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Prevalence of Type 2 Diabetes Mellitus among Women and the Associated Risk Factors

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ABSTRACT

The prevalence of non-communicable disease like Type 2 diabetes mellitus is increasing among woman. The study is aimed at investigating the prevalence of Type 2 Diabetes Mellitus and their associated risk factors among woman, in the states of Andhra Pradesh and Telangana of India. The present study is the part of case control study of Genetic and Non-genetic risk factors for Type 2 Diabetes Mellitus and its related complications. Validation of the single nucleotide polymorphisms in Calpain10 and Adiponectin genes with proven role in predicting Type 2 Diabetes Mellitus in woman in comparison with the men among the discrete diabetic population under the study. The biochemical parameters were also compared. The study was conducted among a total of 180 subjects (96 females and 84 males) out of these, 90 were diabetic cases (54 females and 36 males) and 90 were controls (42 females and 48 males). All these subjects were used for non-genetic risk factor study. Only 41 diabetic cases (28 females and 13 males) and 10 controls were used for the Single Nucleotide Polymorphism (SNP) study.

On measurement of the blood glucose levels (Fasting and Post prandial blood glucose), it was found that the prevalence of diabetes was more among the women than in men. The mean \pm standard deviation value was found to be high in diabetic subjects (both women and men) in comparison to the normal ones. The Lipid concentrations were found to be high in all diabetic cases and some controls showing their susceptibility for Type 2 diabetes Mellitus in future. Only HDL showed low concentrations.

The SNP rs2975760 of CAPN 10 gene is present in 50% of the diabetic women studied where as it is present in 46.1% of the diabetic men. Similarly the SNP rs3792267 of CAPN 10 gene is present in 58.5% of the diabetic women population whereas this SNP is present in 30.7% of diabetic men. The SNP rs3774261 of ADIPOQ gene is present in 42.8% of the women population and whereas this SNP is present in 38.4% of diabetic men. A new SNP was identified in new position of CAPN 10 gene and was found in 39.2% of diabetic women whereas it was found in 15.3% of the men population.

INTRODUCTION

Type 2 Diabetes Mellitus has become a global health issue ^[1]. T2DM is a condition characterized by elevated blood sugar levels. This condition is due to either insulin resistance or absolute or partial deficiency of insulin secretion by the pancreatic β -cell

[2-4].The number of people affected with diabetes is projected to be 438 million by the year 2030 [5]. Prolonged period of diabetes increases the risk for other complications. The frequency is increasing many folds especially in south Asian population due to high genetic and non-genetic risk factors [6]. Diabetes has significant effect on adult population [7-10]. The risk for death is twice in people with diabetes when compared to normal persons [11].

Diabetes among woman

The women with diabetes stand for the second highest mortality in South Asians [12]. Approximately 9% of the South East Asia women were diabetic in 2008 and 10% were of 25 years age. The more prevalence of diabetes among women in the developed and developing countries is attributed to more of the body fat and the increased lipid profile. About 55% women deaths occur due to diabetes [13]. The ninth leading cause of death among women is diabetes which accounts for approximately 2.1 million women deaths worldwide compared to 1.8 million deaths in men [13]. The life span decreases by 8.2 years among diabetic women and by 7.5 years among diabetic men on average than those who don't have the disease. Risk of heart disease increases six times in diabetic women when compared to normal woman.

Risk factors

The major risk factors contributing to diabetes are Biochemical, environmental and genetic factors [14-16]. All of them together or independently are responsible for the development and advancement of the disease. This is because of lipid abnormalities characterized by increase in the Triglycerides, Total Cholesterol, LDL and decrease in the HDL concentrations. They are independent predictors of type 2 diabetes mellitus [17]. Overweight, obesity and physical inactivity along with Lifestyle and diet also will contribute for the disease [18,19]. With the economic development and globalization the dietary habits have changed in India. The more intakes of saturated fats, energy-dense foods and fast foods are responsible for the major cause of concern for diabetes among women. South Asian Indians due to their genotype are more prone to diabetes, especially Indians [20,21]. A subtle variation in the gene sequence is associated with an increased risk of developing diabetes and its related complications [22].

METHODOLOGY

Collection of sample

The Fasting and Postprandial left over blood samples were collected from 180 subjects (96 females and 84 males were considered for the study) of the 200 enrolled subjects visiting diagnostic centers for routine biochemical examination .The people suffering from infectious diseases were excluded from the study. They were aged between 15-85 years.

The samples were collected after taking their written consent. Out of these 90 were diabetic cases (54 females and 36 males) and 90 were normal subjects. The samples were collected in EDTA and non-EDTA vials as per protocol [23]. For the SNP study Only 41 diabetic cases (28 females and 13 males) 10 normal samples were processed by modified Sambrook protocol for DNA extraction and purification [24,25].

Selection of biochemical parameters

The Blood glucose levels were measured using Glucose oxidase peroxidase method for the 90 diabetic cases (54 females and 36 males) and 90 controls (42 females and 48 males) Their concentrations of lipids Total Cholesterol, Triglycerides, Low Density Lipoproteins (LDL) and High density Lipoproteins (HDL) were also analyzed and measured using Star 21 plus auto-analyzer [26].

Selection of single nucleotide polymorphisms

The SNPs rs2975760 and rs3792267 [29] in CAPN10 gene and rs rs3774261 [30] in ADIPOQ gene for were selected for their validation in 41 subjects of which 28 females and 13 males of our study population and 10 controls [27,28].

EXPERIMENTAL DETAILS

Analysis of biochemical parameters

The Biochemical parameters of the women study participants were compared to the men .The data for different parameters are presented in the **Table 1** shown below as mean \pm standard deviation .The subjects of the study were established as diabetic cases based on their biochemical reports which showed FBG of value more than 126 mg/dl or \geq 7.0 mmol/l and PPBG of value more than 200 mg/dl or \geq 11.1 mmol/l in accordance to WHO diagnostic criteria for diabetes.

Table 1. Lipid profile characteristics of the study population.

Parameter	T2DM Cases Mean \pm SD	Controls Mean \pm SD	Normal Range
Total Cholesterol (TC)	176.8 \pm 50.3	163 \pm 51.7	130-250
Triglycerides (TG)	198.1 \pm 87.7	141 \pm 56.9	50-150
HDL	42.5 \pm 4.7	43.2 \pm 5.9	35-70
LDL	86.4 \pm 25.8	44.0 \pm 28.6	Upto140
VLDL	41.8 \pm 20.7	28.6 \pm 13.6	10-40

Analysis of reported SNPs

The purified DNA samples were amplified by Polymerase Chain Reaction and were analyzed qualitatively by Agarose Gel Electrophoresis [29-33]. They were analysed for SNP specific region after the sequencing using different computational tools. The SNPs of the

CAPN10 gene, rs2975760 with nucleotide change from C→T with corresponding amino acid change from Ala→Val was observed in 14 diabetic women cases and rs3792267 the nucleotide change G→A with corresponding amino acid change from Val→Ile in 15 diabetic women cases. The nucleotide change and corresponding amino acid change in the ADIPOQ gene is A→G (Met→Ile) for SNP rs3774261 is noticed in 11 women T2DM cases. The nucleotide change from A→G and the corresponding amino acid change from Arg→Gly identified in a new position were observed in 10 women diabetic cases of T2DM. CAPN10 gene SNPs are not present in controls [34]. All the three SNPs are present in 6 of the women T2DM cases. The BOX SHADE (Figure 1) of the amplified gene shows the presence of SNPs along with the SNPs in new position (Tables 1-3).

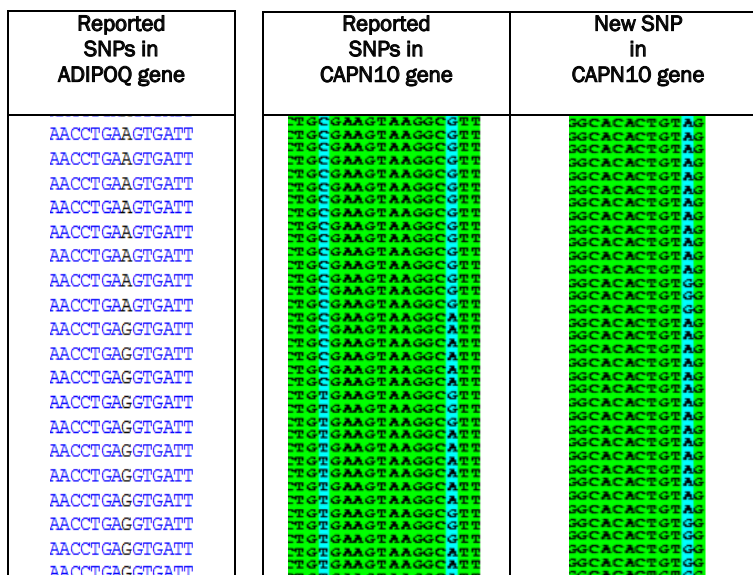


Figure 1. BOX SHADE of SNPs in CAPN10 and ADIPOQ gene.

Table 2. Comparison of distribution of FBG and PPBG among women and men.

	No. of Samples (n)	FBG mg/dl	PPBG mg/dl
Diabetic women	54	165.2 ± 57.4	241.3 ± 76
Diabetic men	36	134.2 ± 40.2	211.13 ± 57.4
Normal Range		70-110	170-200

Table 3. Distribution of SNP among diabetic women and men.

GENE	Rs of reported SNP	Nucleotide change in SNP	Amplicon	New SNP Position	% Positive In Women	% Positive In men
CAPN10	rs2975760	C/T	240591700-240592224	240592222	50	46.1
	rs3792267	A/G			58.5	30.7
ADIPOQ	rs3774261	A/G	186853309-186853804		39.2	15.3
					42.8	38.4

RESULTS

Results of the blood sugar profile showed increased mean value of fasting blood Glucose (FBG) levels in controls and Post Prandial Blood Glucose (PPBG) in the study. For diabetic women cases FBG was 165.2 ± 57.4 and 134.2 ± 40.2 and PPBG was 241.3 ± 76 and 211.13 ± 57.4 (Table 2). FBG and PPBG were slightly higher in women in comparison to men.

Results of Lipid Profile showed the increased value and were almost similar to men.

Thea over all mean ± Standard deviation for women and men diabetic population is TC=176.8 ± 50.3, TG=198.1 ± 87.7, HDL=42.5 ± 4.7, LDL=86.4 ± 25.8, VLDL=41.8 ± 20.7 as shown in Table 1.

The SNP rs3774261 of ADIPOQ gene is present in 42.8% of the women population and whereas this SNP is present in 38.4% of diabetic men. The SNP rs2975760 of CAPN 10 gene is present in 50% of the diabetic women studied where as it is present in 46.1% of the diabetic men. Similarly the SNP rs3792267 of CAPN 10 gene is present in 58.5% of the diabetic women population whereas this SNP is present in 30.7% of diabetic men. A new SNP was identified in new position of CAPN 10 gene and was found in 39.2% of diabetic women whereas it was found in 15.3% of the men population. The distribution of SNP in the study population is shown in Table 3.

*The number of female diabetics outnumber the males in the population study. This is indicated by the presence of 54 females and 36 males in the enrolled population of 90 diabetics. The FBG and PPBG levels among women are more when compared to the men (**Table 2**). The SNPs in the candidate genes CAPN10 and ADIPOQ gene are detected more in women diabetics when compared to the men.*

DISCUSSION

Globally the prevalence of diabetes in woman is increasing at an alarming rate^[32]. The prevalence studies of diabetes among woman showed varying results. Diabetes affects women's health across the life stages. The prevalence of diabetes was more in woman was more in Nepal and Sri Lankan woman^[35]. The number of American women diagnosed with diabetes is expected to reach 27.5 million by 2050^[36]. India is having the second highest number of known diabetic cases worldwide^[37]. GDM prevalence is 3.8 to 21% in different parts of India^[38,39].

In the case control study among the 180 subjects 90 were diabetic cases and 90 were controls, the females and males were 96 and 84 respectively. The number of women in our discrete diabetic population was more owing to increase in the number of women diabetics.

CONCLUSION

The obesity among the woman is responsible for diabetes in diabetic cases and is a risk factor in controls; the lipid abnormalities are the risk factors for cardiovascular disease in diabetic cases and are risk factor for diabetes in controls.

With the results that the FBG and PPBG levels among women are more when compared to the men and more percentage of women positive for SNP from this we can safely conclude that prevalence of diabetes is more among women in discrete diabetic population Telangana and Andhra Pradesh states in India.

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