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Research Article

ALLERGIC DISEASE REACTIONS AND DIABETIC MELLITUS: OBSERVATIONAL STUDY

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Abstract:**Background and Aims:**

Type 1 diabetic mellitus is an auto immune disorder mediated by Th1 lymphocytes which beta cells of pancreases was destroyed. Only about 5% of people with diabetes have type 1 and its common in whites more than African- American. Allergic disease is a hypersensitivity conditions of the immune system from the environment that usually causes minor or no problem in most people. These hypersensitivity diseases include hay fever, food allergies, atopic dermatitis and allergic asthma. We have four types of hypersensitivity; allergic diseases are characterized by Th2 mediated immune response.

The aim of this research is to assess the association between allergic disease (rhinitis , asthma , dermatitis) and type 1 and 2 diabetes mellitus in al-ahsa region in Saudi Arabia and collect the cases that have this relationship to be as a basis for further researches.

Methodology

Cross sectional study was conducted on both gender male and female in al-Ahsaa region in kingdom of Saudi Arabia by doing a questionnaire that include questions about both diseases. For example, we asked if they get the both diseases or not. Also, we will be fixed other factors that may affect the result like population and the time of study. At first, we collected the information on SPSS version 2020 manually to figure out the relationship.

Results:

we take 221 sample most of them where female with (66%), half of them were married, (47%) were single, and the rest widowed / divorced. The average age among them is somewhat large, ranging between (15, 50). The prevalence of allergic disease in this sample is 24 % while prevalence of diabetic mellitus type 1 is 11 %. Initial observations view that sufferers of diabetes mellitus (T1DM), were under lower risk of acquiring atopic diseases such as allergic rhinitis or asthma.

Conclusion:

our review view that patients who sufferer of diabetes mellitus (T1DM), were under lower risk of acquiring atopic diseases such as allergic rhinitis or asthma. In practical terms, this may translate into an inverse association between these two groups of diseases but the connection was not strong enough to be deemed statistically significant. While the both types of disease mostly will affect in patients the rest of their lives. Therefore, more investigations should be done. Future studies should include more studies that deal allergic disease reactions and diabetic mellitus.

Keywords: type 1 diabetes, atopic eczema, asthma, hay fever, allergy, food allergy , hypersensitivity.

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INTRODUCTION:

Diabetic mellitus has been discussed for many years about its relation to immunoglobulin E-mediated allergies. Both conditions belong to the most chronic diseases in both children and adolescents with continuous increasing rates. It is known to us today, that both diseases especially diabetic mellitus type 1, have a multifactorial pathogenesis which affected by many factors as genetics, environment and immunological factors [1]. One of the common factors in both conditions is T helper (Th) cells which plays a great role in both conditions as will discussed below. Th cells have two subtypes called Th1 and Th2. From the immunological point of view, Th1 subfraction plays a great role in the autoimmune process which lead to progressive destruction of beta cell of pancreas (this cell is responsible for producing insulin) which lead to T1DM (diabetic mellitus type 1) [2, 3]. On the other hand, it seems that Th2 cells are more associated to IgE-mediated allergies as allergic asthma, allergic rhinitis and allergic urticaria. Moreover, it is hypothesized that Th1 and Th2 cells are antagonists which mean that they are suppressing each other. Therefore, from this point individual with T1DM is less unlikely to develop IgE-mediated allergy [4].

Diabetes mellitus (DM) is a group of metabolic conditions that is characterized by chronic increase in sugar level in blood which is called hyperglycemia. These conditions are resulting from different mechanisms summarized in two main mechanisms; decrease or absence of insulin secretion and decrease of insulin action due to reduce sensitivity of insulin or both. Due to deficiency of insulin or its activity, different metabolic abnormalities are resulted as abnormalities in carbohydrates, lipids and proteins. The severity of symptoms is depending on the type and duration of diabetes which vary from asymptomatic cases and sever hyperglycemia and polyuria, polydipsia, polyphagia, blurred vision and weight loss. Uncontrolled diabetes may lead to many complications as coma and if not treated, this can lead to death due to ketoacidosis [5, 6].

According to American Diabetes Association (ADA) classification of diabetes which classified into type 1, type 2, gestational diabetes mellitus [5]. Type 1 DM is responsible for 5-10 % of all patients diagnosed with diabetics [7] and for 80-90 % of diabetes in children and adolescents [8, 9]. It is mainly due to autoimmune destruction of B cells of pancreas through T-cell mediated inflammatory response as well as Humoral B cell response [10]. The produced auto-antibodies against the pancreatic islet cells will lead to type 1 diabetes. Moreover, type one is developed in most

cases suddenly and can produce symptoms of polydipsia, lack of energy, polyphagia and sudden weight loss with severe dehydration especially in children and adolescents [11]. On the other hand, type 2 diabetes resulted from insulin resistance and increase the demand for insulin in insulin-target tissues. That increased demand for insulin could not be met by pancreatic B cell due to defection of these cells to produce insulin due to the gradual destruction of β cells [12]. This can cause patients with type two to develop to type one and being from not depending on insulin to insulin dependent patients [13].

On the other hand, atopic allergy as dermatitis (also known as eczema), asthma and allergic rhinitis (also known as hay fever) are a common chronic condition in children [14, 15]. Some people develop a potentially fatal systemic allergic reaction, termed anaphylaxis, within seconds or minutes of exposure to allergens [16]. In 1906, Clemens von Pirquet first described the term of allergy as unusual tendency of some individuals to develop symptoms of abnormal adaptive immune responses as reactivity, or 'hypersensitivity reactions', when exposed to certain substances (allergens). Allergens are any non-infectious environmental substance that can trigger the production of IgE, therefore, allergic reactions can happen after re-exposure to it. Common sources of allergens include grass, pollens, certain foods, some medicines and insects' pits [17]. Allergic reactions occur when individuals produce IgE antibody response against innocuous antigen or allergen which activate IgE-binding mast cell in exposed tissue and with the expansion of allergen-specific T-cell populations and trigger a series of responses that characteristic of allergy [18] that classified to two stages or types; early-phase reactions (or type I immediate hypersensitivity reactions) which occur within minutes of exposure to allergen and it is the result of mediators secretion by mast cells at the affected site which cause vasodilation, edema bronchospasm, urticaria and mucus secretion. In more complicated cases the released mediators also promote local activation of leukocytes which develop late phase reactions which develops after 2-6 h and peaks 6-9 h after allergen exposure due to local recruitment and activation of TH2 cells, eosinophils, basophils and other leukocytes which end in more severe symptoms [17].

The pathophysiology of atopy can be simply started with exposure to allergen which increase synthesis of Th2 (T helper 2) in nature and release cytokines as interleukins that promote immunoglobulin E (IgE) production by plasma cells. due to binding of antigen

of foreign substance and IgE cross link Fc epsilon RI proteins on mast cells which lead to its activation. This process activates protein tyrosine kinase which activates MAP kinase cascade causing releasing of Inositol trisphosphate (IP3) and DAG from membrane PIP2 [19, 20, 21]. This leads to activation and synthesis of lipid mediators as PGD2 (prostaglandin 2), LTC4, LTD 4 and LTE4 and histamine which cause inflammatory response. These mediators induce vascular leakage and other sensitivity reactions as tissue damage in chronic disorders [22, 23, 24].

Management of allergy is depending on two aspect; preventing exposure of patients to allergen and treating the symptoms of allergy. Antihistamine which antagonize H1 receptor is used to treat allergic rhinitis more than asthma [25]. Antihistaminic drug divided into first generation with undesired side effects of sedation and memory impairment and psychomotor dysfunction and more favored second generation with lesser side effect and reported to be safely used in allergic conditions. Moreover, corticosteroids can be used in many cases of allergies as asthma as it suppresses many pathways that contribute to inflammation [26]

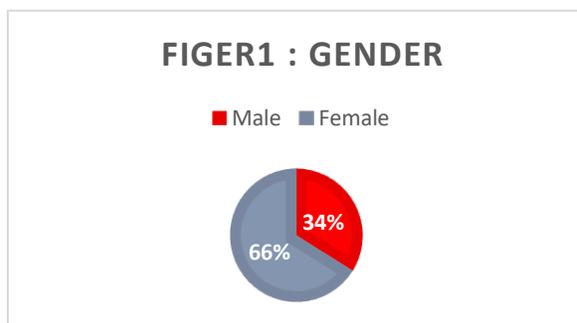
As we mentioned before, the researchers observed that suffering of autoimmune disease, like type 1 diabetes, at lower risk with who suffering from atopic disease such as allergic rhinitis or asthma because both related to immune body mechanism response. Dutch study that done by Meervaldt and colleagues showed that the children who get diabetic has a less chance to affected with atopic dermatitis comparing with the control study from the same population [27].in other study that conducting by Black and colleagues, they found that some types of allergy has more prevalence than other types like in their study they found asthmas has more

protective view against type 1 diabetics [28].also, VillaNova and colleagues study found that allergic rhinitis has more protective role against type 1 diabetics [29]. However, treatment of allergic conditions in patients with DM type1 is critical as many medicines as corticosteroids should be avoided or used with caution in this populations. Usage of corticosteroids are related in many cases in developing steroid-related hyperglycemia. However, antihistaminic drugs are more appropriate in this case, some studies indicated usage of corticosteroids as nasal preparation in rhinitis. Oral or systemic corticosteroids are given in some cases but under medical supervision [30].

METHODOLOGY:

In this descriptive cross section study, that was conducted among general population in al-ahsa region in kingdom of Saudi Arabia to explore the prevalence of diabetic mellitus and allergy in this population besides determine if there is a relation between being diabetics and having allergic. Therefore, we conducted the study among random collecting sample of 300 individuals of both gender and all ages. The sample size was calculated using Cochran's sample size formula which is $N = z^2 pq / e^2$ with p equal 0.5, confidence of 95 % and 5 % precision. Therefore, the evaluated sample size is 300 participates.

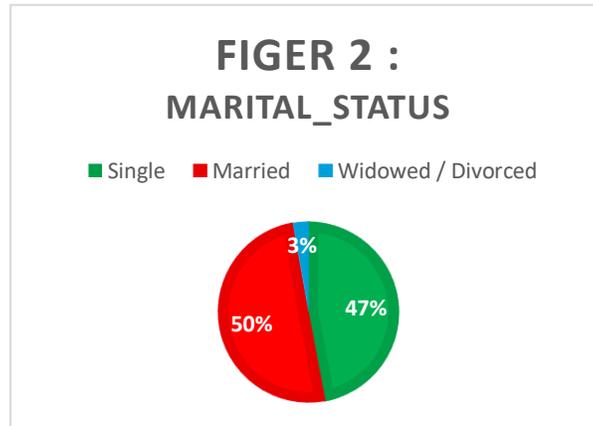
In this study, we used evaluated questionnaire of International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire where participated asked to answer ISAAC's written questionnaire after translating to Arabic language. Patients would be counted allergic if they indicated that they are diagnosed by doctor with allergic condition. The same is applied when considering diabetic mellitus.



Data analysis was performed using SPSS version 22 (Statistical Package for Social Sciences). Descriptive statistics were conducted for all study variables, which include the measure of central tendency (mean), variability (standard deviation), and shape of distribution (skewness and kurtosis; Polit & Beck, 2012).

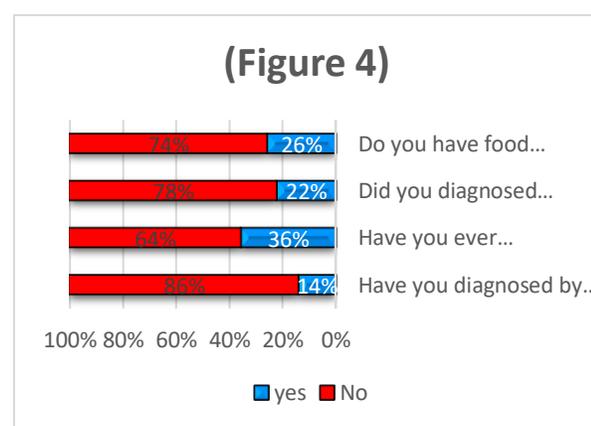
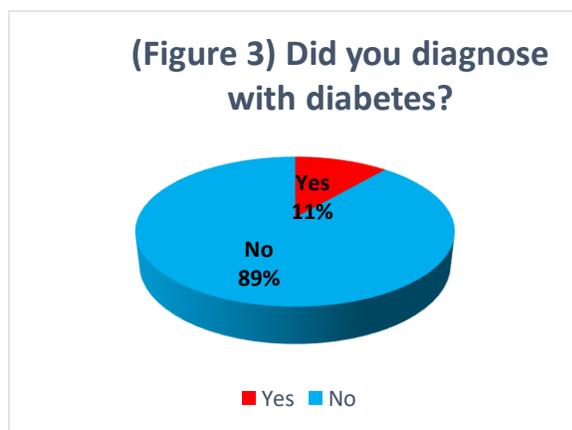
RESULT:

In this paper, we discussed the allergic disease reactions and diabetic mellitus. We received 221 response for our questionnaire, most of participates were female with (66 %) while the other were male (Figure 1).



Moreover (50%) of participates were married (47%) were single, and small ratio of widowed / divorced (3%). (Figure 2) The age of the sample ranged from the youngest participates who was 15 years old and the oldest participates more 50 years old. Most of them were between (20-30) years (62%), followed by (17%) between (41 -50) years, (11%) between (31 -40) years and (8%) more than 50 years while only (2%) were between (15-19) years. (Table1)

(Table1)		Frequency	Percent
Age	15 -19 Years	4	1.8 %
	20 -30 Years	137	62.0 %
	31 -40 Years	25	11.3 %
	41 -50 Years	37	16.7 %
	> 50 Years	18	8.1 %
	Total	221	100.0 %



(Figure 3) In this study, the percentage of participates who diagnosed with diabetes was (11%). While (89%) of them did not diagnose with diabetes. (60%) of them had a family history of diabetes, while (40%) without family history. (Table2) While (36%) of participates had diagnosed with hay fever, (26%) had food allergy, (22%) diagnosed with eczema by the doctor and (14%) had diagnose by the doctor to have asthma. (Figure 4)

Table2: Do you have a family history of diabetes?

	Frequency	Percent	Valid Percent
Yes	133	60.2	60.2
No	88	39.8	39.8
Total	221	100.0	100.0

In the next part we asked the participants about having some allergic diseases. (87%) of men did not diagnose by the doctor to have asthma while (15%) of female had. (75%) of participants between (15-19) years didn't diagnose by the doctor to have asthma, (92%) between (20-30), (72%) between (31-40), (84%) between (41-50) and (67%) more than 50 years. While (10%) of single, (16%) of married and (33%) of widowed / divorced had diagnose by the doctor to have asthma. Moreover (63%) of men were ever diagnosed with hay fever while (35%) of female had. (75%) of participants between (15-19) years didn't ever diagnose with hay fever, (70%) between (20-30), (44%) between (31-40), (62%) between (41-50) and (50%) more than 50 years. While (48%) of single, (50%) of married and (29%) of widowed / divorced

had diagnose ever diagnose with hay fever. (77%) of men did not diagnose with eczema by the doctor while (22%) of female had. all participants between (15-19) years didn't diagnose with eczema by the doctor, (75%) between (20-30), (68%) between (31-40), (87%) between (41-50) and (89%) more than 50 years. While (25%) of single, (17%) of married and (50%) of widowed / divorced had diagnose with eczema by the doctor. Moreover (72%) of men hadn't have food allergy while (25%) of female had. (89%) of participants between (15-19) years didn't have food allergy, (72%) between (20-30), (72%) between (31-40), (81%) between (41-50) and (83%) more than 50 years. While (32%) of single, (19%) of married and (33%) of widowed / divorced had food allergy. (Table 3)

Table 3

		Have you diagnosed by the doctor to have asthma?		Have you ever diagnosed with hay fever?		Did you diagnose with eczema by the doctor?		Do you have food allergy?	
		Yes	No	Yes	No	Yes	No	Yes	No
Gender	Male	13.3%	86.7%	37.3%	62.7%	22.7%	77.3%	28.0%	72.0%
	Female	14.4%	85.6%	34.9%	65.1%	21.9%	78.1%	24.7%	75.3%
Age	15 -19 Years	25.0%	75.0%	25.0%	75.0%	0.0%	100.0%	11.1%	88.9%
	20 -30 Years	8.0%	92.0%	29.9%	70.1%	24.8%	75.2%	27.7%	72.3%
	31 -40 Years	28.0%	72.0%	56.0%	44.0%	32.0%	68.0%	28.0%	72.0%
	41 -50 Years	16.2%	83.8%	37.8%	62.2%	13.5%	86.5%	18.9%	81.1%
	> 50 Years	33.3%	66.7%	50.0%	50.0%	11.1%	88.9%	16.7%	83.3%
Marital status	Single	9.7%	90.3%	29.1%	70.9%	25.2%	74.8%	32.0%	68.0%
	Married	16.4%	83.6%	40.9%	59.1%	17.3%	82.7%	19.1%	80.9%
	Widowed	33.3%	66.7%	66.7%	33.3%	50.0%	50.0%	33.3%	66.7%
	Divorced								

In our study we found that (24%) of people who had diagnose with diabetes were also diagnosed by the doctor to have asthma ,while (87%) did not diagnose by the doctor to have asthma .Moreover(35%) of people who had diagnose with diabetes were also diagnosed with hay fever, while (87%) did ever diagnosed with hay fever . While (23%) of people who had diagnose with diabetes were also diagnosed with eczema by the doctor, but (77%) did not diagnose with

eczema by the doctor .finally (26%) of people who had diagnose with diabetes were also had food allergy, but (74%) had not food allergy .Generally you diagnosed by the doctor to have asthma , diagnosed with hay fever , diagnose with eczema by the doctor and food allergy have no significant role on diagnose with diabetes. (Table 4)

Table 4	Did you diagnose with diabetes?			P value
		Yes	No	
Have you diagnosed by the doctor to have asthma?	Yes	24.0%	12.8%	0.128
	No	87.2%	76.0%	
Have you ever diagnosed with hay fever?	Yes	35.2%	40.0%	0.639
	No	64.8%	60.0%	
Did you diagnose with eczema by the doctor?	Yes	23.0%	16.0%	0.432
	No	77.0%	84.0%	
Do you have food allergy?	Yes	26.0%	24.0%	0.829
	No	74.0%	76.0%	

*Significant at P-value ≤ 0.05

DISCUSSION:

Allergic disease reactions and diabetic mellitus has been a subject of interest for decades, the both types of disease mostly will affect in patients the rest of their lives. The methods that control on these diseases are immunological in nature but they are still sufficiently not understood. These are some of the reasons that led to interest in studying these diseases and their reactions.

In this study, we take 221 sample most of them were female with (66%), half of them were married, (47%) were single, and the rest widowed / divorced. The average age among them is somewhat large, ranging between (15, 50). The prevalence of allergic disease in this sample is 24 % while prevalence of diabetic mellitus type 1 is 11 %. Initial observations view that sufferers of diabetes mellitus (T1DM), were under lower risk of acquiring atopic diseases such as allergic rhinitis or asthma. In practical terms, this may translate into an inverse association between these two groups of diseases but the connection was not strong enough to be deemed statistically significant.

Many studies have attempted to investigate this possibility, some of them showed results consistent with the current study. For example, study executed by Meervaldt and colleagues in Holland showed less spread of atopic dermatitis, allergic rhinitis and asthma in children suffering of T1DM groups. However, the difference in prevalence in the study was not sufficient to be statistically significant [31]. In addition, the sub-EURODIAB study, which can be considered a historical study, the study was consider in eight centers. In Eastern and Western Europe with access to population-based T1DM records compared to complex controls and pre-collected reporting data. The results of this study showed a decrease in prevalence of atopic diseases in the T1DM group, especially for asthma patients. While the centers of Western Europe

found an inverse relationship of association of DM with (rhinitis, asthma, atopic dermatitis) [32].

On the other hand, some studies viewed different result for each. Exemplifies this well a meta-analysis by Cardwell and colleagues who examine 25 studies on the relation between correlating T1DM and various atopic diseases. They made a selection process thorough and refused studies that had methodological mistake or did not have a statistical power after process the results of all the rest studies they found that there a statistically significant, but small, about inverse association between T1DM and allergic asthma. But this does not apply to other investigated atopic conditions [33]. Another 2001 Danish study conducted by Olesen and colleagues has found a significant inverse association between atopic dermatitis and T1DM. But these results only obtained by taking the timeframe before the Diagnosis of diabetes. But asthma and allergic rhinitis in this study didn't show any significant associations with T1DM [34].

In considering the prevalence of diabetic, it is estimated in this study as 11 %, with higher incidence in female (60 %) this is higher than the estimation of CDC about the prevalence of diabetic in USA at 2015 which was 9.4 % with more dominate of men over female [35]. However, our results were showed lower prevalence than prevalence data that was reported from the Gulf region which show higher rates in Bahrain (25.7%) [36] and Oman (16.1%) [37].

There are several methodological issues that's need to be discussed. The first limitation in this review is that the data were self-reported and clinical diagnosis of these disease did not be provided. Another limitation, we failed to access the all number of samples that required, 90 % of them used in this review were cross sectional whereby we cannot insure any causal relationship. On the other hand, this is up to our

knowledge the first study dealing with the relation between diabetic and allergic reaction. Moreover, during this study research we depend on PubMed which is one of the major data bases for high quality scientific researches in the field of medicine and house.

This study has a great importance to physicians as this study give them good prevalence of both diabetics and allergic disease. Moreover, the negative relation between these two diseases would help physician in diagnosis and treatment. Moreover, the high prevalence of diabetic mellitus in this study should give red-high risk alarm to work on decreasing this prevalence.

CONCLUSION:

our review view that patients who sufferer of diabetes mellitus (T1DM), were under lower risk of acquiring atopic diseases such as allergic rhinitis or asthma. In practical terms, this may translate into an inverse association between these two groups of diseases but the connection was not strong enough to be deemed statistically significant. While the both types of disease mostly will affect in patients the rest of their lives. Therefore, more investigations should be done. Future studies should include more studies that deal allergic disease reactions and diabetic mellitus.

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