AN ANALYSIS OF PREDICTORS OF *STAPHYLOCCOCUS AUREUS* AMONG PATIENTS WITH AUTOIMMUNE DISEASES IN NORTH TEXAS

A DISSERTATION

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BY

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To the Dean of the Graduate School:

I am submitting herewith a dissertation written by Susan D. Kehl entitled "An Analysis of Predictors of *Staphylococcus Aureus* Among Patients with Autoimmune Diseases in North Texas." I have examined this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy with a major in Health Studies.

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We have read this dissertation and recommend its acceptance:

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DEDICATION

This dissertation is dedicated to patients who live with autoimmune and other chronic diseases. This research was conducted to identify risks of a vulnerable population in healthcare systems. The results of this inquiry have raised hopes that health educators and healthcare providers can initiate interdisciplinary collaboration for increased quality of care of high-risk patients requiring acute or critical care. This study was completed to increase knowledge needed to educate patients with autoimmune diseases to decrease preventable complications. With fewer complications related to hospitalizations, the overall quality of life of patients with autoimmune diseases can be enhanced.

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ABSTRACT

SUSAN D. KEHL

AN ANALYSIS OF PREDICTORS OF *STAPHYLOCCOCUS AUREUS* AMONG PATIENTS WITH AUTOIMMUNE DISEASES IN NORTH TEXAS

DECEMBER 2010

The prevalence of autoimmunity is increasing, and a comprehensive, definitive understanding of treatment remains elusive to medical and genetic research. Hospitalized autoimmune patients who experience complications are potentially at greater risk for infections. The purpose of this investigation was to evaluate the predictors of *Staphylococcus aureus (SA)* among hospitalized, autoimmune patients in North Texas. This retrospective study assessed secondary data of 65,536 adult patients from 1999 to 2005. Cross-tabulations, chi squares, *t* tests, ANOVAs, and multiple logistic regression analyses were used to find relationships and predictors of SA related infections among the sample. The descriptive characteristics of patients discharged after SA infections were analyzed. Multiple significant relationships were identified. The rate of SA infections discovered in the sample, SA specific infections (2.8%), SA infections without site designation (1.7%), MRSA (.1%), and SA possibly related infections (3.3%) was included in the data presentation. Finally, multiple logistic regression analyses were completed on the full sample, and three random samples. Several covariates were either protective or predictive of a diagnosis of infection in patients with autoimmune diagnoses. Females ($OR = 1.256 - 1.791$, $p < .05$), African-Americans ($OR = 1.231 -$

1.427, $p < .05$), 10 or more day hospital stay (*OR* = 3.955 – 6.911, $p < .001$), $24,000 or more in hospital charges (OR = 2.210 – 2.726, $p < .01$), SLE patients (OR = 1.421 – 2.198, $p < .05$), acute renal failure (1.346 – 3.071, $p < .05$), and patients with acute respiratory failure (OR = 1.416 – 2.664, $p < .05$) were at increased risk for infection.

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CHAPTER I

INTRODUCTION

Autoimmune diseases are comprised of over 80 chronic illnesses that impact at least 5% to 8% of the population, and are the third most common disease classification in the United States (US). Estimates of the population affected by autoimmune diseases range from 14 to 23.5 million people (American Autoimmune Related Diseases Association [AARDA], 2010; Fairweather & Rose, 2004; National Institutes of Health [NIH], 2005). Some of the most common autoimmune diseases in the US population include: Rheumatoid Arthritis (RA) (2.1 million), Type 1 Diabetes Mellitus (DM) (up to 1.5 million), Multiple Sclerosis (MS) (250,000 to 350,000), Systemic Lupus Erythematosus (SLE) (239,000), and Inflammatory Bowel Diseases (IBD) (1.4 million) (NIH, 2010). A higher prevalence of autoimmune diseases affects women. Some experts estimate that 78.8% of the autoimmune patients are women (Fairweather & Rose).

The immune system of adults and children are challenged daily by a variety of antigens that include noninfectious substances and infectious pathogens. The adaptive immune system must recognize foreign or non-self antigens to destroy or inhibit proliferation (McCance, Huether, Brashers, & Rote, 2010). Healthy adults produce a small number of antibodies against self-antigens. Autoimmunity develops when an individual's cells, organs, or tissues are attacked and damaged by an abnormal increase in autoantibodies or T lymphocytes (T cells) that are reactive on self (McCance et al.). The

etiology of autoimmune diseases is unknown, but research has discovered that environmental and infection exposure, as well as hormones and genetics, may have a synergistic effect on risk for autoimmunity (NIH, 2010). Autoimmune diseases are chronic in nature with no known cure. Patients experience exacerbations, remission, and often progressive disability. In addition, many endure loss of physical function and organ function, and a decreased quality of life. The need for consistent outpatient supervision and potential for numerous hospitalizations sets the stage for high medical expenditures (NIH, 2005).

Healthcare Associated Infections

Healthcare associated infections (HAIs) result in increased morbidity and mortality rates, as well as increased healthcare expenditures in the US ($26 to $33 billion annually). Approximately 1.7 million HAIs are reported, and 99,000 deaths are recorded each year (Centers for Disease Control and Prevention [CDC], 2009a). Consequently, HAIs have prompted significant attention at the national, state, and local levels (United States Department of Health and Human Services [USDHHS], 2010). HAIs are defined as "infections that patients acquire during the course of receiving treatment for other conditions within a healthcare setting" (CDC, 2009a, slide 5). A majority of HAIs result from the use of invasive devices for treatment or surgical procedures (CDC, 2009a). Of the numerous pathogens known to cause HAIs, *Staphylococcus aureus* (SA) is commonly identified as a primary source of infection in acute care facilities (Noskin et al., 2005). SA has mutated to a virulent, antibiotic resistant strain known as methicillin resistant *S. aureus* (MRSA). Between the years of 1999 to 2005, estimates of SA-related

hospitalizations doubled, and MRSA-related hospitalization rates increased even more dramatically (Klein, Smith, & Laxminarayan, 2007).

Community-Associated Methicillin Resistant Staphylococcus Aureus

Historically, MRSA infections were acquired nosocomially by patients with known risk factors such as compromised immune system functions, cross-contamination from other inpatients within close proximity, prolonged lengths of stay, admission to intensive care units, frequent antimicrobial treatments, and a history of surgical or other invasive procedures (CDC, 2005; Herman, Kee, Moores, & Ross, 2008; Klein et al., 2007). Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has emerged as an epidemic threat within healthy community, outpatient, and inpatient healthcare settings (Herman et al.; Klein, Smith, & Laxminarayan, 2009; Klevens et al., 2006). Genotyping of MRSA isolates by pulsed-field electrophoresis (PFE) has enabled differentiation of CA-MRSA and hospital acquired (HA)-MRSA (Herman et al.; Seybold et al., 2006). CA-MRSA USA300 genotype has been identified as the cause of more than one-third of MRSA bloodstream infections (BSI) in a 1000-bed, urban public hospital system (Seybold et al.). Evidence suggests that CA-MRSA is complicating and increasing the current burden of HAIs among hospital inpatients (Klein et al.).

Statement of Purpose

This study assessed secondary data of patients hospitalized from 1999-2005 with at least one of 21 autoimmune diseases to: 1) Determine the prevalence at discharge of SA infections (ICD-9-CM code 041.11; *Staphylococcus* ICD-9-CM code 041.1; *Staphylococcus*, unspecified ICD-9-CM code 041.10; other *Staphylococcus* ICD-9-CM code 041.19), including MRSA (ICD-9-CM code V09.0), other SA specific infections (*Staphylococcal* septicemia ICD-9-CM code 038.1; *Staphylococcal* septicemia, unspecified ICD-9-CM code 038.10; *Staphylococcal aureus* septicemia ICD-9-CM code 038.11; Other *Staphylococcal* septicemia 038.19; Pneumonia ICD-9-CM code 482.41) and possibly related SA infections (Vancomycin-resistant *S. aureus* ICD-9-CM code V09.8; *Staphylococcal* enterocolitis ICD-9-CM code 008.41; Bacteremia ICD-9-CM codes 038.1, 790.7, 996.62; Endocarditis ICD-9-CM code 421.0, 996.61; Surgical site infection ICD-9-CM code 998.3, 998.5; Osteomyelitis ICD-9-CM code 730.00 – 730.09, 730.10-730.19; Septic arthritis ICD-9-CM code 711.00-711.09, 996.66; Systemic inflammatory response syndrome (SIRS) ICD-9-CM code 995.9; SIRS unspecified ICD-9-CM code 995.90; SIRS due to infectious process without organ dysfunction.[sepsis] ICD-9-CM code 995.91; SIRS due to infectious process with organ dysfunction [severe sepsis] ICD-9-CM code 995.92 with additional codes to specify organ dysfunction such as: acute renal failure ICD-9-CM code 584.5-584.9; acute respiratory failure ICD-9-CM code 518.81; critical illness myopathy ICD-9-CM code 359.81; critical illness polyneuropathy ICD-9-CM 357.82; Encephalopathy ICD-9-CM 348.31; Hepatic failure ICD-9-CM code 570; Septic shock ICD-9-CM code 785.52) (Hart & Hopkins, 2005;

Noskin et al., 2005); 2) Delineate those with SA infections by descriptive covariates of gender, age, race/ethnicity, autoimmune diagnosis, insurance type, length of stay in days, and total charges; and 3) Determine the predictive effect of descriptive covariates on the presence of diagnosis of SA infection.

Research Questions

1. What are the descriptive characteristics (gender, age, race/ethnicity, autoimmune diagnosis, insurance type, length of hospitalization and total charges) of patients hospitalized with MRSA or SA in North Texas?

2. Which autoimmune diseases resulted in the highest prevalence of MRSA or SA infections (Bacteremia, Septicemia, Pneumonia, Vancomycin-resistant *S. aureus*, Enterocolitis, Endocarditis, Surgical site infection, Osteomyelitis, Septic arthritis, and SIRs)?

Hypothesis

The following null hypothesis was tested at the .05 level of significance:

Ho1. The covariates (autoimmune disease, gender, age, race/ethnicity, insurance type, length of stay in days, and total charges) in hospitalized patients will be neither predictive nor protective of a diagnosis for MRSA or SA infection (Bacteremia, Septicemia, Pneumonia, Vancomycin-resistant *S. aureus*, Enterocolitis, Endocarditis, Surgical site infection, Osteomyelitis, Septic arthritis and SIRs).

Delimitations

This study had the following delimitations:

1. The investigation used secondary data of patients hospitalized in the Dallas Fort Worth (DFW) Metropolitan Statistical Area (MSA) between the years of 1999 to 2005.

2. The patients were 18 years of age or older.

3. The patients had at least one of the following autoimmune diagnoses: Autoimmune hepatitis (ICD-9-CM code 710.0), Graves disease (ICD-9-CM code 242.00), Hashimotos thyroiditis (ICD-9-CM code 245.2), Autoimmune disease, NOS (ICD-9-CM code 279.4), Primary thrombocytopenia (ITP) (ICD-9-CM code 287.3), Multiple sclerosis (MS) (ICD-9-CM code 340), Myasthenia gravis (MG) (ICD-9-CM code 358.0), Raynaud's disease (ICD-9-CM code 443.0), Crohn's disease (ICD-9-CM code 555.0), Ulcerative colitis (ICD-9-CM code 556.0), Primary biliary cirrhosis (ICD-9-CM code 571.6), Celiac disease (ICD-9-CM code 579.0), Ig A nephropathy (ICD-9-CM code 583.9), Discoid lupus erythematosus (ICD-9-CM code 695.4), Systemic lupus erythematosus (SLE) (ICD-9-CM code 710.0), Systemic sclerosis (scleroderma) (SS) (ICD-9-CM code 710.1), Sicca syndrome (primary Sjogrens) (ICD-9-CM code 710.2), Dermatomyositis (ICD-9-CM code 710.3), Polymyositis (ICD-9-CM code 710.4), Rheumatoid arthritis (RA) (ICD-9-CM code 714.0), or Juvenile rheumatoid arthritis (ICD-9-CM code 714.30).

Limitations

The study had the following limitations:

1. The secondary data set is comprised of hospital discharge data coded with the *International Classification of Diseases, 9th Revision, Clinical Modification* (Hart & Hopkins, 2005). This data has the potential to involve input or collection errors. The size of the sample reduces the impact of these errors on data analysis.

2. Patient specific identifiers have been removed from the data, and the data cannot be validated for accuracy.

3. Since the secondary data set is hospital discharge information, the onset timing of SA and MRSA cannot be determined nor differentiated between hospital acquired and community acquired infections.

Assumptions

1. The DFW Hospital Council used trained personnel in ICD -9-CM coding, procedures, and used valid and reliable criteria and instruments for the data collection.

2. Diseases were coded correctly, and data entry was accurate.

Definition of Terms

Bacteremia: The presence of bacteria in the blood (Mosby Elsevier, 2009)

Endocarditis: An acute or sub-acute bacterial infection of the endocardium or heart valves or both (Mosby Elsevier, 2009)

Enterocolitis: Inflammation and bacterial infection involving both the large and small intestines (Mosby Elsevier, 2009)

Human Genome Project: This project was an international research endeavor completed in April 2003 to sequence and map all known human genes as a comprehensive genetic blueprint (National Human Genome Research Institute, 2009).

Methicillin resistant Staphylococcus aureus: Virulent, semi-synthetic penicillinase-resistant (methicillin, oxacillin, nafcillin) strain of *S. aureus* (Kuehnert et al., 2005)

Osteomyelitis: A local or generalized bacterial infection of the bone and bone marrow caused by trauma, surgery, spread from a distant infection or via the blood stream (Mosby Elsevier, 2009)

Pneumonia: Acute infection and inflammation of the lungs (Mosby Elsevier, 2009)

Septic arthritis: Acute bacterial infection of one or more joints due to trauma or penetrating wound. Found most frequently in children (Mosby Elsevier, 2009)

Septicemia: Systemic infection caused by pathogens or bacteria circulating in the blood. If left untreated, this infection can lead to septic shock (Mosby Elsevier, 2009)

Staphylococcus aureus: Humans are the primary reservoir, and this bacterial species is found primarily in nasal mucous membranes and the skin. The common species produces exotoxins that cause toxic shock, rash, renal, hepatic, and central nervous system disease. Enterotoxins cause the clinical manifestations of food poisoning. These bacteria can also cause furunculosis, cellulitis, pyemia, pneumonia, endocarditis, and osteomyelitis (MediLexicon, 2009).

Systemic inflammatory response syndrome: Acute inflammatory reaction as a response to infection with impaired coagulation and potential organ failure (Hart & Hopkins, 2005).

Importance of the Study

With the incidence and prevalence of autoimmune diseases, HAIs, SA, MRSA, and CA-MRSA infections rising, a greater understanding is necessary to clarify additional risks to those patients with immune response deficiencies or those who require pharmacological immunosuppresion. The determination of factors associated with increased risk for HAIs and all SA-related infections will assist in the identification of patients most at risk during hospitalizations. The importance of health promotion and education for preventable complications to patients, families, and healthcare providers is valuable to sustain the individual quality of life of a patient regardless of the unique position on the health and illness continuum (Munster, 2008). Prevention of HAIs and all SA related infections ultimately results in reduced morbidity/mortality, reduced hospital stays, decreased healthcare costs, and improved quality of life for the patients living with autoimmune diseases.

CHAPTER II

REVIEW OF LITERATURE

The prevalence of autoimmune diseases is increasing, and a comprehensive understanding of the risk factors, etiology, manifestations of pathophysiology, diagnosis, and treatment remain elusive to medical research (Fairweather & Rose, 2004; NIH, 2005; Sebastiani & Galeazzi, 2009a). The NIH estimates that as many as 23.5 million Americans live with an autoimmune disease. In comparison, cancer affects 9 million individuals in this country, and heart disease affects 22 million (AARDA, 2010; NIH). Health care costs associated with autoimmune related complications are estimated to reach $100 billion nationally. In contrast, annual healthcare expenditures related to cancer treatments are approximately $57 billion, and costs associated with heart disease and stroke recovery are $200 billion (AARDA). While the impact of autoimmune diseases rivals and exceeds the impact of cancer and heart disease on the American population, national research allocation continues to lag behind. In 2003, $591 million were given for autoimmune disease research, in contrast to cancer funding and heart and stroke related research, that totaled $6.1 billion and $2.5 billion, respectively (AARDA; NIH).

In 1998, the Autoimmune Disease Coordinating Committee (ADCC) was established within the NIH. The ADCC is comprised of NIH directors, and the director of the National Institute of Allergy and Infectious Diseases (NIAID) (NIH, 2005).

Representatives from the CDC, the Food and Drug Administration (FDA), other federal agencies, and private organizations participated with the directors in the ADCC to coordinate research and educational efforts related to autoimmune diseases. Due to the complexity of the impact of autoimmune diseases, and the identification as the leading cause of death in young and middle aged women, the NIH published a strategic plan in 2002 with the federal funding for autoimmune research (NIH). In 2003, $591.2 million was allocated toward immunologic, genetic, and environmental studies related to the understanding of autoimmune diseases. Until risk factors and etiology of these diseases are more fully understood, the prevention, early diagnosis, treatment, and management of autoimmune diseases are primary targets of research and emerging medical science (Fairweather & Rose, 2004; NIH; Sebastiani & Galeazzi, 2009a).

Etiology and Risk Factors of Autoimmune Diseases

Understanding the etiology and risk factors of autoimmune diseases form the foundational basis for prevention of overt disease expression. Genetic inheritance, environmental factors, and lifestyle compound in the development of autoimmune diseases (Fairweather & Rose, 2004; NIH, 2005). Genome wide linkage scans (GWLS) and research studies of twins and families who have RA, found genetic factors to account for 50-60% of risk, with environmental triggers explaining the remaining probability of disease (Kobayashi, Momohara, Kamatani, & Okamoto, 2008). As the study of genetics and the impact of the Human Genome project advances, evidence is mounting that multiple genetic patterns are responsible for common autoimmune diseases, and there are genetic commonalities in autoimmunity (Coenen & Gregersen, 2009). For example,

major histocompatibility complex (MHC) subtypes emerge as important genetic precursors to MS and RA (Coenen & Gregersen; Ramagopalan, Dyment, & Ebers, 2008; Zdanowicz, 2009). However, the manifestation of clinically active autoimmune diseases is a relatively unpredictable interaction and progression of multiple, susceptible genes, and environmental factors (Aggarwal, Sestak, D'Sousa, Dillon, Namjou, & Scofield, 2010; Shepshelovich & Shoenfeld, 2006). Infectious agents, food contaminants, and hazardous environmental exposure have been linked to autoimmune diseases (NIH; Sebastiani & Galeazzi, 2009b).

Immunity Dysfunction in Autoimmune Diseases

Autoimmune disease research inquiry has illuminated the dysfunction of mechanisms of innate and adaptive immune responses as precursors to clinical manifestations (Agmon-Levin & Shoenfeld, 2009; Gregersen, 2007). Frequently unknown to the individual or healthcare provider, specific biomarkers, such as genetic traits or biological dysfunctions, and specific autoantibodies exist within the circulatory serum prior to manifestation of active autoimmune disease (Rose, 2007; Shepshelovich & Shoenfeld, 2006). Differing immunodeficiencies are linked to autoimmune disease expression. The pathophysiology related to these phenomenon include: immune dysfunction in eliminating microbial pathogens, chronic inflammation (Crohn's disease), complement and immunoglobulin (Ig A) deficiency (SLE, arthritis, ITP, pernicious anemia, and vitiligo), and abnormalities in T cell regulation (IBD, RA, hemolytic anemia, and ITP) (Shepshelovich & Shoenfeld).

Innate and adaptive immunity within the human body work in tandem against pathogenic invaders. Innate immunity is differentiated from adaptive defenses as the natural, innate resistance of invading antigens or pathogens that does not require immunologic memory. The innate resistance responds to assaults within minutes while the adaptive immunologic memory is activated within days (McCance et al., 2010). The innate immune system's primary response is inflammation which is mediated by the plasma protein pathways of the complement cascade, the coagulation system, and the kinin system. An example of association to autoimmune diseases relates to the complement cascade of immunity. Complement components are normal, basic responses of a healthy, innate immune system (McCance et al., 2010). Early genetic complement deficiency (C1, C2, and C4) was evident in a large cohort of patients with SLE. Complete complement deficiency was frequent among patients whose onset of SLE was prior to 18 years of age (Aggarwal et al., 2010).

Body cell surfaces are known to have pattern recognition receptors for surface proteins of microorganisms. These cell surface receptors can become reactionary to cellular proteins of the self (Gregersen, 2007; McCance et al., 2010). Examples of groups of pattern recognition receptors include toll-like receptors (TLRs) and nucleotide oligomerization domain (NOD) like receptors. The pattern recognition receptors can react to self proteins such as nuclear antigens that are found in apoptotic debris (Gregersen). Apoptosis is a specific type of cellular death that is programmed, self initiated, and present in normal physiological and pathophysiological cellular and tissue changes (McCance et al.). Apoptotic debris presents as an antigen, and is normally cleared

quickly. If the rate of apoptosis is too high for effective clearance of debris, immunogenicity is increased. Other precipitating factors for this sequence of events include: ultraviolet light and medications (Sebastiani & Galeazzi, 2009b). Deficiency of any component of the complement cascade hinders removal of apoptotic fragments (Mackey, 2000).

Adaptive immunity involves the lymphocytes which are one group of the differentiated white blood cells. Lymphocytes originate as stem cells in the bone marrow of a child or adult (McCance et al, 2010). Lymphocytes migrate through lymphoid tissues and plasma to mature and further differentiate specific roles in the complex immune function. In normal physiological response, B lymphocytes or B cells interact with foreign antigens, further mature into plasma cells, and then produce antigen specific antibodies (McCance et al.). Lymphocytes that travel through the thymus become T. lymphocytes or T cells. T cells recognize specific antigens, and attack directly, and are responsible for cell-mediated immunity (McCance et al.). When any aspect of these processes is compromised, the individual is vulnerable to pathological complications. Although autoimmunity prevalence is increasing in every age population, age-dependent decline in innate and cell mediated immune competence or immunosenescence has increased the incidence of late-onset autoimmunity (Siegel et al., 2008).

Females are clearly more susceptible to autoimmune diseases (Ahmed et al., 1999; NIH, 2005; Rose, 2007; Siegel et al., 2008), and the effect of hormones on the immune system is poorly understood (Fairweather & Rose, 2004). Within ethnic groups, the incidence and prevalence of autoimmune varies, as African-American females have

the highest incidence of SLE (Seshan & Jennette, 2009). As a gender group, females have increased immune responses to pathogens, foreign antigens, and self antigens. Gender differences in physiological systems have been studied extensively. Females have higher B cell mediated immunity and thus immunoglobulin or antibody levels. Females are known to have increased antibody responses, and increased resistance to certain infections (Ahmed et al.). Immune biomarkers for endogenous or exposure to synthetic estrogen include decreased response of T cells to apoptosis, and lessened Natural Killer (NK) cell activation. Due to the use of synthetic estrogen as oral contraception and as a food additive to meat and milk products, estrogen is believed to play a role in the expression of autoimmune diseases (Ahmed et al.).

Several processes in the cell mediated immune response have been linked with autoimmunity (Ercolini & Miller, 2008). Antibody dysregulation has been found as a potential factor in autoimmunity. Cryoglobulins, a type of immunoglobulin or antibody have been associated with systemic vasculitis, Raynaud's disease, arthralgia, and neuropathy related autoimmune diseases (Faguer et al., 2008). In a study comparing patients with allergy and autoimmune diseases, participants with elevated Total Ig E were at increased risk of resulting autoimmune disease, especially Graves' disease and psoriasis. This finding further implicates immune dysregulation as a generalized precursor of autoimmunity (Lindelof, Granath, Trengvall-Linder, Lindelof, & Ekbom, 2008).

Characteristically, autoimmune diseases exhibit autoantibody elevation and T cell activation against self antigens. These distinctions separate autoimmune diseases and

systemic, inflammatory, genetically inherited disorders (Stjernberg-Salmela, Ranki, Karenko, & Pettersson, 2004). A subset of self autoantibodies exists in most autoimmune diseases (Mackay, 2000; Rose, 2007). "These autoantibodies may have a high positive predictive value for disease onset, severity, and organ-specific complications, especially in genetically prone individuals" (Agmon-Levin & Shoenfeld, 2009, p. 57). Examples are the two types of muco-cutaneous autoantibodies. Type I targets cutaneous and extra-cutaneous sites, and are linked to systemic autoimmune diseases (SLE, SS, Sicca syndrome, and Dermatomyositis). Type II muco-cutaneous autoantibodies target epidermal and dermal autoantigens (Agmon-Levin & Shoenfeld).

T cells target self cells as antigen presenting cells (APCs) process self cells into peptides. Cytolytic T cells directly remove targeted self cells, or helper T cells release cytokines that activate macrophages, monocytes, and B cells to target cells, tissues and organs of self (Ercolini & Miller, 2008). Signaling and costimulatory pathways are activated on self antigens (Mackay, 2000). Molecular mimicry of T or B cells has been found to be causative mechanisms for autoimmune diseases (Agmon-Levin & Shoenfeld, 2009; Ercolini & Miller; Mackey). A microorganism or foreign antigen may have a similar amino acid structure to self antigens. Thus, when B and T cells react to the foreign antigen, the cell mediated response is cross reactive to self. This cross reaction leads to cell destruction, chronic inflammation, and clinical manifestations of autoimmune diseases (Ercolini & Miller). In SLE patients, exposure to Epstein-Barr virus (EBV) has initiated autoantibodies from the antibodies developed against Epstein-Barr nuclear antigen-1 (EBNA-1). This example of cross reactive autoantibodies supports a

possibility of one aspect of autoimmunity disease development in SLE patients (Harley, Harley, Guthridge, & James, 2006).

Genetics of Autoimmune Diseases

The immune dysfunction of autoimmune diseases is likely a complex interaction between genetic susceptibility of multigenic phenotype origins, a multiplicity of environmental factors, and differing expression across diverse populations (Sebastiani & Galeazzi; Shepshelovich & Shoenfeld, 2006). The evidence for the genetic contribution to autoimmunity is increased concordance of manifestation of disease in monozygotic twins when compared to dizygotic twins, and a significantly increased frequency in families with one or more affected family members (Cocco et al., 2009; Molina & Shoenfeld, 2005; Rose, 2007; Sebastiani & Galeazzi, 2009a; Shepshelovich & Shoenfeld).

Autoimmune susceptible genes can be divided into 2 groups. The first group affects the response to autoantigens. This group also creates the susceptibility to target organ tissues (Mackay, 2000). The second group is genes that affect inflammatory mechanisms, apoptosis, and tolerance. The genes of MHC normally offer protection against autoimmunity, but the absence or defection of these genes causes susceptibility, as in RA (Mackay). An example of a genetic role in immune tolerance and autoimmune pathogenesis is the inhibitory actions of immunoglobulin-like transcripts (ILT)2 and ILT4 binding to human leukocyte antigen (HLA)-G. ILT6 expression varies in MS, and is normally responsible for T cell proliferation (Kabalak et al., 2007).

For the past 2 decades, the MHC and the HLA complex were the primary genetic loci associated with autoimmune diseases (Maier & Hafler, 2009; Shepshelovich & Shoenfeld, 2006). The class I MHC presents antigenic peptides to CD8 cytotoxic T cells, and class II MHC gene presents to CD4 helper T cells (Rose, 2007). MS has been related to HLA class II variants in several ethnic groups (Cocco et al., 2009). A deficiency of or a defective class III allele, C4AQO, is the most common genetic indicator of SLE in several ethnic groups (40 to 50% of patients compared with 15% of healthy controls). The haplotype, B8.DR3.Dqw2.C4AQO predisposes to SLE in patients with northern European heritage (Shepshelovich & Shoenfeld). A HLA haplotype is a genetic marker for Graves' disease (Rose).

A second major grouping in autoimmune genetic susceptibility is non-MHC alleles. These genes are more difficult to identify due to the heterogenetic nature of the alleles. Examples of non-MHC alleles are NOD2 (CARD15) in Crohn's disease, ADAM33 and GPRA genes in asthma, and IDDM12/CTLA4 in Graves' disease (Shepshelovich & Shoenfeld, 2006). Genome-wide association (GWA) scans have generated current excitement in the search for the heterogeneous genes outside the MHC complex that contribute to autoimmunity. To date, the odds ratio associations have proved weaker than the HLA class II studies. Intracellular phosphatase, PTPN22, demonstrates the most consistent relationship to RA (Coenen & Gregersen, 2009). Interleukin-10 is a cytokine produced by monocytes, and provides both inhibitory and activating effects on T cells. Interleukin-10 genotypes (3575, 2849, and 2763) are linked to SS, and are associated with disease type and severity (Hudson, Rocca, Kuwana, &

Pandey, 2005). A final example involves RNA interference that protects the body against RNA viruses. Mediators of the processes, microRNAs (miRNAs) are important regulators of cell differentiation, growth, proliferation, mobility, and apoptosis. MiRNA 146 and 155 was recently associated with RA and Autoimmune hepatitis (Sebastiani & Galeazzi, 2009a).

Historically, the impact of each genetic factor on the risk of developing full autoimmune disease expression was modest and in some diseases, inconsistent. One particular flaw was the inability to replicate the genetic associations of autoimmune disease in an independent study with a new population sample. The most likely rationale for the failure of replication was lack of sample size, thus decreasing the statistical power of each study (Maier & Hafler, 2009). GWA scans allows for the inquiry into common genetic and variant pathways in autoimmunity. The GWA scans mark a new era of genetic research designs to find genetic clues in autoimmune diseases (Maier & Hafler). Three primary publications and developments have ignited this burst of discovery: release of the public catalog of common genetic variation in the human genome, genome-wide typing technologies that are decreasing in cost, and compilation of large sample sizes, and detailed phenotypes to provide sufficient statistical power to illuminate fine and truthful associations (Maier & Hafler). "Numerous consortia are currently pursuing large-scale genetic association studies of autoimmune diseases in thousands of subjects, using a half a million genetic markers or more per person" (Gregersen, 2007, p. 1266).

Environmental Exposure and Lifestyle Risk Factors of Autoimmune Diseases

Genetic and immunological dysfunction frequently is a precursor to autoimmune diseases. However, clinical manifestations of disease are often triggered by an environmental exposure (Molina & Shoenfeld, 2005). Exposure to infections, vaccines, occupational exposures, and lifestyle factors has been implicated with varying strengths of association (Ercolini & Miller, 2008; Molina & Shoenfeld; Parks & Cooper, 2005). In the complex findings for infection causing autoimmunity, there is evidence-based support for the protective activity of some infections against exacerbation of disease. This finding has been labeled the hygiene hypothesis (Shepshelovich & Shoenfeld, 2006). The relationship of allergy and autoimmunity has been a topic of inquiry, although no definitive relationship has been found in 28 autoimmune diseases, and specifically in MS patients (Alonso, Hernan, & Ascherio, 2008; Lindelof et al., 2008). Environmental exposure is certainly a factor of autoimmunity and disease expression, but frequency, amount, and consistency of exposure have been difficult to quantify, correlate clearly, and is stronger for select autoimmune diseases than for others (Agmon-Levin & Schoenfeld, 2008; Shepshelovich & Shoenfeld).

Challenges by the infectious pathogens on the immune system may cause dysregulation and autoimmune processes in susceptible individuals. Molecular mimicry, epitope spreading, bystander activation, and cryptic antigens are processes in which exposure to infections cause autoimmune diseases (Ercolini & Miller, 2008). Bacterial infections have been identified as a probable cause of autoimmunity. "Approximately, 30% of Gullian Barre Syndrome (GBS) are preceded by *Campylobacter jejuni (C. jejuni)*

as detected by serologic tests" (Molina & Shoenfeld, 2005, p. 237). Bacterial etiology for autoimmunity due to molecular mimicry has been associated with RA, Graves' disease, ankylosing spondylitis, and rheumatic fever. *Helicobacter pylori*, a frequent gastrointestinal bacterial pathogen has been linked to antiphospholipid syndrome (API) (Molina & Shoenfeld). The genetic diverseness of the human population may be the factor in the lack of definitive findings in the investigation of infections as causes of autoimmunity. "Defining the genetic markers that predispose patients to different autoimmune diseases with a suspected infectious trigger would be an important contribution to defining the underlying disease pathogenesis" (Ercolini & Miller, 2008, p. 8).

Viral and parasitic diseases are possible initiators of autoimmune disease. The EBV is strongly related to SLE and RA (Agmon-Levin & Shoenfeld, 2009; Harley et al., 2006; Molina & Shoenfeld, 2005). The EBV accentuates lymphoid responses, and potentially is reactivated in patients with autoimmune diseases. "These patients were also found to have modestly elevated anti-EBV antibody titers and altered antiviral T cell responses" (Molina & Shoenfeld, 2005, p. 236). Other viral associations with autoimmunity include: the human Herpes virus family (MS), the retrovirus family (MS), the human cytomegalovirus (CMV) and human parvovirus B19 (SS) (Molina & Shoenfeld, 2005). Evidence exists that parasitic infections increase the presence of autoantibodies. Chagus' disease has produced autoantibodies that are reactive on the retina. In patients with malaria, high titers of anti-nuclear antibodies and additional autoantibodies were found. A confounding finding, however, was the persistence of

autoantibodies did not correlate with the degree of parasitemia. Pancytopenia without bone marrow suppression was found in patients with leishmaniasis (Molina & Shoenfeld).

Vaccines, occupational exposures, ultraviolet light, smoking, diet (low levels of n-6 fatty acid linoleic acid [18:2n-6], and vitamin D), and high levels of emotional stress contribute to autoimmune disease onset and exacerbation (Agmon-Levin & Shoenfeld, 2009; Molina & Shoenfeld, 2005; Parks & Cooper, 2005; Sawyer, 2010; Shepshelovich & Shoenfeld, 2006). Autoimmune type reactions, such as "arthropathy, vasculitis, thrombocytopenia, and neurological dysfunction" that are mild and self-limiting have been reported after viral immunizations (Shepshelovich & Shoenfeld, 2006, p.186). During 1992-1994, 10.5% of individuals who received the influenza vaccine developed GBS. Overall, 0.01% of all vaccines administered result in autoimmune reactions (Shepshelovich & Shoenfeld).

Crystalline silica, silicone implants, solvents (alcohols, glycols, aromatic hydrocarbons and chlorinated products), mercury, and pesticides have moderate to strong associations to SLE (Molina & Shoenfeld, 2005; Parks & Cooper, 2005). Ultraviolet (UV) light damage to the skin may stimulate autoantibodies in individuals with genetic biomarkers and other triggers of autoimmune diseases (Agmon-Levin & Shoenfeld, 2009; Sawyer, 2010; Shepshelovich & Shoenfeld, 2006). However, low levels of UV light that increase Vitamin D levels may have protective autoimmune properties (Shepshelovich & Shoenfeld). Exposure to the toxic chemicals of cigarette smoke has been identified as a risk factor for SLE, RA, and Crohn's disease (Agmon-Levin &

Shoenfeld; CDC, 2009b; Moorthy, Cappellano, & Rosenberg, 2008; Shepshelovich & Shoenfeld). Smoking's contribution to the mosaic of autoimmunity includes the initiation of the inflammatory responses, cytokine imbalance, and increased apoptosis with DNA damage resulting in anti-DNA antibodies (Agmon-Levin & Shoenfeld). Finally, several retrospective investigations found as many as 86% of individuals stated that high emotional stress occurred prior to autoimmune disease onset (Shepshelovich & Shoenfeld).

Clinical Manifestations of Autoimmune Diseases

In autoimmune diseases, the targets of destruction are tissues, entire organs, or multiple systems (Fred Hutchinson Cancer Research Center [FHCRC], 2010). The 21 autoimmune diseases that are included in the scope of this investigation involve the gastrointestinal system (Autoimmune hepatitis, Crohn's disease, Ulcerative colitis, Primary biliary cirrhosis, Celiac disease and Sicca syndrome), the genitourinary system (Ig A nephropathy), the hematologic system (ITP), the endocrine system (Graves' disease, Hashimotos thyroiditis), the musculoskeletal system (Dermatomyositis, Polymyositis, RA, juvenile RA), the neurological system (MS, MG), the cardiovascular system (Raynaud's disease), and multi-system diseases (SLE, SS) (McCance et al., 2010).

Disease onset may begin with vague, non-specific symptoms related to the tissue, organ, or systems affected. Symptomology may include pain, rash, increased evidence of inflammation, weakness, fatigue, dizziness, general ill feelings, and low grade fever (Medline Plus, 2009; Pountney, 2010; Siegel et al., 2008). At times, symptoms will

logically grow in severity based on pathogenesis of the organ or system affected. However, there are many exceptions to this assumption, and this occurrence contributes to a stochastic explanation of disease progression. This phenomenon contributes to the complexity in the understanding of autoimmunity. An example is celiac disease in which basic gastrointestinal symptoms (vomiting, anorexia, constipation, diarrhea, and recurrent abdominal pain) are often the presenting clinical picture. However, several extraintestinal manifestations of celiac disease contribute to ongoing medical supervision and a decreased quality of life: enamel hypoplasia, anemia, hepatitis, arthritis, osteopenia, epilepsy, ataxia, and psychiatric disorders (Setty, Hormaza, & Guandalini, 2008).

Individuals with autoimmune diseases are faced with remissions and exacerbations, and often progressive complications and disability (NIH, 2005). Clinical manifestations range in severity based on genetic biomarkers, immune dysregulation, and environmental exposure (Ercolini & Miller, 2008; Molina & Shoenfeld, 2005; Parks & Cooper, 2005). In addition to severe symptoms associated with SLE, pain and depression may also significantly impact the daily lives of patients (Ledermen, Lindner, Greenwood, & Philip, 2008). The impact on health related quality of life and health care expenditures has the potential to be devastating. For instance, patients with RA have compromised self-reported health, activity participation, and work performance (CDC, 2009b). From 1998 to 2000, patients hospitalized with SLE increased from <60,000 to <100,000 with approximately 77,000 hospitalizations annually (CDC, 2009c). Crude deaths rates of SLE patients were 5 times higher in woman than men, and 3 times higher among blacks than whites (CDC, 2009c).

Complications of Autoimmune Diseases

The severity of autoimmune diseases varies in individual patients, and in the case of SLE, presents with such complexity that one experienced physician speculated that the diagnosis is multiple diseases entities (Isenberg, 2010; NIH, 2005). A variety of complications arise in the aggressive or advanced forms of autoimmune diseases. In the most recent North American study of mortality among patients with RA, based on data extracted between 1965 and 1990, patients with RA were twice as likely to die as the general population of the same age (CDC, 2009b). Most frequent causes of death in RA patients were cardiovascular disease (CVD), infections, and lymphoproliferative malignancies (leukemia, multiple myeloma). Half of the deaths of patients with RA were caused by CVD which is a similar incidence in control populations (CDC, 2009b). However, patients with RA had more significant evidence of subclinical atherosclerotic disease. Infections are the cause of a fourth of the deaths of patients with RA (CDC, 2009b). Causes of mortality related to infections include pharmacological immunosuppression and immune system dysregulation (CDC, 2009b; Jeong et al., 2009). The increased incidence of lymphoproliferative malignancies has variable explanations (CDC, 2009b; Dalamaga, Karmaniolas, Papadavid, Pelecanos, & Migdalis, 2008; Smedby, Askling, Mariette, & Baecklund, 2008). Death rates due to SLE were the highest with the most substantial increase among African-American women who were aged 45-64 years (CDC, 2009c). In SLE, survival is improving, but causes of death include active disease with organ failure, particularly the kidneys, infection or CVD from accelerated atherosclerosis (CDC, 2009c).

Inflammation has been an identified factor in the pathogenesis of atherosclerosis (Bruce, 2005; Spah, 2008). Additionally, chronic, systemic autoimmune diseases (psoriasis, RA, SLE and Crohn's disease) also have the common foundation of inflammation. Inflammatory cytokines, tumor necrosis factor-alpha (TNF-a), and interleukin (IL-1) are catalysts for the underlying pathology of inflammation. Inflammatory markers that are identified systemically, such as elevation of C-reactive protein, contribute to the acceleration of atherosclerosis in patients with autoimmune diseases (Bruce; Spah). Inflammation also exacerbates dyslipidemia that is common in SLE (Bruce).

In SLE patients, other risk factors for atherosclerosis exist. Treatment with corticosteroids and antimalarial medications, as well as, anticardiolipin antibodies contributes to atherosclerosis risk (Bruce, 2005). Acceleration of atherosclerosis also contributes to increased arterial and venous vessel complications. Chronic leg ulcers are complications of a variety of autoimmune diseases and symptoms (Raynaud's disease, vasculitis, hemolytic anemia, thrombocytopenia, MS, RA, SS) which are the result of chronic venous insufficiency and atherosclerotic disease of the arteries of the lower extremities (Rayner, Carville, Keaton, Prentice, & Santamaria, 2009). Even though risk factors exist for superficial venous thrombosis and venous thromboembolism in patients with autoimmune diseases, the incidence is rare (Decousus et al., 2010; Mignoga et al., 2008).

Renal disease, lupus nephritis, lupus glomerulonephritis, and infections are high risk complications in patients with SLE (Burling et al., 2007; Jeong et al., 2009; Seshan & Jennette, 2009). As many as 50% of SLE patients develop renal involvement within a year of diagnosis. "Glomerular and microvascular lesions similar to lupus may occur, although less frequently, in association with other autoimmune diseases, such as rheumatoid arthritis, progressive systemic sclerosis, dermatomyositis, rheumatic fever, mixed connective tissue disease, and various non-infectious vasculitides" (Seshan & Jennette, 2009, p.233). Damage to the glomeruli, renal tubule interstitial areas, and blood vessels contribute in differing degrees of severity to lupus nephritis. The presence of autoantibodies within the renal system also contributes to lupus glomerulonephritis (Burling et al., 2007; Seshan & Jennette, 2009).

Infections are a major cause of complications and deaths of patients with SLE. A history of exposure to bacterial, viral, and parasitic infections may be instrumental in the manifestation and progression of SLE (Berkun et al., 2009; Jeong et al., 2009). Between 11-23% of SLE patients are hospitalized for serious infections. As many as half of the total number of SLE patients will develop infections during the progression of disease (Jeong et al.). After retrospectively reviewing medical records of 110 adult patients with SLE, a case control study was conducted in Korea. Between the years of 1991 to 2000, 76% of the infections were community acquired, and 24% were HA infections (Jeong et al.). SA was one of the pathogenic organisms in pulmonary infection sites, soft tissue sites, and bacteremia. High dose corticosteroid treatment, other immunosuppressive medications, and the complication of renal disease increased infection susceptibility in

these SLE patients (Jeong et al.). A high score on the instrument, SLE Disease Activity Index (SLEDAI), low levels of serum C3, and the presence of anti-ds DNA antibodies were strong predictors of infection rates among this sample of Korean SLE adult patients (Jeong et al.).

Many autoimmune diseases are associated with an increased risk of malignant lymphomas and multiple myelomas (Dalamaga et al., 2008; Smedby et al., 2008). The risk of lymphomas are occasionally associated with SS, IBD, and psoriasis, and more strongly associated with RA, Sicca syndrome, SLE, celiac disease, dermatitis herpetiformis, and thyroiditis. Risk determinants for lymphoma include severity of disease, unique autoimmune disease characteristics, chronicity and severity of inflammation in the disease process, and treatment related determinants (nonbiologic disease modifying anti-rheumatic medications [DMARDs], corticosteroids, tumor necrosis factor antagonists, monoclonal antiantibodies) (Smedby et al.). Efalizumab, a monoclonal antibody, was related to the occurrence of lymphoma in a psoriasis patient (MacKenzie, Kamili, Menter, & Cooper, 2010). The risk of multiple myeloma in patients with thyroid disease and thyroid autoimmunity was significant [OR=3.23, 95% CI; 1.25-8.31] in 73 patients between 2001 to 2007 (Dalamaga et al.).

Treatment of Autoimmune Diseases

Treatment goals of patients with autoimmune diseases are to control symptoms, to decrease the autoimmune cell and tissue destruction, and to support the immune system's function to protect against opportunistic infections (Medline Plus, 2009). Patients with autoimmune diseases face at least two broad treatment categories to decrease the

autoimmune cell and tissue destruction. The first is to replace or restore the organ or tissue function that is damaged or destroyed. In order to replace function, transplantation is required. Another option seeks to suppress the destructive immune response which, in turn, often suppresses the systemic immune response. As a result, many patients with autoimmune diseases face pharmacological immunosuppression which predisposes these individuals to increased risk of infections and cancers (Merck, 2007; NIH, 2005; Zdanowicz, 2009).

Holistic treatment for MS and other autoimmune diseases includes physical therapy and rehabilitation to maximize functional independence, mobility, and safety; symptom management; promotion of overall health and wellness; and support for emotional, family, and economic issues (Holland, Burks, & Schneider, 2010). Corticosteroids, disease modifying antirheumatic drugs (DMARDs), general immunosuppressants, anti-tumor necrosis factor (TNF) drugs, and monoclonal antibodies which target both T & B lymphocytes are emerging as single and combination treatments to control the pathophysiology of autoimmune diseases (Medline Plus, 2009; Merck, 2007). The onset of RA in the elderly typically is a form of severe disease. Anti-TNF alpha medications decreased pathological progression of disease, and increased functional levels of patients with RA in individuals of all ages. Anti-TNF agents did not increase the risk of infections in age-matched control groups, whereas, patients who took corticosteroids did have increased rates of infection (Radovits, Kievit, & Laan, 2009). Infliximab, an anti-TNF alpha antibody is used globally to treat IBD, RA, ankylosing spondilytis, and psoriasis. Although treatment does relieve signs and symptoms of these

autoimmune diseases, adverse events associated with the medication include infusion reactions, further autoimmune phenomenon, dermatological symptoms, neurological complications, opportunistic infections, and malignancy, primarily lymphoma (Papa et al., 2009; Skidmore-Roth, 2010).

One function of monoclonal antibodies is antigen presentation in T lymphocyte activation. In transplantation, this activity will influence whether the T cell will reject the new tissue, ignore the new tissue, or fight against other T cells (T regulatory cells – Tregs) (Xia et al., 2009). Monoclonal antibodies, therefore, have the potential of increasing Tregs without suppressing immune response to other antigens, thus protecting against opportunistic infections or cancers. The anti-CD45 RB monoclonal antibody accomplishes this interaction by suppressing dendritic cells (Xia et al.). Monoclonal antibodies show promise in the treatment of MS and MG (Lebrun, Bourg, Tieulie, & Thomas, 2009; Mellergard, Edstrom, Vrethem, Ernerudh, & Dahle, 2010). Natalizumab acts by initiating a prolonged marked decline of chemokines and cytokines in the cerebrospinal fluid of MS patients, thus decreasing exacerbations in relapsing-remitting MS by approximately 70% (Mellergard et al.). In patients who are unresponsive to first-line therapies of MG with lymphoma, Rituximab provided successful treatment (Lebrun et al.).

Other investigations reveal complications with humanized monoclonal antibodies. In the administration of Ipilimumab, autoimmune polymyositis occurred in a 51 year old woman with a history of metastatic melanoma and post abdominal laparoscopy (Hunter, Voll, & Robinson, 2009). Both Alemtuzumab and type 1 interferon (miscellaneous

immune modulating agent) caused secondary autoimmunity targeting the thyroid (Jones et al., 2009; Monzani, Caraccio, Dardano, & Ferrannini, 2004; Skidmore-Roth, 2010). In autoimmune hematological disorders, risk factors for infection related to Rituximab administration include a decreased count of Ig M after prolonged therapy and the administration of granulocyte colony-stimulating factor (Kanbayashi et al., 2008). Polyclonal antibodies that are comprised of primarily Ig G are labeled intravenous immunoglobulins (IVIg), and used in treatment of SLE. IVIg has been useful in assisting SLE patients with disease complications and infections (Zandman-Goddard, Blank, & Shoenfeld, 2009).

New targets of immunological research are constantly emerging. In the treatment of IBDs, targeting CD4 T cells with colitogenic memory have a promising outcome for future treatment to prevent recurrences and complications (Kanai, Watanabe, & Hibi, 2009). Mesenchymal stem cell transplantation is emerging in clinical trials for the treatment of MS and SLE (Freedman et al., 2010; Tyndall, 2009). Immunoablation with the subsequent transplantation of autologous hematopoietic stem cells have been attempted on over 1,300 patients (150 patients with SLE) with varying results. Some patients experienced remissions, and others complications or death as responses to treatment (Tyndall, 2009). Mesenchymal stem cell transplantation has the potential to provide repair in the central nervous system of MS patients. Healing occurs in neuro-axonal protection or remyelination. Clinical trials are being planned with small numbers of MS patients in various clinical sites (Freedman et al.).

Healthcare Associated Infections

Patients with autoimmune diseases face numerous challenges related to disease progression and treatment modalities. As complications require frequent hospitalizations with invasive diagnostic and therapeutic tests, patients are at risk for potential exposure to nosocomial pathogens furthering complications. Therefore, patients with autoimmune diseases who experience exacerbations or complications, and are hospitalized, are potentially placed at greater risk for HAIs (Blot, 2007). The most frequent infections related to hospitalization are: urinary tract infections (32%); surgical site infections (22%); pneumonias (15%); and bloodstream infections (14%) (CDC, 2007). HAIs contribute to patient morbidity, mortality, and healthcare expenditures regardless of the reason for admission. Despite national and local educational initiatives to healthcare providers and staff to prevent HAIs, adherence to prevention guidelines and infection rates remain a pervasive issue. In 2008, "the Centers for Medicare and Medicaid Services has chosen to withhold reimbursement for certain hospital-acquired conditions, including catheter-associated urinary tract infections (CAUTs) and central line-associated bloodstream infections (CLABSIs)" (Doshi, Patel, MacKay, & Wallach, 2009, p. 84).

Despite national attention on the issues associated with HAIs, and focused efforts on prevention, HAIs are one of the most important complications associated with hospitalizations (Blot, 2007). Due to increased disease acuity, severity, and longevity of patients in intensive care units (ICUs), life threatening HAIs and multidrug resistance (MDR) has been associated with poor patient outcomes (Blot; Magnason et al., 2008). CLABSIs due to *enterococci* were responsible for the diagnosis of SIRS with septic

shock in 62% of the patients, and severe sepsis in another 18% (N=50 adult patients) (Bar, Wisplinghoff, Wenzel, Bearman, & Edmond, 2006).

In the past ten to twenty years, invasive diagnostic testing and therapy has increased significantly. With advances in genetics and immunotherapy, more patients are receiving immunosuppressive agents for a variety of diseases (Blot, 2007). Over a period of 27 months, an observational research investigation was conducted in a 10 bed general ICU. All patients who resided longer than 48 hours were included in the study. Twenty-nine percent of a total of 278 patients were diagnosed with ICU-acquired infections. CAUTs accounted for 14%, CLABSIs accounted for 9%, surgical site infections for 8%, and pneumonia for 8% (Magnason et al., 2008). SA infections were involved in 7 of the 147 episodes with the highest occurrence of 24 episodes of *Escherichia coli* (EC) infection. Independent risk factors of ICU infection at any site were: therapeutic intervention score (OR=1.022, CI 1.002-1.043; per point); length of time at risk (OR=2.6, CI 1.9-3.7; per double the number of days). There was only one independent risk factor for CLABSI: length of time at risk (OR=3.5, CI 2.1-5.9; per double number of days). Independent risk factors for ICU-acquired pneumonia were: use of ventilator (OR=8.0, CI 1.8-35; risk-time ratio 1 vs 0); lack of enteral nutrition (OR=8.0, CI 1.2-2.8; risk-time ratio 1 vs. 0); and length of time at risk (OR=1.8, CI 1.2-2.8; per double number of days) (Magnason et al.).

The CDC analyzed surveillance data from the National Healthcare Safety Network (NHSN) on HAIs from hospitals all over the nation (CDC, 2009a; Doshi et al., 2009). Of approximately 1,256 hospitals participating, hand hygiene adherence ranged

from 5 to 81% with an average of 40%. For the CDC recommendation of surgical site antimicrobial prophylaxis, the adherence was <50%. Full compliance with CDC evidence-based recommendations for prevention of HAIs ranged from 30.7 to 38.5% with CLABSI adherence at 35.4% (CDC, 2009a). The public disclosure of HAI rates are mandated in only 2 of the states in the continental United States. Only 4 additional states are considering making the mandate law. Advocates of public mandates of HAI infection rates argue that patients as consumers could be better equipped to make informed choices for healthcare (CDC, 2009a; McKibben et al., 2005). Many questions in the reporting of HAI infection rates were raised. Opponents question the reliability of reporting and consistency of the definition of HAIs (McKibben et al., 2005). Over 20 years ago, the reliability of reporting nosocomial infection rates was queried. Risk factors were identified as lack of documentation by healthcare providers and medical record technicians despite obvious pathological findings (Massanari, Wilkerson, Streed, & Hierholzer, 1987).

Staphylococcus Aureus

During 2001-2002, nasal samples for cultures of SA were obtained from 9622 individuals in the National Health and Nutrition Examination Survey (Kuehnert et al., 2006). This investigation was conducted because colonization has been established as a predictor of later infection. The colonization prevalence estimates were 32.4% (95% CI, 30.7-34.1%) (Kuehnert et al.). SA is the leading cause of lower respiratory tract and surgical site HAIs, and is the second leading cause of bacteremia, pneumonia, and cardiovascular infections (Noskin et al., 2005; Rubin et al., 1999). Noskin et al. identified

SA infections were most likely to occur in hospitalized patients who had received neurosurgery (1.4%), and the least likely patients were those who had a history of orthopedic surgery (0.3%). Additionally, SA infection was associated with the exacerbation or etiology of vasculitis which complicates the progression of systemic autoimmune diseases (Lidar, Lipschitz, Langevitz, & Shoenfeld, 2009).

In an analysis of the burden of SA infections in the United States, SA was the discharge diagnosis of 0.8% of inpatients. Patients with SA had three times the length of the average hospital stay, had three times the charges, and five times the risk of in hospital mortality (Noskin et al., 2005). Of the 1,351,362 nonobstetrical hospital discharges for New York City in 1995, 1.0% or 13,550 were patients discharged following SA infections. Direct medical costs were estimated at $435.5 million with an average length of stay (LOS) at approximately 20 days, and the focused cost of the SA infection was $32,100. There were 1,400 reported deaths with a 10% death rate. In comparison, direct medical charges for nonobstetrical hospitalizations that were not SA infections were $13,263 with a mean LOS of 9 days, and a death rate of 4.1% (Rubin et al., 1999). The contrast is astounding given the assumption that these infections were preventable.

Peripheral and central venous catheters are essential to the treatment modalities of current medical care, but are associated with complications. SA infections are the second leading cause of CLABSIs (Gosbell, 2005; Noskin et al., 2005; Rubin et al., 1999). Approximately 150 million venous catheters are purchased in the United States each year, and approximately 5 million are central venous catheters. Mortality estimates

related to CLABSIs are 12% to 25% with direct costs at $25,000 (Gosbell). CLABSIs due to MRSA were associated with 2 times the death rates than CLABSIs with methicillin susceptible SA (MSSA) (Cauda & Garau, 2009). The highest rates of systemic infections occurred in patients with long-term central venous catheters, such as Hickman catheters, subcutaneous infusion ports, and peripherally placed central venous catheters. The sources of CLABSIs were numerous. Cross infection, contaminated equipment or solutions, catheter insertion and maintenance, and host factors (medications, age, co morbidities, immunosuppression, loss of skin integrity, and distant infection) were considered as links in the chain of infection (Gosbell).

Microbiologists have discovered that genetic coding initiates slime production and biofilm formation that is necessary for strains of SA to colonize (Mateo et al., 2008). CLABSIs can progress into bacteremia which is commonly caused by SA. When bacteremia develops, the tandem effects of bacterial toxins and the immune response can result in sepsis, septic shock, hypotension, and finally multiple organ failure. Bacteremia can also result from other SA-related infections such as endocarditis, osteomyelitis, and septic arthritis (Naber, 2008).

Methicillin Resistant *Staphylococcus aureus.* Experts estimate that greater than 95% of patients with SA related infections do not respond to first-line antimicrobial treatment such as penicillin or ampicillin (Rubin et al., 1999). Evidence suggests that the majority of SA isolates are resistant strains to beta lactamase antimicrobial medications such as methicillin or oxacillin (Klein et al., 2007; Lindsay & Holden, 2006). The evolution of bacteria has been in flux at an alarming speed. These processes are

completed by a variety of mechanisms which include mutation, DNA rearrangement or loss, and horizontal transfer of genes between bacterium. There are 6 genome sequences for SA (Boyce & Tiemersma, 2006; Grundmann, Aires-de-Sousa, Lindsay, & Holden, 2006). "Approximately 75% of a *S. aureus* genome comprises a core component of genes present in all of the strains" (Lindsay & Holden, 2006, p. 187). However, genetic diversity within the core genome is responsible for important phenotype varieties within strains of SA. The accessory portion of the genome contains genes that are responsible for many functions which include virulence and drug resistance (Lindsay & Holden). An ethical conflict has arisen in this antimicrobial resistance of bacteria such as SA, and the public and private interests of antimicrobial development (Aiello, King, & Foxman, 2006). Lack of financial incentives and other risks in antimicrobial development hinder the pharmaceutical companies in the prioritization of clinical trials for antimicrobial drug development (Aiello et al.).

Methicillin resistance is the most important phenomenon in SA related infections of the healthy and diseased populations (Gundmann et al., 2006). Globally and nationally, MRSA from HAIs and CA-MRSA are growing in prevalence with a burden of unknown scope (Kuehnert et al., 2005). Research data regarding exact incidence and prevalence of MRSA is lacking. Kuehnert et al. calculated the number of MRSA hospitalizations from ICD-9 codes (Hart & Hopkins, 2005) related to SA infections. The number of MRSA infections was 3.95 per 1,000 hospital discharges in the United States (Kuehnert et al., 2005). In research of hospitalizations and deaths attributed to MRSA between 1999 to

2005 in the United States, the rate of MRSA hospitalizations doubled from 127,036 to 278,203 (Klein et al., 2007).

As prevalence of MRSA is growing at an alarming rate, the understanding of risk populations and the organization of surveillance are moving to the forefront as areas of exploration. A case-control study was completed in a Missouri prison during 2002-2003 regarding risk factors for the spread of MRSA infection rates among inmates (Turabelidze et al., 2006). MRSA isolates were identified by PFGE. Transmission related to hygiene contributed heavily to MRSA rates (Turabelidze et al.). Control of MRSA will necessitate a comprehensive approach which encompasses strategies such as screening of patients in acute and long term care facilities, screening of healthcare providers and staff, rigorous adherence to isolation and barrier nursing, strict adherence to hand hygiene, thorough environmental cleaning of surfaces and reservoirs, and potentially the initiation of decolonization therapy to all who are colonized (Grundmann et al., 2006). Simons and Alcabes (2008) proposed a model of MRSA surveillance which included state coordinating offices, specific, standardized local surveillance reports and data collection, and localized administrative and public laboratories. The factors associated with the burgeoning of MRSA infections was the result of increased use of broad spectrum antibiotics, increased numbers of immunocompromised patients in healthcare settings, and increased use of invasive devices for diagnosis and treatment such as peripheral and central venous lines and shunts (Enright, 2006).

New technologies and a deeper understanding of genetics and genomics offer strategies for control of the ubiquitous nature of SA infections, MSSA, MRSA, and CA-

MRSA (Struelens, Hawkey, French, Witte, & Tacconelli, 2009). Public debate is in progress as to which strategies are the "most efficacious, cost-effective, and achievable" (Cimolai, 2008, p. 481). In healthcare settings, a consensus agreement has been proven regarding transmission of MRSA on the hands of personnel involved in direct patient care. Although not all strains of SA or MRSA are disseminated equally, bacteria may be spread via nose, mouth, skin, or clothing of the healthcare workers. The movement of the SA-related bacteria has been likened to aerosol spread (Cimolai). An additional feature of the organisms is their ability to survive with virulence (Cimolai). Environments include all levels of the healthcare system and places of public domain. The removal of the pathogens from the surfaces will depend on a complexity of factors which include the type of surfaces, porosity, composition, sensitivity to chemical products, exposure time, concentration, humidity, and temperature (Cimolai). Additional factors associated with SA, MRSA, and CA-MRSA were poor hygiene, crowded living conditions, and socioeconomic status (Bubacz, 2007).

Some patients who are colonized or infected with an SA related infection were not detected by cultures that were ordered by physicians for clinical reasons, but were collected from sample body sites such as the anterior nares with 80% efficacy (Grundmann et al., 2006). Due to the costs and lack of strong empirical evidence in randomized clinical trials, this practice occurs in less than 30% of patients. When the complex variables of risk of SA infections are placed in mathematical models, results suggest that universal screening is the best way to control spread and dissemination. Selective culture media and real–time positive culture assays allow for quicker

identification of patients who are colonized or infected (Struelens et al., 2009). The identification of risk factors at hospital admission with the focus of individualized treatment and care may decrease the incidence and prevalence of SA infections. Risk factors that may be important for such individualized isolation and care include: age >60; previous hospitalization in the last year; 2 or more antibiotics in the previous 30 days; hemodialysis; and a previous history of MRSA infection (Tacconelli, 2006).

Community-acquired Methicillin-resistant *Staphylococcus aureus.* CA-MRSA came to public attention with the reports of the deaths of 4 healthy children from 1997 to 1999 (Enright, 2006). Strains of CA-MRSA have been speculated to increase as much as 33% annually. A recent critical surgence occurred from 2003 to 2005 with a significant increase of skin and soft tissue outpatient infections (Klein et al., 2009). CA-MRSA and MRSA due to HAI are genetically different. CA-MRSA typically expresses a toxin called Panton-Valentine leukocidin, and is not generally multi-drug resistant. This toxin is the cause of the necrosis of blood cells, and is linked with necrotizing pneumonia in children and young adults (Enright, 2006). Groups at risk for CA-MRSA include children and adults in overcrowded conditions such as athletes, prisoners, and soldiers; individuals with limited access to healthcare; those of a lower socioeconomic status and certain racial or ethnic minorities (Furugo & Lowry, 2005; Herman et al., 2008). Skin and soft tissue infection of the pulmonary tissue and bloodstream were the most common sites of infections. Sources of infection stemmed from frequent skin to skin contact with compromised skin, sharing of personal items and sexual activity among men (Furugo & Lowry; Herman et al.). Antimicrobial susceptibility is broader in CA-MRSA. CA-MRSA

was typically sensitive to trimethoprim-sulfamethoxazole, tetracyclines and clindamycin (Herman et al.; Klein et al.). Family outbreaks of CA-MRSA have been reported, but are a rare occurrence. Typically, the predicted risk factors are apparent and may warrant prophylactic cultures of the entire family if 2 or more members have confirmed cases of CA-MRSA (Jones et al., 2006).

Due to the current sophistication of genotyping, there is a significant increase of CA-MRSA strains appearing in HAIs (Klevens et al., 2006; Maree, Daum, Boyle-Vavra, Matayoshi, & Miller, 2007; Seybold et al., 2006). Time based definitions have been the tools to differentiate hospital acquired (HA) MRSA to CA-MRSA. "For example, if MRSA was cultured or diagnosed within 24-72 hours after a patient was hospitalized and there were no risk factors for HA-MRSA, the condition was defined as CA-MRSA" (Herman et al., 2008, p. 219). Bratu et al. (2006) sought to discover the extent CA-MRSA isolates were apparent in MRSA infections among patients in New York City. Of 1316 isolates that were identified during the investigation, 217 were sensitive to clindamycin which distinquished CA-MRSA strains from HA-MRSA strains. Seventy-two were identified as the USA300 strain CA-MRSA and 5 USA400 strain. Demographic characteristics of participants of the study were black, Hispanic, <18 years of age and lived in households of $\geq$ 3 persons (Bratu et al.).

In 2005, a population based surveillance was conducted over 9 states with 16.3 million individuals within the study (Klevens et al., 2006). CA-MRSA USA300 was confirmed as present in all healthcare settings. Approximately 18% to 28% of patients with health-related risk factors were infected with CA-MRSA USA300 strain. Twenty-

six percent of patients without health-related risk factors had HA-MRSA USA100 (Klevens et al.). In 2000, Minnesota Department of Health initiated a 12 hospital prospective surveillance for pulse field types (PFTs), case characteristics, and antibiotic susceptibility of CA-MRSA (Como-Sabetti et al., 2009). From 2000 to 2005, CA-MRSA increased from 11% to 33% of cases. CAMRSA USA300 replaced USA400 as the primary PFT during the investigation. Isolates' sensitivity to erythromycin and clindamycin decreased significantly (Como-Sabetti et al.). In a 10 year retrospective review, the mortality related to CA-MRSA and HA-MRSA bacteremia was similar if treatment was specific to strain susceptibility. In this study, 90.4% were categorized as HA-MRSA and 9.6% as CA-MRSA (Robinson, Pearson, Christiansen, Coombs, & Murray, 2009).

Summary

According to the NIH (2005), autoimmune diseases affect as many as 23.5 million Americans, and estimated healthcare expenditures reach $100 billion annually. The impact of prevalence and healthcare expenditures do not match the distribution of federally allocated clinical research dollars (AARDA, 2010). The 2003 research award for autoimmune diseases was the direct result of the efforts of the ADCC. In coordination with the ADCC, the NIH published a strategic plan to research immunologic, genetic, and environmental studies to increase the knowledge base of autoimmune diseases (Fairweather & Rose, 2004; NIH, 2005; Sebastini & Galeazzi, 2009a).

Since autoimmune disease prevalence is increasing, the understanding of the etiology and risk factors is necessary for prevention of overt disease manifestation.

Aberrations in immune system function (innate and adaptive), abnormal genetic patterns, environmental exposure, and lifestyle choices are all pieces in the expression of autoimmune disease (Fairweather & Rose, 2004; NIH, 2005). Examples of immune dysfunction include: abnormalities in eliminating pathogens, the presence of chronic inflammation, complement and immunoglobulin (Ig A) deficiency, and dysfunctional T cell regulation (Shepshelovich & Shoenfeld, 2006). Alterations in the adaptive immunity or immunological memory system affect autoimmunity. Changes in B cell or T cell function can predispose individuals to autoimmune diseases (McCance et al., 2010). Immunosenescence has increased the incidence of late-onset autoimmunity (Siegel et al., 2008). Gender related immune response appears to be a factor in the susceptibility of females. Endogenous and synthetic estrogen is believed to play a role in the high prevalence of females with autoimmune diseases (Ahmed et al., 1999). Finally, antibody dysfunction and the presence of high numbers of autoantibodies have high positive predictive value for the onset, severity and complications of autoimmune diseases (Agmon-Levin & Shoenfeld, 2009).

Autoimmunity has been linked to multigenic phenotype origins (Sebastiani & Galeazzi, 2009; Shepshelovich & Shoenfeld, 2006). Genetic causality for autoimmune diseases was substantiated by the increased manifestation of disease in monozygotic twins compared to dizygotic twins, and a significantly increased frequency in families with one or more affected family members (Cocco et al., 2009; Molina & Shoenfeld, 2005; Rose, 2007; Sebastiani & Galeazzi; Shepshelovich & Shoenfeld). Susceptible genes related to autoimmunity affect response to autoantigens, and influence apoptosis,

inflammatory processes, and tolerance (Mackay, 2000). The most important genetic loci associated with autoimmune diseases are the MCH and HLA complexes (Maier & Hafler, 2009; Shepshelovich & Shoenfeld). Although association calculations, such as odds ratio, are weaker, non-MHC alleles are implicated in relationship to autoimmunity as well (Coenen & Gregersen, 2009). GWA scans enable genetic research design to discover common and abnormal genetic patterns in large studies of patients with autoimmune diseases (Gregersen, 2007).

Evidence of varying strengths has associated exposure to infections, vaccines, occupational exposures, and lifestyle choices with autoimmunity (Ercolini & Miller, 2008; Molina & Shoenfeld, 2005; Parks & Cooper, 2005). Molecular mimicry, epitope spreading, bystander activation, and cryptic antigens are mechanisms in which infections trigger manifestation of autoimmune diseases (Ercolini & Miller). The genetic diverseness of humans complicates the inquiry of the correlation of infections and autoimmune diseases. Identifying which genetic markers are precursors to identified infection triggers would be a victory in autoimmune disease etiology research (Ercolini & Miller).

Viral diseases such as human Herpes virus family, EBV, retrovirus family, CMV, and human parvovirus B19 have been associated with autoimmune diseases (Molina & Shoenfeld, 2005). Parasitic diseases, such as Chagus' disease and malaria have produced autoantibodies that led to the expression of autoimmune diseases (Molina & Shoenfeld). Other triggers of active autoimmunity include vaccines, occupational exposures, ultraviolet light, smoking, low levels of n-6 fatty acid linoleic acid, vitamin D, and

chronically, high emotional stress (Agmon-Levin & Shoenfeld, 2009; Molina & Shoenfeld; Parks & Cooper, 2005; Sawyer, 2010; Shepshelovich & Shoenfeld, 2006). Crystalline silica, silicone implants, solvents, mercury, and pesticides have been associated with SLE (Molina & Shoenfeld; Parks & Cooper).

Autoimmune diseases may target one system or affect multiple systems (FHCRC, 2010) and the clinical manifestations may be vague, nonspecific, and will range in severity (Medline Plus, 2009; Pountney, 2010; Siegel et al., 2008). Patients with autoimmune diseases experience remissions, exacerbations and frequently progressive complications and disability (NIH, 2005), which could include mental health challenges due to a decreased quality of life (Ledermen et al., 2008). Frequent complications related to autoimmunity include accelerated atherosclerosis, cardiovascular disease, infections, and lymphoproliferative malignancies (CDC, 2009b). Renal complications are common in SLE patients (Burling et al., 2007). Infections were identified in two studies of autoimmune patients (Berkun et al., 2009; Jeong et al., 2009). SA was one of the pathogens identified in a study by Jeong et al. High dose corticosteroid treatment, immunosuppressive medications, and complications related to renal disease contributed significantly to those infections (Jeong et al.). Treatment of autoimmune disease with immunosuppressive agents is associated with malignant lymphomas, multiple myelomas, and leukemias (CDC, 2009b; Dalamaga et al., 2008; Smedby et al., 2008).

Treatment of autoimmune disease targets the controlling of symptoms, decreased cell and tissue destruction, and assists the immune system to protect against opportunistic infections and cancers (Medline Plus, 2009). Medication treatment options include

corticosteroids, DMARDs, general immunosuppressants, anti-TNF drugs, and monoclonal antibodies (Medline Plus, 2009; Merck, 2007). Treatment addressing holistic needs such as physical therapy, functional rehabilitation, emotional, and financial counseling are needed to maintain the optimum quality of life (Holland et al., 2010). A new, emerging treatment in the clinical trial phase is mesenchymal stem cell transplantation of autologous hematopoietic stem cells in patients with SLE and MS (Tyndall, 2009).

Autoimmune patients face challenges related to treatments and disease complications. Patients who are immunosuppressed face greater risk for HAIs (Blot, 2007). HAIs increase patient morbidity, mortality, and healthcare expenses (CDC, 2007). Medical advancements have increased longevity of life, and increased invasive diagnostic testing and therapy place compromised patients at further risk of complications (Blot, 2007). The incidence of HAIs is related to many complicated factors in care delivery. Lack of adherence to CDC evidence-based recommendations for infection control remains a constant challenge for healthcare leadership (CDC, 2009a).

SA is a frequent causative agent for HAIs. Patients with SA had three times the length of the average hospital stay, three times the charges, and five times the risk of hospital mortality (Noskin et al., 2005). Nasal colonization of SA is estimated to be 32.4% (Kuehnert et al., 2006). SA is the leading cause of infections in the lower respiratory tract, surgical site HAIs, and is the second leading cause of bacteremia, pneumonia, and cardiovascular infection (Noskin et al.; Rubin et al., 1999). SA infections are the second leading cause of CLABSIs (Gosbell, 2005; Noskin et al.; Rubin et al.).

Bacteremia can occur as a consequence of SA infections of endocarditis, osteomyelitis, and septic arthritis (Naber, 2008).

The majority of strains of SA related infections do not respond to first-line antimicrobial treatment such as penicillin or ampicillin (Rubin et al., 1999). The evolution of resistant SA microorganisms is completed by mutation, DNA rearrangement or loss, and horizontal transfer of genes between bacterium (Klein et al., 2007). Six genome sequences have been identified for SA (Grundmann et al., 2006; Lindsay & Holden, 2006). An understanding of the genome contributes to the understanding of the virulence and resistance of SA infections (Lindsay & Holden). Between 1999 and 2005, the rate of MRSA hospitalizations doubled (Klein et al.).

As the prevalence of MRSA increases, the study of risk populations and the possible organization of surveillance is appearing in scholarly literature. Debate is ongoing regarding strategies to contain and control MRSA transmission (Grundmann et al., 2006). Models of MRSA surveillance and control include state and local coordinating offices, standardized reporting and data collections, and the use of public laboratories. Factors noted in the spread of MRSA include frequent use of broad spectrum antimicrobials, increased numbers of immunocompromised patients in healthcare settings, and increased use of invasive devices for diagnosis and treatment (Enright, 2006).

CA-MRSA is speculated to increase 33% annually (Klein et al., 2009). CA-MRSA is genetically different from MRSA, and is not typically multi-drug resistant (Enright, 2006). Advances in gentotyping led to the identification of a significant increase

in CA-MRSA strains in HAIs. (Klevens et al., 2006; Maree et al., 2007; Seybold et al., 2006). Time based definitions, and the identification of genetic strains alert scientists to the origin of HAIs (Herman et al., 2008). A common CA-MRSA strain identified in HAIs was CA-MRSA USA300 (Klevens et al.). In a 10 year retrospective review, mortality rates of CA-MRSA and HA-MRSA were similar if treatment was sensitive to strain susceptibility (Robinson et al., 2009).

Patients with autoimmune disease face additional challenges and risks during hospitalization. HAIs are a threat to all patient populations, but the risk is increased with the disease progression, complications, and treatments experienced by autoimmune disease patients. SA, MRSA, and CA-MRSA are formidable threats for those hospitalized with autoimmune diseases. The analysis of predictors of SA-related infections of hospitalized patients with autoimmune diseases will further the knowledge of health educators and healthcare providers seeking to preserve and optimize the quality of life for patients living with autoimmune diseases.

CHAPTER III

METHODOLOGY

The proposed retrospective study analyzed secondary hospital discharge data of patients with at least one of twenty-one autoimmune diseases. The secondary data was evaluated in groupings related to autoimmune diseases, infectious diseases (SA or MRSA at any site), and descriptive data (gender, age, race/ethnicity, type of autoimmune disease, insurance type, length of stay in days, and total charges). Nested case control studies comprised of three random samples were explored within the retrospective investigation. The cases were patients with SA or MRSA at any site. The controls were patients without any diagnosis of an SA-related diagnosis. This chapter describes the data protection procedures for this study, human patient protection measures, description of variables in the study, and the statistical analysis conducted.

Data Collection Procedures

The secondary data for this study was obtained from the Dallas Fort Worth Hospital Council [DFWHC]. Twenty-one hospitals from multiple counties in the geographic area were included in the DFWHC. Faculty from the Department of Health Studies at Texas Woman's University at Denton, Texas secured the data of patients with autoimmune diseases from 1999 to 2005. This study analyzed the total sample (N=65,536) of patients hospitalized with autoimmune diseases. The goal of securing the data was to further the knowledge and understanding of risk factors and experiences of

hospitalized patients with autoimmune diseases. This information has the potential for use in the field of health education and related disciplines of allied health.

Human Participant Protection

As all individual identifying data were removed from the data set prior to acquisition from the DFWHC, an exempt status application was submitted for this study and approved by the Texas Woman's University Institutional Review Board (IRB). The data were stored on an Excel spreadsheet with all identifying data removed, and uploaded to a statistical software program for analysis.

Description of Variables

The two primary research questions that initiated this investigation were:

1. What are the descriptive characteristics (gender, age, race/ethnicity, autoimmune diagnosis, insurance type, length of hospitalization and total charges) of patients hospitalized with MRSA or SA in North Texas?

2. Which autoimmune diseases resulted in the highest prevalence of MRSA or SA infections (Bacteremia, Septicemia, Pneumonia, Vancomycin-resistant *S. aureus*, Enterocolitis, Endocarditis, Surgical site infection, Osteomyelitis, Septic arthritis and SIRs)?

Each descriptive characteristic was coded for input into the statistical software system as independent variables. For the DFWHC data initiative, an autoimmune disease data extract- data dictionary was provided. Each patient had one primary diagnosis and up to 8 secondary diagnoses that were identified by the ICD-9-CM coding structure with the decimal added (Hart & Hopkins, 2005). The SA, MRSA, and SA-related infections

with ICD-9-CM coding represented multiple dependent variables of this investigation (Hart & Hopkins, 2005).

Data Analysis Strategies

Statistical Package for Social Sciences (SPSS) software package Version 17.0 was used in data analysis. Descriptive statistical analysis included were measures of central tendency, standard deviation, range, and frequency distribution. One way ANOVAs were calculated of age at discharge by categorical demographic variables. Independent sample *t* tests were calculated of age at discharge by SA specific infection diagnosis. A series of logistic regressions, were conducted on three randomized samples within the data set to determine if autoimmune disease diagnosis, gender, age, race/ethnicity, insurance type, length of stay in days or total charges were predictive or protective of the presence of SA or MRSA at any site. Odds ratio was utilized to determine the degree of the measure of association between covariates and SA infection.

Summary

This retrospective investigation utilized existing patient data collected from 1999 to 2005 to explore the descriptive characteristics and prevalence of SA, MRSA and SA-related infections in patients hospitalized with 21 autoimmune diseases. All patient identifiers had been removed from the data spread sheet prior to TWU faculty acquisition from the DFWHC. Statistical analysis included measures of central tendency, calculation of standard deviation, range, frequency distribution, one-way ANOVAs, and independent *t* tests. A series of logistic regressions were completed to determine if any descriptive characteristics were predictive of SA, MRSA or SA-related infection. The highest

prevalence of SA, MRSA or SA-related infections were calculated by type of autoimmune disease.

CHAPTER IV

RESULTS

The data analyses of this study will be grouped by preliminary analyses, primary analyses for research question one, primary analyses for research question two, and the analyses of the hypothesis. The data will be presented in tables interspersed with descriptive narrative to explain the significance of the findings. Frequencies, percentages, cross-tabulations, chi squares, *t* tests, ANOVAs, and multiple logistic regression analyses will be used to find the relationships and predictors of SA specific infections and potentially related SA infections among hospitalized autoimmune patients in north Texas.

Preliminary Analyses

The sample population of this study included 65,535 patients hospitalized with autoimmune diseases. Tables 1 through 28 will display the preliminary analysis of this study. As demonstrated in Table 1, the majority of the patients were females (79.2%), with Caucasians (67.3%) and African-Americans (19.8%) representing the largest ethnic groups in the sample. Additionally, Hispanics (8.4%), Asian Pacific Islanders (1.1%), and American Indian Eskimo/Aleutians (.1%) were represented. Non-identified ethnic groups (3.3%) were labeled in the final category.

Table 1

Frequencies and Percentage for Gender, Ethnicity, and Insurance Type

	n	%
Gender		
Female	51917	79.2
Male	13618	20.8
Ethnicity		
Caucasian	44086	67.3
African-American	12971	19.8
Hispanic	5508	8.4
Asian or Pacific Islander	694	1.1
American Indian/Eskimo/Aleut	75	.1
Other	2171	3.3
Insurance Type		
Missing	39	.1
Self Pay	4072	6.2
Other Non-Federal Program	378	.6
Preferred Provider Organization	10534	16.1
Point of Service	8	.0
Exclusive Provider	8	.0
Indemnity Insurance	2	.0
Health Maintenance Organization	9699	14.8
Blue Cross/Blue Shield	2818	4.3
Champus	261	.4
Commercial Insurance	4582	7.0
Medicare Part A	28052	42.8
Medicare Part B	18	.0
Medicaid	4104	6.3
Other Federal Programs	65	.1
Worker's Comp Health Claim	131	.2
Unknown	764	1.2

Note: Frequencies not summing to 65,535 and percentages not summing to 100 reflect missing data

Descriptors of the patient population included the age at discharge, length of stay in the hospital, and total hospital charges (Table 2). The average age of the full sample was 56 years (M=56.02, SD = 17.80), with a range of 18 to 109 years. The mean length of the hospital stay in days was 6 days (M = 6.07; SD = 7.06) and varied from 1 to 373 days. The range of total hospital charges was 0 to $1,281,330 with an average charge of $24,340.35 ($M$ = 24,340.35; SD = 36,863.49).

Table 2

Means and Standard Deviations for Age at Discharge, Length of Stay, and Total Hospital Charges

	N	Mean	*SD*	Min	Max
Age at Discharge	65535	56.02	17.80	18	109
Length of Stay	65535	6.07	7.06	1	373
Total Hospital Charges	65531	24340.35	36863.49	0	1281330

Table 3 illustrates the frequencies and percentages for SA specific infections and SA potentially related infections. All SA specific infections (n = 1825, 2.8%), SA infections (n=1135; 1.7%), MRSA (n = 60; .1%), and SA possibly related infections (n = 2168; 3.3%) were included in the data analysis. The highest frequencies of infections that were >.5% included: Septicemia (n = 500; .8%), Bacteremia (n = 1131; 1.7%), Septic

arthritis (n = 392; .6%), and SIRS (n = 412; .6%). As autoimmune diseases and SIRS may be associated with organ failure, Table 4 describes the frequencies and percentages of organ dysfunction. Overall organ dysfunction of the sample was 5.3% (n = 3474). Acute renal failure (n = 1994; 3.0%), Acute respiratory failure (n = 1612; 2.5%), Hepatic failure (n = 94; .1%), and Septic shock (n = 119; .2%) were the highest frequencies of organ dysfunction in the autoimmune patient sample.

Table 3

Frequencies and Percentage for SA Specific Infections and SA Possibly Related Infections

	n	%
All SA Specific Infections		
No	63710	97.2
Yes	1825	2.8
SA Infection		
No	64400	98.3
Yes	1135	1.7
MRSA		
No	65475	99.9
Yes	60	.1
Pneumonia		
No	65358	99.7
Yes	177	.3
Septicemia		
No	65035	99.2
Yes	500	.8

(Table 3, continued)

Table 3, continued

Frequencies and Percentage for SA Specific Infections and SA Possibly Related Infections

	n	%
SA Possibly Related Infection		
No	63367	96.7
Yes	2168	3.3
Enterocolitis		
No	65526	100.0
Yes	9	.0
Bacteremia		
No	64404	98.3
Yes	1131	1.7
Endocarditis		
No	65428	99.8
Yes	107	.2
Surgical Site Infection		
No	65442	99.9
Yes	93	.1
Osteomyelitis		
No	65343	99.7
Yes	192	.3
Septic Arthritis		
No	65143	99.4
Yes	392	.6
SIRS		
No	65123	99.4
Yes	412	.6

Note: Frequencies not summing to 65,535 and percentages not summing to 100 reflect missing data

Table 4

Frequencies and Percentage for Organ Dysfunctions

	n	%
Any Organ Dysfunction		
No	62061	94.7
Yes	3474	5.3
Acute Renal Failure		
No	63541	97.0
Yes	1994	3.0
Encephalopathy		
No	65503	100.0
Yes	32	.0
Critical Illness Polyneuropathy		
No	65532	100.0
Yes	3	.0
Critical Illness Myopathy		
No	65532	100.0
Yes	3	.0
Acute Respiratory Failure		
No	63923	97.5
Yes	1612	2.5
Hepatic Failure		
No	65441	99.9
Yes	94	.1
Septic Shock		
No	65416	99.8
Yes	119	.2

Note: Frequencies not summing to 65,535 and percentages not summing to 100 reflect missing data

Each patient in the sample had at least one of twenty-one autoimmune diseases. The frequencies and percentages for autoimmune diseases are presented in Table 5. The highest prevalence of autoimmune diseases were RA (n = 24,122; 36.8%), SLE (n = 14,829; 22.6%), MS (n = 8529; 13.0%), and ITP (n = 3797; 5.8%). Graves' disease (n = 2068; 3.2%), MG (n = 1835; 2.8%), Raynaud's disease (n = 1798; 2.7%), Crohn's disease (1749; 2.7%), Ig A nephropathy (n = 1315; 2.0%), SS (n = 2347; 3.6%), and Sicca syndrome (n = 1563; 2.4%) were clustered in prevalence. The proportion of patients diagnosed with each of the remaining autoimmune diseases was less than 2%.

Table 5

Frequencies and Percentage for Autoimmune Diagnoses

	n	%
Autoimmune Hepatitis		
No	65273	99.6
Yes	262	.4
Graves' Disease		
No	63467	96.8
Yes	2068	3.2
Hashimotos Thyroiditis		
No	64638	98.6
Yes	897	1.4
Autoimmune Disease - Nonspecific		
No	65126	99.4
Yes	409	.6

(Table 5, continued)

Table 5, continued

Frequencies and Percentage for Autoimmune Diagnoses

	n	%
Primary Thrombocytopenia		
No	61738	94.2
Yes	3797	5.8
Multiple Sclerosis		
No	57006	87.0
Yes	8529	13.0
Myasthenia Gravis		
No	63700	97.2
Yes	1835	2.8
Raynaud's Disease		
No	63737	97.3
Yes	1798	2.7
Crohn's Disease		
No	63786	97.3
Yes	1749	2.7
Ulcerative Colitis		
No	65466	99.9
Yes	69	.1
Primary Biliary Cirrhosis		
No	64653	98.7
Yes	882	1.3
Celiac Disease		
No	64991	99.2
Yes	544	.8
Ig A Nephropathy		
No	64220	98.0
Yes	1315	2.0
Discoid Lupus Erythematosus		
No	64957	99.1
Yes	578	.9

(Table 5, continued)

Table 5, continued

Frequencies and Percentage for Autoimmune Diagnoses

	n	%
Systemic Lupus Erythematosus		
No	50706	77.4
Yes	14829	22.6
Systemic Sclerosis		
No	63188	96.4
Yes	2347	3.6
Sicca Syndrome		
No	63972	97.6
Yes	1563	2.4
Dermatomyositis		
No	65008	99.2
Yes	527	.8
Polymyositis		
No	64620	98.6
Yes	915	1.4
Rheumatoid Arthritis		
No	41413	63.2
Yes	24122	36.8
Juvenile Rheumatoid Arthritis		
No	65079	99.3
Yes	456	.7

Note: Frequencies not summing to 65,535 and percentages not summing to 100 reflect missing data

The frequencies, percentages, and relationships between categorical demographic variables by gender are presented in Table 6. Analysis of gender and ethnicity revealed a significant relationship between gender and ethnicity, $\chi^2(2) = 289.85$, $p < .001$, Cramer's $V = .07$. An unusual finding related to autoimmunity demonstrated a greater proportion of

the Caucasian patients were males (72.5%) compared to females (65.9%). Conversely, a higher percentage of African-American patients were females (21.1%) compared to males (14.8%). Despite the statistical significance found in the relationship of gender and insurance type, χ^2 (4) = 156.59 $p < .001$, Cramer's $V = .05$, and between gender and length of stay, x^2 (3) = 37.48, $p < .001$, Cramer's $V = .02$, no notable differences (> 5%) were found between males and females for any of the insurance or length of stay categories. Significant results were found for total hospital charges, x^2 (3) = 206.59, $p < .001$, Cramer's $V = .06$ when compared with gender. Men had higher percentages (33.9%) of charges of $24,000 or more compared to women (28.0%).

The relationships between ethnicity and the categorical variables of gender, χ^2 (2) = 289.85, $p < .001$, Cramer's $V = .07$; insurance type, χ^2 (6) = 888.46, $p < .001$, Cramer's $V = .08$; length of stay, χ^2 (6) = 165.84, $p < .001$, Cramer's $V = .04$; and total hospital charges, χ^2 (6) = 16.16, $p = .013$, Cramer's $V = .01$ were significant (Table 7). The percentage of African-American females (84.5%) was proportionally higher than other ethnic groups (79.5%), and Caucasians (77.6%). The percentage of African-American males (15.5%) was significantly lower than Caucasian males (22.4%), and males in other ethnic groups (20.5%). A smaller proportion of those who self-pay were Caucasians (3.6%) compared to African-Americans (9.7%). A smaller proportion of both Caucasians and African-Americans who self-pay were compared to those of other ethnicity (15.7%). In the PPO/POS payment category, Caucasians (30.3%) had the highest proportion compared to African-Americans (23.0%). Of the patients who claimed Medicare, each ethnicity was significantly different and ranked as follows: Caucasians (47.0%), African-

Americans (41.0%), and other ethnic groups (30.9%). Finally, of those with Medicaid, a smaller proportion were Caucasian (3.3%) compared to African-American (13.2%), or other ethnicity (12.6%).

Table 6

Frequencies and Percentages for Categorical Demographic Variables by Gender

	Female		Male			
	n	%	n	%	χ^2	*p*
Ethnicity					289.85	<.001
Caucasian	34212	65.9	9874	72.5		
African-American	10960	21.1	2011	14.8		
Other	6719	12.9	1729	12.7		
Insurance Type					156.59	<.001
Self-Pay	3070	6.0	1002	7.5		
PPO/POS	14537	28.6	3676	27.7		
HMO	7687	15.1	2012	15.1		
Medicare	22059	49.9	6011	49.0		
Medicaid	3523	6.9	581	4.4		
Length of Stay					37.48	<.001
1-2 Days	13834	26.6	3410	25.0		
3-5 Days	19510	37.6	4959	36.4		
6-9 Days	10514	20.3	2990	22.0		
10 or More Days	8059	15.5	2259	16.6		
Total Hospital Charges					206.59	<.001
$7999 or Less	12508	24.1	2806	20.6		
$8000 - $15999	16131	31.1	3893	28.6		
$16000 - $23999	8748	16.8	2304	16.9		
$24000 or More	14530	28.0	4615	33.9		

Table 7

Frequencies and Percentages for Categorical Demographic Variables by Ethnicity

	Caucasian		African-American		Other			
	n	%	n	%	n	%	χ^2	*p*
Gender							289.85	<.001
Female	34212	77.6	10960	84.5	6719	79.5		
Male	9874	22.4	2011	15.5	1729	20.5		
Insurance Type							4592.18	<.001
Self-Pay	1571	3.6	1223	9.7	1278	15.7		
PPO/POS	13144	30.3	2905	23.0	2164	26.6		
HMO	6894	15.9	1647	13.1	1158	14.2		
Medicare	20382	47.0	5179	41.0	2509	30.9		
Medicaid	1419	3.3	1663	13.2	1022	12.6		
Length of Stay							165.84	<.001
1-2 Days	11919	27.0	3041	23.4	2275	26.9		
3-5 Days	16571	37.6	4680	36.1	3205	37.9		
6-9 Days	9044	20.5	2874	22.2	1583	18.7		
10 or More Days	6552	14.9	2376	18.3	1385	16.4		
Total Hospital Charges							16.16	.013
$7999 or Less	10172	23.1	3080	23.7	2047	24.2		
$8000 - $15999	13472	30.6	4017	31.0	2529	29.9		
$16000 - $23999	7498	17.0	2198	16.9	1351	16.0		
$24000 or More	12944	29.4	3676	28.3	2521	29.8		

The comparison of length of stay and total hospital charges by ethnicity resulted in a close distribution (< 5%) by ethnic grouping. The highest percentages for each ethnic group, Caucasians (37.6%), African-Americans (36.1%), and other ethnic groups (37.9%) were placed in the three to five days category. Mid-range percentages by ethnicity,

Caucasians (27.0%), other ethnic groups (26.9%), and African-Americans (23.4%) were associated with shorter lengths of stay (1-2 days). The lowest percentages by ethnic group, African-Americans (18.3%), other ethnic groups (16.4%), and Caucasians (14.9%) were categorized by the longest lengths of stay (10 or more days). When analyzed by ethnicity, most patients were charged $8,000 to $15,999: African-Americans (31.0%), Caucasians (30.6%), and other ethnic groups (29.9%). Nearly a third of patients in each ethnicity, other ethnic groups (29.8%), Caucasians (29.4%), and African-Americans (28.3%) were charged $24,000 or more.

Table 8 illustrates the cross tabulations and chi square results of the frequencies and percentages for categorical demographic variables by insurance type. A greater proportion of females had Medicaid insurance (85.9%) compared to the other four insurance types, self-pay (75.4%), PPO/POS (79.8%), HMO (79.3%), and Medicare (78.6%), χ^2 (1) = 156.59, $p < .001$, Cramer's $V = .05$, and the relationship was significant. In contrast, the lowest proportion of males had Medicaid (14.2%) insurance compared with self-pay (24.6%), PPO/POS (20.2%), HMO (20.7%), and Medicare (21.4%). The relationship between ethnicity and insurance type was significant, χ^2 (8) = 4592.18, $p <$ .001, Cramer's $V = .19$. Of those who were Caucasian, a smaller proportion had self-pay (38.6%) and Medicaid (34.6%) compared to PPO/POS (72.2%), HMO (71.1%), and Medicare (72.6%). A greater percentage of African-Americans claimed Medicaid (40.5%) and self-pay insurance (30.0%) compared to PPO/POS (16.0%), HMO (17.0%), and Medicare (18.5%).

Table 8

Frequencies and Percentages for Categorical Demographic Variables by Insurance Type

	Self-Pay		PPO/POS		HMO		Medicare		Medicaid			
	n	%	n	%	n	%	n	%	n	%	$\chi 2$	*p*
Gender											156.59	<.001
Female	3070	75.4	14537	79.8	7687	79.3	22059	78.6	3523	85.8		
Male	1002	24.6	3676	20.2	2012	20.7	6011	21.4	581	14.2		
Ethnicity											4592.18	<.001
Caucasian	1571	38.6	13144	72.2	6894	71.1	20382	72.6	1419	34.6		
African-American	1223	30.0	2905	16.0	1647	17.0	5179	18.5	1663	40.5		
Other	1278	31.4	2164	11.9	1158	11.9	2509	8.9	1022	24.9		
Length of Stay											1034.58	<.001
1-2 Days	1121	27.5	5849	32.1	2930	30.2	6011	21.4	956	23.3		
3-5 Days	1523	37.4	6855	37.6	3652	37.7	10412	37.1	1509	36.8		
6-9 Days	809	19.9	3204	17.6	1831	18.9	6487	23.1	896	21.8		
10 or More Days	619	15.2	2305	12.7	1286	13.3	5160	18.4	743	18.1		
Total Hospital Charges											401.37	<.001
$7999 or Less	1121	27.5	4496	24.7	2666	27.5	5704	20.3	1092	26.6		
$8000 - $15999	1317	32.3	5424	29.8	2981	30.7	8630	30.7	1272	31.0		
$16000 - $23999	637	15.6	2963	16.3	1570	16.2	5014	17.9	596	14.5		
$24000 or More	997	24.5	5330	29.3	2482	25.6	8722	31.1	1144	27.9		

In addition, length of stay was significantly related to insurance type, χ^2 (12) = 1034.58, $p < .001$, Cramer's $V = .07$. A greater proportion of patients who stayed in the hospital for one to two days had a PPO/POS (32.1%) or HMO (30.2%) compared to those with Medicaid (23.3%) or Medicare (21.4%). In the six to nine days category, a greater proportion of patients had Medicare (23.1%) compared to those with PPO/POS (17.6%) insurance. Finally, a smaller proportion of those with a PPO/POS (12.7%) or HMO (13.3%) stayed 10 or more days compared to those with Medicare (18.4%) or Medicaid (18.1%). The relationship between insurance type and total charges was also significant, χ^2 (12) = 401.37, $p < .001$, Cramer's $V = .05$. Of the patients who paid the least, ($7,999 or less), a smaller percentage had Medicare (20.3%) compared to Medicaid (26.6%), HMO (27.5%), or self-pay (27.5%). Finally, of the patients who paid the highest charges ($24,000 or more), a smaller proportion had self-pay (24.5%) compared to those with Medicare (31.1%).

Categorical demographic variables were cross tabulated by length of stay in the hospital (Table 9). Females and males were proportionally represented in each length of stay category, and the comparison was significant, χ^2 (3) = 37.48, $p < .001$, Cramer's $V =$ .02. Slightly more females (80.2%) had a shorter hospital stay (1-2 days) than females (78.1%) with longer stays (10 or more days). In contrast, slightly more males (21.9%) were hospitalized for 10 or more days than males (19.8%) in the shortest stay category (1-2 days). Ethnicity compared to length of stay was significant (χ^2 (6) = 165.84, $p <$ .001, Cramer's $V = .04$). More Caucasians (69.2%) were hospitalized one to two days compared to stays of ten or more days (63.5%). African-Americans (23.0%) had the

highest percentage in the longest stay category (10 or more days) compared with 17.6% in shorter stay groupings (1-2 days). Overall, the relationship between insurance type and length of stay was significant, χ^2 (12) = 1034.58, $p < .001$, Cramer's $V = .07$. Of patients with a PPO/POS insurance plan, a greater percentage stayed one to two days (34.7%) compared to three to five days (28.6%), six to nine days (24.2%), and ten or more days (22.8%). In the Medicare insurance group, a lower percentage stayed one to two days (35.65) compared to three to five days (43.5%), six to nine days (49.0%), or ten or more days (51.0%). As expected, total hospital charges compared significantly with length of stay, $\chi 2$ (9) = 27,118.70, $p < .001$, Cramer's $V = .37$. The highest percentages of cost increased as the length of stay increased. Patients who were charged $7999 or less had the highest percentage in the one to two days category (51.6%) compared with (.9%) in the ten days or more stays in the hospital. The $8000 to $15999 grouping had the highest proportion in the three to five days category (37.9%) contrasted with those (7.8%) in the longest hospital stay category. The $16,000 to $23,999 category had the highest percentage in the six to nine days category (25.9%) compared to one to two days (8.6%), three to five days (19.0%), and ten or more days (13.7%). Finally, a proportionally larger percentage of the patients who spent $24,000 or more (77.6%) were hospitalized for ten or more days in contrast to patients who spent that amount in the one to two days category (6.4%), the three to five days category (18.2%), and the six to nine days category (41.3%).

Table 9

Frequencies and Percentages for Categorical Demographic Variables by Length of Stay

	1-2 Days		3-5 Days		6-9 Days		10 or More Days			
	n	%	n	%	n	%	n	%	χ^2	*p*
Gender									37.48	<.001
Female	13834	80.2	19510	79.7	10514	77.9	8059	78.1		
Male	3410	19.8	4959	20.3	2990	22.1	2259	21.9		
Ethnicity									165.84	<.001
Caucasian	11919	69.2	16571	67.8	9044	67.0	6552	63.5		
African-American	3041	17.6	4680	19.1	2874	21.3	2376	23.0		
Other	2275	13.2	3205	13.1	1583	11.7	1385	13.4		
Insurance Type									1034.58	<.001
Self-Pay	1121	6.6	1523	6.4	809	6.1	619	6.1		
PPO/POS	5849	34.7	6855	28.6	3204	24.2	2305	22.8		
HMO	2930	17.4	3652	15.2	1831	13.8	1286	12.7		
Medicare	6011	35.6	10412	43.5	6487	49.0	5160	51.0		
Medicaid	956	5.7	1509	6.3	896	6.8	743	7.3		
Total Hospital Charges									27118.70	<.001
$7999 or Less	8902	51.6	5642	23.1	681	5.0	89	.9		
$8000 - $15999	5767	33.4	9712	39.7	3744	27.7	801	7.8		
$16000 - $23999	1479	8.6	4658	19.0	3498	25.9	1417	13.7		
$24000 or More	1096	6.4	4457	18.2	5581	41.3	8011	77.6		

Table 10 describes the frequencies and percentages of the demographic variables by total hospital charges. The relationship between total charges and gender was significant, χ^2 (3) = 206.59, $p < .001$, Cramer's $V = .06$. A greater percentage of females were in the $7,999 or less (81.7%) category compared to the $24,000 or more group (75.9%). Ethnicity and total charges, χ^2 (6) = 16.16, $p = .013$, Cramer's $V = .01$, were significant, and were similarly distributed in each cost grouping. The relationship between total charges and insurance type was significant, χ^2 (12) = 401.37, $p < .001$, Cramer's $V = .05$. A smaller percentage of patients with Medicare had total charges of $7,999 or less (37.8%) compared to those with charges of $8,000 to $15,999 (44.0%), $16,000 to $23,999 (46.5%), or $24,000 or more (46.7%). Again, total charges by length of stay were significantly related, χ^2 (9) = 27,118.68, $p < .001$, Cramer's $V = .37$. Total cost increased proportionally by the length of stay. For patients who stayed in the hospital for one or two days, a higher percentage paid $7, 9999 or less (58.1%) compared to $8,000 to $15,999 (28.8%), $16,000 to $23,999 (13.4%), and > $24,000 (5.7%). For those hospitalized for three to five days, the highest percentage of patients paid $8,000 to $15,999 (48.5%) in contrast with < $7,999 (36.8%), $16,000 to $23,999 (42.1%), and > $24,000 (23.3%). For lengths of stays between six and nine days, the highest cost was $16,000 to $23,999 (31.7%) compared with < $7,999 (4.4%), $8,000 to $15,999 (18.7%), and ten days or more (29.2%). Finally, for patient stays for ten or more days, total charges were > $24,000 (41.8%) for the highest proportion of patients contrasted with < $7,999 (.6%), $8,000 to $15,999 (4.0%), and $16,000 to $23,999 (12.8%).

Table 10

Frequencies and Percentages for Categorical Demographic Variables by Total Charges

	$7999 or less		$8000 – $15999		$16000 – $23999		$24000 or more			
	n	%	n	%	n	%	n	%	χ^2	*p*
Gender									206.59	<.001
Female	12508	81.7	16131	80.6	8748	79.2	14530	75.9		
Male	2806	18.3	3893	19.4	2304	20.8	4615	24.1		
Ethnicity									16.16	.013
Caucasian	10172	66.5	13472	67.3	7498	67.9	12944	67.6		
African-American	3080	20.1	4017	20.1	2198	19.9	3676	19.2		
Other	2047	13.4	2529	12.6	1351	12.2	2521	13.2		
Insurance Type									401.37	<.001
Self-Pay	1121	7.4	1317	6.7	637	5.9	997	5.3		
PPO/POS	4496	29.8	5424	27.6	2963	27.5	5330	28.5		
HMO	2666	17.7	2981	15.2	1570	14.6	2482	13.3		
Medicare	5704	37.8	8630	44.0	5014	46.5	8722	46.7		
Medicaid	1092	7.2	1272	6.5	596	5.5	1144	6.1		
Length of Stay									27118.68	<.001
1-2 Days	8902	58.1	5767	28.8	1479	13.4	1096	5.7		
3-5 Days	5642	36.8	9712	48.5	4658	42.1	4457	23.3		
6-9 Days	681	4.4	3744	18.7	3498	31.7	5581	29.2		
10 or More Days	89	.6	801	4.0	1417	12.8	8011	41.8		

One-way ANOVAs were used to compare the age of the patients at discharge by categorical demographic variables (see Table 11). The discharge age of males (M = 57.66; SD = 17.17) was significantly higher than that of females (M = 55.59; SD = 17.93), F (1, 65,533) = 146.84, $p < .001$. Significant differences were also found in the discharge age of those with different ethnicities, F (2, 65,502) = 3146.05, $p < .001$. Caucasians' discharge age (M = 59.69; SD = 16.98) was significantly higher than both African-Americans (M = 48.36; SD = 16.50) and those of other ethnic groups (M = 48.62; SD = 17.83). Patients' age at discharge was significantly related to type of insurance, F (4, 64,153) = 7562.18, $p < .001$. As expected, patients with Medicare (M = 67.17, SD = 15.13) were significantly older than those with an HMO (M = 52.36, SD = 16.55). Both those with Medicare and an HMO were significantly older than those with a PPO/POS (M = 47.65, SD = 13.72). Those with self-pay were significantly younger (M = 42.64, SD = 13.63) than those with Medicare, HMOs, or PPO/POS. Finally, those patients with Medicaid (M = 41.21, SD = 13.63) were significantly younger than all other groups.

Length of stay was significantly related to increased age of patients at discharge, F (3, 65,531) = 303.73, $p < .001$. Patients' ages were higher in longer hospital stays of six to nine days (M = 58.28; SD = 17.77), and ten or more days (M = 57.30; SD = 16.86). Younger patients had stays of one to two days (M = 52.95; SD = 17.41) when compared to patients with three to five days (M = 55.97; SD = 17.83) in the hospital. Finally, age was related to total hospital charges, F (3, 65,531) = 161.20, $p < .001$. Higher total charges, $16,000 - $23,999 ($M$ = 57.25; SD = 17.46), and costs of $24,000 or more ($M$ = 57.30; SD = 16.86) were associated with increased age at discharge. The mean age of

patients' decreased significantly with each smaller category of total hospital charges, $8,000 - $15,999 ($M$ = 56.11; SD = 17.95), and $7,999 or less ($M$ = 53.42; SD = 18.68).

Table 11

Means and Standard Deviations of Age at Discharge by Categorical Demographic Variables

	n	Mean	*SD*	*F*	*p*
Gender				146.84	<.001
Male	13618	57.66	17.17		
Female	51917	55.59	17.93		
Ethnicity				3146.05	<.001
Caucasian	44086	59.69 [a]	16.98		
African-American	12971	48.36 [b]	16.50		
Other	8448	48.62 [b]	17.83		
Insurance Type				7562.18	<.001
Self-Pay	4072	42.64 [b]	13.72		
PPO/POS	18213	47.65 [c]	13.32		
HMO	9699	52.36 [d]	16.55		
Medicare	28070	67.17 [e]	15.12		
Medicaid	4104	41.21 [a]	13.63		
Length of Stay				303.73	<.001
1-2 Days	17244	52.95 [a]	17.41		
3-5 Days	24469	55.97 [b]	17.83		
6-9 Days	13504	58.28 [c]	17.77		
10 or More Days	10318	58.30 [c]	17.61		
Total Hospital Charges				161.20	<.001
$7999 or Less	15314	53.42 [a]	18.68		
$8000 - $15999	20024	56.11 [b]	17.95		
$16000 - $23999	11052	57.25 [c]	17.46		
$24000 or More	19145	57.30 [c]	16.86		

Note: Means with different superscripts are significantly different, $p < .05$

Tables 12 through 16 present the frequencies and percentages for autoimmune diagnoses by categorical demographic variables. Due to variations in sample sizes of patients who have the autoimmune diagnoses and those that do not, all significant relationships in this section of tables were addressed. Gender is an identified factor in autoimmunity, and specific autoimmune diseases are more prevalent among each gender population (Table 12). SLE (Females = 25.8%; Males = 10.4%), χ^2 (1) = 1475.57, $p <$ .001, Cramer's V = .15; Hashimotos thyroiditis (Females = 1.6%; Males = .7%),χ^2 (1) = 65.13, $p <$ .001, Cramer's V = .03; Raynaud's disease (Females = 3.0%; Males = 1.6%), χ^2 (1) = 86.30, $p <$ .001,Cramer's V = .04; Primary biliary cirrhosis (Females = 1.5%; Males = .9%), χ^2 (1) = 23.71, $p <$ .001, Cramer's V = .02; Discoid lupus erythematosus (Females = .9%; Males = .7%), χ^2 (1) = 10.26, p = .001, Cramer's V = .01; SS (Females = 4.0%; Males = 1.9%), χ^2 (1) = 136.75, $p <$ .001, Cramer's V = .05; and Sicca syndrome (Females = 2.8%; Males = .7%),χ^2 (1) = 219.48, $p <$ .001, Cramer's V = .06, were autoimmune diagnoses with the highest percentages of females, and the relationships were significant. Conversely, ITP (Female = 5.0%; Male = 9.0%), χ^2 (1) = 313.99, $p <$ .001, Cramer's V = .07; Crohn's disease (Female = 1.9%; Male = 5.5%), χ^2 (1) = 514.10, $p <$ .001, Cramer's V = .09; Ig A nephropathy (Females = 1.2%; Males = 5.0%), χ^2 (1) = 803.09, $p <$ .001, Cramer's V = .11;Autoimmune hepatitis (Females = .3%; Males = .8%), χ^2 (1) = 71.85, $p <$ .001, Cramer's V = .033; MS (Females = 12.5%; Males = 14.8%), χ^2 (1) = 49.03, $p <$ .001, Cramer's V = .03; MG (Females = 2.2%; Males = 5.1%), χ^2 (1) = 322.44, $p <$ .001, Cramer's V = .07; Ulcerative colitis (Females = .1%; Males = .3%), χ^2 (1) = 37.62, $p <$ .001, Cramer's V = .02; Celiac disease (Females = .7%; Males = 1.2%),

χ^2 (1) = 36.53, $p < .001$, Cramer's $V = .02$; and polymyositis (Females = 1.2%; Males = 2.0%), χ^2 (1) = 42.95, $p < .001$, Cramer's $V = .03$, autoimmune diagnoses had the highest percentages of males, and the relationships were significant. The highest percentages of males (36.8%) and females (36.8%) had RA. In summary, sixteen of the twenty-one autoimmune diagnoses had significant relationships by gender.

Table 12

Frequencies and Percentages for Autoimmune Diagnoses by Gender

	Female		Male			
	n	%	n	%	χ^2	*p*
Autoimmune Hepatitis					71.85	<.001
No	51765	99.7	13508	99.2		
Yes	152	.3	110	.8		
Graves' Disease					.57	.450
No	50265	96.8	13202	96.9		
Yes	1652	3.2	416	3.1		
Hashimotos Thyroiditis					65.13	<.001
No	51109	98.4	13529	99.3		
Yes	808	1.6	89	.7		
Autoimmune Disease –Nonspecific					3.37	.066
No	51608	99.4	13518	99.3		
Yes	309	.6	100	.7		
Primary Thrombocytopenia					313.99	<.001
No	49339	95.0	12399	91.0		
Yes	2578	5.0	1219	9.0		
Multiple Sclerosis					49.03	<.001
No	45405	87.5	11601	85.2		
Yes	6512	12.5	2017	14.8		

(Table 12, continued)

Table 12, continued

Frequencies and Percentages for Autoimmune Diagnoses by Gender

	Female		Male			
	n	%	n	%	χ^2	*p*
Myasthenia Gravis					322.44	<.001
No	50771	97.8	12929	94.9		
Yes	1146	2.2	689	5.1		
Raynaud's Disease					86.30	<.001
No	50335	97.0	13402	98.4		
Yes	1582	3.0	216	1.6		
Crohn's Disease					514.10	<.001
No	50911	98.1	12875	94.5		
Yes	1006	1.9	743	5.5		
Ulcerative Colitis					37.62	<.001
No	51883	99.9	13583	99.7		
Yes	34	.1	35	.3		
Primary Biliary Cirrhosis					23.71	<.001
No	51160	98.5	13493	99.1		
Yes	757	1.5	125	.9		
Celiac Disease					36.53	<.001
No	51543	99.3	13448	98.8		
Yes	374	.7	170	1.2		
Ig A Nephropathy					803.09	<.001
No	51288	98.8	12932	95.0		
Yes	629	1.2	686	5.0		
Discoid Lupus Erythematosus					10.26	.001
No	51428	99.1	13529	99.3		
Yes	489	.9	89	.7		
Systemic Lupus Erythematosus					1475.57	<.001
No	38500	74.2	12206	89.6		
Yes	13417	25.8	1412	10.4		

(Table 12, continued)

Table 12, continued

Frequencies and Percentages for Autoimmune Diagnoses by Gender

	Female		Male			
	n	%	n	%	χ^2	*p*
Systemic Sclerosis					136.75	<.001
No	49832	96.0	13356	98.1		
Yes	2085	4.0	262	1.9		
Sicca Syndrome					219.48	<.001
No	50444	97.2	13528	99.3		
Yes	1473	2.8	90	.7		
Dermatomyositis					1.05	.306
No	51509	99.2	13499	99.1		
Yes	408	.8	119	.9		
Polymyositis					42.95	<.001
No	51272	98.8	13348	98.0		
Yes	645	1.2	270	2.0		
Rheumatoid Arthritis					.01	.912
No	32813	63.2	8600	63.2		
Yes	19104	36.8	5018	36.8		
Juvenile Rheumatoid Arthritis					.00	.977
No	51556	99.3	13523	99.3		
Yes	361	.7	95	.7		

Frequencies and percentages for autoimmune diseases by ethnicity illustrated differences in prevalence (Table 13). Caucasians had the highest percentages of RA (40.8%), SLE (16.1%), MS (15.0%), and ITP (5.5%). In comparison, African-Americans had the highest prevalence of SLE (40.5%), RA (25.5%), MS (10.5%), and ITP (5.1%). Other ethnic groups demonstrated further differences, RA (33.3%), SLE (29.5%), ITP (8.5%), and MS (6.6%). All autoimmune diagnoses had significant relationships by

ethnicity. The discussion of Table 13 will be divided by ethnic group, and will rank the autoimmune diseases beginning with the highest prevalence. The significant chi square results will be integrated within the discussion of prevalence among African-Americans, and among autoimmune diagnoses by ethnicity in differences > 5%.

Table 13

Frequencies and Percentages for Autoimmune Diagnoses by Ethnicity

	Caucasian		African-American		Other			
	n	%	n	%	n	%	χ^2	*p*
Autoimmune Hepatitis							13.34	.001
No	43930	99.6	12918	99.6	8395	99.4		
Yes	156	.4	53	.4	53	.6		
Graves' Disease							72.63	<.001
No	42873	97.2	12457	96.0	8107	96.0		
Yes	1213	2.8	514	4.0	341	4.0		
Hashimotos Thyroiditis							90.62	<.001
No	43364	98.4	12901	99.5	8343	98.8		
Yes	722	1.6	70	.5	105	1.2		
Autoimmune Disease-Nonspecific							7.56	.023
No	43794	99.3	12912	99.5	8390	99.3		
Yes	292	.7	59	.5	58	.7		
Primary Thrombocytopenia							135.49	<.001
No	41678	94.5	12305	94.9	7727	91.5		
Yes	2408	5.5	666	5.1	721	8.5		
Multiple Sclerosis							524.53	<.001
No	37485	85.0	11608	89.5	7887	93.4		
Yes	6601	15.0	1363	10.5	561	6.6		

(Table 13, continued)

Table 13, continued

Frequencies and Percentages for Autoimmune Diagnoses by Ethnicity

	Caucasian		African-American		Other			
	n	%	n	%	n	%	χ^2	*p*
Myasthenia Gravis							59.54	<.001
No	42711	96.9	12729	98.1	8230	97.4		
Yes	1375	3.1	242	1.9	218	2.6		
Raynaud's Disease							73.23	<.001
No	42714	96.9	12736	98.2	8260	97.8		
Yes	1372	3.1	235	1.8	188	2.2		
Crohn's Disease							172.39	<.001
No	42656	96.8	12769	98.4	8332	98.6		
Yes	1430	3.2	202	1.6	116	1.4		
Ulcerative Colitis							12.52	.002
No	44026	99.9	12967	100.0	8443	99.9		
Yes	60	.1	4	.0	5	.1		
Primary Biliary Cirrhosis							88.01	<.001
No	43476	98.6	12883	99.3	8264	97.8		
Yes	610	1.4	88	.7	184	2.2		
Celiac Disease							110.75	<.001
No	43608	98.9	12946	99.8	8407	99.5		
Yes	478	1.1	25	.2	41	.5		
Ig A Nephropathy							402.19	<.001
No	43530	98.7	12466	96.1	8194	97.0		
Yes	556	1.3	505	3.9	254	3.0		
Discoid Lupus Erythematosus							105.94	<.001
No	43788	99.3	12759	98.4	8380	99.2		
Yes	298	.7	212	1.6	68	.8		

(Table 13, continued)

Table 13, continued

Frequencies and Percentages for Autoimmune Diagnoses by Ethnicity

	Caucasian		African-American		Other			
	n	%	n	%	n	%	χ^2	*p*
Systemic Lupus Erythematosus							3690.79	<.001
No	37010	83.9	7714	59.5	5956	70.5		
Yes	7076	16.1	5257	40.5	2492	29.5		
Systemic Sclerosis							19.96	<.001
No	42606	96.6	12454	96.0	8099	95.9		
Yes	1480	3.4	517	4.0	349	4.1		
Sicca Syndrome							140.49	<.001
No	42844	97.2	12839	99.0	8260	97.8		
Yes	1242	2.8	132	1.0	188	2.2		
Dermatomyositis							34.75	<.001
No	43793	99.3	12821	98.8	8364	99.0		
Yes	293	.7	150	1.2	84	1.0		
Polymyositis							74.51	<.001
No	43558	98.8	12687	97.8	8347	98.8		
Yes	528	1.2	284	2.2	101	1.2		
Rheumatoid Arthritis							1059.24	<.001
No	26100	59.2	9664	74.5	5632	66.7		
Yes	17986	40.8	3307	25.5	2816	33.3		
Juvenile Rheumatoid Arthritis							11.38	.003
No	43777	99.3	12902	99.5	8370	99.1		
Yes	309	.7	69	.5	78	.9		

A substantial portion of patients with SLE (40.5%) were African-Americans, χ^2 (2) = 3690.79, $p < .001$, Cramer's $V = .24$, and the percentage was the highest by ethnicity with differences >5%. In patients with diagnoses of RA (25.5%), χ^2 (2) = 1059.24, $p < .001$, Cramer's $V = .13$, and MS (10.5%), χ^2 (2) = 524.53, $p < .001$, Cramer's $V = .09$, African-Americans were the second highest grouping following Caucasians, and the differences varied by > 5%. African-Americans had the lowest prevalence within patients with ITP (5.1%), χ^2 (2) = 135.49, $p < .001$, Cramer's $V = .04$. The remaining prevalence of autoimmune diagnoses among African-Americans was < 5%, and the difference among ethnic groups was not notable. African-Americans with Graves' disease (4.0%), χ^2 (2) = 72.63, $p < .001$, Cramer's $V = .03$, Ig A nephropathy (3.9%), χ^2 (2) = 402.19, $p < .001$, Cramer's $V = .08$, and SS (4.0%), χ^2 (2) = 19.96, $p <$ .001, Cramer's $V = .02$, had similar prevalence by percentage.

African-Americans with Polymyositis (2.2%), χ^2 (2) = 74.51, $p < .001$, Cramer's $V = .03$, MG (1.9%), χ^2 (2) = 59.54, $p < .001$, Cramer's $V = .03$, Raynaud's disease (1.8%), χ^2 (2) = 73.23, $p < .001$, Cramer's $V = .03$,Crohn's disease (1.6%), χ^2 (2) = 172.39, $p < .001$, Cramer's $V = .05$, and Discoid lupus erythematosus (1.6%), $\chi 2$ (2) = 105.94, $p < .001$, Cramer's $V = .04$, had prevalence percentages that were between 1.5% and 2.5%. Lastly, Dermatomyositis (1.2%), χ^2 (2) = 34.75, $p < .001$, Cramer's $V =$ .02,Sicca syndrome (1.0%), χ^2 (2) = 140.49, $p < .001$, Cramer's $V = .05$, Primary Biliary Cirrhosis (.7%), χ^2 (2) = 88.01, $p < .001$, Cramer's $V = .04$, Hashimotos thyroiditis (.5%), χ^2 (2) = 90.62, $p < .001$, Cramer's $V = .04$, Autoimmune disease, nonspecific (.5%), χ^2 (2) = 7.56, $p = .023$, Cramer's $V = .01$, Juvenile RA (.5%), $\chi 2$ (2) = 11.38, $p = .003$, Cramer's

$V = .01$, Autoimmune hepatitis (.4%), χ^2 (2) = 13.34, $p < .001$, Cramer's $V = .01$, and Celiac disease (.2%) χ^2 (2) = 110.75, $p < .001$, Cramer's $V = .04$, were the lowest prevalence percentages among African-Americans.

The highest prevalence percentages of autoimmune diagnoses among Caucasians differed from African-Americans. RA (40.8%) was the highest compared to SLE (16.1%) and MS (15.0%). Among Caucasians, ITP (5.5%), SS (3.4%), Crohn's disease (3.2%), Raynaud's disease (3.1%), MG (3.1%), Sicca syndrome (2.8%), and Graves' disease (2.8%) were similar in prevalence. Caucasians with Hashimotos thyroiditis (1.6%), Primary biliary cirrhosis (1.4%), Ig A nephropathy (1.3%), Polymyositis (1.2%), and Celiac disease (1.1%) were clustered similarly. Lastly, Caucasians with nonspecific autoimmune disease (.7%), Discoid lupus erythematosus (.7%), Dermatomyositis (.7%), Juvenile RA (.7%), autoimmune hepatitis (.4%), and Ulcerative colitis (.1%) were < 1% in prevalence.

All other ethnic groups were included in the third category of Table 13. The highest ranked prevalence percentages again differed from either African-Americans or Caucasians. Approximately a third of patients in other ethnic groups had RA (33.3%) or SLE (29.5%). In this grouping, ITP (8.5%) and MS (6.6%) were third and fourth ranked prevalence percentages. Patients in other ethnic groups with SS (4.1%), Graves' disease (4.0%), Ig A Nephropathy (3.0%) had similar percentages. Patients in this ethnicity category with MG (2.6%), Raynaud's disease (2.2%), Primary biliary cirrhosis (2.2%), and Sicca syndrome (2.2%) were clustered. Finally, the smallest prevalence percentages of patients with autoimmune diagnoses from other ethnic groups were Crohn's disease

(1.4%), Hashimotos thyroiditis (1.2%), Polymyositis (1.2%), Dermatomyositis (1.0%), Juvenile RA (.9%), nonspecific autoimmune diseases (.7%), Discoid lupus erythematosus (.8%), autoimmune hepatitis (.6%), Celiac disease (.5%), and Ulcerative colitis (.1%).

Autoimmune diagnoses by insurance type are presented in Table 14. A comparison of twenty of the twenty-one autoimmune diseases by insurance type resulted in significant relationships. A higher proportion of patients with Graves' disease used self-pay (7.9%) for the hospitalization compared to Medicare patients (1.6%), $\chi 2$ (4) = 599.04, $p < .001$, Cramer's $V = .01$. A significant relationship was evident between patients with MS and insurance type, $\chi 2$ (4) = 207.88, $p < .001$, Cramer's $V = .06$. Proportionally more MS patients claimed PPO/POS (14.8%), HMO (15.1%), and Medicaid (14.6%) compared to self-pay (9.4%). Patients with SLE demonstrated a significant relationship by insurance type, $\chi 2$ (4) = 823.33, $p < .001$, Cramer's $V = .11$. Self-pay (31.8%) and Medicaid (35.6%) patients were more prevalent than PPO/POS (23.8%), HMO (20.4%), and Medicare (19.2%) patients when hospitalized with SLE. Patients hospitalized for RA were significantly related by insurance type, $\chi 2$ (4) = 2811.03, $p < .001$, Cramer's $V = .21$. RA patients with Medicare (47.5%) were significantly higher than RA patients with all other insurance types, Medicaid (19.7%), self-pay (21.0%), PPO/POS (29.3%), and HMO (34.4%). RA HMO patients were proportionally higher than Medicaid, self-pay, and PPO/POS patients, and less than RA Medicare patients. RA PPO/POS patients were higher than self-pay and Medicaid and less than RA HMO and Medicare patients.

Table 14

Frequencies and Percentages for Autoimmune Diagnoses by Insurance Type

	Self-Pay		PPO/POS		HMO		Medicare		Medicaid			
	n	%	n	%	n	%	n	%	n	%	χ^2	*p*
Autoimmune Hepatitis											121.42	<.001
No	4021	98.7	18114	99.5	9667	99.7	28019	99.8	4081	99.4		
Yes	51	1.3	99	.5	32	.3	51	.2	23	.6		
Graves' Disease											599.04	<.001
No	3751	92.1	17460	95.9	9365	96.6	27628	98.4	3942	96.1		
Yes	321	7.9	753	4.1	334	3.4	442	1.6	162	3.9		
Hashimotos Thyroiditis											395.39	<.001
No	4021	98.7	17748	97.4	9500	97.9	27928	99.5	4080	99.4		
Yes	51	1.3	465	2.6	199	2.1	142	.5	24	.6		
Autoimmune Disease-Nonspecific											30.48	<.001
No	4043	99.3	18053	99.1	9640	99.4	27937	99.5	4083	99.5		
Yes	29	.7	160	.9	59	.6	133	.5	21	.5		
Primary Thrombocytopenia											123.91	<.001
No	3712	91.2	17132	94.1	9138	94.2	26659	95.0	3793	92.4		
Yes	360	8.8	1081	5.9	561	5.8	1411	5.0	311	7.6		

(Table 14, continued)

Table 14, continued

Frequencies and Percentages for Autoimmune Diagnoses by Insurance Type

	Self-Pay		PPO/POS		HMO		Medicare		Medicaid			
	n	%	n	%	n	%	n	%	n	%	χ^2	*p*
Multiple Sclerosis											207.88	<.001
No	3691	90.6	15520	85.2	8232	84.9	24859	88.6	3503	85.4		
Yes	381	9.4	2693	14.8	1467	15.1	3211	11.4	601	14.6		
Myasthenia Gravis											82.83	<.001
No	3977	97.7	17834	97.9	9417	97.1	27108	96.6	4012	97.8		
Yes	95	2.3	379	2.1	282	2.9	962	3.4	92	2.2		
Raynaud's Disease											74.57	<.001
No	3961	97.3	17591	96.6	9383	96.7	27444	97.8	4018	97.9		
Yes	111	2.7	622	3.4	316	3.3	626	2.2	86	2.1		
Crohn's Disease											754.49	<.001
No	3907	95.9	17352	95.3	9330	96.2	27843	99.2	4016	97.9		
Yes	165	4.1	861	4.7	369	3.8	227	.8	88	2.1		
Ulcerative Colitis											21.15	<.001
No	4066	99.9	18182	99.8	9684	99.8	28056	100.0	4103	100.0		
Yes	6	.1	31	.2	15	.2	14	.0	1	.0		
Primary Biliary Cirrhosis											8.25	0.083
No	4026	98.9	17958	98.6	9579	98.8	27704	98.7	4032	98.2		
Yes	46	1.1	255	1.4	120	1.2	366	1.3	72	1.8		

(Table 14, continued)

Table 14, continued

Frequencies and Percentages for Autoimmune Diagnoses by Insurance Type

	Self-Pay		PPO/POS		HMO		Medicare		Medicaid			
	n	%	n	%	n	%	n	%	n	%	χ^2	*p*
Celiac Disease											20.94	<.001
No	4044	99.3	18017	98.9	9613	99.1	27863	99.3	4081	99.4		
Yes	28	.7	196	1.1	86	.9	207	.7	23	.6		
Ig A Nephropathy											161.12	<.001
No	3940	96.8	17892	98.2	9532	98.3	27578	98.2	3927	95.7		
Yes	132	3.2	321	1.8	167	1.7	492	1.8	177	4.3		
Discoid Lupus Erythematosus											69.38	<.001
No	4013	98.6	18045	99.1	9621	99.2	27890	99.4	4033	98.3		
Yes	59	1.4	168	.9	78	.8	180	.6	71	1.7		
Systemic Lupus Erythematosus											823.33	<.001
No	2779	68.2	13872	76.2	7723	79.6	22691	80.8	2645	64.4		
Yes	1293	31.8	4341	23.8	1976	20.4	5379	19.2	1459	35.6		
Systemic Sclerosis											13.52	0.009
No	3924	96.4	17626	96.8	9358	96.5	27001	96.2	3938	96.0		
Yes	148	3.6	587	3.2	341	3.5	1069	3.8	166	4.0		

(Table 14, continued)

Table 14, continued

Frequencies and Percentages for Autoimmune Diagnoses by Insurance Type

	Self-Pay		PPO/POS		HMO		Medicare		Medicaid			
	n	%	n	%	n	%	n	%	n	%	χ^2	*p*
Sicca Syndrome											90.62	<.001
No	4017	98.6	17686	97.1	9484	97.8	27357	97.5	4074	99.3		
Yes	55	1.4	527	2.9	215	2.2	713	2.5	30	.7		
Dermatomyositis											32.11	<.001
No	4029	98.9	18080	99.3	9609	99.1	27886	99.3	4047	98.6		
Yes	43	1.1	133	.7	90	.9	184	.7	57	1.4		
Polymyositis											14.87	0.005
No	4005	98.4	17950	98.6	9568	98.6	27725	98.8	4027	98.1		
Yes	67	1.6	263	1.4	131	1.4	345	1.2	77	1.9		
Rheumatoid Arthritis											2811.03	<.001
No	3216	79.0	12882	70.7	6362	65.6	14725	52.5	3297	80.3		
Yes	856	21.0	5331	29.3	3337	34.4	13345	47.5	807	19.7		
Juvenile Rheumatoid Arthritis											106.72	<.001
No	4045	99.3	18034	99.0	9597	98.9	27979	99.7	4058	98.9		
Yes	27	.7	179	1.0	102	1.1	91	.3	46	1.1		

Table 15 identifies the frequencies and percentages for autoimmune diagnoses by length of stay. For lengths of stay of one to two days, patients with RA (35.0%), SLE (23.0%), and MS (12.7) were the highest diagnoses represented. At three to five days, patients with RA (39.7%), SLE (21.5%), and MS (13.3%) documented the highest proportional percentages. Similarly, for the six to nine days stays, the highest percentages were documented for patients with RA (38.2%), SLE (22.1%), and MS (12.3%). For the longest stays, ten or more days, again, RA (31.1%), SLE (25.2%), and MS (13.8%) were the proportional percentages calculated.

Sixteen of the twenty-one autoimmune diseases had significant chi square results, but the differences in percentage by length of stay were < 3%. Two of the autoimmune diagnoses had a significant relationship by length of stay with important differences by days in the hospital. Hashimotos thyroiditis, χ^2 (3) = 914.96, $p < .001$, Cramer's $V = .12$, and RA, $\chi 2$ (3) = 264.16, $p < .001$, Cramer's $V = .06$, had significant cross tabulated chi square results, and >3% distribution by length of stay. A proportionally higher percentage of patients with Hashimotos thyroiditis stayed one to two days in the hospital (3.6%) when compared to ten or more days (.3%), and six to nine days (.6%). A greater proportion of RA patients were hospitalized for three to five days (39.7%) and six to nine days (38.2%) in contrast to one to two days (35.0%) and the longest stay of ten or more days (31.1%).

Table 15

Frequencies and Percentages for Autoimmune Diagnoses by Length of Stay

	1-2 Days		3-5 Days		6-9 Days		10 or More Days			
	n	%	n	%	n	%	n	%	χ^2	*p*
Autoimmune Hepatitis									18.50	<.001
No	17148	99.4	24375	99.6	13470	99.7	10280	99.6		
Yes	96	.6	94	.4	34	.3	38	.4		
Graves' Disease									142.27	<.001
No	16478	95.6	23735	97.0	13172	97.5	10082	97.7		
Yes	766	4.4	734	3.0	332	2.5	236	2.3		
Hashimotos Thyroiditis									914.96	<.001
No	16615	96.4	24287	99.3	13444	99.6	10292	99.7		
Yes	629	3.6	182	.7	60	.4	26	.3		
Autoimmune Disease-Nonspecific									18.56	<.001
No	17147	99.4	24331	99.4	13426	99.4	10222	99.1		
Yes	97	.6	138	.6	78	.6	96	.9		
Primary Thrombocytopenia									28.36	<.001
No	16288	94.5	23110	94.4	12735	94.3	9605	93.1		
Yes	956	5.5	1359	5.6	769	5.7	713	6.9		

(Table 15, continued)

Table 15, continued

Frequencies and Percentages for Autoimmune Diagnoses by Length of Stay

	1-2 Days		3-5 Days		6-9 Days		10 or More Days			
	n	%	n	%	n	%	n	%	χ^2	*p*
Multiple Sclerosis									15.04	.002
No	15057	87.3	21215	86.7	11841	87.7	8893	86.2		
Yes	2187	12.7	3254	13.3	1663	12.3	1425	13.8		
Myasthenia Gravis									135.99	<.001
No	16896	98.0	23865	97.5	13053	96.7	9886	95.8		
Yes	348	2.0	604	2.5	451	3.3	432	4.2		
Raynaud's Disease									44.30	<.001
No	16668	96.7	23819	97.3	13140	97.3	10110	98.0		
Yes	576	3.3	650	2.7	364	2.7	208	2.0		
Crohn's Disease									65.93	<.001
No	16899	98.0	23829	97.4	13033	96.5	10025	97.2		
Yes	345	2.0	640	2.6	471	3.5	293	2.8		
Ulcerative Colitis									6.40	.094
No	17232	99.9	24446	99.9	13487	99.9	10301	99.8		
Yes	12	.1	23	.1	17	.1	17	.2		
Primary Biliary Cirrhosis									24.47	<.001
No	17065	99.0	24143	98.7	13303	98.5	10142	98.3		
Yes	179	1.0	326	1.3	201	1.5	176	1.7		

(Table 15, continued)

Table 15, continued

Frequencies and Percentages for Autoimmune Diagnoses by Length of Stay

	1-2 Days		3-5 Days		6-9 Days		10 or More Days			
	n	%	n	%	n	%	n	%	χ^2	*p*
Celiac Disease									3.01	.391
No	17087	99.1	24269	99.2	13391	99.2	10244	99.3		
Yes	157	.9	200	.8	113	.8	74	.7		
Ig A Nephropathy									12.97	.005
No	16934	98.2	23973	98.0	13187	97.7	10126	98.1		
Yes	310	1.8	496	2.0	317	2.3	192	1.9		
Discoid Lupus Erythematosus									19.34	<.001
No	17071	99.0	24231	99.0	13393	99.2	10262	99.5		
Yes	173	1.0	238	1.0	111	.8	56	.5		
Systemic Lupus Erythematosus									63.42	<.001
No	13273	77.0	19210	78.5	10515	77.9	7708	74.7		
Yes	3971	23.0	5259	21.5	2989	22.1	2610	25.3		
Systemic Sclerosis									80.64	<.001
No	16716	96.9	23654	96.7	13019	96.4	9799	95.0		
Yes	528	3.1	815	3.3	485	3.6	519	5.0		

(Table 15, continued)

Table 15, continued

Frequencies and Percentages for Autoimmune Diagnoses by Length of Stay

	1-2 Days		3-5 Days		6-9 Days		10 or More Days			
	n	%	n	%	n	%	n	%	χ^2	*p*
Sicca Syndrome									42.39	<.001
No	16769	97.2	23866	97.5	13178	97.6	10159	98.5		
Yes	475	2.8	603	2.5	326	2.4	159	1.5		
Dermatomyositis									63.53	<.001
No	17139	99.4	24316	99.4	13377	99.1	10176	98.6		
Yes	105	.6	153	.6	127	.9	142	1.4		
Polymyositis									79.38	<.001
No	17069	99.0	24180	98.8	13277	98.3	10094	97.8		
Yes	175	1.0	289	1.2	227	1.7	224	2.2		
Rheumatoid Arthritis									264.16	<.001
No	11203	65.0	14758	60.3	8347	61.8	7105	68.9		
Yes	6041	35.0	9711	39.7	5157	38.2	3213	31.1		
Juvenile Rheumatoid Arthritis									5.27	.153
No	17141	99.4	24302	99.3	13402	99.2	10234	99.2		
Yes	103	.6	167	.7	102	.8	84	.8		

Autoimmune diseases are compared to total charges in Table 16. Nineteen of the diagnoses were related significantly to total hospital charges. Patients with RA were related significantly to hospital charges, χ^2 (3) = 94.15, $p < .001$, Cramer's $V = .04$, and accounted for the highest percentages per cost category. More RA patients spent $16,000 to $23,999 (39.8%) compared to patients who were charged $7,999 or less (34.4%), $8,000 to $15,999 (37.8%), and $24,000 or more (36.0%). MS patients were related significantly to total hospital charges, χ^2 (3) = 142.98, $p < .001$, Cramer's $V = .05$. The highest percentage of MS patients paid $7,999 or less (15.4%) in contrast with charges of $24,000 or more (11.1%). The remaining significant relationships of autoimmune diseases by total charges reported variations in percentages < 3%.

The frequencies and percentages of SA possibly related infections (Enterocolitis, Bacteremia, Endocarditis, Surgical site infections, Osteomyelitis, Septic arthritis, and SIRS) are calculated by gender in Table 17. Only one infection was related significantly by gender. Patients with Osteomyelitis were related significantly by gender, χ^2 (1) = 12.82, $p < .001$, Cramer's $V = .01$, but the proportions were similar (<3%). Table 18 identified SA possibly related infections by ethnicity. Bacteremia, χ^2 (2) = 204.15, $p < .001$, Cramer's $V = .06$, Endocarditis, χ^2 (2) = 39.51, $p < .001$, Cramer's $V = .02$, and SIRs, χ^2 (2) = 24.05, $p < .001$, Cramer's $V = .02$, were related significantly to SA potentially related infections. All three associations presented proportional percentages that were closely distributed among ethnic groupings.

Table 16

Frequencies and Percentages for Autoimmune Diagnoses by Total Charges

	$7999 or less		$8000 – $15999		$16000 – $23999		$24000 or more			
	n	%	n	%	n	%	n	%	χ^2	*p*
Autoimmune Hepatitis									16.32	.001
No	15229	99.4	19948	99.6	11005	99.6	19091	99.7		
Yes	85	.6	76	.4	47	.4	54	.3		
Graves' Disease									107.75	<.001
No	14667	95.8	19348	96.6	10789	97.6	18663	97.5		
Yes	647	4.2	676	3.4	263	2.4	482	2.5		
Hashimotos Thyroiditis									232.33	<.001
No	15028	98.1	19608	97.9	10946	99.0	19056	99.5		
Yes	286	1.9	416	2.1	106	1.0	89	.5		
Autoimmune Disease-Nonspecific									20.22	<.001
No	15243	99.5	19912	99.4	10984	99.4	18987	99.2		
Yes	71	.5	112	.6	68	.6	158	.8		
Primary Thrombocytopenia									147.71	<.001
No	14431	94.2	19092	95.3	10487	94.9	17728	92.6		
Yes	883	5.8	932	4.7	565	5.1	1417	7.4		

(Table 16, continued)

Table 16, continued

Frequencies and Percentages for Autoimmune Diagnoses by Total Charges

	$7999 or less		$8000 – $15999		$16000 – $23999		$24000 or more			
	n	%	n	%	n	%	n	%	χ^2	*p*
Multiple Sclerosis									142.98	<.001
No	12956	84.6	17356	86.7	9676	87.5	17018	88.9		
Yes	2358	15.4	2668	13.3	1376	12.5	2127	11.1		
Myasthenia Gravis									107.34	<.001
No	14933	97.5	19562	97.7	10794	97.7	18411	96.2		
Yes	381	2.5	462	2.3	258	2.3	734	3.8		
Raynaud's Disease									15.63	.001
No	14884	97.2	19462	97.2	10705	96.9	18686	97.6		
Yes	430	2.8	562	2.8	347	3.1	459	2.4		
Crohn's Disease									32.56	<.001
No	14999	97.9	19453	97.1	10710	96.9	18624	97.3		
Yes	315	2.1	571	2.9	342	3.1	521	2.7		
Ulcerative Colitis									8.87	.031
No	15303	99.9	20010	99.9	11037	99.9	19116	99.8		
Yes	11	.1	14	.1	15	.1	29	.2		

(Table 16, continued)

Table 16, continued

Frequencies and Percentages for Autoimmune Diagnoses by Total Charges

	$7999 or less		$8000 – $15999		$16000 – $23999		$24000 or more			
	n	%	n	%	n	%	n	%	χ^2	*p*
Primary Biliary Cirrhosis									22.25	<.001
No	15150	98.9	19753	98.6	10918	98.8	18832	98.4		
Yes	164	1.1	271	1.4	134	1.2	313	1.6		
Celiac Disease									2.23	.525
No	15183	99.1	19845	99.1	10967	99.2	18996	99.2		
Yes	131	.9	179	.9	85	.8	149	.8		
Ig A Nephropathy									7.71	.052
No	15046	98.2	19617	98.0	10809	97.8	18748	97.9		
Yes	268	1.8	407	2.0	243	2.2	397	2.1		
Discoid Lupus Erythematosus									15.74	.001
No	15162	99.0	19821	99.0	10958	99.1	19016	99.3		
Yes	152	1.0	203	1.0	94	.9	129	.7		
Systemic Lupus Erythematosus									14.93	.002
No	11890	77.6	15605	77.9	8583	77.7	14628	76.4		
Yes	3424	22.4	4419	22.1	2469	22.3	4517	23.6		

(Table 16, continued)

Table 16, continued

Frequencies and Percentages for Autoimmune Diagnoses by Total Charges

	$7999 or less		$8000 – $15999		$16000 – $23999		$24000 or more			
	n	%	n	%	n	%	n	%	χ^2	*p*
Systemic Sclerosis									22.69	<.001
No	14818	96.8	19326	96.5	10684	96.7	18360	95.9		
Yes	496	3.2	698	3.5	368	3.3	785	4.1		
Sicca Syndrome									10.59	.014
No	14929	97.5	19508	97.4	10794	97.7	18741	97.9		
Yes	385	2.5	516	2.6	258	2.3	404	2.1		
Dermatomyositis									40.38	<.001
No	15212	99.3	19893	99.3	10978	99.3	18925	98.9		
Yes	102	.7	131	.7	74	.7	220	1.1		
Polymyositis									39.69	<.001
No	15138	98.9	19782	98.8	10907	98.7	18793	98.2		
Yes	176	1.1	242	1.2	145	1.3	352	1.8		
Rheumatoid Arthritis									94.15	<.001
No	10050	65.6	12454	62.2	6658	60.2	12251	64.0		
Yes	5264	34.4	7570	37.8	4394	39.8	6894	36.0		
Juvenile Rheumatoid Arthritis									18.79	<.001
No	15214	99.3	19918	99.5	10972	99.3	18975	99.1		
Yes	100	.7	106	.5	80	.7	170	.9		

Table 17

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by Gender

	Female		Male			
	n	%	n	%	χ^2	*p*
Enterocolitis					.01	.915
No	51910	100.0	13616	100.0		
Yes	7	.0	2	.0		
Bacteremia					.01	.942
No	51022	98.3	13382	98.3		
Yes	895	1.7	236	1.7		
Endocarditis					3.43	.064
No	51840	99.9	13588	99.8		
Yes	77	.1	30	.2		
Surgical Site Infection					.88	.347
No	51847	99.9	13595	99.8		
Yes	70	.1	23	.2		
Osteomyelitis					12.82	<.001
No	51785	99.7	13558	99.6		
Yes	132	.3	60	.4		
Septic Arthritis					3.29	.069
No	51621	99.4	13522	99.3		
Yes	296	.6	96	.7		
SIRS					.43	.512
No	51596	99.4	13527	99.3		
Yes	321	.6	91	.7		

Table 18

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by Ethnicity

	Caucasian		African-American		Other			
	n	%	n	%	n	%	χ^2	*p*
Enterocolitis							3.64	.162
No	44082	100.0	12969	100.0	8445	100.0		
Yes	4	.0	2	.0	3	.0		
Bacteremia							204.15	<.001
No	43537	98.8	12576	97.0	8263	97.8		
Yes	549	1.2	395	3.0	185	2.2		
Endocarditis							39.51	<.001
No	44034	99.9	12924	99.6	8440	99.9		
Yes	52	.1	47	.4	8	.1		
Surgical Site Infection							2.3	.317
No	44020	99.9	12952	99.9	8441	99.9		
Yes	66	.1	19	.1	7	.1		
Osteomyelitis							0.93	.629
No	43954	99.7	12938	99.7	8421	99.7		
Yes	132	.3	33	.3	27	.3		
Septic Arthritis							0.21	.899
No	43819	99.4	12897	99.4	8397	99.4		
Yes	267	.6	74	.6	51	.6		
SIRS							24.05	<.001
No	43852	99.5	12853	99.1	8388	99.3		
Yes	234	.5	118	.9	60	.7		

SA possibly related infection diagnoses were compared by insurance type in Table 19. There were four possibly related SA infections that related significantly by insurance type. Bacteremia demonstrated a significant relationship with insurance type, χ^2 (4) = 61.24, $p < .001$, Cramer's $V = .03$.The proportional percentages were similarly expressed (<3% difference). Surgical site infection was significantly related by insurance type, χ^2 (4) = 10.75, $p < .001$, Cramer's $V = .01$, but the percentages were closely matched. Similarly, Osteomyelitis was significantly related to insurance type, χ^2 (4) = 14.02, $p = .007$, Cramer's $V = .01$, but the percentages were nearly identical. The fourth significant relationship of related infection and insurance type was SIRS, χ^2 (4) = 44.13, $p < .001$, Cramer's $V = .03$ but all the proportional percentages were < 1.0%.

The frequencies and percentages of patients with possibly related SA infections by length of stay in the hospital are illustrated in Table 20. All diagnoses when compared to length of stay were significant, Enterocolitis, χ^2 (3) = 18.14, $p < .001$, Cramer's $V = .02$; bacteremia, χ^2 (3) = 784.60, $p < .001$, Cramer's $V = .11$; Endocarditis, χ^2 (3) = 105.86, $p < .001$, Cramer's $V = .01$; Surgical site infection, χ^2 (3) = 121.69, $p < .001$, Cramer's $V = .04$; Osteomyelitis, χ^2 (3) = 115.14, $p < .001$, Cramer's $V = .04$; Septic arthritis, χ^2 (3) = 232.27, $p < .001$, Cramer's $V = .06$; and SIRS, χ^2 (3) = 158.33, $p < .001$, Cramer's $V = .05$. The percentages of diagnoses increased with each increased length of stay category. Bacteremia had the highest percentage in the ten or more days group (4.7%) compared with patients diagnosed with bacteremia with one to two day stays (.4%), three to five day stays (1.1%), and six to nine day stays (2.2%). In all remaining infection diagnoses, the proportional percentages were closely distributed.

Table 19

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by Insurance Type

	Self-Pay		PPO/POS		HMO		Medicare		Medicaid			
	n	%	n	%	n	%	n	%	n	%	χ^2	*p*
Enterocolitis											2.44	.655
No	4072	100.0	18211	100.0	9699	100.0	28066	100.0	4104	100.0		
Yes	0	.0	2	.0	0	.0	4	.0	0	.0		
Bacteremia											61.24	<.001
No	4017	98.6	17967	98.6	9577	98.7	27484	97.9	4009	97.7		
Yes	55	1.4	246	1.4	122	1.3	586	2.1	95	2.3		
Endocarditis											7.00	.136
No	4064	99.8	18186	99.9	9689	99.9	28021	99.8	4092	99.7		
Yes	8	.2	27	.1	10	.1	49	.2	12	.3		
Surgical Site Infection											10.75	.013
No	4066	99.9	18190	99.9	9675	99.8	28040	99.9	4099	99.9		
Yes	6	.1	23	.1	24	.2	30	.1	5	.1		
Osteomyelitis											14.02	.007
No	4064	99.8	18171	99.8	9678	99.8	27962	99.6	4094	99.8		
Yes	8	.2	42	.2	21	.2	108	.4	10	.2		
Septic Arthritis											7.92	.095
No	4057	99.6	18113	99.5	9645	99.4	27882	99.3	4084	99.5		
Yes	15	.4	100	.5	54	.6	188	.7	20	.5		
SIRS											44.13	<.001
No	4048	99.4	18107	99.4	9681	99.8	27847	99.2	4077	99.3		
Yes	24	.6	106	.6	18	.2	223	.8	27	.7		

Table 20

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by Length of Stay

	1-2 Days		3-5 Days		6-9 Days		10 or More Days			
	n	%	n	%	n	%	n	%	χ^2	*p*
Enterocolitis									18.14	<.001
No	17244	100.0	24467	100.0	13503	100.0	10312	99.9		
Yes	0	.0	2	.0	1	.0	6	.1		
Bacteremia									784.60	<.001
No	17170	99.6	24198	98.9	13203	97.8	9833	95.3		
Yes	74	.4	271	1.1	301	2.2	485	4.7		
Endocarditis									105.86	<.001
No	17236	100.0	24451	99.9	13476	99.8	10265	99.5		
Yes	8	.0	18	.1	28	.2	53	.5		
Surgical Site Infection									121.69	<.001
No	17240	100.0	24452	99.9	13484	99.9	10266	99.5		
Yes	4	.0	17	.1	20	.1	52	.5		
Osteomyelitis									115.14	<.001
No	17230	99.9	24417	99.8	13458	99.7	10238	99.2		
Yes	14	.1	52	.2	46	.3	80	.8		
Septic Arthritis									232.27	<.001
No	17227	99.9	24364	99.6	13385	99.1	10167	98.5		
Yes	17	.1	105	.4	119	.9	151	1.5		
SIRS									158.33	<.001
No	17190	99.7	24365	99.6	13399	99.2	10169	98.6		
Yes	54	.3	104	.4	105	.8	149	1.4		

The frequencies and percentages presented in Table 21 support the findings in the previous table. All SA possibly related infections compared significantly with total hospital charges. Interestingly, the number of patients and proportional percentage increased with each increased cost category. Although only nine patients total were identified with enterocolitis, seven of the patients paid $24,000 or more for charges, and the relationship was significant, χ^2 (3) = 10.48, p = .015, Cramer's V = .01. Patients with bacteremia had the highest percentage (3.4%) in the $24,000 or more category compared with the lowest group of $7,999 or less (.5%). The relationship with bacteremia and total charges was significant, χ^2 (3) = 487.63, p < .001, Cramer's V = .09. Patients with both Endocarditis, χ^2 (3) = 68.85, p < .001, Cramer's V = .03, and Surgical site infections, χ^2 (3) = 40.54, p < .001, Cramer's V = .02, were each related significantly to cost of hospitalization. Osteomyelitis diagnoses were related significantly to charges, χ^2 (3) = 70.91, p < .001, Cramer's V = .03. Patients with septic arthritis had percentages that increased with total hospital charges, $7, 9999 or less (.1%), $8.000 to $15,999 (.4%), $16,000 to $23,999 (.7%), and $24,000 or more (1.2%), and were related significantly, χ^2 (3) = 171.32 p < .001, Cramer's V = .05. Similarly, SIRS percentages increased with total charges, $7,999 or less (.2%), $8,000 to $15,999 (.3%), $16,000 to $23,999 (.5%), and $24,000 or more, (1.4%) with a significant relationship, χ^2 (3) = 245.21, p < .001, Cramer's V = .06.

Table 21

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by Total Charges

	$7999 or less		$8K – $15999		$16K – $23999		$24K or More			
	n	%	n	%	n	%	n	%	χ^2	*p*
Enterocolitis									10.48	.015
No	15313	100.0	20023	100.0	11052	100.0	19138	100.0		
Yes	1	.0	1	.0	0	.0	7	.0		
Bacteremia									487.63	<.001
No	15232	99.5	19819	99.0	10851	98.2	18502	96.6		
Yes	82	.5	205	1.0	201	1.8	643	3.4		
Endocarditis									68.85	<.001
No	15310	100.0	20002	99.9	11040	99.9	19076	99.6		
Yes	4	.0	22	.1	12	.1	69	.4		
Surgical Site Infection									40.54	<.001
No	15307	100.0	20006	99.9	11038	99.9	19091	99.7		
Yes	7	.0	18	.1	14	.1	54	.3		
Osteomyelitis									70.91	<.001
No	15303	99.9	19975	99.8	11025	99.8	19040	99.5		
Yes	11	.1	49	.2	27	.2	105	.5		
Septic Arthritis									171.32	<.001
No	15292	99.9	19948	99.6	10980	99.3	18923	98.8		
Yes	22	.1	76	.4	72	.7	222	1.2		
SIRS									245.21	<.001
No	15285	99.8	19960	99.7	10994	99.5	18884	98.6		
Yes	29	.2	64	.3	58	.5	261	1.4		

Table 22 presents the frequencies and percentages for SA possibly related infection diagnoses by enterocolitis. One patient hospitalized with enterocolitis reported bacteremia (11.1%) with significant results, χ^2 (1) = 4.67, $p < .031$, Cramer's $V = .01$. There were no additional significant relationships for SA possibly related infection diagnoses by enterocolitis. The frequencies and percentages for SA possibly related infections by bacteremia are presented in Table 23. Patients with bacteremia experienced other co-morbidities of possibly related SA infections, Enterocolitis (.1%), χ^2 (1) = 4.67, $p < .031$, Cramer's $V = .01$; Endocarditis (2.4%), χ^2 (1) = 349.21, $p < .001$, Cramer's $V = .07$; Surgical site infection (.8%), χ^2 (1) = 34.72, $p < .001$, Cramer's $V = .02$; Septic arthritis (2.1%), χ^2 (1) = 44.95, $p < .001$, Cramer's $V = .03$; SIRs (6.8%), χ^2 (1) = 703.46, $p < .001$, Cramer's $V = .10$, and the relationships were statistically significant. There were three significant co-morbidity results of additional SA-related infections in patients with endocarditis (Table 24). In rank order, patients with endocarditis had the highest frequency of bacteremia (25.2%). χ^2 (1) = 349.21, $p < .001$, Cramer's $V = .07$, and the relationship was significant. Secondly, patients with endocarditis had septic arthritis (4.7%), χ^2 (1) = 29.93, $p < .001$, Cramer's $V = .02$ with significant results. And thirdly, patients who were also diagnosed with SIRS (2.8%), χ^2 (1) = 8.12, $p = .004$, Cramer's $V = .01$, and endocarditis were related significantly.

Table 22

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by Enterocolitis

	No		Yes			
	n	%	n	%	χ^2	*p*
Bacteremia					4.67	.031
No	64396	98.3	8	88.9		
Yes	1130	1.7	1	11.1		
Endocarditis					.01	.903
No	65419	99.8	9	100.0		
Yes	107	.2	0	.0		
Surgical Site Infection					.01	.910
No	65433	99.9	9	100.0		
Yes	93	.1	0	.0		
Osteomyelitis					.03	.871
No	65334	99.7	9	100.0		
Yes	192	.3	0	.0		
Septic Arthritis					.05	.816
No	65134	99.4	9	100.0		
Yes	392	.6	0	.0		
SIRS					.06	.811
No	65114	99.4	9	100.0		
Yes	412	.6	0	.0		

Table 23

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by Bacteremia

	No		Yes			
	n	%	n	%	χ^2	*p*
Enterocolitis					4.67	.031
No	64396	100.0	1130	99.9		
Yes	8	.0	1	.1		
Endocarditis					349.21	<.001
No	64324	99.9	1104	97.6		
Yes	80	.1	27	2.4		
Surgical Site Infection					34.72	<.001
No	64320	99.9	1122	99.2		
Yes	84	.1	9	.8		
Osteomyelitis					.15	.703
No	64216	99.7	1127	99.6		
Yes	188	.3	4	.4		
Septic Arthritis					44.95	<.001
No	64036	99.4	1107	97.9		
Yes	368	.6	24	2.1		
SIRS					703.46	<.001
No	64069	99.5	1054	93.2		
Yes	335	.5	77	6.8		

Table 24

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by Endocarditis

	No		Yes			
	n	%	n	%	χ^2	*p*
Enterocolitis					.01	.903
No	65419	100.0	107	100.0		
Yes	9	.0	0	.0		
Bacteremia					349.21	<.001
No	64324	98.3	80	74.8		
Yes	1104	1.7	27	25.2		
Surgical Site Infection					.15	.696
No	65335	99.9	107	100.0		
Yes	93	.1	0	.0		
Osteomyelitis					1.51	.219
No	65237	99.7	106	99.1		
Yes	191	.3	1	.9		
Septic Arthritis					29.93	<.001
No	65041	99.4	102	95.3		
Yes	387	.6	5	4.7		
SIRS					8.12	.004
No	65019	99.4	104	97.2		
Yes	409	.6	3	2.8		

Surgical site infections were compared with possibly related SA infection diagnoses in Table 25. Only two significant relationships were presented. Patients with surgical site infections were identified with bacteremia (9.7%), as the highest frequency percentage of the possibly related infections, χ^2 (1) = 34.72, $p < .001$, Cramer's $V = .02$. Osteomyelitis (4.3%) was the second ranked, and only additional significant relationship with patients with surgical site infection, χ^2 (1) = 51.22, $p < .001$, Cramer's $V = .03$. In both relationships, the sample size was less than ten. Table 26 presents the frequencies and percentages for SA possibly related infection diagnoses by osteomyelitis. There were significant relationships with samples sizes less than 15. In patients with osteomyelitis, the proportional percentage of patients that also were diagnosed with septic arthritis was (6.8%), χ^2 (1) = 123.40, $p < .001$, Cramer's $V = .04$. Again, osteomyelitis diagnoses and surgical site infections (2.1%), χ^2 (1) = 51.22, $p < .001$, Cramer's $V = .03$, were significantly related with a sample size of four.

SA potentially related infection diagnoses were compared to patients with septic arthritis (Table 27). There were three significant relationships in this comparison. Patients with septic arthritis had bacteremia (6.1%) with the highest frequency, χ^2 (1) = 44.95, $p < .001$, Cramer's $V = .03$, and the relationship was significant. Patients with osteomyelitis (3.3%) were associated with septic arthritis, χ^2 (1) = 123.40, $p < .001$, Cramer's $V = .04$. Diagnoses of endocarditis (1.3%) were also related to septic arthritis, χ^2 (1) = 29.93, $p < .001$, Cramer's $V = .02$, but the sample was five. Table 28 presents the frequencies and percentages for SA possibly related infection diagnoses by SIRS. The frequency and percentage of bacteremia (18.7%) with patients with SIRS was notably high, and the

relationship was significant, χ^2 (1) = 703.46, $p < .001$, Cramer's $V = .01$. Patients with SIRS and endocarditis (.7%) were also significantly related, χ^2 (1) = 8.12, $p = .004$, Cramer's $V = .01$, and the sample size was three.

Table 25

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by Surgical Site Infection

	No		Yes			
	n	%	n	%	χ^2	*p*
Enterocolitis					.01	.910
No	65433	100.0	93	100.0		
Yes	9	.0	0	.0		
Bacteremia					34.72	<.001
No	64320	98.3	84	90.3		
Yes	1122	1.7	9	9.7		
Endocarditis					.15	.696
No	65335	99.8	93	100.0		
Yes	107	.2	0	.0		
Osteomyelitis					51.22	<.001
No	65254	99.7	89	95.7		
Yes	188	.3	4	4.3		
Septic Arthritis					.36	.550
No	65051	99.4	92	98.9		
Yes	391	.6	1	1.1		
SIRS					.59	.443
No	65030	99.4	93	100.0		
Yes	412	.6	0	.0		

Table 26

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by Osteomyelitis

	No		Yes			
	n	%	n	%	χ^2	*p*
Enterocolitis					.03	.871
No	65334	100.0	192	100.0		
Yes	9	.0	0	.0		
Bacteremia					.14	.703
No	64216	98.3	188	97.9		
Yes	1127	1.7	4	2.1		
Endocarditis					1.51	.219
No	65237	99.8	191	99.5		
Yes	106	.2	1	.5		
Surgical Site Infection					51.22	<.001
No	65254	99.9	188	97.9		
Yes	89	.1	4	2.1		
Septic Arthritis					123.40	<.001
No	64964	99.4	179	93.2		
Yes	379	.6	13	6.8		
SIRS					.53	.468
No	64933	99.4	190	99.0		
Yes	410	.6	2	1.0		

Table 27

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by Septic Arthritis

	No		Yes			
	n	%	n	%	χ^2	*p*
Enterocolitis					.05	.816
No	65134	100.0	392	100.0		
Yes	9	.0	0	.0		
Bacteremia					44.95	<.001
No	64036	98.3	368	93.9		
Yes	1107	1.7	24	6.1		
Endocarditis					29.93	<.001
No	65041	99.8	387	98.7		
Yes	102	.2	5	1.3		
Surgical Site Infection					.36	.550
No	65051	99.9	391	99.7		
Yes	92	.1	1	.3		
Osteomyelitis					123.40	<.001
No	64964	99.7	379	96.7		
Yes	179	.3	13	3.3		
SIRS					.12	.731
No	64734	99.4	389	99.2		
Yes	409	.6	3	.8		

Table 28

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by SIRS

	No		Yes			
	n	%	n	%	χ^2	*p*
Enterocolitis					.06	.811
No	65114	100.0	412	100.0		
Yes	9	.0	0	.0		
Bacteremia					703.46	<.001
No	64069	98.4	335	81.3		
Yes	1054	1.6	77	18.7		
Endocarditis					8.12	.004
No	65019	99.8	409	99.3		
Yes	104	.2	3	.7		
Surgical Site Infection					.59	.443
No	65030	99.9	412	100.0		
Yes	93	.1	0	.0		
Osteomyelitis					.53	.468
No	64933	99.7	410	99.5		
Yes	190	.3	2	.5		
Septic Arthritis					.12	.731
No	64734	99.4	409	99.3		
Yes	389	.6	3	.7		

Primary Analyses of Research Question One

Tables 29 through 33 will address the primary analysis for the first research question presented in this study. The frequencies and percentages for gender, ethnicity, insurance type, length of stay, and total charges by SA specific infection diagnoses are

presented in Table 29. The relationship of gender to SA specific infection was significant, χ^2 (1) = 27.59, $p < .001$, Cramer's $V = .02$. The percentage of females (79.4%) without a SA specific infection diagnosis was higher than the percentage of females (74.3%) with the SA specific infection. Conversely, the percentage of males (20.6%) without the SA specific diagnosis was lower than the percentage of males (25.7%) with a SA specific infection. The comparison of ethnicity and SA specific infections was similar (< 4.4%) and significant, χ^2 (2) = 22.00, $p < .001$, Cramer's $V = .02$. The highest percentage of Caucasians (67.4%) did not have an SA specific infection when compared to Caucasians (63.0%) with an SA specific infection. A higher percentage of African-Americans (24.0%) had a SA specific infection as a co-morbidity than those that did not (19.7%). Other ethnic groups had similar percentages, SA specific infections (12.9%), and without infection (13.0%).

The relationship of SA specific infections and insurance type was significant, $\chi 2$ (1) = 47.10, $p < .001$, Cramer's $V = .03$. Patients with SA specific infections claimed Medicare (50.4%) more frequently when compared to those that did not have an infection (43.6%). A lower proportion of patients with SA infections used PPO/POS insurance (23.3%) in contrast with those that did not (28.5%). Medicare was the highest percentage claimed followed by PPO/POS, and then HMO (13.3%) insurance. The relationship of SA specific infections and length of stay was interesting and significant, χ^2 (3) = 1008.43, $p < .001$, Cramer's $V = .12$. Higher percentages of patients with SA specific infections had longer length of stays in the hospital. For hospital stays for 10 or more days, 38.5% had an SA specific infection and 15.1% did not. Similarly, 28.7% had a SA specific

infection and 20.4% did not have this diagnosis in the six to nine days category. In contrast, 7.1% had an SA specific diagnosis and 26.9% did not have the infection in the one to two days length of stay category.

Table 29

Frequencies and Percentages for Gender, Ethnicity, Insurance Type, Length of Stay, and Total Charges by SA Specific Infection Diagnosis

	No		Yes			
	n	%	n	%	χ^2	*p*
Gender					27.59	< .001
Male	13149	20.6	469	25.7		
Female	50561	79.4	1356	74.3		
Ethnicity					22.00	<.001
Caucasian	42937	67.4	1149	63.0		
African-American	12533	19.7	438	24.0		
Other	8210	12.9	238	13.0		
Insurance Type					47.10	< .001
Self-Pay	3978	6.4	94	5.3		
PPO/POS	17798	28.5	415	23.3		
HMO	9462	15.2	237	13.3		
Medicare	27173	43.6	897	50.4		
Medicaid	3967	6.4	137	7.7		
Length of Stay					1008.43	<.001
1-2 Days	17114	26.9	130	7.1		
3-5 Days	24000	37.7	469	25.7		
6-9 Days	12981	20.4	523	28.7		
10 or More Days	9615	15.1	703	38.5		
Total Charges					432.88	<.001
$7999 or Less	15123	23.7	191	10.5		
$8000 - $15999	19607	30.8	417	22.8		
$16000 - $23999	10737	16.9	315	17.3		
$24000 or More	18243	28.6	902	49.4		

In line with results for length of stay, hospital charges increased significantly when compared to SA specific infections, χ^2 (3) = 432.88, $p < .001$, Cramer's $V = .08$. Nearly half (49.4%) of patients with SA specific diagnoses had charges of $24,000 or more compared to (28.6%) less than one-third of patients who did not have that diagnosis. In the $7,999 or less category, 10.5% had an SA specific infection compared to 23.7% who did not. Fewer SA infection patients (22.8%) were charged $8,000 to $15,999 than those who did not have the infection (30.8%). Higher frequencies and percentages were evident in higher total hospital charges. The most significant relationship was evident in the $24,000 or more category.

Table 30 presents the means and standard deviations of age at discharge by SA specific infection diagnosis. Independent sample *t* tests identified the age at discharge from the hospital was significantly lower, $t = 4.28$, $p < .001$, in patients with an SA specific diagnosis ($M = 54.34$, $SD = 16.97$) when compared to those patients without the SA diagnosis ($M = 56.07$, $SD = 17.82$). The frequencies and percentages for patients with and without SA possibly related infection diagnoses were compared to those with and without SA specific infection diagnoses in Table 31. The overall percentages of those with SA possibly related infections by SA specific infections was the highest percentage category (31.1%), and was statistically significant, χ^2 (1) = 4540.62, $p < .001$, Cramer's $V = .26$, indicating the commonality of co-morbidities of infections. The proportional percentages of those with septicemia (27.4%) and bacteremia (18.2%) demonstrated that blood originated infections were associated with SA specific infection diagnoses. Both Septicemia, χ^2 (1) = 17588.99, $p < .001$, Cramer's $V = .52$, and Bacteremia, χ^2 (1) =

3021.07, $p < .001$, Cramer's $V = .21$, were significantly related to SA specific infections. Less than ten percent (9.7%) of the patients with SA specific infections had pneumonia, and this relationship was significant, χ^2 (1) = 6195.73, $p < .001$, Cramer's $V = .31$. Septic arthritis (7.0%), χ^2 (1) = 1299.54, $p < .001$, Cramer's $V = .14$; SIRS (4.5%), χ^2 (1) = 461.59, $p < .001$, Cramer's $V = .08$; and Osteomyelitis (3.0%), χ^2 (1) = 456.74, $p < .001$, Cramer's $V = .08$, were significantly related to SA specific infections. Endocarditis, χ^2 (1) = 332.73, $p < .001$, Cramer's $V = .07$, Surgical site infection, χ^2 (1) = 16.34, $p < .001$, Cramer's $V = .02$, and Enterocolitis, χ^2 (1) = 12.56, $p < .001$, Cramer's $V = .01$, resulted in significance when compared with SA specific infections, but the percentages were < 2%. There were no records of Vancomycin-resistant SA by SA specific diagnosis.

Table 30

Means and Standard Deviations of Age at Discharge by SA Specific Infection Diagnosis

	n	Mean	*SD*	*t*	*p*
Age at Discharge				4.28	<.001
No	63710	56.07	17.82		
Yes	1825	54.34	16.97		

Table 31

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by SA Specific Infection Diagnosis

	No		Yes			
	n	%	n	%	χ^2	*p*
SA Possibly Related Infection					4540.62	< .001
No	62110	97.5	1257	68.9		
Yes	1600	2.5	568	31.1		
Bacteremia					3021.07	< .001
No	62912	98.7	1492	81.8		
Yes	798	1.3	333	18.2		
Septicemia					17588.99	<.001
No	63710	100.0	1325	72.6		
Yes	0	.0	500	27.4		
Pneumonia					6195.73	< .001
No	63710	100.0	1648	90.3		
Yes	0	.0	177	9.7		
Vancomycin-Resistant *S. Aureus*					.00	.000
No	63710	100.0	1825	100.0		
Yes	0	.0	0	.0		
Enterocolitis					12.56	< . 001
No	63703	100.0	1823	99.9		
Yes	7	.0	2	.1		
Endocarditis					332.73	< .001
No	63637	99.9	1791	98.1		
Yes	73	.1	34	1.9		
Surgical Site Infection					16.34	< .001
No	63626	99.9	1816	99.5		
Yes	84	.1	9	.5		

(Table 31, continued)

Table 31, continued

Frequencies and Percentages for SA Possibly Related Infection Diagnoses by SA Specific Infection Diagnosis

	No		Yes			
	n	%	n	%	χ^2	*p*
Osteomyelitis					456.74	< .001
No	63572	99.8	1771	97.0		
Yes	138	.2	54	3.0		
Septic Arthritis					1299.54	< .001
No	63446	99.6	1697	93.0		
Yes	264	.4	128	7.0		
SIRS					461.59	< .001
No	63381	99.5	1742	95.5		
Yes	329	.5	83	4.5		

Table 32 presents the frequencies and percentages for autoimmune diseases by SA specific infection diagnosis. Ten autoimmune diagnoses were related significantly by SA specific infection. Three of the autoimmune diagnoses had a higher prevalence of SA specific infection than those who did not. Patients with the diagnosis of SLE had a higher proportional percentage (27.1%) of SA specific infections contrasted with SLE patients who did not (22.5%) with significant results, χ^2 (1) = 21.67, $p < .001$, Cramer's $V = .02$. More patients with MS (16.5%) had a SA specific infection compared with those who did not (12.9%), and the results were significant, χ^2 (1) = 20.07, $p < .001$, Cramer's $V = .02$. Finally, a higher proportional percentage of patients with Dermatomyositis (1.5%) had an SA specific infection than those who do did not (.8%), and the relationship was significant, χ^2 (1) = 12.54, $p < .001$, Cramer's $V = .01$.

Table 32

Frequencies and Percentages for Autoimmune Diagnoses by SA Specific Infection Diagnosis

	No		Yes			
	n	%	n	%	χ^2	*p*
Autoimmune Hepatitis					.41	.521
No	63457	99.6	1816	99.5		
Yes	253	.4	9	.5		
Graves' Disease					23.36	<.001
No	61664	96.8	1803	98.8		
Yes	2046	3.2	22	1.2		
Hashimotos Thyroiditis					18.38	<.001
No	62817	98.6	1821	99.8		
Yes	893	1.4	4	.2		
Autoimmune Disease - Nonspecific					.52	.470
No	63310	99.4	1816	99.5		
Yes	400	.6	9	.5		
Primary Thrombocytopenia					4.02	.045
No	59999	94.2	1739	95.3		
Yes	3711	5.8	86	4.7		
Multiple Sclerosis					20.69	<.001
No	55482	87.1	1524	83.5		
Yes	8228	12.9	301	16.5		
Myasthenia Gravis					.99	.321
No	61933	97.2	1767	96.8		
Yes	1777	2.8	58	3.2		
Raynaud's Disease					4.79	.029
No	61947	97.2	1790	98.1		
Yes	1763	2.8	35	1.9		
Crohn's Disease					21.81	<.001
No	61978	97.3	1808	99.1		
Yes	1732	2.7	17	.9		

(Table 32, continued)

Table 32, continued

Frequencies and Percentages for Autoimmune Diagnoses by SA Specific Infection Diagnosis

	No		Yes			
	n	%	n	%	χ^2	*p*
Ulcerative Colitis					.62	.430
No	63644	99.9	1822	99.8		
Yes	66	.1	3	.2		
Primary Biliary Cirrhosis					.28	.598
No	62850	98.7	1803	98.8		
Yes	860	1.3	22	1.2		
Celiac Disease						
No	63176	99.2	1815	99.5	1.81	.180
Yes	534	.8	10	.5		
Ig A Nephropathy					2.01	.156
No	62440	98.0	1780	97.5		
Yes	1270	2.0	45	2.5		
Discoid Lupus Erythematosus						
No	63141	99.1	1816	99.5	3.25	.072
Yes	569	.9	9	.5		
Systemic Lupus Erythematosus						
No	49376	77.5	1330	72.9	21.67	<.001
Yes	14334	22.5	495	27.1		
Systemic Sclerosis						
No	61440	96.4	1748	95.8	2.21	.137
Yes	2270	3.6	77	4.2		
Sicca Syndrome						
No	62169	97.6	1803	98.8	11.22	.001
Yes	1541	2.4	22	1.2		
Dermatomyositis						
No	63211	99.2	1797	98.5	12.54	<.001
Yes	499	.8	28	1.5		

(Table 32, continued)

Table 32, continued

Frequencies and Percentages for Autoimmune Diagnoses by SA Specific Infection Diagnosis

	No		Yes			
	n	%	n	%	χ^2	*p*
Polymyositis						
No	62828	98.6	1792	98.2	2.31	.128
Yes	882	1.4	33	1.8		
Rheumatoid Arthritis						
No	40217	63.1	1196	65.5	4.43	.035
Yes	23493	36.9	629	34.5		
Juvenile Rheumatoid Arthritis						
No	63273	99.3	1806	99.0	3.24	.072
Yes	437	.7	19	1.0		

Patients with RA had the highest percentage (34.5%) of SA specific infections, but less than those who did not (36.9%), and the results were statistically significant, χ^2 (1) = 4.43, p = .035, Cramer's V = .01. Fewer patients with ITP (4.7%) developed a SA specific infection than those who did not (5.8%), and the result was statistically significant, χ^2 (1) = 4.02, p = .045, Cramer's V = .01.Other autoimmune diseases were significantly related to SA specific diagnoses, but their percentage differences were < 2%. Fewer patients with Graves' disease (1.2%) had SA infections contrasted with those who did not (3.2%), and the result was significant, χ^2 (1) = 23.36, p < .001, Cramer's V = .02. Similarly, less patients with Hashimoto's thyroiditis had SA specific infections (.2%)

than those without the infection (1.4%), and the results were significant, χ^2 (1) = 18.38, p < .001, Cramer's V = .02. Raynaud's disease (1.9%), χ^2 (1) = 4.79, p = .029, Cramer's V = .01, Crohn's disease (.9%), χ^2 (1) = 21.81, p < .001, Cramer's V = .02, and Sicca syndrome (1.2%), χ^2 (1) = 11.22, p < .001, Cramer's V = .01, had lower proportional percentages of SA infections, and the results were significant.

Several diagnoses are associated with organ dysfunction as a result of SIRS. Table 33 describes the frequencies and percentages for organ dysfunction diagnoses by SA specific infection. Five diagnoses resulted in significant relationships with SA specific diagnoses. More patients with organ dysfunction (10.4%) had a SA specific infection diagnosis than did not have the infection (5.2%), and the results were statistically significant, χ^2 (1) = 95.56, p < .001, Cramer's V = .04. More patients with acute renal failure had SA specific infections (4.7%) than those who did not (3.0%) and results were significant, χ^2 (1) = 16.59, p < .001, Cramer's V = .02. A greater proportion of patients with acute respiratory failure (6.5%) had a SA specific infection than those who did not (2.3%) and the results were significant, χ^2 (1) = 125.57, p < .001, Cramer's V = .04. Patients with hepatic failure and SA infection (.4%), χ^2 (1) = 7.56, p = .006, Cramer's V = .01, and patients with septic shock and SA infections (.6%), χ^2 (1) = 18.37, p < .001, Cramer's V = .02, were related significantly as well.

Table 33

Frequencies and Percentages for Organ Dysfunction Diagnoses by SA Specific Infection Diagnosis

	No		Yes			
	n	%	n	%	χ^2	*p*
Any Organ Dysfunction						
No	60425	94.8	1636	89.6	95.56	<.001
Yes	3285	5.2	189	10.4		
Acute Renal Failure						
No	61801	97.0	1740	95.3	16.59	<.001
Yes	1909	3.0	85	4.7		
Encephalopathy						
No	63679	100.0	1824	99.9	.01	.907
Yes	31	.0	1	.1		
Critical Illness Polyneuropathy						
No	63707	100.0	1825	100.0	.09	.769
Yes	3	.0	0	.0		
Critical Illness Myopathy						
No	63707	100.0	1825	100.0	.09	.769
Yes	3	.0	0	.0		
Acute Respiratory Failure						
No	62216	97.7	1707	93.5	125.57	<.001
Yes	1494	2.3	118	6.5		
Hepatic Failure						
No	63623	99.9	1818	99.6	7.56	.006
Yes	87	.1	7	.4		
Septic Shock					18.37	<.001
No	63602	99.8	1814	99.4		
Yes	108	.2	11	.6		

Primary Analysis of Research Question Two

Tables 34 through 36 will illustrate the primary analysis related to the second research question of this study. Table 34 presents the frequencies and percentages of autoimmune diseases and organ dysfunctions by SA specific diagnoses. A bolded row within the table indicates the significant relationship with a difference that is (> 5%). Patients with at least one organ dysfunction demonstrated the only statistically significant relationship with SA specific infections, χ^2 (1) = 95.56, $p < .001$, Cramer's $V = .04$, and a difference of (>5%). More patients with at least one organ dysfunction (10.4%) had a SA specific infection than patients with organ dysfunction that did not have an SA specific infection (5.2%).

Three statistically significant relationships were found in Table 35 that describes the frequencies and percentages of autoimmune diseases and organ dysfunction diagnoses by at least one possibly related SA infection. Bolded rows within the table identify significant relationships with differences (>5%). More SLE patients (36.0%) had a potentially related SA infection compared with SLE patients (22.2%) that did not have the infection diagnosis, χ^2 (1) = 228.26, $p < .001$, Cramer's $V = .06$. The presence of at least one organ dysfunction diagnosis was evident in (14.4%) of the patients with at least one possibly related SA infection when contrasted with (5.0%) of the patients that did not have the infection diagnosis, χ^2 (1) = 369.07, $p < .001$, Cramer's $V = .07$. The third relationship identified was patients with acute renal failure and a potentially related SA infection. A greater percentage of patients with acute renal failure (8.1%) had a possible

SA infection compared with patients with renal failure (2.9%) who did not have the infection, χ^2 (1) = 192.24, $p < .001$, Cramer's $V = .05$.

Table 34

Frequencies and Percentages of Autoimmune and Organ Dysfunction Diagnoses by SA Specific Disease

	SA Specific Infection			
	No		Yes	
	n	%	n	%
Autoimmune Diagnosis				
Autoimmune Hepatitis	253	0.4	9	0.5
Graves' Disease	2,046	3.2	22	1.2
Hashimotos Thyroiditis	893	1.4	4	0.2
Autoimmune Disease, Nonspecific	400	0.6	9	0.5
Primary Thrombocytopenia	3,711	5.8	86	4.7
Multiple Sclerosis	8,228	12.9	301	16.5
Myasthenia Gravis	1,777	2.8	58	3.2
Raynaud's Disease	1,763	2.8	35	1.9
Crohn's Disease	1,732	2.7	17	0.9
Ulcerative Colitis	66	0.1	3	0.2
Primary Biliary Cirrhosis	860	1.3	22	1.2
Celiac Disease	534	0.8	10	0.5
Ig A Nephropathy	1,270	2.0	45	2.5
Discoid Lupus Erythematosus	569	0.9	9	0.5
Systemic Lupus Erythematosus	14,334	22.5	495	27.1
Systemic Sclerosis	2,270	3.6	77	4.2
Sicca Syndrome	1,541	2.4	22	1.2
Dermatomyositis	499	0.8	28	1.5
Polymyositis	882	1.4	33	1.8
Rheumatoid Arthritis	23,493	36.9	629	34.5
Juvenile Rheumatoid Arthritis	437	0.7	19	1.0

(Table 34, continued)

Table 34, continued

Frequencies and Percentages of Autoimmune and Organ Dysfunction Diagnoses by SA Specific Disease

	SA Specific Infection			
	No		Yes	
	n	%	n	%
Organ Dysfunction (at least one)	**3,285**	**5.2**	**189**	**10.4**
Acute Renal Failure	1,909	3.0	85	4.7
Encephalopathy	31	0.0	1	0.1
Critical Illness Polyneuropathy	3	0.0	0	0.0
Critical Illness Myopathy	3	0.0	0	0.0
Acute Respiratory Failure	1,494	2.3	118	6.5
Hepatic Failure	87	0.1	7	0.4
Septic Shock	108	0.2	11	0.6

Note. Organ Dysfunction $\chi^2(1) = 95.56, p < .001$

Table 36 presents the frequencies and percentages of autoimmune and organ dysfunction diagnoses by bacteremia, endocarditis, and surgical site infection. Bolded rows within the table identify significant relationships with differences (>5%). A significant relationship was established between patients with SLE and Bacteremia, χ^2 (1) = 318.83, $p < .001$, Cramer's $V = .07$. A greater proportional percentage of SLE patients were diagnosed with bacteremia (44.7%) than were not diagnosed (22.2%). In addition, a significant relationship was discovered for patients with at least one organ dysfunction and Bacteremia, χ^2 (1) = 103.65, $p < .001$, Cramer's $V = .04$. For the patients who were diagnosed with at least one organ dysfunction, a higher proportional percentage (12.0%) was diagnosed with bacteremia compared to those who were not (5.2%).

Table 35

Frequencies and Percentages of Autoimmune and Organ Dysfunction Diagnoses by at Least One Possibly Related Infection

	At Least One Possibly Related Infection			
	No		Yes	
	n	%	n	%
Autoimmune Diagnosis				
Autoimmune Hepatitis	259	.4	3	.1
Graves' Disease	2,042	3.2	26	1.2
Hashimotos Thyroiditis	895	1.4	2	.1
Autoimmune Disease, Nonspecific	389	.6	20	.9
Primary Thrombocytopenia	3,685	5.8	112	5.2
Multiple Sclerosis	8,290	13.1	239	11.0
Myasthenia Gravis	1,777	2.8	58	2.7
Raynaud's Disease	1,770	2.8	28	1.3
Crohn's Disease	1,724	2.7	25	1.2
Ulcerative Colitis	67	.1	2	.1
Primary Biliary Cirrhosis	844	1.3	38	1.8
Celiac Disease	535	.8	9	.4
Ig A Nephropathy	1,241	2.0	74	3.4
Discoid Lupus Erythematosus	568	.9	10	.5
Systemic Lupus Erythematosus	**14,049**	**22.2**	**780**	**36.0**
Systemic Sclerosis	2,240	3.5	107	4.9
Sicca Syndrome	1,525	2.4	38	1.8
Dermatomyositis	513	.8	14	.6
Polymyositis	877	1.4	38	1.8
Rheumatoid Arthritis	23,466	37.0	656	30.3
Juvenile Rheumatoid Arthritis	440	.7	16	.7
Organ Dysfunction (at least one)	**3,162**	**5.0**	**312**	**14.4**
Acute Renal Failure	**1,819**	**2.9**	**175**	**8.1**
Encephalopathy	29	.0	3	.1
Critical Illness Polyneuropathy	3	.0	0	.0
Critical Illness Myopathy	3	.0	0	.0
Acute Respiratory Failure	1,468	2.3	144	6.6
Hepatic Failure	85	.1	9	.4
Septic Shock	58	.1	61	2.8

Note. Systemic Lupus Erythematosus $\chi^2(1) = 228.26$, $p < .001$, Organ Dysfunction $\chi^2(1) = 369.07$, $p < .001$; Acute Renal Failure $\chi^2(1) = 192.24$, $p < .001$

Table 36

Frequencies and Percentages of Autoimmune and Organ Dysfunction Diagnoses by Bacteremia,, Endocarditis, and Surgical Site Infection

	Bacteremia				Endocarditis				Surgical Site Infection			
	No		Yes		No		Yes		No		Yes	
	n	%	n	%	n	%	n	%	n	%	n	%
Autoimmune Diagnosis												
Autoimmune Hepatitis	259	.4	3	.3	262	.4	0	.0	262	.4	0	.0
Graves' Disease	2,058	3.2	10	.9	2,066	3.2	2	1.9	2,066	3.2	2	2.2
Hashimotos Thyroiditis	897	1.4	0	.0	897	1.4	0	.0	895	1.4	2	2.2
Autoimmune Disease, Nonspecific	396	.6	13	1.1	409	.6	0	.0	409	.6	0	.0
Primary Thrombocytopenia	3,737	5.8	60	5.3	3,787	5.8	10	9.3	3,794	5.8	3	3.2
Multiple Sclerosis	8,425	13.1	104	9.2	8,522	13.0	7	6.5	8,521	13.0	8	8.6
Myasthenia Gravis	1,793	2.8	42	3.7	1,829	2.8	6	5.6	1,832	2.8	3	3.2
Raynaud's Disease	1,790	2.8	8	.7	1,797	2.7	1	.9	1,795	2.7	3	3.2
Crohn's Disease	1,731	2.7	18	1.6	1,749	2.7	0	.0	1,745	2.7	4	4.3
Ulcerative Colitis	69	.1	0	.0	69	.1	0	.0	69	.1	0	.0
Primary Biliary Cirrhosis	856	1.3	26	2.3	882	1.3	0	.0	881	1.3	1	1.1
Celiac Disease	538	.8	6	.5	544	.8	0	.0	544	.8	0	.0
IgA Nephropathy	1,257	2.0	58	5.1	1,308	2.0	7	6.5	1,314	2.0	1	1.1
Discoid Lupus Erythematosus	574	.9	4	.4	578	.9	0	.0	578	.9	0	.0
Systemic Lupus Erythematosus	**14,324**	**22.2**	**505**	**44.7**	**14,776**	**22.6**	**53**	**49.5**	14,802	22.6	27	29.0
Systemic Sclerosis	2,276	3.5	71	6.3	2,346	3.6	1	.9	2,341	3.6	6	6.5

(Table 36, continued)

Table 36, continued

Frequencies and Percentages of Autoimmune and Organ Dysfunction Diagnoses by Bacteremia,, Endocarditis, and Surgical Site Infection

	Bacteremia				Endocarditis				Surgical Site Infection			
	No		Yes		No		Yes		No		Yes	
	n	%	n	%	n	%	n	%	n	%	n	%
Autoimmune Diagnosis (cont)												
Sicca Syndrome	1,541	2.4	22	1.9	1,562	2.4	1	.9	1,558	2.4	5	5.4
Dermatomyositis	516	.8	11	1.0	527	.8	0	.0	527	.8	0	.0
Polymyositis	891	1.4	24	2.1	912	1.4	3	2.8	913	1.4	2	2.2
Rheumatoid Arthritis	23,913	37.1	209	18.5	24,103	36.8	19	17.8	24,088	36.8	34	36.6
Juvenile Rheumatoid Arthritis	450	.7	6	.5	455	.7	1	.9	455	.7	1	1.1
Organ Dysfunction (at least one)	**3,338**	**5.2**	**136**	**12.0**	**3,457**	**5.3**	**17**	**15.9**	3,469	5.3	5	5.4
Acute Renal Failure	1,924	3.0	70	6.2	**1,983**	**3.0**	**11**	**10.3**	1,992	3.0	2	2.2
Encephalopathy	31	.0	1	.1	32	.0	0	.0	32	.0	0	.0
Critical Illness Polyneuropathy	3	.0	0	.0	3	.0	0	.0	3	.0	0	.0
Critical Illness Myopathy	3	.0	0	.0	3	.0	0	.0	3	.0	0	.0
Acute Respiratory Failure	1,544	2.4	68	6.0	1,606	2.5	6	5.6	1,608	2.5	4	4.3
Hepatic Failure	93	.1	1	.1	93	.1	1	.9	94	.1	0	.0
Septic Shock	109	.2	10	.9	119	.2	0	.0	119	.2	0	.0

Note. Bacteremia: *Systemic Lupus Erythematosus* $\chi^2(1) = 318.83, p < .001$; *Organ Dysfunction* $\chi^2(1) = 103.65, p < .001$. Endocarditis: *Systemic Lupus Erythematosus* $\chi^2(1) = 44.31, p < .001$; *Organ Dysfunction* $\chi^2(1) = 23.93, p < .001$; *Acute Renal Failure* $\chi^2(1) = 19.03, p < .001$

A higher percentage of patients with SLE had endocarditis (49.5%) in contrast with those who did not have the infection (22.6%). Endocarditis was significantly related to the SLE diagnosis, χ^2 (1) = 44.31, $p < .001$, Cramer's V =.03. For the patients who were diagnosed with at least one organ dysfunction, more patients proportionally (15.9%) had endocarditis in contrast to those who did not have the complication (5.3%). The relationship of organ dysfunction and endocarditis was significant, χ^2 (1) = 23.93, $p <$ .001, Cramer's V = .02. The relationship of acute renal failure and endocarditis was significant, χ^2 (1) = 19.03, $p < .001$, Cramer's V = .02. A greater proportional percentage of patients with acute renal failure were also diagnosed with endocarditis (10.3%) compared with those that did not have the diagnosis (3.0%). Patients with bacteremia and SLE and at least one organ dysfunction had increased significant differences than similar patients without the infection. Finally, patients with endocarditis, SLE, at least one organ dysfunction, and specifically, acute renal failure had increased percentages of co-morbidity than similar patients without endocarditis.

The frequencies and percentages of autoimmune and organ dysfunction diagnoses compared to osteomyelitis, septic arthritis, and SIRS are displayed in Table 37. Bolded rows within the table identify significant relationships with differences (>5%). Patients with RA and osteomyelitis had a significant relationship, χ^2 (1) = 10.22, $p < .01$, Cramer's V = .01. Proportionally, more patients with RA had osteomyelitis (47.9%) than RA patients without the bone infection (36.8%). RA patients also demonstrated a significant relationship with the complication of Septic arthritis, χ^2 (1) = 171.61, $p < .001$,

Cramer's $V = .05$. A substantially higher percentage of RA patients were also diagnosed with septic arthritis (68.6%) compared to those who did not have the infection (36.6%).

There were six significant relationships of autoimmune diseases and organ dysfunctions by SIRS. MS patients were significantly related to the complication of SIRS, χ^2 (1) = 40.60, $p < .001$, Cramer's $V = .02$. A greater proportional percentage of MS patients were diagnosed with SIRS (23.5%) than those MS patients without SIRS (12.9%). Patients hospitalized with SLE were significantly related to SIRS, χ^2 (1) = 53.24, $p < .001$, Cramer's $V = .03$. More patients with the diagnoses of SLE and SIRS (37.6%) were hospitalized than proportionally those without the complication of SIRS (22.5%). As expected, patients with at least one organ dysfunction were significantly related to patients with SIRS, χ^2 (1) = 726.10, $p < .001$, Cramer's $V = .10$. The proportional percentage difference was substantial in this relationship. More patients with at least one organ dysfunction and SIRS (35.0%) were hospitalized compared to patients without the diagnosis of SIRS (5.1%). Specifically, three organ dysfunctions were related significantly with SIRS. A higher percentage of patients with acute renal failure and SIRS (19.9%) were reported than those without SIRS (2.9%), and the relationship was significant, χ^2 (1) = 399.51, $p < .001$, Cramer's $V = .08$. The relationship of patients with acute respiratory failure and SIRS was significant, χ^2 (1) = 284.52, $p < .001$, Cramer's $V = .07$. Again, a higher percentage of patients with acute respiratory failure and SIRS (15.3%) were in the hospital than those without SIRS (2.4%). Lastly, patients with septic shock were related significantly to the SIRS diagnosis, χ^2 (1) = 4417.10, $p < .001$,

Cramer's $V = .26$. More patients with septic shock also were diagnosed with SIRS (14.1%) compared to those with septic shock without SIRS (.1%).

Analyses of the Hypotheses

Tables 38 and 39 present the multiple logistic regression analyses predicting SA specific and SA possibly related infection diagnoses stemming from the hypothesis written for this study. Due to the size of the full sample of patients with autoimmune diseases, and as strategy to determine the consistency of the regression models, a kfold cross-validation was conducted. Three nested case control studies were completed. First, the model was run on the full sample of patients hospitalized with autoimmune and other diagnoses. Secondly, three random samples were identified to verify the findings of the regression analyses. Each random sample was comprised of 1,200 patients from the full sample. In Table 38, in each random sample, six hundred of the patients were randomly selected with a SA specific diagnosis, and six hundred patients were randomly selected without a SA specific diagnosis. In Table 39, for each random sample, six hundred patients were randomly selected with a SA possibly related infection diagnosis, and six hundred patients were selected without such designation. Odds ratio are listed for the full sample and each random sample. All significant odds ratios are designated with asterisks (*, $p < .05$), (**, $p < .01$), (***, $p < .001$). Odds ratio results (<.9) or (> 1.2) will be discussed as significant results.

Table 37

Frequencies and Percentages of Autoimmune and Organ Dysfunction Diagnoses by Osteomyelitis, Septic Arthritis, and SIRS

	Osteomyelitis				Septic Arthritis				SIRS			
	No		Yes		No		Yes		No		Yes	
	n	%	n	%	n	%	n	%	n	%	n	%
Autoimmune Diagnosis												
Autoimmune Hepatitis	262	.4	0	.0	262	.4	0	.0	262	.4	0	.0
Graves' Disease	2,064	3.2	4	2.1	2,064	3.2	4	1.0	2,063	3.2	5	1.2
Hashimotos Thyroiditis	897	1.4	0	.0	897	1.4	0	.0	897	1.4	0	.0
Autoimmune Disease, Nonspecific	408	.6	1	.5	407	.6	2	.5	403	.6	6	1.5
Primary Thrombocytopenia	3,790	5.8	7	3.6	3,782	5.8	15	3.8	3,778	5.8	19	4.6
Multiple Sclerosis	8,499	13.0	30	15.6	8,518	13.1	11	2.8	**8,432**	**12.9**	**97**	**23.5**
Myasthenia Gravis	1,829	2.8	6	3.1	1,832	2.8	3	.8	1,833	2.8	2	.5
Raynaud's Disease	1,792	2.7	6	3.1	1,793	2.8	5	1.3	1,792	2.8	6	1.5
Crohn's Disease	1,748	2.7	1	.5	1,749	2.7	0	.0	1,747	2.7	2	.5
Ulcerative Colitis	69	.1	0	.0	69	.1	0	.0	67	.1	2	.5
Primary Biliary Cirrhosis	881	1.3	1	.5	882	1.4	0	.0	874	1.3	8	1.9
Celiac Disease	544	.8	0	.0	543	.8	1	.3	542	.8	2	.5
IgA Nephropathy	1,311	2.0	4	2.1	1,314	2.0	1	.3	1,309	2.0	6	1.5
Discoid Lupus Erythematosus	577	.9	1	.5	576	.9	2	.5	575	.9	3	.7
Systemic Lupus Erythematosus	14,794	22.6	35	18.2	14,751	22.6	78	19.9	**14,674**	**22.5**	**155**	**37.6**
Systemic Sclerosis	2,338	3.6	9	4.7	2,334	3.6	13	3.3	2,327	3.6	20	4.9

(Table 37, continued)

Table 37, continued

Frequencies and Percentages of Autoimmune and Organ Dysfunction Diagnoses by Osteomyelitis, Septic Arthritis, and SIRS

	Osteomyelitis				Septic Arthritis				SIRS			
	No		Yes		No		Yes		No		Yes	
	n	%	n	%	n	%	n	%	n	%	n	%
Autoimmune Diagnosis (cont)												
Sicca Syndrome	1,557	2.4	6	3.1	1,560	2.4	3	.8	1,556	2.4	7	1.7
Dermatomyositis	527	.8	0	.0	526	.8	1	.3	525	.8	2	.5
Polymyositis	912	1.4	3	1.6	910	1.4	5	1.3	912	1.4	3	.7
Rheumatoid Arthritis	**24,030**	**36.8**	**92**	**47.9**	**23,853**	**36.6**	**269**	**68.6**	24,045	36.9	77	18.7
Juvenile Rheumatoid Arthritis	456	.7	0	.0	451	.7	5	1.3	451	.7	5	1.2
Organ Dysfunction (at least one)	3,465	5.3	9	4.7	3,453	5.3	21	5.4	**3,330**	**5.1**	**144**	**35.0**
Acute Renal Failure	1,988	3.0	6	3.1	1,981	3.0	13	3.3	**1,912**	**2.9**	**82**	**19.9**
Encephalopathy	31	.0	1	.5	32	.0	0	.0	31	.0	1	.2
Critical Illness Polyneuropathy	3	.0	0	.0	3	.0	0	.0	3	.0	0	.0
Critical Illness Myopathy	3	.0	0	.0	3	.0	0	.0	3	.0	0	.0
Acute Respiratory Failure	1,610	2.5	2	1.0	1,604	2.5	8	2.0	**1,549**	**2.4**	**63**	**15.3**
Hepatic Failure	94	.1	0	.0	94	.1	0	.0	86	.1	8	1.9
Septic Shock	118	.2	1	.5	119	.2	0	.0	**61**	**.1**	**58**	**14.1**

Note. Osteomyelitis: *Rheumatoid Arthritis* $\chi^2(1) = 10.22$, $p < .01$. Septic Arthritis: *Rheumatoid Arthritis* $\chi^2(1) = 171.61$, $p < .001$. SIRS: *Multiple Sclerosis* $\chi^2(1) = 40.60$, $p < .001$; *Lupus* $\chi^2(1) = 53.24$, $p < .001$; *Organ Dysfunction* $\chi^2(1) = 726.10$, $p < .001$; *Acute Renal Failure* $\chi^2(1) = 399.51$, $p < .001$; *Acute Respiratory Failure* $\chi^2(1) = 284.52$, $p < .001$; *Septic Shock:* $\chi^2(1) = 4417.10$, $p < .001$

Table 38 presents multiple logistic regression analyses predicting SA specific infection diagnoses from demographics, autoimmune diagnoses, and organ dysfunction diagnoses. Several categories of demographics, autoimmune diagnoses, and organ dysfunction diagnoses were significant, χ^2 (32) = 1202.23, $p < .001$, $R^2 = .083$. Females as compared to males had increased odds of having a specific SA infection (*OR* = 1.377, $p < .001$; *OR* = 1.684, $p < .001$; *OR* = 1.524, $p < .05$) in the full sample and in two random samples. Medicare patients as compared to those who self paid had increased odds of having a SA specific infection diagnosis (*OR* = 1.753, $p < .001$; *OR* = 1.793, $p < .05$; *OR* = 2.298, $p < .01$) in the full samples and two random samples. Patients who stayed in the hospital for three days or longer compared to those who stayed one to two days had increased odds of an SA specific infection in all four samples. The increase in odds was sequential with each longer stay category as compared to a one to two day stay. Patients who were hospitalized for three to five days (*OR* = 2.445, $p < .001$; *OR* = 2.317, $p < .001$; *OR* = 3.267, $p < .001$; *OR* = 2.158, $p < .001$) demonstrated at least twice the odds of having a SA specific diagnosis. Patients that were hospitalized for six to nine days (*OR* = 4.992, $p < .001$; *OR* = 4.693, $p < .00$; *OR* = 7.746, $p < .001$; *OR* = 4.653, $p < .001$) had at least four times the odds of those who stayed less in the hospital. For patient stays of ten or more days (*OR* = 8.349, $p < .001$; *OR* = 9.931, $p < .001$; *OR* = 13.087, $p < .001$; *OR* = 9.9791, $p < .001$), the odds of a SA specific infection were even higher. Patients spending $24,000 or more on the hospitalization had an increased risk (*OR* = 1.214, $p < .05$) of having a SA specific diagnosis in the full sample compared to those who spent $7999 or less. In the full sample, as compared to those without each disorder,

MS patients had increased odds (OR = 1.283, $p < .05$) of having a SA specific diagnosis. In a random sample, MG patients had increased risks (OR = 2.614, $p < .05$) of having the SA specific infection during hospitalization. Lastly, patients with acute respiratory failure had increased odds (OR = 1.676, $p < .001$; OR = 2.737, $p < .01$) of a SA specific infection diagnosis in the full sample and in one random sample.

Patients with Graves' disease in the full sample had a decreased risk (OR = .472, $p < .01$) of having a SA specific infection. Similarly, patients with ITP in a random sample (OR = .416, $p < .05$) had a decreased risk for a SA specific diagnosis. Interestingly, patients with Crohn's disease had substantially decreased odds (OR = .274, $p < .001$; OR = .178, $p < .01$; OR = .260, $p < .05$) of having a SA specific diagnosis in three of the four samples, patients with Sicca syndrome (OR = .285, $p < .05$), and RA (OR = .234, $p < .05$) had decreased odds of having a SA infection in one random sample.

Table 38

Multiple Logistic Regression Analyses Predicting SA Specific Infection Diagnosis from Demographics, Autoimmune Diagnoses, and Organ Dysfunction Diagnoses

	Full Sample Odds Ratio	Random Sample 1 Odds Ratio	Random Sample 2 Odds Ratio	Random Sample 3 Odds Ratio
Female[a]	1.377 ***	1.684 ***	1.524 *	.977
Discharge Age	.982 ***	.983 ***	.982 ***	.979 ***
African-American[b]	.994	1.062	1.005	.927
Other[b]	.899	.872	.724	.693
PPO/POSc	1.167	1.457	.663	1.440

(Table 38, continued)

Table 38, continued

Multiple Logistic Regression Analyses Predicting SA Specific Infection Diagnosis from Demographics, Autoimmune Diagnoses, and Organ Dysfunction Diagnoses

	Full Sample Odds Ratio	Random Sample 1 Odds Ratio	Random Sample 2 Odds Ratio	Random Sample 3 Odds Ratio
HMO[c]	1.297 *	1.365	.837	1.510
Medicare[c]	1.753 ***	1.793 *	1.065	2.298 **
Medicaid[c]	1.282	1.326	.633	1.426
3-5 Days[d]	2.445 ***	2.317 ***	3.267 ***	2.158 ***
6-9 Days[d]	4.992 ***	4.693 ***	7.746 ***	4.653 ***
10 or More Days[d]	8.349 ***	9.931 ***	13.087 ***	9.791 ***
$8000 - $15999[e]	1.101	.981	.838	1.093
$16000 - $23999[e]	1.078	1.285	.633	.931
$24000 or More[e]	1.214 *	.977	1.002	.956
Graves' Disease[f]	.472 **	.982	.492	.543
Primary Thrombocytopenia[f]	.789	.416 *	.820	1.347
Multiple Sclerosis[f]	1.283 *	1.409	1.510	1.414
Myasthenia Gravis[f]	.964	.934	.508	2.614 *
Raynaud's Disease[f]	.817	.753	.497	1.285
Crohn's Disease[f]	.274 ***	.178 **	.260 *	.454
Primary Biliary Cirrhosis[f]	.878	.876	1.555	.795
Celiac Disease[f]	.765	.533	1.395	.919
Ig A Nephropathy[f]	1.064	.803	1.128	1.800
Systemic Lupus Erythematosus[f]	1.196	.899	1.406	1.265
Systemic Sclerosis[f]	1.171	1.118	1.125	1.218
Sicca Syndrome[f]	.649	1.369	.281	.285 *
Dermatomyositis[f]	1.564 *	.601	.939	4.816 *
Polymyositis[f]	1.118	.966	1.403	1.014
Rheumatoid Arthritis[f]	1.203	1.008	1.573	1.483
Juvenile Rheumatoid Arthritis[f]	1.184	.234 *	.650	1.974
Acute Renal Failure[f]	.888	1.476	1.074	.895
Acute Respiratory Failure[f]	1.676 ***	1.182	1.628	2.737 **

Note: Model χ^2 (32) = 1202.23 $p < .001$, R^2=.083; [a]Compared to males; [b]Compared to Caucasian; [c]Compared to Self-pay; [d]Compared to 1-2 Days; [e]Compared to $7999 or less; [f]Compared to not having the diagnosis

Table 39 illustrates multiple logistic regression analyses predicting SA possibly related infection diagnoses by demographics, autoimmune diagnoses, and organ dysfunction diagnoses. Again, there were several significant predictors of the potentially related SA diagnoses, χ^2 (33) = 1826.14, $p < .001$, $R^2 = .112$. In three of the four samples, females had increased odds (*OR* = 1.234, $p < .001$; *OR* = 1.470, $p < .05$; *OR* = 1.805, $p < .01$) of having a potentially related SA infection. African-American patients had increased risk (*OR* = 1.253, $p < .001$; *OR* = 1.451, $p < .05$) of a related SA infection in the full sample and in one random sample as compared to Caucasian patients. Patients claiming PPO/POS insurance (*OR* = 1.319, $p < .05$) had increased odds of a SA related infection in the full sample as compared to those who self paid their insurance. Medicare patients also had a higher risk (*OR* = 2.094, $p < .001$; *OR* = 2.143, $p < .05$) of a related SA infection diagnosis in the full and one random sample as compared to those who self paid.

The length of stay and total hospital charges correlated with increased odds of a possibly related SA infection diagnosis. Patients with stays of three to six days had a higher risk (*OR* = 1.901, $p < .001$; *OR* = 2.453, $p < .001$) of a potential SA related diagnosis in the full and in one random sample compared to those who stayed one to two days. Patients who were hospitalized six to nine days (*OR* = 3.104, $p < .001$; *OR* = 2.988, $p < .001$ *OR* = 2.472, $p < .001$; *OR* = 3.370, $p < .001$) and patients who stayed for ten or more days (*OR* = 5.122, $p < .001$; *OR* = 4.099, $p < .001$ *OR* = 5.136, $p < .001$; *OR* = 7.169, $p < .01$) had significant results and increased odds in all four samples compared to those who stayed one to two days. The total hospital charges significantly predicted a

potentially SA related infection diagnosis. As compared to patients who were charge $7999 or less, patients who were charged $8,000 to $15,999 had increased risk (*OR* = 1.508, $p < .001$; *OR* = 1.618, $p < .05$ *OR* = 1.599, $p < .05$) in three of the four samples. Patients charged $16,000 to $23,999 had increased odds (*OR* = 1.919, $p < .001$; *OR* = 2.066, $p < .01$; *OR* = 2.074, $p < .01$) of related SA infection in the full sample and two of the random samples as compared to patients who were charge $7999 or less. Patients charged $24,000 or higher had at least twice the risk (*OR* = 2.658, $p < .001$; *OR* = 2.153, $p < .01$ *OR* = 2.274, $p < .01$; *OR* = 2.575, $p < .001$) of a potentially related SA infection in all four samples as compared to patients who were charge $7999 or less.

Patients in the hospital with SLE had increased odds (*OR* = 1.407, $p < .001$; *OR* = 2.202, $p < .01$; *OR* = 1.801, $p < .05$) of contacting a potentially related SA infection in the full sample and in two of the random samples. SS patients had increased risk (*OR* = 1.345, $p < .05$; *OR* = 2.608, $p < .05$) for SA-related infection in the full and in one random sample. Lastly, organ dysfunction was predictive of possibly related SA infection. Patients with acute renal failure had increased risk (*OR* = 1.394, $p < .001$; *OR* = 3.155, $p < .01$; *OR* = 1.984, $p < .05$) of SA-related infection in the full sample and in two random samples. Patients hospitalized with acute respiratory failure had increased odds (*OR* = 1.433, $p < .001$; *OR* = 2.644, $p < .05$) of a potentially related SA infection in the full sample and in one random sample.

Patients in the hospital with Graves's disease had decreased risk (*OR* = .478, $p < .01$) of a SA-related diagnosis in the full sample. The patients with Raynaud's diagnosis had decreased risk (*OR* = .499, $p < .001$; *OR* = .192, $p < .01$) for SA-related infection in

the full sample and in one random set. Patients with Crohn's disease had decreased risk (*OR* = .345, $p < .001$) of SA-related infection in the full sample. Patients with Dermatomyositis had decreased risk (*OR* = .531, $p < .05$) for SA-related infection in the full sample.

Table 39

Multiple Logistic Regression Analysis Predicting SA Possibly Related Infection Diagnoses from Demographics, Autoimmune Diagnoses, and Organ Dysfunction Diagnoses

	Full Sample Odds Ratio	Random Sample 1 Odds Ratio	Random Sample 2 Odds Ratio	Random Sample 3 Odds Ratio
Female[a]	1.234 ***	1.217	1.470 *	1.805 **
Discharge Age	.982 ***	.985 **	.984 **	.990 *
African-American[b]	1.253 ***	1.334	.809	1.451 *
Other[b]	1.077	1.158	.801	.860
PPO/POS[c]	1.319 *	1.377	1.026	1.269
HMO[c]	1.262	.970	1.093	.933
Medicare[c]	2.094 ***	1.443	2.143 *	1.381
Medicaid[c]	1.230	1.071	1.741	.645
3-5 Days[d]	1.901 ***	1.517	1.455	2.453 ***
6-9 Days[d]	3.104 ***	2.988 ***	2.472 ***	3.370 ***
10 or More Days[d]	5.122 ***	4.099 ***	5.136 ***	7.169 ***
$8000 - $15999[e]	1.508 ***	1.562	1.618 *	1.599 *
$16000 - $23999[e]	1.919 ***	2.066 **	2.074 **	1.616
$24000 or More[e]	2.658 ***	2.153 **	2.274 **	2.575 ***
Graves' Disease[f]	.478 **	.320	.716	1.280

(Table 39, continued)

Table 39, continued

Multiple Logistic Regression Analysis Predicting SA Possibly Related Infection Diagnoses from Demographics, Autoimmune Diagnoses, and Organ Dysfunction Diagnoses

	Full Sample Odds Ratio	Random Sample 1 Odds Ratio	Random Sample 2 Odds Ratio	Random Sample 3 Odds Ratio
Autoimmune Disease, Nonspecific[f]	1.334	1.872	1.184	1.076
Primary Thrombocytopenia[f]	.809	1.482	.980	1.141
Multiple Sclerosis[f]	.828	1.255	1.233	.780
Myasthenia Gravis[f]	.811	.877	1.153	.736
Raynaud's Disease[f]	.499 ***	.629	.192 **	.831
Crohn's Disease[f]	.345 ***	.538	.892	.347
Primary Biliary Cirrhosis[f]	1.220	1.018	1.856	1.668
Ig A Nephropathy[f]	1.286	1.746	.866	2.134
Discoid Lupus Erythematosus[f]	.634	.661	1.526	3.668
Systemic Lupus Erythematosus[f]	1.407 ***	1.723	2.202 **	1.801 *
Systemic Sclerosis[f]	1.345 *	1.621	1.639	2.608 *
Sicca Syndrome[f]	.946	1.706	1.185	.962
Dermatomyositis[f]	.531 *	.786	.152	1.375
Polymyositis[f]	1.058	1.385	1.175	.861
Rheumatoid Arthritis[f]	.983	1.190	1.318	1.356
Juvenile Rheumatoid Arthritis[f]	.742	.505	.973	3.860
Acute Renal Failure[f]	1.394 ***	3.155 **	1.984 *	1.196
Acute Respiratory Failure[f]	1.433 ***	2.644 *	1.581	2.122

Note: Model χ^2 (33) = 1826.14 p < .001, R^2=.112; [a]Compared to males; [b]Compared to Caucasian; [c]Compared to Self-pay; [d]Compared to 1-2 Days; [e]Compared to $7999 or less; [f]Compared to not having the diagnosis

Summary

Table presentations and narrative were documented to address the preliminary analysis, the primary analysis, research questions one and two, and the hypothesis. Frequencies, percentages, cross-tabulations, chi squares, *t* tests, ANOVAs, and multiple logistic regression analyses were used to understand relationships and predictors of SA specific infections and potentially related SA infections among hospitalized patients in north Texas. Several significant relationships among demographic variables, autoimmune diseases, and organ dysfunctions were predictive of SA specific and SA related infections and will be further explored in the following chapter.

CHAPTER V

SUMMARY, DISCUSSION, AND RECOMMENDATIONS

Summary

This retrospective investigation assessed secondary data of patients hospitalized from 1999 to 2005 with at least one of twenty-one autoimmune diagnoses. The purposes of this epidemiological study were to: 1) Determine the prevalence at discharge of SA infections and possibly related SA infections; 2) Delineate those with SA infections by descriptive covariates of gender, age, race/ethnicity, autoimmune diagnosis, insurance type, length of stay in days, and total hospital charges; and 3) Determine the predictive effect of descriptive covariates on the presence of diagnosis of SA infection.

The sample of this study included 65,535 patients with at least one autoimmune diagnosis. In the preliminary analysis (Tables 1 to 28), frequencies and percentages were calculated for all autoimmune diagnoses, SA specific infections, SA possibly related infections, gender, ethnicity, insurance type, and length of stay. Means and standard deviations for age at discharge, length of stay, and total hospital charges were also completed. Frequencies, percentages, cross-tabulations, and chi square values were calculated for categorical demographic variables by each demographic variable; for autoimmune diagnoses by categorical demographic variables; for possibly related SA infections by categorical demographic variables, and by each potential SA infection.

Means, standard deviations, and one-way ANOVAs were calculated for age at discharge by demographic variables.

Tables 29 to 33 focused on the primary analyses related to the first research question. Means, standard deviations, and an independent sample *t* test of age at discharge by SA specific infection diagnosis were presented. Frequencies, percentages, cross-tabulations, and chi square values of demographic variables, autoimmune diagnoses, and organ dysfunction diagnoses by SA specific infection diagnoses completed the analysis of the first research question. Tables 34 to 37 addressed the second research question. The frequencies, percentages, cross-tabulations, and chi square values were calculated for autoimmune diagnoses and organ dysfunction diagnoses by SA specific infections, by at least one possibly related SA infection, and by each potential SA infection. Tables 38 and 39 addressed the null hypothesis presented in this study, and sought to analyze whether the covariates were predictive or protective of SA infections. The results were statistically significant, and the null hypothesis was rejected. Several covariates were either protective or predictive of a diagnosis of a SA specific or potentially related infection.

Conclusions

Preliminary Analyses

Autoimmune diagnoses. The frequencies and percentages of the twenty-one autoimmune diagnoses represented in this study are presented in Table 5. In rank order, RA patients (36.8%), SLE (22.6%), and MS (13.0%) represented the highest prevalence in the sample. These percentages are consistent with national numbers that place those

three as the most prevalent autoimmune diseases. The CDC (2009b) reported that 1.293 million adults (0.6%) of the United States population had RA in 2005. This prevalence had decreased since 1990 due to more specific diagnostic criteria, and an acknowledged global decline in prevalence (CDC, 2009b). The incidence of SLE is difficult to record consistently since onset of disease may be insidious without predictable clinical manifestations (CDC, 2009c). Estimates of incidence vary across the continental United States. The Mayo Clinic in Rochester, Minnesota reported that the incidence of SLE in Caucasians tripled from the 1950 to 1979 cohort (1.5/100,000) to 1980 to 1992 (5.6/100,000) (CDC, 2009c). In 2005, the estimated prevalence was 161,000 with definitive SLE and 322,000 with definite or probable SLE (CDC, 2009c). Prevalence of patients with MS was also difficult to delineate. According to the National Institute of Neurological Disorders and Stroke (NINDS) there are approximately 250,000 to 350,000 MS patients in the US with nearly 200 new cases each week (NINDS, 2010).

Several autoimmune diagnoses had prevalence percentages that were clustered. ITP (5.8%) was ranked fourth, followed by SS (3.6%), Graves ' disease (3.2%), MG (2.8%), Raynaud's disease (2.7%), Crohn's disease (2.7%), Sicca syndrome (2.4%) and Ig A nephropathy (2%) were at least 2%. The rank order of prevalence for the remaining diagnoses were as follows: Hashimotos thyroiditis (1.4%), Polymyositis (1.4%), Primary biliary cirrhosis (1.3%), Discoid lupus erythematosus (.9%), Celiac disease (.8%), Dermatomyositis (.8%), Juvenile RA (.7%), Autoimmune disease – Nonspecific (.6%), Autoimmune hepatitis (.4%), Ulcerative colitis (.1%).

SA infections. Table 3 reported the frequencies and percentages for SA specific infections and SA possibly related infection diagnoses. The percentage of SA specific infections (n = 1825; 2.8%) included all SA ICD-9-CM coding, MRSA, and SA specific Septicemia and Pneumonia. The percentage of SA infection only (n = 1135; 1.7%) included all ICD-9-CM coding of SA infections without a site designation. Few patients were identified as having MRSA (n = 60; .1%). Due to low sample numbers, MRSA was not included as a separate category in the primary analyses. SA possibly related infections (n = 2168; 3.3%) included SA enterocolitis (n = 9; .0%), Bacteremia (n = 1131; 1.7%), Endocarditis (n = .107; .2%), SSI (n = 93; .1%), Osteomyelitis (n = 192; .3%), Septic arthritis (n = 392; .6%), and SIRS (n = 412; .6%). Noskin et al. (2005) reported a retrospective analysis of the burden of SA infections on hospitals in the United States for 2000 and 2001. Discharge data from over 900 hospitals approximating 14 million inpatients represented the sample population. SA infection was reported as a discharge diagnosis for 0.8% of those hospital inpatients. The percentage of SA specific (2.8%) and SA related discharge diagnoses (3.3%) was higher in this investigation than the comprehensive study by Noskin et al. Autoimmune disease inpatients represent a higher risk for SA infections than the general inpatient population due to abnormalities in the innate and adaptive immune responses, and the potential need for pharmacological immunosuppression (Agmon-Levin & Shoenfeld, 2009; Gregersen, 2007; Zdanowicz, 2009).

The low prevalence of MRSA in this study was likely primarily due to inaccurate ICD-9-CM coding of the patient sample. In a review of discharge and microbiology

databases from July and August of 2005 to 2007, ICD-9-CM codes designating MRSA were compared with laboratory confirmation (Schaefer et al., 2010). Medical records were reviewed as further confirmation. The authors identified 571 potential infections with 403 (71%) confirmed MRSA infections. The onset of HA-MRSA totaled 61 (15%). Choosing from fifteen possible ICD-9-CM codes, the capability of capture was 59% for all MRSA cases identified. When only nine of the ICD-9-CM codes were used in the analysis, only 31% of the established cases were confirmed. The overall sensitivity of all the ICD-9-CM codes for HA-MRSA was 33% in contrast with 62% of CA–MRSA (Schaefer et al.).

Some scholars estimated that as many as 95% of SA infections over the globe did not respond to first-line treatment of penicillin or ampicillin, as well as, the majority do not respond to narrow spectrum beta lactamase resistant antimicrobial drugs (e.g., methicillin, oxacillin) in the time preceding the data collection of this sample (Klein et al., 2007; Rubin et al., 1999). Klein et al. explored the hospitalizations and mortality caused by MRSA in the United States between 1999 to 2005. Over this time period, the number of hospitalizations related to SA infections increased 62% or approximately 8.4% each year. The number of hospitalizations related to MRSA increased 119% or approximately 14% per year (Klein et al.). Researchers then suggested that the emergence CA-MRSA strains in healthcare settings likely added to the burden of SA infection rates in acute care hospitals (Klein et al.; Klevens et al., 2006; Maree et al., 2007). Either a prospective research design or improved training and validation of healthcare ICD-9-CM

coding staff are needed to truly capture the growing phenomenon of MRSA rates in the hospital setting.

Tables 22 through 28 presented the frequencies and percentages for SA possibly related infection diagnoses by each individual infection. Table 23 displayed the percentages for SA possibly related infection diagnoses by Bacteremia. More patients with bacteremia were also diagnosed with SIRS (6.8%) when compared to septic arthritis (2.1%) and endocarditis (2.4%), and each relationship was significant. More patients with SIRs were also diagnosed with bacteremia (18.7%), and the relationship was significant (Table 28). Some patients with bacteremia from MRSA have been difficult to treat even though the infections were susceptible to vancomycin. In a retrospective cohort analysis, MRSA bacteremia was compared to nonpersistant bacteremia (Neuner, Casabar, Reichly, & McKinnon, 2010). By multivariate analysis, the authors found that endocarditis (OR = 2.3, p = .021), complicated bacteremia (OR = 2.6, p = .009), Vancomycin susceptibility (OR = 2.6, p = .009), and septic shock (OR = 2.2, p = .031) increased the odds of MRSA bacteremia that lasted longer than three to seven days (Neuner et al.). Blaine et al. (2010) studied the role of Panton-Valentine leukocidin (PVL), a gene producing a virulent endotoxin, in MRSA bacteremia. PVL has been found in CA-MRSA strains of HA-MRSA (Blaine et al.; Herman et al., 2008). The colonization of PVL MRSA increased the risk of bacteremia (OR = 2.40, CI 1.23-4.57) in a sample of 266 patients (Blaine et al.).

Gender. According to the National Hospital Discharge Survey (NHDS) in 2005, all hospital discharge rates per 1,000 population demonstrated that more females (138.3)

were discharged from the hospital than males (95.9) (DeFrances, Cullen, & Kozak, 2007). Females (79.2%) were clearly more likely than males (20.8%) to have an autoimmune disease in this study (Table 1) and percentages for gender and autoimmune diagnoses were consistent with other reports (Ahmed et al., 1999; NIH, 2005; Rose, 2007; Siegel et al., 2008). Basic processes of both innate and the adaptive immune responses are known to differ by gender. Women have an increased strength in immune responses, and a higher antibody production (Fairweather & Rose, 2004). In studies involving animal models, estrogen significantly increased proinflammatory cytokines, and may be a factor in the expression of autoimmune diseases after an infection (Fairweather & Rose). In contrast, hormones may also have a protective effect in the manifestation of some autoimmune diseases. There has been mixed evidence on four estrogenic factors in RA etiology. Oral contraceptives and hormonal replacement therapy have been inconclusive in regard to risk of RA. There is slight evidence of increased risk of RA in women with a live birth history, and RA is less frequent in women who breast feed (CDC, 2009b).

Table 6 specifically addressed the calculations for categorical demographic variables by gender. A surprising finding was that a higher proportion of Caucasian males had an autoimmune diagnosis than Caucasian females. In comparison, a higher proportion of African-American females had an autoimmune diagnosis than African-American males. Nationally, among patients with SLE, death rates and severity of disease were highest among African-American women aged 45 to 64 years of age (CDC, 2009c).

Table 12 displayed the proportional calculations for autoimmune diagnoses by gender. Although females accounted for a higher number of diagnoses among most of the autoimmune diseases, the following diseases had a higher proportion of male patients (>3%): ITP, Crohn's disease, and Ig A nephropathy. In literature, ITP has a higher incidence in women than men (Ando et al., 2003, Fujimura, 2005; Medline Plus, 2010). In a study analyzing the burden of inflammatory bowel disease between 1998 to 2005, more females (59.7%) had Crohn's disease and more females had Ulcerative colitis (54%) than males (Cannon, Kaiser, Ault, & Etzioni, 2009). In contrast and in support of the findings of this study, the National Institute of Diabetes and Digestive and Kidney Diseases (2008) wrote that more males than females have Ig A nephropathy.

The greatest significance by gender was demonstrated for SLE diagnosis, with a significantly greater percentage of women diagnosed with the disease. Nationally, women have five times the risk of mortality related to SLE than men (CDC, 2009c). There was no evidence in this study that gender was related to a possibly related SA infection diagnosis (Table 17). Osteomyelitis was the single significant relationship, but the proportional percentage differences by gender were negligible.

Ethnicity. According to the United States Census 2000 profile for the Dallas Fort Worth area in the state of Texas, the percentage of Caucasians (69.5%) was higher when compared to African-Americans (13.8%). According to the Office of Minority Health (OMH) (2009), African-Americans (13.5%) are the second largest ethnic group following Hispanics (15%). African-Americans hospitalized with at least one autoimmune disease in this study (19.8%) were higher than the national demographic (Table 1). Caucasian

patients (69.5%) in this study were consistent with population demographics of the time period, in contrast with the Hispanic patients (8.4%) who numbered less than national demographic percentages (15 %). Texas ranks second in the nation for resident Hispanics (OMH, 2009).

Table 7 presented the categorical variables by ethnicity. The Office of Minority Health (2009) documented that fewer African-Americans (49%) have employer sponsored insurance than Caucasians (66%). This finding was supported in this study, with a higher percentage of Caucasians (30.3%) on PPO/POS insurance than African-American (23.0%) or other ethnic group (26.6%) patients. Nationally, nearly one-fourth (23.8%) of African-Americans have public health insurance compared to Caucasians (9.0%) (OMH, 2009). In this study, Caucasian (3.3%) patients were much less likely to have Medicaid when compared with African-American (13.2%) and other ethnic group (12.6%).

Table 13 addressed the relationship of autoimmune diagnoses by ethnicity. African-American patients were more likely to be diagnosed with SLE, while Caucasian patients were more likely to be diagnosed with RA and MS. The CDC (2009c) reported that African-Americans are more affected by SLE than Caucasians and potentially Hispanics, Asians, and Native Americans. Lupus nephritis is a common and serious complication of SLE that requires hospital intervention and African-Americans, Afro-Caribbean, and Hispanics have a higher risk for this complication (Burling et al., 2007). MS commonly has caused neurological disability in young white populations. The island of Sardinia has established a high incidence of MS with early onset and severe

progressive disability validating genetic predisposition (Cocco et al., 2009). Lastly, a higher proportion of ITP was evident in other ethnic groups when compared with Caucasians and African-Americans.

Insurance type. The 2005 NHDS presented the number of discharges from short-stay hospitals by expected principal payment sources (DeFrances et al., 2007). From this document, the percentages were calculated by payment source from total discharges in the thousands. In the 2005 NHDS, Medicare (39.8%) was the highest payment source for discharges compared with Blue Cross Blue Shield (BCBS) (18.5%), Medicaid (16.8%), HMO/PPO (13.8%), Self-pay (4.3%), Workers' Compensation (2.1%) and other payment or no charge (2.3%) (DeFrances et al.). The percentages of insurance type varied in this sample of patients with autoimmune diagnoses (Table 1). Medicare Part A (42.8%) was similar to the national percentage of 2005. A striking difference was the percentage of Medicaid patients in the study (6.3%) was lower than the national percentage, but the percentage of self-pay patients (6.2%) in this study was higher than the NHDS study. Given the mean age of patients in the study was less than required for Medicare eligibility, that finding is important. Private insurance providers varied by type in this study of north Texas patients. PPO/POS patients (16.1%) and HMO (14.8%) were higher than BCBS patients (4.3%) in this study. Regional insurance types may account for these differences.

Table 8 illustrates the calculations of demographic variables by insurance type. The greatest gender difference by insurance type occurred on Medicaid. Females were significantly more likely than males to have Medicaid as their payment source in this

study. In contrast, a higher percentage of males were self-pay compared to females (Table 6). African–American patients claimed Medicaid as their insurance type more frequently than both Caucasians and other ethnic groups. In contrast, Caucasians were billed as self-pay more so than other ethnic groups and African-Americans. These findings are in contrast to findings from the CDC (2009c) that African-Americans (19.5%) were more likely to be uninsured compared to Caucasians (10.4%).

According to the 2005 NHDS, the average length of stay by all insurance types was 4.8 days. In this survey, Medicare patients averaged 5.6 days, Medicaid 4.7days, HMO/PPO averaged 3.8 days, and self-pay patients averaged 5.0 days in the hospital (DeFrances et al., 2007). Consistent with this data, the highest percentage of Medicaid patients (36.8%) was discharged after three to five days in the hospital. A higher percentage of PPO/POS and HMO patients had a hospital stay of 1-2 days. The highest percentage of self-pay patients had hospital stays of 3-5 days (37.4%) or 1-2 days (27.5%), and this is congruent with national discharge data of 2005 (DeFrances et al.). Fewer patients with Medicare (20.3%) were charged $7,999 or less when compared to all other forms of coverage. In comparison, a greater percentage of Medicare patients (31.1%) were charged $24,000 or more for the hospital stay in contrast with self-pay (24.5%), PPO/POS (29.3%), HMO (25.6%), and Medicaid (27.9%).

Table 14 shows the percentages of autoimmune diseases by insurance type. SLE patients were more likely to have Medicaid as payment source, suggesting a younger sample not eligible for Medicare coverage. This is in contrast to RA patients, most of whom had Medicare coverage. Incidence investigations using three separate populations

demonstrated that the incidence of RA peaks for men and women after 60 years of age (CDC, 2009c). A greater proportion of patients with Graves' disease used self-pay as a payment source compared to Medicare, Medicaid, PPO/POS, and HMO. There were no notable differences (> 3%) for SA possibly related infections by insurance type, although patients with bacteremia, SSI, osteomyelitis, and SIRS were related significantly to insurance type (Table 19).

Length of stay. The average length of stay in this investigation (6.1 days) was greater than the 2005 NHDS average length of stay for all hospital discharges (4.8 days) (DeFrances et al., 2007). Table 9 presented the percentages for descriptive variables by length of stay. Although both gender and ethnicity demonstrated significant relationships by length of stay, only ethnicity expressed a notable difference (> 3%). More Caucasians were only in the hospital for one to two days compared to 10 or more days stays. Conversely, more African-Americans were hospitalized for 10 or more days compared to shorter stays of one to two days. Insurance type by length of stay revealed that a greater proportion of Medicare patients were hospitalized for ten or more days compared to shorter stays of one to two days.

Percentages for autoimmune diagnoses by length of stay are presented in Table 15. A higher proportion of SLE patients had a hospital stay of ten or more days, while a higher proportion of patients with Hashimoto's thyroiditis had a hospital stay of only one to two days. Table 20 presents the percentages for SA possibly related infection diagnoses by length of stay. The 2005 NHDS lists the average length of stay (6.6 days) for all infectious and parasitic diseases as a first diagnosis (DeFrances et al., 2007). In

this study, patients with bacteremia were more likely to have a hospital stay of ten or more days compared with shorter stays. No other potentially related SA infection diagnosis was related to length of stay.

Total charges. The average total hospital charge in this study was over $24,000. The Agency for Healthcare Research and Quality (AHRQ) (2002) stated that average hospital charges in that year were $17,300. Therefore, the average charges of this sample were higher than the national average in the mid-point of the data collection period (1999 to 2005). Table 10 documented the calculations for descriptive variables by total hospital charges. Gender was inversely related to total charges. In comparison with female patients, a higher proportion of males were charged $24,000 or greater. As mentioned previously, a significantly greater proportion of Medicare patients had higher hospital charges ($16,000 to $23,000 = 46.5%; $24,000 or more = 46.7%). In 2002, Medicare was billed for 34% of all hospital charges (AHRQ, 2002). As discussed in the length of stay section, higher charges are associated with longer hospital stays.

Table 16 presented the percentages for autoimmune diagnoses by total charges. Although there were several significant relationships for autoimmune diagnoses by total charges, most diagnoses had evenly distributed charges among categories. Percentages for SA possibly related infections by total charges were addressed in Table 21. A higher percentage of patients with bacteremia (3.4%) had charges of $24,000 or more compared with lesser charges of $7,999 or less (0.5%). Due to small numbers in samples, no other notable differences were found in total charge categories.

Age. The mean age at discharge of this sample was 56 years of age, with a range of 18 to 109 years (Table 2). According to the 2005 NHDS, there were more discharges in patients who were 65 years of age or older (13,288/numbers in the thousands) compared to patients who were 45 – 64 years old (8,349/numbers in the thousands) (DeFrances et al., 2002). The early onset of many autoimmune diseases may be one explanation for the lower mean age at discharge in this study.

One-way ANOVAs were conducted on patients' age by descriptive variables, and all relationships were significant (Table 11). Female patients were slightly younger than the male patients. Of interest, African-American patients and other ethnic group patients were significantly younger than Caucasian patients. As expected, patients who self-paid and those with Medicaid were significantly younger than patients with PPP/POS, HMO, and Medicare. Additionally, longer hospital stays and higher hospital charges were associated with older patients.

Research is needed to comprehensively identify the categorical, demographic factors of the most vulnerable patients for autoimmune diseases and infections. When these factors are understood, research strategies could progress to the testing of effective strategies and interventions within complex healthcare systems to protect the most vulnerable against complications such as infections. If infections are prevented, the quality of life of patients could be improved, and loss decreased related to time and money spent for hospitalizations.

Discussion

Research Question 1

What are the descriptive characteristics (gender, age, race/ethnicity, autoimmune diagnosis, insurance type, length of hospitalization and total charges) of patients hospitalized with MRSA or SA in North Texas?

Tables 29 to 33 focused on the primary analyses related to the first research question. Table 29 presented the percentage for gender, ethnicity, insurance type, length of stay, and total charges by SA specific infection diagnosis. A higher proportion of males were diagnosed with a SA specific infection. Sacar et al. (2010) found that males (*OR* = 2.000, 95% CI 1.081-3,699, *p* = .027) had a higher risk of MRSA infection. This finding supported the gender differences in immune response, with females having a higher production of antibodies (Fairweather & Rose, 2004). A higher proportion of African-Americans had a SA infection diagnosis, with overall higher percentages of bacteremia, endocarditis, and SIRS (Table 18). In addition, there is evidence that African-Americans have increased disease severity, have increased incidence of complications such as lupus nephritis, and have a higher mortality from SLE (Burling et al., 2007; CDC, 2009c; Crosslin & Wiginton, 2009).

A greater proportion of Medicare patients had a SA specific infection and this finding is supported by national data. The 2005 NHDS revealed that patients 65 years or older had higher rates of hospitalizations counted by discharges (DeFrances et al., 2007). Vulnerable populations such as the elderly and immunocompromised are at increased risk for HA infections such as SA infections (Duffy, 2002). The factors of increased risk of

infection for the elderly are related to age related decline in the immune system and the presence of co morbidities. Other risk factors identified in HA infections were patient acuity level, longer lengths of stay, malnutrition, previous antibiotic usage, and sleep deprivation (Duffy).

In this study, significant differences were found between length of stay and total hospital charges by SA specific infections. A greater proportion of patients who stayed in the hospital ten or more days and had charges of $24,000 or more had a SA specific infection, while a greater proportion of patients who had stays of only one to two days did not have a SA infection diagnosis. Noskin et al. (2005) stated that on average, patients with SA infections had three times the length of stay in the hospital, and three times the total charges than the patients without the SA infection diagnosis.

The epidemiology and predictive factors for HA–MRSA were studied in a tertiary hospital from 2004 to 2006 (Sacar et al., 2010). There were 265 confirmed cases of HA-MRSA infections, showing a significant increase in MRSA diagnoses from 2004 (44.3%) to 2006 (77.3%). Multivariate analysis calculated that prolonged hospitalization (OR = 3.982, 95% CI 2.235-7.094, $p < .001$), mechanical ventilation (OR = 3.052, 95% CI 1.666-5.590, $p < .001$), surgery (OR = 2.032, 95% CI 1.102-3.748, $p = .023$), and male gender (OR = 2.000, 95% CI 1.081-3.699, $p = .027$) increased the odds of HA-MRSA in the tertiary-care hospital (Sacar et al.). An independent t test was conducted to analyze the mean age at discharge by SA specific infection diagnosis (Table 30). The ages of the patients with the diagnosis were similar to those without the infection. However, the

average age of patients with a SA infection ($M = 54.34$, $SD = 16.97$) was younger compared to those without the infection ($M = 56.07$, $SD = 17.82$).

A higher percentage of patients were identified as having both SA specific and a possibly related infection diagnosis (Table 31). The complicated nature of the immune response, the immune dysfunctions related to autoimmunity, and exposure to risk in the hospital are likely factors in this finding. Patients with bacteremia (18.2%) were more likely to have a SA specific diagnosis. Even more importantly, all of the patients with septicemia had a SA specific diagnosis. Bacteremia is a diagnosis that is established with the laboratory finding of bacteria in the blood and septicemia describes an acute illness state in which the presence of bacteria in the blood overwhelms the immune system responses (Avery, 2009). A confounding reality in hospital laboratory services is that only 28% of patients with sepsis have the confirmation of a positive blood culture. Prior use of antibiotics, and issues of sample retrieving or processing may affect the results of blood cultures (Avery). Additionally in this study, a higher proportion of patients had pneumonia with a SA specific diagnosis and SIRS with a SA specific infection. SIRS is the systemic inflammatory response that occurs with trauma or infection. Patients with SIRS have symptoms such as fever, tachycardia, tachypnea, and leukocytosis. SIRS can potentially cause organ failure, as well as, sepsis (Avery, 2009). Patients with septic arthritis or osteomyelitis had a higher proportion of SA infections.

SLE patients had the highest proportional percentage for SA specific infections (Table 32). Multiple studies have demonstrated the increased risk of infection for patients with SLE (Burling et al., 2007; Jeong et al., 2009; Seshan & Jennette, 2009). Between

11-23% of SLE patients will be hospitalized for serious infections and as many as half of SLE patients will develop significant infections during the progression of disease (Jeong et al.). Additionally, a higher proportion of MS patients had a SA specific infection. Currently MS patients are being recruited for a clinical trial in Israel to study infections in selected autoimmune diseases (Achiron & Shoenfeld, 2006). The researchers are investigating the seropositivity for toxoplasmosis, rubella, CMV, HSV-1, HSV-2, EPV, and H. pylori in autoimmune patients (Achiron & Shoenfeld). Although RA patients have been noted to be at high risk for infections (CDC, 2009b), this study revealed that fewer RA patients had a SA specific infection.

A greater proportion of patients with organ dysfunction had a SA specific infection (Table 33). Patients with severe sepsis are known to have organ dysfunction or failure due to hypotension or hypoperfusion to vital organs. Sepsis can progress to septic shock which is a critical disequilibrium in hemodynamic and metabolic physiologic processes characterized by cardiovascular failure (Avery, 2009). The highest significant, proportional percentages for organ dysfunction by SA specific infection were acute renal failure and acute respiratory failure. Multiple organ dysfunction syndrome (MODS) is the dysfunction of at least two body systems as a response to uncontrolled inflammation processes after severe illness or trauma. Sepsis and septic shock are the most common causes (Mc Cance et al., 2010).

The magnitude of the infection rate in the vulnerable population of this study warrants further validation of varied sources of infection rates in hospitalized autoimmune patients and other patients with known immune dysfunction or inadequacies.

The patients with significant co morbidities and a history of infections or other complications should receive the highest standard of care related to infection control upon each entry in the healthcare system. This population should be identified early, and clearly identified to all staff and providers caring for these patients and communicated to patient visitors.

Research Question 2

Which autoimmune diseases resulted in the highest prevalence of MRSA or SA infections (Bacteremia, Septicemia, Pneumonia, Vancomycin-resistant *S. aureus*, Enterocolitis, Endocarditis, Surgical site infection, Osteomyelitis, Septic arthritis, and SIRs)?

Tables 34 to 37 addressed the second research question. Table 34 presented the percentages of autoimmune and organ dysfunction diagnoses by SA specific infection diagnoses. Only the relationship between at least one organ dysfunction and SA specific infections was significant, revealing that a higher proportion of patients with at least one organ dysfunction had a SA specific infection. More significant relationships were exposed for autoimmune diseases and organ dysfunction diagnoses by at least one possibly related SA infection (Table 35). Significantly more SLE patients had at least one related SA infection (36.0%) than had no possibly related infections (22.2%). This exemplifies earlier findings that infections are a high risk complication for SLE patients (Burling et al., 2007; Jeong et al., 2009; Seshan & Jennette, 2009). As infections may precipitate organ failure, patients with a diagnosis for at least one organ dysfunction or a diagnosis for acute renal failure had at least one related SA infection (McCance, 2010). In

general, SLE patients are at high risk for renal complications and infections (CDC, 2009b).

Table 36 presented the percentages of autoimmune diseases and organ dysfunction diagnoses by bacteremia, endocarditis, and surgical site infection. There were two significant relationships with SLE patients. A greater proportion of SLE patients had bacteremia and endocarditis. The prevention of potentially related SA infections would be important in the SLE inpatient population of this study. Chen et al. (2008) studied the survival rates and long term outcomes of 1,442 SLE patients between 2000 and 2005 after an episode of bacteremia. A greater percentage of SLE patients (17%) had one at least one episode of bacteremia compared to the general patient population (9.3%) with that infection diagnosis. Chen et al. wrote that patients with a SLE had a 92% survival rate after five years. In contrast, SLE patients with bacteremia had lower survival rates of 76% at 30 days, and 67% at 360 days. Bacteremia was associated with poor long term outcomes in SLE patients in the six year follow up study (Chen et al.). Additionally, a greater percentage of patients with at least one organ dysfunction had bacteremia and endocarditis, while patients with acute renal failure were more likely to have endocarditis.

Table 37 presented the percentages for autoimmune diseases and organ dysfunctions by osteomyelitis, septic arthritis, and SIRS. A greater percentage of MS patients had SIRS, and the relationship was significant. Infection, trauma, or severe illness can precipitate SIRS (Avery, 2009). Having an SLE diagnosis was also significantly related to a higher incidence of a SIRS diagnosis. Based on these findings,

patients hospitalized with both MS and SLE should be monitored for early signs of SIRS to decrease mortality and further complications. Patients hospitalized with RA demonstrated higher and significantly related percentages of osteomyelitis and septic arthritis. The incidence of septic arthritis is increasing, and treatment is becoming more complicated due to increased immunosuppression in patients and increased microbial resistance of pathogens. RA is a significant risk factor in septic arthritis and osteomyelitis (Ader, Salomon, Perronne, & Bernard, 2004; Mathews, Westin, Jones, Field, & Coakley, 2010). Most frequent causes of death in RA patients were cardiovascular disease (CVD), infections, and lymphoproliferative malignancies (leukemia, multiple myeloma) (CDC, 2009b).

Finally there were four significant relationships of at least one organ dysfunction that were related to SIRS. Substantially higher percentages of patients with at least one organ dysfunction, acute renal failure, respiratory failure, and septic shock also had the SIRS diagnosis. The results related to SIRS were consistent with the definition and patient sequelae related to that complication (McCance et al, 2010). SIRS activates extensive inflammatory processes and proinflammatory mediators, and the systemic inflammation produces multiple organ dysfunction and failure if not addressed quickly. Stephenson et al. (2010) conducted a study of 179 patients to predict outcomes related to SIRS in acute surgical admissions. Patients with SIRS had more surgical interventions, longer hospital stays, and more frequent deaths in this study (Stephenson et al.).

Hypothesis

The following null hypothesis was tested at the .05 level of significance:

Ho1. The covariates (autoimmune disease, gender, age, race/ethnicity, insurance type, length of stay in days, and total charges) in hospitalized patients will be neither predictive nor protective of a diagnosis for MRSA or SA infection (Bacteremia, Septicemia, Pneumonia, Vancomycin-resistant *S. aureus*, Enterocolitis, Endocarditis, Surgical site infection, Osteomyelitis, Septic arthritis and SIRs).

Several covariates were either protective or predictive of a diagnosis of an SA related infection. Table 38 displayed multiple regression analysis predicting SA specific infection diagnosis from demographics, autoimmune diagnoses and organ dysfunction diagnoses. Multiple logistic regression analyses were conducted on the full sample and three random samples with 1,200 patients in each random sample. Half of the random sample was patients with a SA infection, and half of the sample was patients without the infection diagnoses. The following descriptive variables were predictive of a SA specific infection and resulted in increased odds for the diagnosis: being female (1.4 to 1.7 times); patients with Medicare (1.7 to 2.3 times); and lengths of stay of three to five days (2.2 to 2.4 times); six to nine days (4.6 to 7.7 times); and ten or more days (8.3 to 13.0 times). Females had increased odds of an SA specific infection in this logistic regression analysis while analyses related to research question one presented that proportionally more males had a SA specific infection (Table 29). The higher numbers of females in this study likely contributed to this finding. The remaining demographic variables were previously discussed, and validated in literature.

Although descriptive variables had significant relationships with SA infection, certain autoimmune diseases were predictive, as well. MS patients in the full sample had slight increased odds (1.2 times) of a specific SA infection. Patients with Dermatomyositis had increased odds of 1.5 to 4.8 times the risk of SA specific infection in two samples. SA positive blood cultures are the most common in HA bacteremia, and the second most common isolate in CA bacteremia. SA bacteremia can have extravascular origins (cellulitis, ulcers, wounds, osteomyelitis, or pneumonia), intravascular origins, or no apparent origin (Mitchell & Howden, 2005). Several autoimmune diseases were protective of SA specific diagnoses. Patients with Graves' disease (47%), Crohn's disease (17-27%), Sicca syndrome *(28%)*, and juvenile RA (23%) were protective against SA specific diagnoses in at least one sample. Finally, patients with acute respiratory failure had 1.6 to 2.7 times the risk, and were predictive of a SA specific diagnosis. A common cause of MODS is sepsis or septicemia (Mc Cance et al., 2010). The model outcome for the multiple regression analyses was significant (Model (32) = 1202.23, $p < .001$, $R2 = .083$). The low R2 variance (.083) confirmed that the prediction of SA specific infection is complex and varied in the analyses presented in Table 38.

More significant relationships were identified in Table 39 using multiple logistic regressions predicting SA possibly related infection diagnoses from demographics, autoimmune diagnoses, and organ dysfunction diagnoses. Females were identified to be at increased risk (1.2 to 1.8 times) for a related SA infection. African-Americans were at increased odds (1.2 to 1.4 times) for having a related SA infection in the full sample and

one random sample. This finding related to African-Americans differs from SA specific infections analyses. Medicare patients were again at increased risk for a SA related infection (2.1 times). Patients who stayed in the hospital for longer stays were at increased risk (4.1 to 7.2 times) for SA related infection. Additionally, higher charges are predictive of a SA related infection in this sample. Differing from SA specific infections, SLE patients were at significant risk (1.4 to 2.2 times) of having a SA related infection. SS patients were also at increased odds (1.3 to 2.6 times) of having a SA infection. In these analyses of Table 39, Graves' disease (48%), Raynaud's disease (50%), Crohn's disease (34%), and Dermatomyositis (53%) were protective of acquiring a SA related infection diagnosis. Both acute renal failure (1.4 to 3.1 times) and acute respiratory failure (1.4 to 2.6 times) were predictive of a SA related infection diagnosis. The model analyses for SA related infections were significant (Model (33) = 1826.14, $p < .001$, R2 = .112), with the low R2 variance. Again, the prevalence of SA related infections is related to multiple factors which include but are not limited to high patient acuity, invasive procedures, immunosuppression, corticosteroids, liver disease, antibiotic therapy, prolonged hospitalizations, and recent surgery (Mitchell & Howden, 2005).

Increasing the scope of analyses in Table 39 to the SA-related infections resulted in increased number of factors that were predictive of infection. In addition to factors identified related to SA specific infections, systemic autoimmune diseases, SLE and SS, and organ dysfunction had higher odds of infection in the larger inclusion of possibly related types of SA infection. Given the varied factors that increase the risk for SA infection, these findings suggest the need for the development and testing of additional

protection strategies in hospital settings for autoimmune patients and other high risk groups.

Limitations

The large secondary data used in this study consisted of hospital discharge information captured by ICD-9-CM coding. In this retrospective study, the data were subject to human input errors that were complicated by barriers to accurately code SA-related infections (Avery, 2009; Schaefer, 2010). These errors were at least partially compensated by the total sample size. However, in cells with small sample numbers, the risk for errors was greater. All patients in the sample had at least one autoimmune diagnosis. Since discharge data were obtained for this study, the origin (HA or CA) of the SA infections could not be identified. The prevalence, predictors, and protectors of SA specific and SA related infections would likely differ in other selected patient populations or the general patient population.

Recommendations for Future Research

The estimates of the impact of autoimmune diseases, and the present issues related to rising infection rates in all healthcare settings warrant continued investigation in these areas. The retrospective design could be improved in a future study. A future prospective, longitudinal design would further validate the findings of this study, and provide the sample size needed for generalizability of results. In a prospective study organizing various hospital systems, standardized training and recurrent validation of staff for the accurate identification of ICD-9-CM coding for SA-related infections would be required to decrease input errors. Randomized medical record review and laboratory

confirmation of SA infection diagnoses could ensure the data were accurately assembled. In a prospective design, the timing of infection onset could differentiate community acquired infections and hospital acquired infections which are useful information for healthcare facilities, and policy planning. The inclusion of all pathogens that are common in acute healthcare facilities and identification of all patient groups at high-risk for infections would be other potential studies that would offer valuable insight.

The high SA infection prevalence identified in this study provide further rationale for the importance of current efforts in healthcare research to design organizational, staff, and patient education and interventions to provide high-quality and safe care for patients (Pronovost et al., 2006). Despite educational and on-the-job training in infection control practices, knowledge deficits exist among healthcare workers at all levels (Burkitt et al., 2010). Inadequate healthcare staff adherence to infection control guidelines was identified. Communication failures among healthcare providers and staff have been identified as leading causes of poor quality care. Provonost et al. asserted that systemic changes in organizational culture are needed to implement education and effective, evidence-based interventions to improve patient care and increase safety standards. Multidisciplinary teams from acute and community healthcare organizations must collaborate on processes and culture changes needed to limit infection-related complications in vulnerable patients. Health educators are well-equipped in educational strategies, and can facillitate communication of expected infection control practices with patients, families, and even unlicensed healthcare assistive personnel. The roles of the

health educator can potentially provide valuable expertise in the progress of addressing these persistent and critical issues.

Practical, clearly communicated strategies are required to prevent infection in high-risk patient groups. Whereas all hospitalized patients are cared for with standardized universal precautions (CDC, 2009d), the findings of this study suggest that additional accountability or documentation by healthcare personnel of isolation or infection control practices are needed for vulnerable patients such as those with autoimmune diseases. This assertion has precedent in the development of prevention measures called Protective Environment designed to protect the allogenic hematiopoietic stem cell transplant patients, an extremely high-risk group, from opportunistic infections (CDC, 2009d). Given the enormous cost of healthcare stays related to infections identified in this study, new strategies and guidelines could be studied for effectiveness and adherence of implementation for autoimmune and other patients at risk.

Implications for Health Educators

The Healthy People 2020 objectives that are under consideration include the reduction of HA infections for national focus (USDHHS, 2010). The National Commission for Health Education Credentialing (NCHEC) (2010) has published responsibilities and competencies for health educators, and these delineations are important for this and further investigative studies for patients with autoimmune diseases, as well as the study of infection rates in hospitals. The first responsibility of health educators is the assessment of individual and community needs for health education (NCHEC). The results of this study have important implications for patients with

autoimmune diseases and have raised awareness of the potential risk for infection when these patients are faced with acute or critical care needs. The health educator is poised to organize and facilitate the ongoing data collection needed to assess continued risk of these patients and other high-risk groups in acute and community health care settings. Health educators can initiate dialogue in local healthcare organizations to encourage voluntary submission of infection rates and other quality indicators to National Nosocomial Infections Surveillance (NNIS) which is coordinated by the CDC (NNIS, 2004). In addition, health educators can collaborate with nursing professionals to provide infection information to the American Nurses Association (ANA) National Database of Nursing Quality Indicators (NDNQI) (ANA, 2007). The reporting of infection rates within healthcare facilities increases the accountability of those who have the greatest impact related to invasive risk and infection rates.

The third competency within the first responsibility is to distinguish between behaviors that promote or compromise health (NCHEC). Health educators can implement these competencies on both the levels of the individual autoimmune patients, and the group of vulnerable patients who are admitted to acute care or long-term facilities. Health educators can work with individual patients or groups to identify behaviors that promote quality of life in those living with chronic illness. Health educators can also play an important role in educating patients and families regarding the standards of care to expect that prevent infection while hospitalized. Furthermore, health educators can participate in multidisciplinary collaboration to identify barriers to infection control for staff in

healthcare settings. Identifying communication breakdown and effective methods of communication will be important contributions of health educators.

The second and third responsibilities of health educators are related to planning and implementing education strategies, interventions, and programs (NCHEC, 2010). The identification of high risk populations, such as autoimmune patients, is important in planning for educational needs. The identification of technologies, strategies, and media needed to communicate with and educate patients at high-risk for infection are important health educator responsibilities (NCHEC). The competencies of a health educator are also needed in acute care facilities. Educational needs of patients with chronic illnesses, such as autoimmune diseases, change as the disease progresses; and complications, such as infections, increase risk for further hospitalizations. The health educator can be a vital member of the acute care team to educate patients with changing or progressing conditions, to maximize the current quality of life and contribute to the prevention of further hospitalizations. As patients transition from hospitals to communities, health educators can also provide communication for successful transition. As new questions and information needs arise with new living arrangements, health educators have the knowledge and skills to address those needs. Finally, health educators can assist patients at home to connect with community support resources.

The fourth responsibility of a health educator is to conduct evaluation and research related to health education. Health educators with advanced degrees are positioned to be leaders in researching the effectiveness of health education strategies, including the impact these strategies have on the quality of life of patients and individuals

facing acute and chronic illnesses. For example, research of the effectiveness of an intermediate level of isolation precautions for immune compromised patients would be a valuable contribution to infection prevention in hospital settings. Health educators are prepared to continue research investigation of selected population groups to understand health-related needs. Educated in both qualitative and quantitative evaluation methodology, health educators can provide a solid foundation for assisting multidisciplinary collaboration in infection control quality improvement strategies.

The fifth responsibility for health educators is the administration of health education strategies, interventions, and programs (NCHEC, 2010). Health educators are prepared to assist in strategic planning and organizational leadership for facilities committed to the health of patients. An important contribution in this area would be the coordination and development of volunteer opportunities. Encouraging and facilitating support groups for local autoimmune disease patients would be an important step.

The sixth and seventh responsibilities are related to communication, advocacy, and serving as a health education resource (NCHEC, 2010). Health educators must maintain a comprehensive knowledge of the most current health-related resources. An important competency is the evaluation of the implications of healthcare providers' messages to consumers and patients (NCHEC). Health educators are prepared to address health literacy issues of patients with chronic diseases. For example, the improvement of health literacy of autoimmune patients can facilitate the location of appropriate providers and services, and knowledge to implement important preventative care (USDHHS, 2010b). Health educators are prepared to assess social, cultural, demographic, and

political factors that influence health of patients with autoimmune diseases (NCHEC). Health educators can participate in legislative advocacy by lobbying for more research dollars for autoimmune diseases and improved infection control. Therefore, health educators have the potential to fill a vital role in the care of patients with autoimmune disease and SA-related infections.

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