Granzyme B Gene Polymorphisms Are Associated With Severe Non-segmental Vitiligo

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BACKGROUND: Granzyme B (GZMB) gene is related to human immunity and is considered as one of the genes indulged in vitiligo. **OBJECTIVE:** To evaluate the association between GZMB (R55Q) and (P94Q) gene polymorphisms with vitiligo development in a sample of vitiligo Egyptian patients. **METHODS:** This study was a case-control study which included 100 non-segmental vitiligo patients as well as a control group consisted of 100 healthy, sex and age matched vitiligo free individuals. The polymorphism of GZMB gene at (R55Q) and (P94A) were analyzed by polymerase chain reaction. **RESULTS:** P94Q and R55Q gene polymorphisms were significantly associated with higher VASI scores. **CONCLUSION:** GZMB (Q55R) and P94A) gene polymorphisms are associated with the susceptibility to develop vitiligo in the Egyptian population and could help predicting more extensive forms of the disease.

Vitiligo is a chronic amelanocytic skin disorder which is usually acquired. The main pathology in the vitiliginous patches is the complete melanocytes loss, however, the exact cause of this loss is still under debate. Depigmentation may affect both skin and hair to different extents.[1,2]

Several theories to explain the occurrence of this disorder were proposed. They include genetic predisposition, autoimmunity, autocytotoxicity, neurogenic elements, microenviromental factors, viral infection, melanocytes apoptosis and adhesion disorders.[3] The most accepted theory of vitiligo pathogenesis is the occurrence of one or more of the mentioned hypotheses in a genetically predisposed person.[4]

Many genetic studies are directed to map the susceptibility loci for vitiligo in order to understand the genetic background of the diseases more clearly. However, these studies could not provide the full explanation of the disorder[5-9], so this field needs more attention and more studies are required.

Granzyme B enzyme; a serine protease, is secreted with perforin by natural killer cells and cytotoxic lymphocytes. They act together to induce apoptosis of cells.[10] Perforin helps the internalization of Granzyme B in the target cell, then Granzyme B induces apoptosis of this cell by caspase- dependent and or -independent pathways.[11,12] GZMB can cleave melanocytic proteins attributing to the initiation and propagation of autoimmune reaction towards self melanocytes.[13]

GranzymeB (GZMB) gene is located at 14q12 and it has five exons. It is related to the immune system functions, so it was proposed to be one of the genes involved in the etiopathogenesis of vitiligo.[14,15]

Xu et al[16] studied the relation between 15 GZMB SNPs with the development of vitiligo and the progress in its course in a sample of Chinese Han ancestry. They concluded that this gene polymorphism may play a role in vitiligo cases in that race.

This work was designed to evaluate the association between GZMB (R55Q) and (P94Q) gene polymorphisms with vitiligo occurrence and to assess the clinical significance of these polymorphisms among a sample of Egyptian vitiligo patients.

METHODS

This case control study included 100 patients with non-segmental vitiligo as well as a control group consisting of 100 healthy, sex, and age-matched vitiligo individuals without vitiligo. Patients were recruited from the outpatient clinic and the phototherapy unit of Dermatology, Venereology, and Andrology Department of Benha University Hospitals. An informed consent was obtained from all participants after explanation of the study and before collecting blood samples. The protocol of this study obtained the approval of the local ethics committee on research involving human subjects of Benha Faculty of Medicine (Ethical Approval: Ms.27.1.2019).

Subjects with any of the following criteria were excluded from the study; other autoimmune or inflammatory skin or systemic disease, chronic infectious diseases, malignancy and chronic systemic diseases (e.g. hepatic, renal, cardiac, etc).

All patients in our sample were subjected to complete history taking, complete cutaneous examination to evaluate the extent and clinical type of vitiligo, the presence of halo nevi or leukotrichia and the involvement of mucous membranes, eye and ears. Vitiligo severity was assessed by Vitiligo

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