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RESEARCH ARTICLE

IS GENDER AND RELIGION SIGNIFICANT IN DEVELOPMENT OF DIABETES IN OFFSPRINGS OF PATIENTS WITH TYPE 2 DIABETES MELLITUS? A DISCUSSION.

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Abstract

Background: The purpose of this study was to observe any association of gender and religion with the development of Type 2 Diabetes Mellitus in offsprings of Type 2 Diabetic patients. To the best of our knowledge, no such study on this topic has been done before

Methods: One twenty one patients and one twenty one controls were taken. Three parameters were chosen to observe any trend towards development of Type 2 Diabetes Mellitus in cases and controls. The parameters chosen were Fasting Blood Glucose (FBG), Glycosylated Hemoglobin (HbA1c) and Insulin. The cases and controls were divided into two separate groups, on the basis of gender i.e. males and females and on the basis of religion i.e. Hindus and Muslims.

Results: FBG was statistically insignificant thus failing to establish any relationship of gender and religion with FBG in offsprings of patients with Type 2 Diabetes Mellitus. There was no association of gender and religion affecting HbA1c in offsprings of patients with Type 2 Diabetes Mellitus. Insulin was statistically insignificant thus, once again, failing to establish any association of gender and religion with development of Type 2 Diabetes Mellitus in offsprings of patients with Type 2 Diabetes Mellitus.

INTRODUCTION

This study was aimed to analyze any association between gender, religion and occurrence of Type 2 Diabetes Mellitus in offsprings of patients with Type 2 Diabetes Mellitus.

Diabetes mellitus is one of the major risk factors for cardiovascular disease (Ueshima H et al., 2008), which in turn is the most common cause of morbidity and mortality worldwide (Bonow RO et al., 2002). Type 2 DM along with insulin resistance is generally accompanied by low HDL levels and high plasma triglycerides (Diabetologia 28, 1985; Ganda OP., 1980; Singleton JR et al., 2003; Shaw JT et al., 1999; Pontiroli AE et al., 2000; Eckel RH et al., 2005) Similar findings mainly attributed to glucose intolerance, hyper-insulinemia and obesity have been found in the off springs of individuals with type 2 DM (Shaw JT et al., 1999; Haffner SM et al., 1990; Chathurvedi D et al., 2009; Jouret B et al., 2007).

Approximately 150 million people had T2DM in the year 2000; this number could double by 2025 (Zimmet P et al 2001). The potential for increase in the number of cases of T2DM is highest in Asia; India and China facing the greatest challenges. (Hossain P, et al 2007).The diabetes mellitus epidemic that has enveloped westernized societies is believed to be related to obesity and decrease in physical activity (James WP, 2008). Today more than 1.1 billion adults are overweight and 312 million of them are obese. In addition at least 155 million children worldwide are

overweight or obese (Haslam DW, James WP, 2005). Unlike their western counterparts, the Indian patients with diabetes mellitus have lower body mass index and are younger. (The DECODE-DECODA Study Group, Diabetologia 2003). The financial burden and human suffering due to diabetes mellitus and its complications are enormous.

Clinical progression from normal glucose tolerance to overt T2DM takes years and involves an intermediate stage of impaired glucose tolerance (impaired glucose tolerance and/or impaired fasting glucose). Subjects with IGT also have increased risk for macro vascular disease. Dyslipidemia, hypertension and central obesity are also more common in these subjects. Impaired fasting glucose is another category like IGT, which is also a risk factor for cardiovascular disease and future T2DM (Zimmet P et al 2001). Several randomized controlled trials conducted to test the impact of behavioral and pharmacological interventions in high-risk groups have demonstrated that it is possible to reduce the number of people who develop diabetes by 25–62% over 3 to 6 year time frames (Tuomilehto J et al, 2001). As a result, discussions on mitigating the growing public health problem of diabetes mellitus have expanded from a relatively narrow focus on disease treatment to a broader focus on disease prevention. (Buchanan TA, 2005). Data from the UKPDS indicate that pancreatic β-cell function is substantially reduced at the time of clinical diagnosis of diabetes mellitus (UKPDS overview of 6 years'). Even at earlier stage of IGT, β-cell function is already impaired and intervention at this stage may also be too late for prevention (Sicree RA et al, 1987). Intensive intervention programmes using well-developed life style modification approaches for subjects with IFG/IGT often show high relapse rates; weight gain and increase in blood glucose occurring 1 to 2 years after an initially encouraging response (Mann J. Stemming, 2000). Therefore it is important to identify earlier detectable defects and develop strategies for preventing IGT and IFG .

Subjects with family history of T2DM, members of certain ethnic/racial groups, women with history of gestational diabetes, polycystic ovary syndrome subjects with obesity, dyslipidemia and hypertension are at increased risk for developing diabetes mellitus.

Those with family history of T2DM, members of certain ethnic/racial groups, women with history of gestational diabetes, polycystic ovary syndrome, Obesity, dyslipidemia and hypertension are at increased risk for developing diabetes mellitus. Parental diabetes is one of the dominant genetic factors in the causation of T2DM (Meigs JB et al, 2000). The effect of maternal diabetes on offspring health has been extensively investigated (Dabelea D et al 2000,Dabelea D et al 2008)

Diabetes mellitus is one of the major risk factors for cardiovascular disease (Ueshima H et al, 2008), which in turn is the most common cause of morbidity and molality worldwide (Bonow RO et at, 2002). In patients with Type 2 DM, low HDL levels and high plasma triglycerides are generally accompanied by Insulin resistance (Diabetes drafting group, 1985, Ganda OP, 1980, Singleton JR et al, 2003, Shaw JT et al, 1999,Pontiroli AE et al 2000, Eckel RH et al 2005).

In other studies, Glucose intolerance, Hyper-insulinemia and obesity have been found in the offsprings of individuals with type 2 DM (Shaw JT et al, 1999, Haffner SM et al 1990, Chathurvedi D et al 2009, Jouret B et al 2007, Chiasson et al 2007).

The offspring of type 2 diabetic patients appear to be a good group to study to learn about the abnormalities in the absence of the confounding effects of hyperglycemia. In fact, they have 30-40% chances of developing type 2 diabetes and frequently show abnormal glucose tolerance and several metabolic abnormalities, such as low insulin release or insulin resistance. However, insulin resistance is a risk factor for the development of type 2 diabetes. Children from families with diabetes mellitus are at risk for obesity. Hyperinsulinemia, by its action on the brain induces behaviors and lifestyles conducive to obesity. Low HDL cholesterol values along with overweight and glucose intolerance in offspring of diabetics is well documented.

Gender also influences the likelihood of developing heart disease:
Men under the age of 55 are more likely to develop heart disease than women under the age of 55. Estrogen provides women some level of protection against heart disease before menopause. Once a woman reaches menopause, the risk for developing heart disease increases

MATERIALS AND METHODS:

Sample Collection

Blood samples were collected in a fasting state from healthy subjects in EDTA vials kept in ice, centrifuged

immediately and plasma was stored at -20°C until assayed. All basal parameters like Insulin, HDL, Cholesterol, LDL, VLDL, TG, Glycosylated Hemoglobin (HbA1c) and Cortisol were estimated in the sample. The subclasses of HDL as HDL2 and HDL3 were also included in the study. Blood samples for plasma glucose were collected in potassium oxalate/ sodium fluoride vials.

Ethical Approval

The study was approved by the institutional ethics committee as per ICMR guidelines. Written informed consent was obtained from all subjects who wished to participate in the study. In case of children less than 18 years, consent was obtained from one of the parents and verbal assessment of the child was also done.

Inclusion and Exclusion Criteria

All non-diabetic children and grandchildren of the index cases were included in the study. Subjects diagnosed with diabetes or other systemic disorders and pregnant women were excluded. Controls comprised normal subjects without a family history of diabetes in two generations. The controls were normal in all aspects except for minor ailments. Details of medical history were collected and physical examination including anthropometry was performed. Height was measured with a Stadiometer to the nearest centimeter and weight was also measured. BMI was calculated as weight (kg) divided by the square of the height in meters. A value of 25 or more was considered as overweight for the adult population for BMI. For children and adolescents up to 18 years cut-offs recommended by the International Obesity Task Force (IOTF) were used (Cole et al., 2000).

Size

One hundred and twenty one subjects with family history of DM volunteered for the study and were enrolled as cases and one hundred twenty one matched subjects without family history of DM were enrolled as controls.

Biochemical Analysis

Fasting glucose was estimated on a fully–automated Cobas Integra 400 plus (Roche) by using standard commercially available kits or a standard methodology was adopted wherever necessary. HbA1c was estimated by D-10 dual HbA1c program. Plasma insulin was measured by electro-chemiluminescence assay employing ELECSYS 2010 (Roche Diagnostics, Indianapolis, USA). This assay uses monoclonal antibodies against insulin. (The Insulin kit used in ELECSYS 2010 was procured from Vikas Enterprises in New Delhi, India)

Statistical Analysis

The statistical analysis was carried out using SPSS version 16 software and the technique applied was student t-test to compare continuous data in two groups. Log transformation was applied to the skewed data. A chi square test was done to evaluate the difference in frequency between the two groups.

RESULTS:

One hundred and twenty one cases and controls completed the study. Out of 121 cases, 62 were females whereas 59 were males. On the other hand, out of 121 controls, 59 were females and 62 were males. Equal number of these cases and controls were from two major religions in the country i.e. Muslims and Hindus. Out of the already mentioned 121 cases, there were 61 Hindus and 60 Muslims whereas out of the above mentioned 121 controls, 60 of them were Hindus and Muslims comprised of 61 controls. This equality in sample collection was maintained to accurately correlate gender and religion.

The parameters upon which the study was based included Fasting Blood Glucose (FBG), Glycosylated Hemoglobin (HbA1c) and Insulin.

FBG:

As far as cases are concerned, mean FBG values of males and females were 88.10 ± 12.48 and 88.46 ± 8.66 respectively. Both were statistically insignificant ($p>0.05$). On the other hand, on the basis of religion, mean FBG values of Hindus and Muslims were 88.91 ± 8.12 and 87.67 ± 12.79 respectively. This was again statistically insignificant ($p<0.05$).
As far as Controls are concerned, mean FBG of male controls was 87.40 ± 10.92 and that of female controls was 85.00 ± 6.99. That of Hindu controls were 88.45 ± 10.37 and Muslim controls was 83.97 ± 7.29.
Hence FBG comparison between cases and controls on the basis of gender ($p>0.05$) and on the basis of religion ($p>0.05$), both were statistically insignificant.

	CASES		CONTROLS	
	Mean ± SD	Min-Max	Mean ± SD	Min-Max
MALES	88.10 ± 12.48	69 - 153	87.40 ± 10.92	70 – 118
FEMALES	88.46 ± 8.66	63 - 104	85.00 ± 6.99	71 – 104
MUSLIMS	87.67 ± 12.79	63 - 153	83.97 ± 7.29	74 – 108
HINDUS	88.91 ± 8.12	75 - 108	88.45 ± 10.37	70 – 118

Table I.- FBG comparison in cases and controls

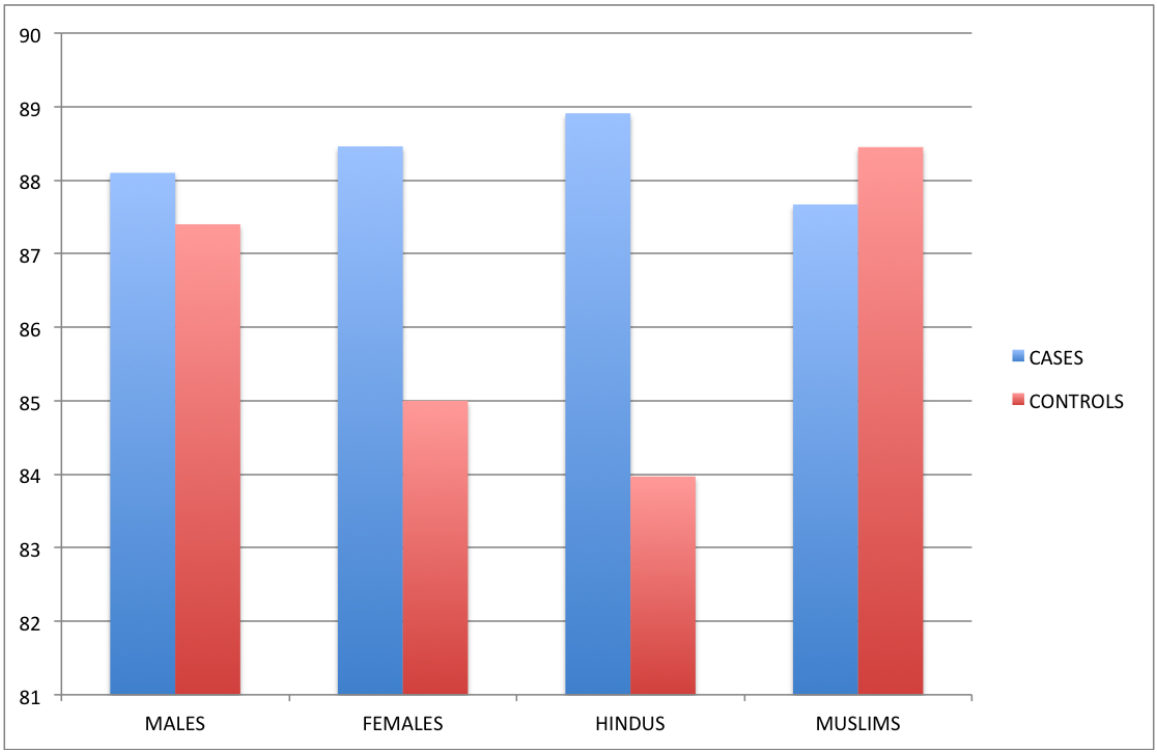

Fig. 1 – Graph depicting FBG values in cases and controls.

HbA1c:

Mean HbA1c value of male cases was 5.06 ± 0.46 and of female cases was 5.16 ± 0.47. That of Hindu cases were 5.06 ± 0.51 and Muslim cases was 5.14 ± 0.42.

On the other hand, as far as controls are concerned, mean HbA1c of male cases was 5.13 ± 0.52 and female cases were 5.09 ± 0.43. As far as religion is concerned, mean HbA1c values of Hindus and Muslims were 5.21 ± 0.47 and 5.00 ± 0.46 respectively.

The comparison between cases and controls on the basis of gender and religion was again statistically insignificant with p>0.05 for both gender and religion.

	CASES		CONTROLS	
	Mean ± SD	Min-Max	Mean ± SD	Min-Max
MALES	5.06 ± 0.46	4 - 6	5.13 ± 0.52	4 – 6
FEMALES	5.16 ± 0.47	4 – 7	5.09 ± 0.43	4 – 6
MUSLIMS	5.14 ± 0.42	4 – 6	5.00 ± 0.46	4 – 6
HINDUS	5.06 ± 0.51	4 – 7	5.21 ± 0.47	4 – 6

Table II. -HbA1C comparison in cases and controls

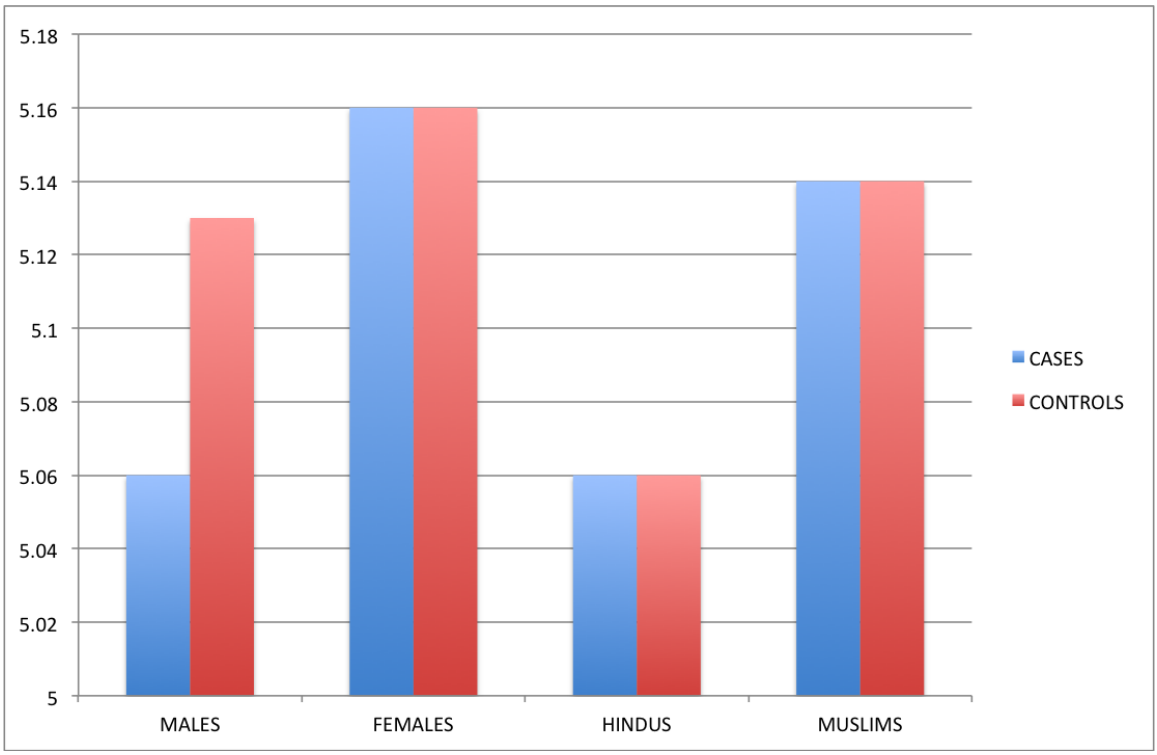

Fig. 2 – Graph depicting HbA1c values in cases and controls.

Insulin:
Mean Insulin of male cases was 10.46 ± 5.79 and female cases were 11.63 ± 10.76. While as mean Insulin values of Hindu cases was 12.24 ± 11.07 and Muslim cases was 9.83 ± 5.27.
As far as controls were concerned, mean Insulin of male controls was 9.97 ± 7.85 and female controls were 8.67 ± 3.82. Mean Insulin values of Hindu and Muslim controls were 9.54 ± 6.70 and 9.09 ± 5.63 respectively.
On comparing cases and controls purely on the basis of their Insulin values, it was observed that their Insulin values were statistically significant. ($p<0.05$). However the relation on the basis of gender and religion was statistically insignificant with $p>0.05$ when comparing on the basis of gender and again $p>0.05$ on the basis of religion.

	CASES		CONTROLS	
	Mean ± SD	Min-Max	Mean ± SD	Min-Max
MALES	10.46 ± 5.79	2 – 28	9.97 ± 7.85	3 – 40
FEMALES	11.63 ± 10.76	2 – 74	8.67 ± 3.82	3 – 20
MUSLIMS	9.83 ± 5.27	2 – 31	9.09 ± 5.63	3 – 40
HINDUS	12.24 ± 11.07	2 – 74	9.54 ± 6.70	3 – 40

Table III. -Insulin comparison in cases and controls

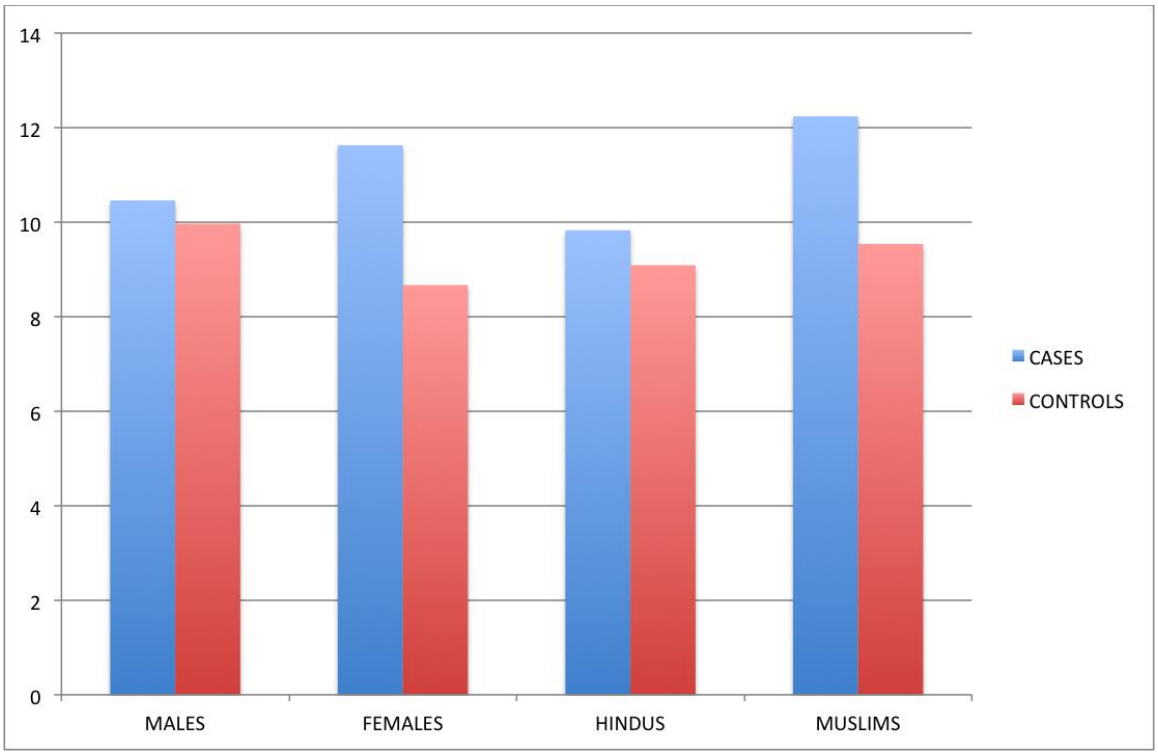

Fig. 3 – Graph depicting Insulin values in cases and controls.

DISCUSSION:

The purpose of this study was to study the association of gender and religion with the development of Type 2 Diabetes Mellitus in offsprings of Type 2 Diabetic patients. To the best of our knowledge, no such study on this topic has been done before. In a study done on Trinidadian population, gender was found irrelevant when evaluated as a risk factor for the development of Type 2 DM (Nayak BS et al 2014)
In another study done on a Japanese work-based cohort, it was studied that the in offsprings of patients with Type 2 Diabetes Mellitus, sex of the affected parent affected the incidence of Type 2 Diabetes Mellitus in the offspring (Wang C et al 2015).

Yet another study done on a Spanish population revealed that incidence of Type 2 Diabetes Mellitus is slightly higher in men and the same peaks in middle age(Vega T et al 2015).
In yet another study done on the Mauritius population observing gender differences in the prevalence of impaired fasting glucose and glucose tolerance, it was studied that Impaired Glucose tolerance (IGT) was more common in women than in men (Williams JW, et al2003)
The basis for this could be the fact that women have a smaller mass of muscle than men and therefore less muscle available for the uptake of the fixed glucose load (75 g) used in the oral glucose-tolerance test (Færch K et al)
Women have also been observed to have a low whole-body Insulin sensitivity. This could be attributed to relatively high levels of Estrogen and Progesterone, which can reduce Insulin sensitivity resulting in Impaired Glucose Tolerance (van Genugten RE et al, 2006).
Physical inactivity and unhealthy diet in Saharan Africa (Esayas Haregot Hilawe et al) have also both been associated with impaired glucose tolerance. Since, in may countries such as the sub-Saharan African countries, women are less physically active than men, this could be another reason for increased incidence of impaired glucose tolerance in women as compared to men (Guthold R et al, 2008, Kruger A et al)
In the present study, our main aim was to establish an association between gender, religion and occurrence of Type 2 Diabetes Mellitus, if there is any, in offsprings of patients with Type 2 Diabetes Mellitus. We selected three parameters to observe any trend towards development of Type 2 Diabetes Mellitus in cases and controls. The parameters chosen were FBG, HbA1c and Insulin. We divided the cases and controls in two separate groups, on the basis of gender i.e. males and females and on the basis of religion i.e. Hindus and Muslims.
Mean FBG in Male cases (88.10 ± 12.48) was almost similar to male controls (87.40 ± 10.92) whereas in female cases was slightly higher (88.46 ± 8.66) as compared to female controls (85.00 ± 6.99). As far as on the basis of religion is considered, mean FBG value of Hindu cases (88.91 ± 8.12) and Hindu controls (88.45 ± 10.37) was almost similar. On the other hand, mean FBG of Muslim cases was more (87.67 ± 12.79) as compared to Muslim controls (83.97 ± 7.29). All these values were however statistically insignificant thus failing to establish any relationship of gender and religion with FBG in offsprings of patients with Type 2 Diabetes Mellitus.
As far as HbA1c is concerned, mean HbA1c in male cases was slightly lower (5.06 ± 0.46) as compared to male controls (5.13 ± 0.52). In Female cases, mean HbA1c was slightly higher (5.16 ± 0.47) as compared to controls (5.09 ± 0.43). As far as religion is concerned, mean HbA1c of Muslim cases was slightly higher (5.14 ± 0.42) as compared to Muslim controls (5.00 ± 0.46). Regarding Hindu cases, their mean HbA1c was slightly lower (5.06 ± 0.51) than Hindu controls (5.21 ± 0.47). Again, none of these comparisons were statistically significant based upon their p values and hence no association of gender and religion affecting HbA1c in offsprings of patients with Type 2 Diabetes Mellitus could be established.
Our last parameter was Insulin estimation. Mean Insulin value in Male cases was slightly higher (10.46 ± 5.79) as compared to male controls (9.97 ± 7.85). As far as female cases are concerned, mean Insulin was marginally higher (11.63 ± 10.76) when compared with female controls (8.67 ± 3.82). In Hindus cases, on the other hand, mean Insulin was again higher (12.24 ± 11.07) when compared with Hindu controls (9.54 ± 6.70). Mean Insulin of Muslim cases (9.83 ± 5.27) was slightly higher than Muslim controls (9.09 ± 5.63). Although the comparison between cases and controls based upon these total Insulin values was significant, when compared with controls independently based upon gender and religion, again it was observed to be statistically insignificant thus, once again, failing to establish any association of gender and religion with development of Type 2 Diabetes Mellitus in offsprings of patients with Type 2 Diabetes Mellitus.
Lastly, based upon statistical analysis using SPSS software, as mentioned above, it was further observed that, while comparing cases and controls, P value for gender and religion was calculated to be >0.05 Since statistical significant level of $p<0.05$ was followed, both gender and religion were found out to be statistically insignificant thus, once again, failing to establish any association of gender and religion with the occurrence of Type 2 Diabetes Mellitus in the offsprings of patients with Type 2 Diabetes Mellitus.
Thus, based upon the above statistics of our study, it can be safely assumed that gender and religion, both, are not significant in the occurrence of Type 2 Diabetes Mellitus in offsprings of patients with Type 2 Diabetes Mellitus.

DECLARATION OF INTEREST:

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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