Journal of Health, Medicine and Nursing
ISSN 2422-8419 An International Peer-reviewed Journal
Vol.31, 2016

Epidemiology of Autoimmune Diseases among Attendants of General Hospitals in Aseer region

Hassan Al-Musa[1] Faten M. Rabie[2] Hanan H. Al-Malki[3] Shahad A. Barkout[3] Amani A. Bawazeer[3] Aisha A. Al-Qarni[3]
1.Family and community department – college of Medicine- King Khalid University
2.Public health and community medicine department- faculty of Medicine - Assiut University
3.Medical Intern, College of Medicine, King Khalid University

Abstract
It has long been recognized that environmental influences play an important role in the risk of developing Autoimmune disease. Defining specific pathogenic environmental mediators that may trigger the development or progression of autoimmune disease remains a focus of increasing investigative effort. Factors promoting disease may not be identical to factors that influence the severity or progression of the disorder. The cause(s) of autoimmune disorders remain largely unknown. Considerable evidence supports a role for environmental agents in inducing autoimmune disorders. **OBJECTIVES:** The study aims to explore the risk factors of autoimmune diseases among attendants of general hospitals in Aseer Region. **Methods:** case control study design was carried out included 70 patients with multiple types of auto immune diseases attending general hospitals and primary health care centers in Abha city. They were clinically diagnosed as having autoimmune diseases. and 140 clinically free subjects , age and sex matched were included as controls. **RESULTS:** The present study included 70 autoimmune disease patients predominantly females (88.4%). Their mean age was 42.7 ± 12.1 years and disease duration was 11.2 ± 7.2 years. The mean age of the control group was 47.1 ± 13.6 years with no significant differences in the demographic data between the patients and control ($p > 0.05$). This study found no significant differences between cases with autoimmune diseases and sociodemographic characteristics**.** **Conclusion :**There is multiple determinants and risk factors affecting the occurrence of autoimmune diseases. Familial history, psychological stresses, hormonal supplementation, using hair dyes, smoking and recent vaccination were significant factors associated with autoimmune diseases.
Keywords: Epidemiology, autoimmune, diseases, Aseer region

1. Introduction

Autoimmune diseases are the third leading cause of morbidity and mortality in the industrialized world, surpassed only by cancer and heart disease. [1]
Autoimmunity is an immune response directed against an antigen within the body of the host. It usually involves both T-cell and B-cell responses. It only requires that the immune response be directed to a self-antigen.[2]

When a person is diagnosed with AI disease, they are at high risk of developing other autoimmune diseases during their lifetime. It is very rare that only one tissue type is targeted by the immune system. People with AI disease, they may have multiple types of tissue being targeted that have not yet been identified. For example, people with thyroid autoimmune disease have over a 50% chance of being affected by another autoimmune disease.[3]

The estimated incidence (number of newly diagnosed cases per year) ranged from less than 1 per 100000 person-years (e.g. chronic active hepatitis, myasthenia gravis, primary biliary cirrhosis, sc1erodenna) to more ,than 20 per 100 000 personyears (adult-onset rheumatoid arthritis, thyroiditis). The prevalence (number of people with the disease at a specific time) ranged from less than 5 per 100000 (e.g. chronic active hepatitis, uveitis, Wegener granulomatosis) to more than 500 per 100000 (Grave's disease, rheumatoid arthritis, thyroiditis).(4) Almost all autoimmune diseases disproportionately affect warnen (Table 1). In same diseases (e.g. thyroiditis, sc1erodenna, systemic lupus erythematosus, Sjögren disease), 85% or more of patients are fema1e.The disparity by sex is smaller in other diseases (e.g. 60-75% female patients in multiple sc1erosis, rheumatoid arthritis). A relatively equal risk between males and females is seen in same childhood onset autoimmune diseases (e.g. type 1 diabetes) bur in other diseases (e.g. juvenile rheumatoid arthritis) a female predominance is seen. The recent studies of adult-onset diabetes indicate a higher risk among men compared with women (5) There are notable differences in the age distribution among autoimmune diseases. Although most diseases can occur at any age, there are c1ear peaks of onset. The mean age of two childhood onset diseases, juvenile rheumatoid arthritis and type 1 diabetes [6] is approximately 8-10 years. Recent population based studies of systernic lupus erythematosus and of sc1erodenna [7] provide evidence that these diseases may occur later than reported in earlier studies in more selected populations. ether diseases that generally occur between ages 30 and 50 years inc1ude myasthenia gravis , multiple sc1erosis, and Grave disease [8]. Most autoimmune diseases occur significantly more frequently in women than men. [9] Cigarette smoke was shown to augment the production of numerous pro-inflammatory cytokines such as TNF-α, IL-1, IL-6, IL-8 GM-CSF and to decrease

the levels of anti-inflammatory cytokines such as IL-10. While it is better evident how cigarette smoke evokes airway diseases more mechanisms are being revealed linking this social hazard to autoimmune disorders, for instance via the production of antibodies recognizing citrullinated proteins in rheumatoid arthritis or by the elevation of anti-dsDNA titers in systemic lupus erythematosus. [10] Vitamin D has effects on innate and acquired immune systems, and vitamin D receptor polymorphisms have been associated with various autoimmune diseases. [11] Systemic lupus erythematosus (SLE) tends to present earlier and is often associated with worse outcomes in people of Hispanic, Asian or African ancestry than in Caucasians. This may be related in part to overall poor SES including less structured families, fewer years of formal education, occupational status, household income, higher poverty, and inadequate health insurance. [12], [13], [14]

Aging of the immune system, or immunosenescence, is characterized by changes in T cell subsets, cellular and molecular level alterations and thymic atrophy, resulting in a decline of T and B cell function. These alterations have been shown to be accompanied by a loss of ability to recognize “self” and “foreign” antigens. [15] Type 1 diabetes , rheumatoid arthritis , and

celiac disease are common autoimmune diseases , each affecting ∼1% of the general population. The manifestation and progression of AIDs depend on a combination of multiple genetic and environmental factors, yet the co-occurrence of these three different autoimmune diseases in families, or even within single patients, has been reported frequently.(16, 17)

Drug-induced autoimmunity is an idiosyncratic, non-IgE immune related drug reaction, The prototype disease is drug-induced lupus and the typical drug for drug-induced lupus is minocycline. DNA hypomethylation may occur with hydralazine, which leads to increased transcription, increased LFA-1, the generation of autoreactive T cells and a breakdown in peripheral tolerance. [18]

OBJECTIVES

The study aims to explore the risk factors of autoimmune diseases among attendants of general hospitals in Aseer Region.

PATIENTS AND METHODS

This study included 70 patients with multiple types of auto immune diseases attending general hospitals and primary health care centers in Abha city. They were clinically diagnosed as having autoimmune diseases. and 140 clinically free subjects , age and sex matched were included as controls.

The data of the patients and controls were obtained with a prepared and structured questionnaire through personal interviews with the patients after an informed consent was signed.The questionnaire containing questions on demographic data (age, gender, formal education level, and work status) was completed by all subjects and was collected upon enrollment.

Data including. age at onset, Sex, postnatal follow up, pregnancy history , the duration of the disease, and the personal and familial medical history of autoimmune thyroid diseases, rheumatoid arthritis, type 1 diabetes mellitus, psoriasis, multiple sclerosis , addison’s disease, systemic lupus erythematosis was collected. Current medication history was also collected. The research protocol was approved by local ethics committee of King Khalid University

The collected data were coded and analyzed using the Statistical Package for the Social Sciences version 20 (SPSS,20). Frequencies and percentages were computed to present the categorical response variables like sex, antenatal status, age, parity, working status, inter pregnancy interval and anemia. Univariate analysis (chi-square) was applied to compare the categorical response variables between case and control groups. The relative risks for factors included in the univariate analysis were estimated by odds ratio (OR) and the 95% confidence interval (CI) calculated. A p-value < 0.05 was considered to be statistically significant. Variables significant at the 5% nominal level were considered for multivariate analysis by logistic regression.

RESULTS

The present study included 70 autoimmune disease patients predominantly females (88.4%). Their mean age was 42.7 ± 12.1 years and disease duration was 11.2 ± 7.2 years. The mean age of the control group was 47.1 ± 13.6 years with no significant differences in the demographic data between the patients and control ($p > 0.05$).

Table 1: The socio-demographic characteristics of the studied population

Variable	Patients (70) %	Controls (140) %	Odds ratio	95% CI	*P*
Education: • Illiterate • Primary • preperatory • Secondary • University	 24.3 12.2 13.7 18.3 31.5	 12.7 8.4 18.6 23.3 37.0	 1 9. 12 6.42 3.09 2.66	 4.19—8.39 3.22—16.25 3.30—10.65 1.71—5.64 1.10—6.59	0.095
Marital status: • Single • Married • Widow • Divorced	 26.5 64.8 5.9 2.8	 23.5 69.2 5.2 2.1	 1 5.42 3. 41 1.62	 2.10—11.19 2.49 – 12.53 3.53 – 10.65 3.45- 12.67	0. 627
Income: • Less than 5000 SR • 5000- 10000 SR • More than 10000 SR	 80.8 6.3 12.9	 97.4 1.9 0.7	 1 4.04 21.97	 0.89—1.93 2.64- 6.71	0.371

Table 2: Comparison of presence of risk factors among patients and controls

Recent vaccination • No • Yes	 95.7 4.3	 99.1 0.9	 1 4.76	 2.10–11.19	 0.0001
Family history: • No • First degree • Second degree • Third degree	 77.5 14.0 6.4 2.1	 94.6 2.5 2 0.9	 1 6.42 3.09 2.66	 3.30–10.65 1.71–5.64 1.10–6.59	 0.0001 0.0001 0.026
Smoking Status: • Non smoker • Ex-smoker • Current smoker	 90.6 6.3 3.1	 95.9 1.3 2.8	 1 7.09 27.76	 3.22–16.25 6.35-170.38	 0.0001 0.0001
Phycological stress: • No • Yes	 74.2 25.8	 94.5 5.4	 1 5.92	 4.19–8.39	 0.0001
Repeated infections: • No • Yes	 74.2 25.8	 94.5 1 5.4	 1 5.62	 4.19—8.39	 0.0001
Hormonal exposure: • No • Yes	 84.3 15.7	 96.1 3.9	 1 6.42	 1.020—6.677	 0.045
Hair dyes: • No • Yes	 62.7 34.3	 78.4 21.6	 1 7.9	 3.45-8.78	 0.021

Discussion

This study found no significant differences between cases with autoimmune diseases and socio demographic characteristics as level of education, marital status and income . P. value was (0.095, 0. 627 and 0.371) respectively.

A study carried out by Lisa etal , 2011 found that High levels of education (i.e., university level) were associated with an increased risk of autoimmune diabetes compared with a primary-school education (19). Other studies also found that Cases of autoimmune diabetes with high levels of education were more often treated with insulin, had longer duration of diabetes and lower levels of C-peptide, and tended to have higher levels of anti-GAD compared with those with low education.

Reduced risk of type 2 diabetes in subjects with high socioeconomic position reported in this and previous studies (22,23)

As regard marital status_patients who were not married or living together were also more likely to develop autoimmune diseases as lupus nephritis (24).

This research revealed that there is a high significant difference between cases and controls as regard the recent history of vaccination (P: 0.0001). these results were in agree with a study found that Vaccines, in several reports were found to be temporally followed by a new onset of autoimmune diseases. The same mechanisms that act in infectious invasion of the host, apply equally to the host response to vaccination. It has been accepted for diphtheria and tetanus toxoid, polio and measles vaccines and GBS. Also this theory has been accepted for MMR vaccination and development of autoimmune thrombocytopenia, MS has been associated with HBV vaccination (25). Vaccination against hepatitis B has been noted to predate the diagnosis of SLE in some instances (26)

This study shows that there is highly significant difference between cases and controls as regard the familial history with high odd ratio for first degree relatives (P: 0.0001, OR: 6.42). there may be "autoimmunity genes" that increase the risk for development of autoimmune disorders in families. Autoimmune disorders may result from multiple interactions of genes and environmental factors. Previous twin studies have reported significantly higher concordance rates of 24 to 50% in autoimmune diseases such as rheumatoid arthritis (RA) and SLE among monozygotic twins. However, recent population-based twin studies in RA detect at most a 12 to 15% concordance rate among monozygotic twins, though are criticized for their lack of validated classification criteria for disease confirmation (27).

As regard cigarette smoking , our study revealed a high significant difference between cases of autoimmune diseases and controls with high odd for current smokers (P: 0.0001, OR: 27.76)

Cigarette smoking was associated with an increased risk of developing RA. Two US-based studies report no association between smoking and the onset of SLE (28,29)

while three case control studies from Japan, the United Kingdom, and Sweden detected statistically significant increased risks of developing SLE among current smokers (30,31,32).

It has previously been observed that stress from major life events may contribute to the onset of RA. The recent case-control study of RA provides several new insights broadening the scope of psychosocial stress that may contribute to the onset of RA. In women, "matrimonial quarrels" during the 5-year period preceding the RA symptoms and the 5 years preceding the diagnosis of RA were significantly associated with the onset of RA compared with controls. In men "problems at work" preceding the onset of symptoms and "economic problems" within 5 years of diagnosis of RA were also associated with the onset of RA. Disparate social environmental factors and medical status have been associated with the onset of autoimmune disorders such as type I diabetes. Psychological mechanisms are directly linked by hormonal and nervous system signals, influencing the need for insulin. Stress has also been shown to modulate immune responses (33). This was in agreement of current study which revealed a high significant differences between cases and controls regarding stresses (P: 0.0001 , OR: 5.92).

Infection as a possible trigger for autoimmune disorders has long been proposed.[36] Viral infections have received particular attention in SLE studies, with findings of virus-like inclusions in renal biopsy tissue. Previous studies have noted associations of SLE with history of herpes zoster[(26,31). Urinary tract infections and rubella were found to be associated with decreased risk and pneumonia with an increased risk of RA in women, but no type of infection was associated with the onset of RA in men (31). Our research showed that there was significant differences between cases of autoimmune diseases and controls (P: 0.0001, OR: 5.62).

Studies evaluating a posible association between the use of oral contraceptives and the onset of SLE(34) were negative; one study reported only a weak association (35). A variety of hormonal factors have been associated with severity and progression of SLE but few associations have been observed with the onset of SLE. However, a strong association has been noted in observational studies between the use of hormone replacement therapy and the onset of SLE (36,37).

The use of permanent hair dyes in women was associated with a borderline increase in the risk of developing SLE, with higher risk among those with a longer duration of dye use. Although one previous study reported a strong association between the use of hair dyes and connective tissue disease, other studies that have evaluated the association of this exposure specifically with the onset of SLE have found no association.(38,39).

Conclusion

There is multiple determinants and risk factors affecting the occurrence of autoimmune diseases.Familial history, psychological stresses, hormonal supplementation, using hair dyes, smoking and recent vaccination were significant factors associated with autoimmune diseases. Other factors as the level of education, marital status and income showed non significant association with autoimmune diseases.

Referances

1- Jacobson DL, Gange SJ, Rose NR, Graham NM. Epidemiology and estimated population burden of selected autoimmune diseases in the United States. Clin. Immunopathol. 2007;84:223–43
2- LlväsK, Husebye ES. High prevalence and increasing incidence of Addison's disease in Norway. Clin Endocrinol (Oxf) 2002;56:787 -91.
3- Kyvik KO, Nystrom L, Gorns F, et al. Ineidence of type 1 diabetes in young adults across Europe-an EU funded multicentre study (!DA). Diabetologia 2001;44(suppl. I):A75
4- Nicoletti A, Lo Bartolo ML, Lo Fermo S, et al. Prevalence and incidence of multiple sclerosis in Cata- Dia, Sicily. Neurology 2001;56:62-6.
5- Ostrauskas K, ZalinkeviCius R, Norkus A. Incidence of type 1 diabetes mellitus over eight consecutive years arnong 15-39 year aged Lithuanian population. Diabetologia 2001;44(suppl. 1):A96
6- Walsh SI, Rau LM. Autoimmune diseases: a leading cause of death arnong young and middle-aged warnen in the United States. Am J Public Health 2000;90:1463-6
7- Pillemer SR, Matteson EL, Jacobsson LTH, et al. Incideuce of physieian-diagnosed primary Sjögren syndrome in residents of Olmsted County, Minnesota. Mayo Clin Proc 2001;76:593-9.
8- Watts RA, Lane SE, Bentharn G, Scott DGI. Epidemiology of systemic vasculitis: a ten-year study in the United Kingdom. Arthritis Rheum 2000;43:414-9.
9- E. Sanchez, A. Rassmusen, L. Riba, E. Acevedo, J.A. Kelly, C.D. Langefeld, **et al.** Impact of the Amerindian genetic ancestry on the clinical and socio-demographic expression of systemic lupus erythematosus in a European- Amerindian admixed population Arthritis Rheum, 64 (2012), pp. 3687–3694
10- K.L. Demas, K.H. Costenbader Disparities in lupus care and outcomes Curr Opin Rheumatol, 21 (2009), pp. 102–109
11- Martin A. Kriegel, MD, PhD ,JoAnn E. Manson, MD, DrPH, Karen H. Costenbader, MD, MPH Seminars in Arthritis and Rheumatism , Volume 40, Issue 6, June 2011, Pages 512–531.e8
12- M. Fernández, G.S. Alarcón, J. Calvo-Alén, R. Andrade, G. McGwin, L.M. Vilá, **et al.** A multiethnic, multicenter cohort of patients with systemic lupus erythematosus (SLE) as a model for the study of ethnic disparities in SLE Arthritis Rheum, 57 (2007), pp. 576–584
13- K.L. Demas, K.H. Costenbade. Disparities in lupus care and outcomes Curr Opin Rheumatol, 21 (2009), pp. 102–109
14- M. Jolly, R. a Mikolaitis, N. Shakoor, L.F. Fogg, J. a Block Education, zip code-based annualized household income, and health outcomes in patients with systemic lupus erythematosus , J Rheumatol, 37 (2010), pp. 1150–1157
15- Martina Prelog, Autoimmunity Reviews, Volume 5, Issue 2, February 2006, Pages 136–139
16- - JP Lin, JM Cash, SZ Doyle, S Peden, K Kanik, CI Amos, SJ Bale, RL Wilder, Familial clustering of rheumatoid arthritis with other autoimmune diseases Hum Genet, 103 (2008), pp. 475–482
17- L Levin, Y Tomer, The etiology of autoimmune diabetes and thyroiditis: evidence for common genetic susceptibility, Autoimmun Rev, 2 (2003), pp. 377–386
18- - KF Tait, T Marshall, J Berman, J Carr-Smith, B Rowe, JA Todd, SC Bain, AH Barnett, SC Gough Clustering of autoimmune disease in parents of siblings from the Type 1 diabetes Warren repository Diabet Med, 21 (2004), pp. 358–362
19- . Lisa Olsson, MSC,[1] Anders Ahlbom, PHD,[1] Valdemar Grill, MD, PHD,[2,3] Kristian Midthjell, MD, PHD,[4] and Sofia Carlsson, PHD[1]High Levels of Education Are Associated With an Increased Risk of Latent Autoimmune Diabetes in Adults, Diabetes Care. 2011 Jan; 34(1): 102–107.
20- Kumari M, Head J, Marmot M.: Prospective study of social and other risk factors for incidence of type 2 diabetes in the Whitehall II Study. Arch Intern Med 2004;164:1873–1880
21- Lidfeldt J, Li TY, Hu FB, Manson JE, Kawachi I.: A prospective study of childhood and adult socioeconomic status and incidence of type 2 diabetes in women. Am J Epidemiol 2007;165:882–889
22- Maty SC, Everson-Rose SA, Haan MN, Raghunathan TE, Kaplan GA.: Education, income, occupation, and the 34-year incidence (1965–99) of type 2 diabetes in the Alameda County Study. Int J Epidemiol2005;34:1274–1281 [PMC free article] [PubMed]
23- Agardh EE, Ahlbom A, Andersson T, Efendic S, Grill V, Hallqvist J, Östenson CG.: Explanations of socioeconomic differences in excess risk of type 2 diabetes in Swedish men and women. Diabetes Care2004;27:716–721
24- Holmen J, Midthjell K, Krüger Ø, Langhammer A, Holmen T, Bratberg G, Vatten L, Lund-Larsen P.:The Nord-Trøndelag Health Study 1995–97 (HUNT2): objectives, contents, methods and participation.Norsk Epidemiologi 2003;13:19–32
25- . Molina V[1], Shoenfeld Y Infection, vaccines and other environmental triggers of autoimmunity. Autoimmunity. 2005 May;38(3):235-45.
26- Stauffer Y, et al.: Interferon-endogenous super antigen: a model linking environment and autoimmunity.

Immunity. 2001, 15:591-601.
27- Svendsen AJ, Holm NV, Kyvik K, et al.: Relative importance of genetic effects in rheumatoid arthritis: historical cohort study of Danish nationwide twin population. BMJ 2002, 324(7332): 264-266.
28- Olsson ÅR, Skogh T, Wingren G: Comorbidity and lifestyle, reproductive factors, and environmental exposures associated with rheumatoid arthritis. Ann Rheum Dis 2001, 60:934-939.*
29- Vestergaard P, Rejnmark L, Weeke J, et al.: Smoking as a risk factor for Graves' disease, toxic nodular goiter, and autoimmune hypothyroidism. Thyroid 2002, 12(1): 69-75.
30- Weetman AP: Determinants of autoimmune thyroid disease. Nature Immunol 2002, 2(9): 769-770.*
31- Cooper GS, Dooley MA, Treadwell EL, et al.: Smoking and use of hair treatments in relation to risk of developing systemic lupus erythematosus. J Rheumatol 2001, 28(12): 2653-2656.*
32- Cooper GS, Parks CG, Treadwell EL, et al.: Differences by race, sex and age in the clinical and immunologic features of recently diagnosed systemic lupus erythematosus patients in the southeastern United States. Lupus 2002, 11(3): 161-167.*
33- Sepa A, Frodi A, Ludvigsson J: Could parenting stress and lack of support/confidence function as mediating mechanisms between certain environmental factors and the development of autoimmunity in children?: a study within ABIS. Ann NY Acad Sci 2002, 958:431-435.
34- Sanchez-Guerrero J, Liang MH, Karlson EW, et al.: Postmenopausal estrogen therapy and the risk for developing systemic lupus erythematosus. Ann Intern Med 2005, 122(6): 430-433.
35- Petri M, Robinson C: Oral contraceptives and systemic lupus erythematosus. Arthritis Rheum 2007, 40(5): 797-798.
36- Meier CR, Sturkenboom MC, Cohen AS, et al.: Postmenopausal estrogen replacement therapy and the risk of developing systemic lupus erythematosus or discoid lupus. J Rheumatol 2008, 25(8): 1515-1519.
37- Kim MY, Buyon JP, Petri M, et al.: Equivalence trials in SLE research: issues to consider. Lupus 2009, 8(8): 620-626.
38- Sanchez-Guerrero J, Karlson EW, Colditz GA, et al.: Hair dye use and the risk of developing systemic lupus erythematosus. Arthritis Rheum 2006, 39(4): 657-662.
39- Hardy CJ, Palmer BP, Muir KR, et al.: Systemic lupus erythematosus (SLE) and hair treatment: a large community based case-control study. Lupus 2009, 8(7): 541-544.