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Original Article

ELUCIDATION OF THE BIOCHEMICAL MECHANISMS INVOLVED IN GENETIC BASIS OF LOW INCIDENCE OF DIABETES MELLITUS WITH SPECIFIC REFERENCE TO RAICA COMMUNITY OF RAJASTHAN

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ABSTRACT

Objective: The purpose of this study is to evaluate the genotypic variables linked to lower type-2 diabetes prevalence in the raica population in Rajasthan, India.

Methods: 150 participants from outside the Raica community and 114 participants from it were recruited for this study for ARNT gene and 112 from Raica and 86 from non-Raica for GLUT4 gene. Their age and sex, body mass index, waist-to-hip ratio, and laboratory results for fasting blood glucose were all taken into account. RFLP was used for genetic study.

Results: In this study, 114 participants from Raica community and 150 from non-Raica community were recruited. There were 40 females and 74 males in Raica group and 52 females and 98 males in non-Raica group for ARNT gene. For GLUT4 gene, 112 participants were recruited from Raica and 86 participants from non-Raica community. Raica community showed lower number of participants with fasting glucose>126 mg/dl, BMI>23. Allelic distribution of ARNT and GLUT4 was also lower among Raica.

Conclusion: The examined genetic variation is equally prevalent in Raica and non-Raica individuals, diabetes circumstances included.

Keywords: ARNT gene, GLUT4 gene, Camel milk, Type-2 diabetes

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INTRODUCTION

Diabetes mellitus (DM) is a chronic endocrinological disease with a high prevalence and rapid development that is characterized by abnormal blood glucose levels [1]. Type 2 diabetes (T2DM) is a chronic condition with an alarmingly high global prevalence. The International Diabetes Federation estimates that 536.6 million adults worldwide in 2021 had T2DM, a threefold rise from 20 y before to the report [2].

T2DM is a complex aetiology and is affected by a wide range of risk factors, some of which are changeable, like adopting a balanced diet and exercising and others of which are unavoidable like age and genetic variety [3]. Genetic or environmental factors may contribute to the dysregulation of the metabolisms of proteins, lipids, carbohydrates, and nucleic acids, which may result in metabolic disorders. The two main risk factors for type 2 diabetes, high body fat and insulin resistance, both contribute to non-alcoholic fatty liver disease (NAFLD). Other factors that contribute to T2DM include overeating, a poor diet, and a sedentary lifestyle, particularly in people with genetic predispositions [4].

Mendelian randomization (MR) and genome-wide association studies (GWAS) have shown that genetic variants are risk factors for human diseases [5]. GWAS and other sequencing studies have currently connected over 140 gene loci to T2DM [6]. In fifteen of these loci, membrane transport proteins-known or fictitious-are encoded. According to thorough GWAS, T2DM is a polygenic condition affected by more than 400 genetic variants [7].

In the last 15 y, researchers have identified a large number of chromosomal loci and variations linked to T2D, as well as the underlying biomarker features of fasting glucose, insulin, and glycated haemoglobin (HbA1c), which define the disease, its antecedent pathophysiology, and its mechanisms of complications [8].

Studies show low prevalence of T2DM in Raica community of Rajasthan [9, 10]. In this study, we tried to evaluate the association between genetic polymorphism implicated in low level of T2DM among Raica community.

MATERIALS AND METHODS

It was a case-control investigation. Samples and clinical data from a subset of patients were compared to those from healthy persons who were age and sex-matched.

This study was collaboratively done by the Department of Biochemistry and the Diabetes Care and Research Centre at the S. P. Medical College in Bikaner. Diabetes type 2 patients were enrolled in the trial. Pregnant women and patients with concomitant illnesses like renal, hepatic, or coronary heart disease were excluded from the study. Important study-related demographic, biochemical, and anthropologic characteristics were noted.

Blood samples were collected from study participants. The polymerase chain reaction (PCR), DNA quantification, and DNA isolation procedures were applied to the samples. For PCR amplification, the forward and reverse primers were ARNT-511F 5'-TATTTGTCTTGTCAACTGGCCTTT-GAC-3' and ARNT-511R 5'-CTGGCCAGTCCTCTTCCTGGG-AC-3. The ARNT polymorphism and the GLUT4 genes GLUT4F 5'-CCATCCTGATGACTGTGGCTCT-3' and GLUT4R 5'-GCCACGATGAACCAAGGAATGG-3' were both detected using RFLP on amplified products [fig. 1].

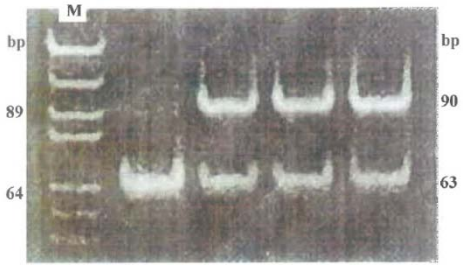

Fig. 1: Restriction fragment length polymorphism (RFLP) detecting ARNT polymorphism and PCR bands

Ethical statement

Patients' consent was obtained before the study began. The research section at Rajasthan University of Health Sciences gave its approval to this work. Dated 29 January 2008, letter No. F-7/Research/RUHS/2007-08/5675.

RESULTS

The study involved delineating te clinical and anthropometric features seen in Raica community members as opposed to the members of non-Raica community.

In this study, 114 participants from Raica community and 150 from non-Raica community were recruited. There were 40 females and 74 males in Raica group and 52 females and 98 males in non-Raica group for ARNT gene. For GLUT4 gene, 112 participants were recruited from Raica and 86 participants from non-Raica community.

Only 4 (3.5%) participants ad abnormal fasting glucose i.e.>126 mg/dl among Raica group while 84 (56%) participants were found to be having impaired fasting glucose. Same findings are also noted for BMI where Raica community has lower number of participants have BMI higher than 23 [table 1].

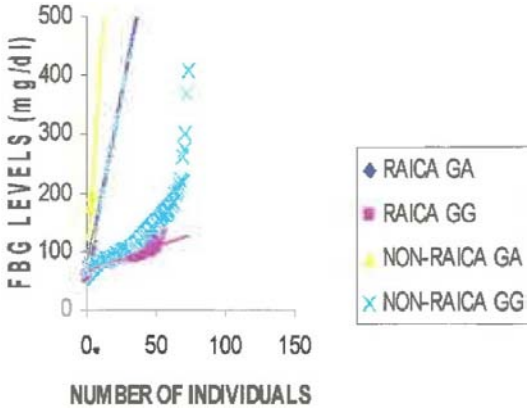

Fig. 2: Distribution of ARNT genotype alleles

The allelic distribution of ARNT gene shows almost similar distribution among both genders in Raica and non-Raica communities [fig. 3]

Table 1: Distribution of ARNT genotype among Raica and non-Raica community

	Raica (n)	Non-Raica (n)	P value
FBG>126 mg/dl	04	84	<0.0001
BMI>23	18	98	<0.0001
WHR>0.85	48	32	0.0004

Fig. 2 shows distribution of ARNT genotype alleles among Raica and non-Raica communities. Result shows higher number of non-Raica participants with impaired glucose express ARNT alleles.

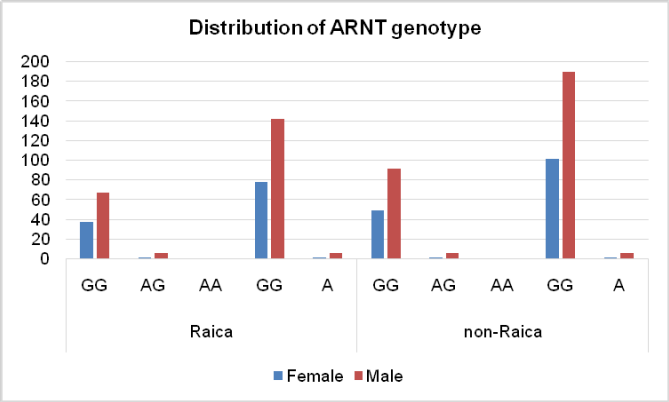

Fig. 3: Distribution of ARNT genotype and allele type in males and females of Raica and non-Raica communities, the difference in GLUT4 genotype and allelic distribution in males and females of Raica and non-Raica communities were similar to ARNT genotype distribution [fig. 4]

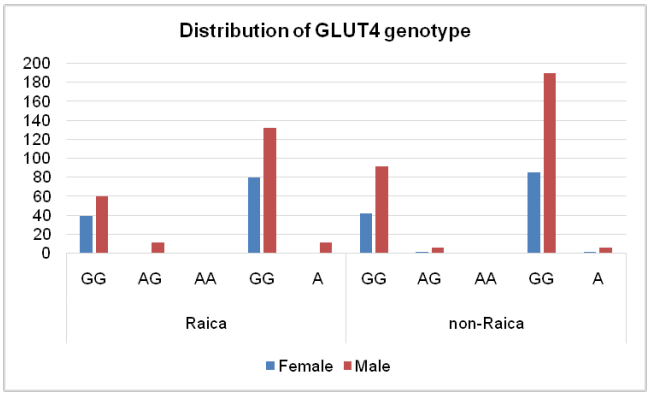

Fig. 4: Distribution of GLUT4 genotype and allele type in males and females of Raica and non-Raica communities

DISCUSSION

Diabetes has become one of the most dangerous and prevalent chronic diseases of our day, lowering life expectancy and creating life-threatening, disabling, and expensive complications. The prevalence of diabetes among adults aged 20 to 79 over the world was predicted to be 10.5% (536.6 million) in 2021 and 12.2% (783.2 million) in 2045. Diabetes prevalence was comparable between genders and was highest in people aged 75 to 79. In 2021, International Diabetes Federation predicted the T2DM prevalence to be higher in urban (12.1%) than rural (8.3%) areas and high-income (11.1%) than low-income (5.5%) nations [2].

Studies show ethnic and racial variability to developing T2DM [11, 12]. The Raica community in our study region is known to have a negligible prevalence of T2DM, so we compared Raica and non-Raica community participants with respect to anthropometric, clinical, and genotypic parameters to draw a conclusion as to why the Raica community has a lower T2DM prevalence.

Members of the Raica community had more control over the anthropometric and clinical traits that serve as risk factors for diabetes. It was found that there was a highly significant difference in the distribution of BMI, FBS, and WHR ($p<0.001$). Using the PCR-RFLP method, the frequency of the GG, AG, and AA alleles of the GLUT4 and ARNT genes was investigated. In the non-Raica community, the frequency of the GG allele was not statistically significant. The distribution of the AG allele in the Raica group and non-Raica community was also statistically insignificant. Our findings were in line with data published by Cao *et al.* [13] among Caucasians and Africans, where the distribution of GG allele and AG allele was virtually identical as no AA allele was reported by them. However, our study's differences from Cao *et al.*'s study in terms of BMI, FBS, WHR, and other variables are more significant.

In patients from the Raica and Non Raica communities with fasting blood sugar, the distribution of ARNT genotype and allele type was compared. Only 3.5% of participants in the Raica community had fasting blood sugar levels over 126 mg/dl, compared to 56% of participants in the non-Raica group. This finding further supports the Raica participants' low incidence of type 2 diabetes mellitus. Only 2 recorded instances of diabetes in the Raica community have been found; hence, statistical analysis was not feasible [13, 14]. Our investigation came to the conclusion that the GG allele appears to be linked to increased FBG levels. Low FBG carriers are more likely to have the AG allele. It's remarkable that none of the study subjects carried the AA allele.

In Raica communities, WHR with the GG allele and the AG allele were less common; but, in non-Raica communities, WHR with the GG allele and the AG allele were more common. Again, a significant difference was discovered. Other studies have also backed up the results [15-17]. This may account for the extremely low incidence of diabetes mellitus in the Raica population, but larger cohort studies are required for conclusive proof.

LIMITATIONS OF THE STUDY

According to sample size calculation at 80% study power and relative risk of 2 we need to analyze at least 516 Raica and non-Raica to ascertain any possible differences in the frequency of Glut4-30G/A in the two communities. This mutation also does not change any transcription factor binding sites in the promoter of the glut4 gene.

CONCLUSION

According to the results of the current study, the polymorphism under investigation has the same frequency distribution in Raica and non-Raica individuals, diabetes situations included. Along with genetic considerations, the socioeconomic and occupational environments of the participants need to be further investigated since they may provide a more accurate explanation for the Raica community's tendency towards leanness and improved glucose regulation.

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AUTHORS CONTRIBUTIONS

Dr. Mili Jain: Literature search, Writing-original draft preparation, data collection, statistical analysis, final approval of manuscript. Dr. Raj Kumar Vyas: Conceptualization, Statistical analysis, Writing-original draft and editing, final approval of manuscript, Supervision.

CONFLICT OF INTERESTS

Declared none

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