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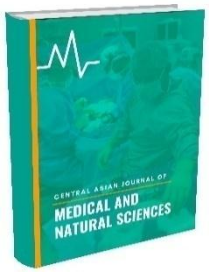

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Evaluation of Torch Infections and Specific Humoral Responses Against HSV in Patients with Nonsegmental Vitiligo

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Abstract: The aim of this study was to assess the TORCH infections and specific humoral responses against HSV in patients with nonsegmental vitiligo. The research consist of 18 to 60 years old 46 patients with nonsegmental vitiligo and 25 healthy individuals were enrolled. General clinico-laboratory results collected from all participants which CBC, biochemical analysis, specific skin test for depigmented patches-mexametria. ELISA was used for detection of IgG antibodies against TORCH infections (cytomegalovirus, herpes simplex viruses (HSV), rubella, toxoplasma gondii, chlamydia trachomatis) in sera of participants. HSV were detected from the sera of 31% of the patients and 12% of the controls. There was no significant difference between TORCH infections in patients and controls ($P > 0.05$). HSV was detected from the sera of 23% of the patients and 6% of the controls ($P > 0.05$). There were no significant differences between serum levels of IgM and IgA in patients and controls ($P > 0.05$). Serum level of IgG was significantly lower in patients than in controls ($P > 0.05$). Type of TORCH infections can change in patients with nonsegmental vitiligo. In addition, these patients have abnormalities in the production of antibodies against HSV that may have a role in the pathogenesis of nonsegmental vitiligo.

Introduction. Vitiligo is caused by both genetic and non-genetic multifactorial and poligenic nature. Our scientific data is mainly based on autoimmune, oxidative stress, genetic and neurochemical hypotheses. The destruction of melanocytes in vitiligo lesion is directly related to the increase of anti-melanocyte bodies, T-lymphocyte (CD4+/CD8+, IL) imbalance and defects in their activity [10, 11]. The pathogenetic characteristic of vitiligo disease that needs to be studied is related to the loss of melanocytes. Vitiligo affects the quality of life of the patient with the formation of skin depigmentation. Several theories have been proposed to explain the pathogenesis of the disease, taking into account the role of increased inflammatory and cytotoxic immune reactions, neuropeptides, microvascular abnormalities, intrinsic abnormalities in the activity of melanocytes and keratinocytes, as well as oxidative stress [2, 3]. In recent decades, clinical, basic, and translational studies using

patient analyses, as well as in vitro and in vivo models, have significantly improved our understanding of the pathophysiology of the disease and demonstrated its complexity. Laboratory data is critical to identifying appropriate therapeutic targets and treatments to halt disease progression and enhance repigmentation. [1, 6, 10] In vitiligo, loss of melanocytes is associated with persistent T-lymphocyte infiltration. Factors leading to infiltration are also important, environmental factors (such as physical, mechanical, infections), genetic polymorphisms, metabolic changes and autoimmune processes. In general, epidermal cell signaling through the production of excess products in response to stress triggers the innate immune system, which leads to the loss of melanocytes in vitiligo through the properties of the immune response itself. Innate immunity has receptors for detecting damaged genetic information and is involved in the inflammatory-autoimmune condition. [5, 17] TORCH infections is a cluster of congenital infection with toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and other organisms including syphilis, parvovirus, and Varicella zoster.[15, 18] Zika virus is considered the most recent member of TORCH infections. TORCH syndrome may develop before birth, causing stillbirth, in the neonatal period, or later in life.[4, 16] Each infectious agent may also cause additional abnormalities that may vary in degree and severity, depending upon the stage of development or procsess at time of infection and/or other factors. Therefore, we aimed to study the clinic of vitiligo disease associated with TORCH triggers, which have an affect on the immune state in the body.

Materials and Methods. 46 patients with vitiligo and 25 healthy individuals as control group from april 2022 to december 2023 were enrolled in the study. The patients and controls filled out the consent form to participate in research and the study was approved by the committee of Bukhara University of Medical Sciences, Bukhara, Uzbekistan. Control subjects were selected from persons who were referred for cosmetic problems and separated clinical nonsegmental vitiligo groups according to specific skin test for depigmented patches-mexametria results. People who had diabetes and those who had used broad spectrum antibiotics and steroids as well as pregnant patients were excluded from the study. In order to assess clinical severity of the disease, the DLQ (dermatological life quality) of nonsegmental vitiligo patients index was calculated as elucidated by Friz et al. in 2010 [3, 12, 19]. Based on this definition, clinical severity of vitiligo was categorized to mild (DLQ index < 10), moderate (DLQ 10–18), and severe (DLQ > 18). Serum IgG levels were measured with enzyme-linked immunosorbent assay (ELISA) test kits (Genesis Diagnostic, England) according to the manufacturer's instructions. Numbers of individuals with infections were compared with the Chi-Square test. Independent -test was used to compare the results of IgG assay in two groups. Values less than 0.05 were considered significant. The correlation between TORCH infections and levels of antibodies against HSV with the severity of disease (DLQ index) were examined by means of Chi-Square test and Pearson's_correlation_test, respectively. Logistic regression was used to control confounding effects of age and sex.

Results. In this study, 46 patients (12 male and 34 female; age 29.7±10.3 years) and 25 controls (12 male and 13 female; age mean 39.9 ± 11.45 years) were examined. By logistic regression analysis, age and sex do not influence TORCH infections and levels of antibodies. 31% of patients and 24% of controls were analysed for TORCH infections. TORCH infections were isolated from the sera of 2 (4%) patients and 2 (8%) of controls. Twenty-nine percent of patients and 22% of controls were analysed by only HSV. Two percent of patients and 2% of controls were analysed by two different infections. HSV and Cytomegaloviruses were the most common infection species isolated from patients and control, respectively. Isolated species are listed in Table 1.

Table 1. Evaluation of blood result against TORCH infections in sera (Ig G).

TORCH -species	Vitiligo patients *N(%)*	Controls *N(%)*	Nonsegmental vitiligo *N(%)*
Cytomegalovirus	3 (17.6%)	2 (18.2%)	3 (33.3%)
Herpes simplex viruses (HSV)	9 (52.9%)	5 (23%)	5 (55.6%)
Rubella	2 (11.8%)	1 (9%)	0 (0%)
Toxoplasma gondii	1 (5.9%)	0 (0%)	0 (0%)
chlamydia trachomatis	2 (11.8%)	3 (27.2%)	1 (11.1%)
Total	**17** (100%)	**11** (100%)	**9** (100%)

DLQ index < 10, DLQ index 10–18, and DLQ index > 18 were observed in 20%, 70%, and 10% of the patients with nonsegmental vitiligo, respectively. 20% of patients with mild disease, 17.5% of patients with moderate disease, and 10% of patients with severe disease were analysed by TORCH species. IgG titers against HSV show normal distribution in patients and control group. The mean level of IgG against HSV in patients and controls was 42.64 and 90.01 U/mL, respectively. The Pearson correlation between levels of IgG and IgA and severity of disease was 0.071 and − 0.022, respectively. Fourteen percent of patients and 12% of controls with TORCH infections showed IgG level less than 10 U/mL (Figure 1). Fourteen percent of patients and 6% of controls with Candida colonization had IgA level less than 10 U/mL (Figure 1). The IgG levels of 15% of patients and 4% of controls with TORCH infections were less than 30 U/mL (Figure 1).

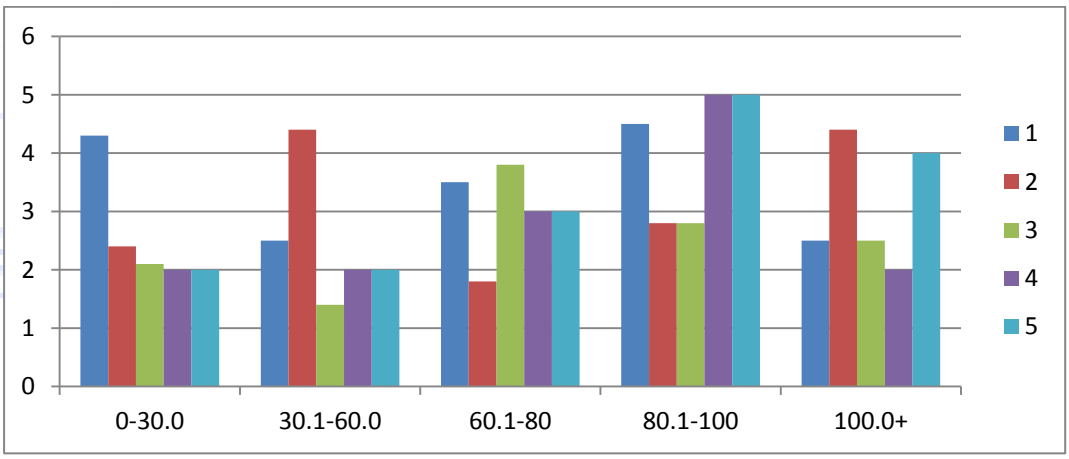

Figure 1.

Distribution of serum level of IgG specific against HSV in patients with vitiligo and control (mean of IgG in patients: and mean of IgG in controls:)

Discussion. In the present study, there was no significant difference between the rate of TORCH infections in the sera of patients with vitiligo and controls. This result is incompatible with Henseler and Tausch's study [8] and is compatible with Leibovici et al.'s study [7]. However, the differences in the results of these studies may be due to differences in race, age, and disease severity of the study population. In the present study although there was no significant difference between the TORCH species in the patients and controls, impaired immune systems of patients with vitiligo can react to the normal rate of TORCH species and alter the course of the disease [2]. In the present study, HSV colonization in the blood of patients was significantly higher than controls. HSV is the most common and important species [13]. Protein compounds of this species such as proteins 27, 37,

125, and 75 kDa can play an important role in the pathogenesis of vitiligo via stimulation of immune system and reaction with immunoglobulins [13]. Some researchers have reported that increased severity of vitiligo is associated with the production of HSV-specific antibodies [2, 9, 14]. In Taeib et al.'s study [14], level of IgE antibody against HSV in patients with nonsegmental vitiligo was significantly higher than in controls. In Levit's study, patients with severe vitiligo had higher level of IgE antibody against HSV than those with mild disease and controls [2]. In Taeib et al.'s study [14] 85% of patients with vitiligo have a high level of IgE antibody against HSV. As noted above, most studies examined specific IgE to HSV and its immunoglobulin-reactive protein in patients with nonsegmental vitiligo. Hence, in this study, the production of other classes of antibody to HSV including IgG was evaluated. In the present study, there were no significant differences between the levels of IgG and IgA antibodies against TORCH infections in serum of the patient and control groups, but level of specific IgG to HSV was significantly lower in patients than in controls. IgG is the major immunoglobulin in normal human serum and is a key player in the humoral immune response [6]. The reduction in specific IgG production may be the etiology for the increased TORCH infections in patients with vitiligo. According to the survey which was conducted, so far the levels of specific antibodies against HSV have not been evaluated in serum of patients with nonsegmental vitiligo. So it seems that the present study is the only study that has addressed this issue. In our study, there were no significant differences among antibody levels, severity of illness, and intensity of TORCH infections. In present study, we applied logistic regression to control confounding effects of age and sex. Therefore age and gender had no effect on the results of this study.

Conclusion. The results of this study showed that type of TORCH infections can change in patients with vitiligo. Moreover, these patients with nonsegmental vitiligo have abnormalities in the production of antibodies against HSV that may have a role in the pathogenesis of vitiligo.

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