The connection of polymorphism locations in certain genes with type 1 diabetes in an Egyptian kid sample

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Received: 25-Jan-2023, Manuscript No. jdm-23-22190; **Editor assigned:** 28-Jan-2023, PreQC No. jdm-23-22190(PQ); **Reviewed:** 11-Feb-2023, QC No. jdm-23-22190; **Revised:** 21-Feb-2023, Revised Manuscript No. jdm-23-22190 (R); **Published:** 28-Feb-2023, DOI: 10.35248/2155-6156.1000981

Abstract

Background: It has been hypothesized that the major histocompatibility complex (MHC) genes are the primary genetic factor in the predisposition to type 1 diabetes mellitus (T1DM). It had also been reported that other loci outside the MHC contributed to T1DM susceptibility. In this study, we looked at a sample of Egyptian children to see how some variants of polymorphic sites in some genes that are linked to T1DM played a role.

Methods and subjects: This study included 60 healthy participants and 60 T1DM patients from Alexandria University Children's Hospital's diabetes clinic. The method of isopropanol precipitation was used to extract genomic DNA. Genotyping was performed on cytotoxic T-lymphocyte antigen-4 (CTLA-4) as well as the vitamin D receptor (VDR), interleukin 10 (IL-10), protein tyrosine phosphatase non-receptor 22 (PTPN22), and interleukin 18 (IL-18).

Results: The PTPN22 gene single nucleotide polymorphisms SNP-137 G>C (rs#187238), VDR Fok1 SNP T>A (rs#2228570), and SNP-1123 C>G (rs#2488457) showed a significant difference between patients and controls (P = 0.026, 0.030, and 0.003, respectively), according to the results of the logistic regression analysis. There was no significant difference between the genotype distributions of PTPN22 SNP-1858, CTLA-4 SNP 49, IL-10 SNP-819, IL-18 SNP-607, and VDR BsmI SNP G>A.

Conclusion: The presence of T1DM in Egyptian children may be influenced by the PTPN22 gene's SNP-1123 C>G (rs#2488457), VDR SNP-Fok1 T>A (rs#2228570), and IL-18 SNP-137 G>C (rs#187238). More population-based, large-scale case-control studies are required.

Keywords: Genes; Genomic DNA; Single nucleotide polymorphism; Type 1 diabetes mellitus

Introduction

Hyperglycemia is a major biochemical feature of type 1 diabetes mellitus (T1DM), which is a common chronic metabolic disorder characterized by disturbances in the metabolism of carbohydrates, fats, and proteins and either absolute or relative deficiencies in insulin secretion and/or action. This typically results from the autoimmune destruction of type 1A beta cells in the pancreas.

The frequency differs from more than 40 for every 100,000 kids in Finland to fewer than 2 for each 100,000 in Japan. An ascent in the quantities of kids and youths with T1DM has been seen since the mid-1950s, both in high-as well as okay nations. For children under the age of 15, the global prevalence rate is currently 0.025%, with an annual incidence rate increase of 3% on average [1,2].

Because T1DM is a complex polygenic disorder that cannot be strictly classified as dominant, recessive, or intermediate, it is challenging to identify genes that are either disease susceptibility or resistance.

Although the major histocompatibility complex (MHC) genes have been suggested to play a major role in the predisposition to type 1 diabetes, other genes, such as interleukin-10 (IL-10), interleukin-18 (IL-18), cytotoxic T-lymphocyte antigen-4 gene (CTLA-4), toll-like receptors 2 (TLR2) [3], insulin gene (INS), protein tyrosine phosphatase non-receptor 22 (PTPN22), These loci have all been demonstrated significant in the pathogenesis of autoimmunity when worldwide considered, while the insulin quality is a sickness explicit T1DM inclination locus [4].

No less than 20 distinct chromosomal locales have been connected to T1DM weakness in people, utilizing genome screening, applicant quality testing and investigations of human homologues of mouse helplessness qualities.

Numerous genome-wide association (GWA) studies have been published since 2001. More than 40 loci that affect the previously identified regions associated with T1DM susceptibility were found in data from The International Type 1 Diabetes Genetics Consortium (T1DGC), which was gathered from multiple GWA studies and large-scale meta-analyses. In addition, there was a strong correlation between 18 additional regions and T1DM, and several of these regions contain new candidate genes that might be relevant to T1DM (IL19, IL20, GLIS3, CD69, and IL27). The majority of the genes on the list control the immune system, some play a role in the destruction of pancreatic cells, and some play both roles. Numerous cytokines and their receptors, as well as an immunomodulatory molecule, were found to be causally linked by additional functional studies within established loci. However, the most likely causal gene still needs to be determined for the majority of associated regions [5].

The point of this study was to look at the job of certain variations of polymorphic destinations in certain qualities related with T1DM in an example of Egyptian youngsters.

Patients and methods

This study included sixty healthy individuals (33 males and 27 females) and sixty patients with type 1 diabetes (25 males and 35 females) from the Diabetes Clinic at Alexandria University Children's Hospital (El-Shatby). The WHO's criteria were used to diagnose patients. All subjects' demographic information was gathered; including age, gender, duration of diabetes, and diabetes-related first-degree family history [6]. The controls lacked any personal or first-degree diabetes history. From September 2012 to December 2012, blood samples were taken. Each patient or healthy control received an EDTA tube containing one milliliter of venous blood, which was stored as whole blood at 20 °C for DNA isolation.

As described by Sambrook et al., isopropanol precipitation was used to extract genomic DNA. The dbSNP, an online single nucleotide polymorphism database, contained a partial fragment of the gene of interest. Control forward, common reverse, and two allele specific primers were designed for allele specific PCR. Except for the final nucleotide at the 3' prime end, the two allele-specific primers for each SNP shared the same nucleotide sequence.

The target SNPs were amplified using two molecular methods: PCR that is allele specific as well as restriction fragment length polymorphism PCR

(RFLP PCR). Using allele specific PCR, IL-18, IL-10, and CTLA-4 antigen SNPs were analyzed for their genotype. Utilizing methods, PTPN22 and VitD receptor SNPs were genotyped [7].

Results

As shown there was a significant age difference between the two groups (P = 0.0001); the controls' mean age was 27.2 6.4 to ensure that they did not have T1DM. Sexe was not significantly different between the two groups that were being studied (P = 0.173). The average age at diagnosis was 5.3 3.5 years, with a range of 0.2 to 17 years.

For the SNP 607 C>A (rs#1946518), there was no significant difference in the genotype distributions of IL-18 between T1DM patients and control subjects (P = 0.641). On the other hand, the genotype level of the SNP-137 G>C (rs#187238) showed a difference between the two groups that was statistically significant (P = 0.001). For the SNP 819 C>T (rs#3021097), the genotypic distributions of IL-10 did not significantly differ between the two groups (P = 0.208) [8]. On the other hand, the SNP 1082 G>A (rs#1800896) showed a statistically significant difference between the two groups (P 0.0001) for the genotypic distributions of polymorphisms in vitamin D receptors; patients and controls didn't essentially contrast for the SNP BsmI G>A (rs#1544410), yet there was a genuinely massive distinction between the two gatherings (P = 0.004) for the SNP Fok1 T>A (rs#2228570).

The participant groups were genotyped for three PTPN22 SNPs: SNP-2740 C>T (rs#1217412), SNP-1123 C>G (rs#2488457), and SNP 1858 C>T (rs#2476601). For the SNP-1858 C>T (rs#2476601), it was discovered that the genotypic distributions did not significantly differ between the two groups (P = 1.0) [9]. On the other hand, the SNP-2740 C>T (rs#1217412) and SNP-1123 C>G (rs#2488457) showed a statistically significant difference between the two groups (P 0.000).

For significant results, a logistic regression model was used. Only the vitamin D receptor SNP Fok1 T>A (rs#2228570), the IL-18 SNP-137 G>C (rs#187238), and the PTPN22 gene SNP-1123 C>G (rs#2488457) distinguished patients from controls.

Discussion

Although the cause of type 1 diabetes in humans is still poorly understood, it is known that both genetic and environmental factors play a significant role in determining disease risk. It is possible that the regions showing some evidence of linkage harbor variants that are not common SNPs well covered by the currently available genotyping platforms. This is a major focus of the current research, which is focused on identifying putative risk genes with rarer or structural variants that could contribute to disease [10].

The purpose of this study was to examine a sample of Egyptian children for polymorphic sites in some genes that are linked to type 1 diabetes.

SNP-137 G>C (rs# 187238) genotype and allele levels showed a statistically significant difference between patients and controls in the IL-18 gene, according to the findings. According to Novota et al.'s findings, the genotype CC appears to be a T1DM risk factor found in 2005 that the two IL-18 gene variants SNP-607 C>A (rs#1946518) and SNP 137 G>C (rs#187238) have no connection to adult type 1 diabetes or latent autoimmune diabetes in adults (LADA) susceptibility. On the other hand, Dong et al. discovered in 2007 that Chinese Han children with T1DM had a significantly higher (risk factor) CC genotype at position 607 in the promoter region of the IL-18 gene than controls, whereas the AA genotype at position 607 may have a protective role for T1DM [11].

Mojtahedi et al.'s findings were partially consistent with the current findings in 2006 found that there was no significant difference in the distribution of alleles and genotypes at positions -137 and -607 of the IL-18 gene between T1DM patients and control subjects in the Iranian population, regardless of age. In contrast, the current results regarding the genotype and allele of the IL-18 gene at position -137 were consistent with those of Massoud et al. in 2009 among the Iranian populace and Kretowski et al. in the Polish population in 2002. The two of them found that the recurrence of GG and CC genotypes at position 137 might be related with defenselessness to diabetes [12].

Conclusion

To close, IL-18 SNP-137G>C (rs#187238), VDR SNP - Fok1T>A (rs#2228570), and the SNP - 1123 C>G (rs#2488457) in PTPN22 quality might affect the event of T1DM in Egyptian kids. Large-scale, population-based case-control studies are required for additional research.

Acknowledgement

None

Conflict of Interest

None

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Cite this article: Abraham Kalfoury. The connection of polymorphism locations in certain genes with type 1 diabetes in an Egyptian kid sample. J Diabetes Metab, 2023, 14(2): 981.