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Vitiligo and anti-tissue Transglutaminase of celiac disease in Al-Nasiriyah city, Iraq

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Abstract

Vitiligo is acquired pigmentation disorder characterized by sharply defined white spots of irregular shape and variable dimensions, increasing in volume and number over time. The causes of vitiligo are still unknown. But it involve some theories like autoimmunity, this study was aimed to detection the relationship between the vitiligo and celiac disease by investigating the presence of celiac tissue transglutaminase IgA(tTGA) autoantibody in patients of vitiligo by using ELISA technique . The study was conducted on 100 patients with vitiligo and 100 healthy individual as control , the mean age of vitiligo patient was 19.4 year and control was 26.3 year .The results of study were showed , twenty six of cases have family history of vitiligo , 53 of cases have family history of other autoimmune disorders, as well as 4 of cases have positive family history of vitiligo with diabetes and thyroid disorders. Tissue transglutaminase IgA antibody test was showed ,12 out of 100 of vitiligo cases were registered Seropositivity result to tTGA antibody, while 4 out of 100 of control were Seropositive to this antibody ,other cases and control were negative for IgA antibody.

Keywords : Vitiligo, autoimmune disease , celiac , tissue transglutaminase, IgA

Introduction

Vitiligo is a common autoimmune disease that gradually destroys melanocytes in the skin, resulting in the appearance of incomplete pigmentation. This deformed condition often affects the face and other visible areas of the body (Rodrigues *et al*., 2017). Histological picture showing melanocytes and melanin loss in white spots and lympho-mononuclear infiltrates in advanced margins of vitiligo (Ogg *et al*.,1998).

Vitiligo has been categorized depend on clinical grounds into two main forms, segmental vitiligo (SV) & non-segmental vitiligo (NSV). non-segmental vitiligo, the commonest form of this unpredictable disorder, is characterized by symmetrical and bilateral white patches. Various clinical subtypes have been qualified, including universalis, acrofacial, and generalized types. Segmental vitiligo is lower common than non-segmental vitiligo and it is usually unilateral distribution. Overall, gradual incomplete loss of pigmentation of the skin, and hair covering, And sometimes the mucosa still the basis for vitiligo diagnosis (Ezzedine *et al*., 2015) . More recently, another form , mixed vitiligo (MV) has been identified as a combination of primary SV followed by NSV spots several months, or more rarely, years later (Ezzedine *et al*., 2011).

Generally ,vitiligo affects about 1% of the world's population. It does not include, sexual or regional and racial differences among the population. Some reports is indicated to higher occurrence of vitiligo in India , Egypt and Japan. Ranging from 1.25% to 6% of the population. The onset of vitiligo is usually more in childhood or in young adults (20- 30 years of age) and at about 30% there is a positive family history (Gerard and Bryan, 2006). An important side of vitiligo is the psychological effect of the disease. Those with Vitiligo may suffer from social and emotional consequences Including low self-esteem, Stigmatization, social anxiety ,depression (Papadopoulos *et al*.,1999). Loss of function of melanocytes responsible for vitiligo

but the real cause of vitiligo is unknown. However, some conditions including autoimmune, Hereditary, viral infection, neural and oxidative stress have an important role in Vitiligo (Halder & Chappell ,2009).

Studies on generalized vitiligo patients from people around the world showed a strong epidemiological association with Many other autoimmune diseases such as autoimmune thyroid diseases, , adult- onset type 1 diabetes mellitus, systemic lupus erythematosus (SLE), rheumatoid arthritis , psoriasis, and Addison's disease (Betterle *et al*., 1985; Mosca *et al*., 2008). Some authors have described Vitiligo cases in patients with celiac illness, (Reunala & Collin , 1997; Akbari *et al*., 2006) .

Celiac Disease (CD) is a small bowel disorder caused by adapting and innate immune responses to ingested gluten proteins found in wheat, oats, barley, and rye(Alaedini& Green, 2005). Celiac pathogenesis involves interactions between the environment, genetic and immunological Factors. one treatment at present is a lifelong rigorous and adhere to a gluten-free diet (GFD), which allows Recovery of the intestinal mucosa (Kagnoff, 1992). The transglutaminase enzyme tissue (tTG) played an important role in the breakdown of proteins in small intestine. Gliadin food triggers formation of a gliadin peptide–tTG complex in the small intestine. In celiac disease, antibodies to this peptide-tTG complex (Anti-tTG antibodies) are formed, leading to the mucosa inflammation. Removal of gliadin from the food causes down regulation of anti-tTG antibody production degradation of inflammation.(Fleckenstein *et al*., 2004).

The active phase of the CD is associated with elevated serum levels of immunoglobulin A (IgA) autoantibodies against endomysium (IgA-EmA) and tissue transglutaminase (IgA-tTG) and the presence of these antibodies is often used as the standard of choice for the jejunal biopsy (**Sulkanen *et al*.,** 1998**; Catassi, *et al*.,** 2000). Iranian revealed that, The serum of two vitiligo patients (3.1%) was positive for anti endomysial and anti transglutaminase of CD disease and concluded there may be a relationship between celiac disease and vitiligo (Shahmoradi *et al*., 2013). Because to the fact that some people have vitiligo in my province and because the specific causes of vitiligo are still unclear ,this study aimed at finding the relationship between vitiligo and celiac disease by detection frequency of celiac autoantibodies in patient with vitiligo.

MATERIALS AND METHODS

It was a case –control study in which the sera of 100 patients with vitiligo (52male and 48 female) and 100 individual (59 male and 41 female) without skin disease as control, the control group are matched with patient group in according to gender and age . The patients and control groups were attending the out patient of the department of dermatology and venereology in the Al-Hussain teaching hospital in Al-Nasiriyah city ,Thi –Qar province , Iraq. In 2015- 2017 . The patients enrolled after obtaining an informed consent from the patients and/or their parents, these were include a relevant data such as age, gender, duration of disease and family history of disease ,e.g. diabetes mellitus and thyroid dysfunction were collected in a Proforma. All patients with vitiligo and control group were referred to laboratory for screening the IgA –anti transglutaminase (anti-tTG)by ELISA with tTG as the antigen.

RESULTS

The results showed that the mean age of vitiligo cases and control was 19.4 year and 26.3 year respectively , Twenty six of cases have family history of vitiligo ,in

compared with control .3% have family history of vitiligo, and it was appeared, 53 of cases have family history of other autoimmune disorders, the higher number (35%) of cases have family history of diabetes . Four of cases have positive family history of vitiligo with diabetes and thyroid disorders (as shown in table 1) .

Table 1 : Characteristics of case and control population

	Case(n=100) No.&(%)	**Control(n=100) No.&(%)**
Family history of vitiligo	26(26%)	3(3%)
Family history of diabetes	35(35%)	16(16%)
Family history of thyroid disorders	18(18%)	11(11%)
Family history of Vitiligo+D.M.+ Thyroid disorders	4(4%)	0
Mean age	19.4 year	26.3 year

D.M: Diabetes mellitus

Table 2 displayed the Seropositivity in cases of vitiligo and control groups , it was appeared that , 12 out of 100 of vitiligo cases were registered Seropositivity result to tissue transglutaminase IgA antibody, while 4 out of 100 of control were Seropositive to this antibody, other cases and control were negative for this Ab , the statistical analysis was showed significant differences ($P \leq 0.05$) between patients and control .

Table 2: Levels of tTGA autoantibody in case and control**.**

tTGA Tests	Cases		Control		Total	
	No.	%	No.	%	No.	%
Sero negative	88	88.0	96	96.0	184	92.0
Sero positive	12	12.0	4	4.00	16	8.00
Total	100	100	100	100	200	100
CalX2= 4.348	**TalX2= 3.84**		**DF = 1**	**P. value = 0.037**		

Figure 1 revealed Comparison between vitiligo cases and control depending on Seronegative and Seropositive of tTGA autoantibody, It shows that the number of control with Seronegative of tTGA autoantibody was higher than that in case , but the number of cases with Seropositive of tTGA autoantibody was higher in compared with control .

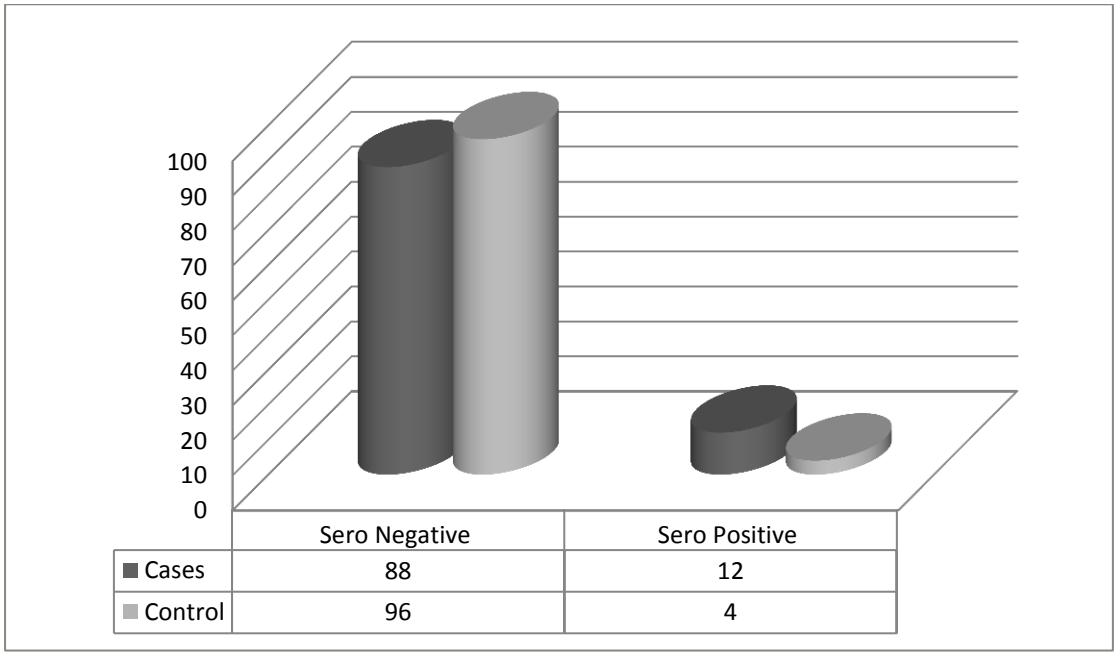

Figure 1: Comparison between case and control anti tissue transglutaminase IgA antibody.

Discussion

The exact pathogenesis of vitiligo is unknown and the question, "What are the causes Vitiligo? "It remains ambiguous. (Kaur *et al*., 2013)**.** Vitiligo has multi-factor etiology and polygene inheritance. The more likely theory of causality suggests that changes in cellular or humoral immunity lead to autoimmune processes that attack melanocytes, causing dysfunction or absence of melanocytes in the influenced area (Van den Wijngaard *et al*.**,** 2000**).** There is rising evidence to support the opinion that Vitiligo Is an autoimmune disease, and it shows a family trait In about 18% of cases (Mason and Gawkrodger, 2005).The results of this study were showed ,the mean age of vitiligo patients was 19.4 year , this was lower than mean age(24.5) years of 135 patients had vitiligo were reported in Hera General Hospital, Makkah, Saudi Arabia by (Fatani *et al*., 2014) and in other study has registered a mean age of onset, namely 23 years (Gopal *et al*., 2007). Nevertheless, a study in India record a later the beginning of the disease, with an average age of 55 years(Dogra *et al*.,2005). These data support that vitiligo is a disease that can occur at any age **(**Dash *et al*., 2015).

In our study, 26% of vitiligo patients had positive family history of vitiligo ,these results are accordance with those results of Butt *et al* .(2015) who found positive family history of vitiligo in 22% of patients. Tanioka *et al*.(2009) registered positive family history in 26% of vitiligo patients, this conclusion proves that vitiligo is a genetically determined disease (Fitzpatrick *et al*., 2001; Nordlund and Majumder 1997). The autoimmune etiology of vitiligo are the most widely accepted as there is a variable autoimmune diseases that are linked with vitiligo. Another important argument in the support of this theory is the existence of Circulating autoantibodies against surface antigen of melanocyte cell in the Serum of vitiligo patients (Halder & Chappell 2009)**.**

The results of this study were finding that, 35(35%) of vitiligo cases have family history of diabetes and 18(18%) have family history of thyroid disorders. Four of cases have positive family history of vitiligo with diabetes and thyroid disorders

,these results were similar the results of Narita *et al*. (2011) who founded twenty of vitiligo patients had a family history of only autoimmune disorders. Earliest evidence suggests a genetic basis for vitiligo was associated with a number of other autoimmune diseases known to have genetic predispositions, such as diabetes mellitus (Ramaiah *et al*.,1988). Presence of organ specific autoantibodies in serum vitiligo patients it was well established in adults and children(Gottumukkala *et al*., 2003; Broniarczyk-Dyla *et al*.,1994).

The Celiac disease is considered an autoimmune disorder with both genetic and environmental factors (Kumar *et al*., 2012). Serum immunoglobulin A-tissue transglutaminase (tTGA) and Endomysial antibody (EMA) test play a major role in the diagnostic evaluation of CD. High serologic tTGA are exclusively associated with CD (Volta *et al*. ,1997). The relationship between CD and vitiligo is controversial, there may be a link between CD and vitiligo, This may indicate a common autoimmune mechanism that is common explanation of a few status reports that gluten-free diets were effective in Treatment of patients with vitiligo (Shahmoradi *et al*.,2013).

This study was showed ,12 out of 100 of vitiligo patients were registered Seropositivity to tTGA . In Turkish study found 5(9.1%) of celiac patients had vitiligo(Seyhan *et al*., 2007) .Other Egyptian study by Attwa *et al*. (2014) reported one patient was seropositive for both anti Endomysial and tTGA from 50 patients with vitiligo , Seyhan *et al*. (2011) reported 11(18.0%) out of 61 patients (21 children) with vitiligo and 1 from 60 control (1.7%) were seropositive for CD.

The present study conclude that, the frequency of autoantibodies for celiac disease was higher in vitiligo patients than in controls .

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