Research Article

TYPE 2 DIABETES WITH AND WITHOUT HYPERTENSION IN A NORTH INDIAN POPULATION: A DESCRIPTIVE STUDY

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A R T I C L E   I N F O

A B S T R A C T

Introduction: Type 2 DM is a disorder of global magnitude and is now considered a major health challenge in the developing countries. The complex correlation between glucose intolerance, hypertension and obesity, as seen in metabolic syndrome, points towards a possible relationship between hypertension and diabetes mellitus. Studies on the subject have shown mixed results in western populations. The Indian scenario remains obscure with little work on the subject.

Methods: A cross sectional study was done in MMIMSR, Mullana, Ambala in which descriptive data was collected and serum insulin, c-peptide, fasting blood glucose levels were estimated on 50 diabetic hypertensives and 50 diabetic normotensives. Statistical analysis of the data was done by SPSS and MS Excel.

Results: In our study we found that hypertensive status of the patients was significantly associated with duration of diabetes (P=0.001) and BMI. (P=0.003). We also found elevated levels of insulin and c-peptide in diabetic patients with their mean levels being 11.24±10.57 μIU/ml (reference interval = 0-10 μIU/ml). and 2.59 ± 1.45 ng/ml (reference interval = 0.78-1.89 ng/ml) respectively. Hypertensive patients had mean serum C-peptide levels of 2.72 ± 1.57 (median 1.9 interquartile range 2.4). Normotensive patients had serum C-peptide levels of 2.45±1.31 ng/ml (median 2.1, interquartile range 1.2). The difference was statistically insignificant (P=0.449). No relationship could be elucidated between hypertension and serum insulin levels either. (P = 0.212).

Conclusion: The descriptive parameters in our study were in accordance with the norms. Hypertensive status of the patients was significantly associated with duration of diabetes and BMI. Although insulin, c-peptide levels were raised, no association with hypertension could be elucidated. This could possibly be because beta cell activity tends to vary considerably in different populations. Studies with a broader patient base could throw further light on the subject and are a need of the hour.

INTRODUCTION

Diabetes Mellitus (DM) is a group of metabolic disorders that share hyperglycaemia as the major presentation (1). It is a disorder of global magnitude and is now considered a major health challenge in the developing countries (2). According to recent estimates, 72.1 million diabetics live in India, and the number is expected to rise to 134.3 million by 2045 (3).

Type 2 DM is a disease with an extremely complex pathophysiology. Complications are also common, generally in untreated cases. The complications may be macrovascular like atherosclerosis and hypertension or microvascular like nephropathy, neuropathy and retinopathy. Many studies have found that micro vascular complications are associated to a

greater extent with stimulated C-peptide levels than with basal levels (4), the reverse has also been observed in some studies (5). Different variants of C-peptide with contrasting phenotypic associations have also been reported (6,7). C-peptide is believed to induce smooth muscle cell proliferation and thus lead to atherosclerotic lesions in type 2 diabetic patients although the exact mechanism is still unclear. It can thus be used as a marker of subclinical atherosclerosis in patients with T2DM. Alteration in levels of C-peptide in hypertensive patients of type 2 DM has also been reported (8). A possible mechanism could be the activation of endothelial nitric oxide synthetase (eNOS) by C-peptide (9). However, contrary findings have also been reported (10). Administration of C-Peptide in animal models has been shown to exert beneficial effects on RBCs by release of ATP thereby stimulating the production of nitric oxide (NO) (11). The complex correlation between glucose intolerance, hypertension and obesity, as seen in metabolic syndrome, points towards a

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possible relationship between hypertension and insulin resistance in diabetic patients. A number of studies have been performed to evaluate the possible role of hypertension with regards these analytes. Mixed results have been reported. (8,10,12)

MATERIALS AND METHODS

The study was conducted in the Department of Biochemistry in collaboration with the department of General Medicine, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala, Haryana. The study was performed on fifty hypertensive type 2 diabetics and fifty normotensive type 2 diabetics. Prediagnosed diabetic patients admitted in General Medicine ward or attending the Medical OPD were chosen for the study. Type 1 diabetics, patients on insulin, pregnant and lactating women and patients with thyroid abnormalities were excluded. American Diabetic Association (ADA) (13) and WHO (14) criteria, as under, were used to define DM., which are as under:

- HbA1C >6.5%.   OR
- FPG >126 mg/dL (>7.0 mmol/L). (Fasting = no caloric intake for at least 8 h.)*OR
- 2-h plasma glucose>200mg/dL (>11.1mmol/L).
    OR
- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose >200 mg/dl (>11.1 mmol/L).

A patient was considered hypertensive if he had a systolic blood pressure > 140 mm Hg or diastolic blood pressure > 90 mmHg or was on anti hypertensive drugs. A cross sectional study was carried out.

The following demographic and clinical data were collected with a self designed, pretested questionnaire standardized: age, gender, cigarette smoking, alcohol intake, diet history (vegetarian/ non-vegetarian), duration of diabetes, family history of diabetes, drug history, physical activity. The level of physical activity during the leisure time was defined using a three-category scale: 1- No exercise and sedentary activities at home/work; 2- Mild to moderate exercise / regular physical activity at home/work; 3-Vigorous exercise or strenuous labour at home/work. Weight (to the nearest 0.5 kg) and height (to the nearest 0.5 cm) were measured while the subjects were fasting overnight and wearing light clothes. BMI was calculated as weight (kg) divided by height (m^2).

Fasting morning serum samples were obtained asceptically after an overnight fast of atleast 8 hrs.

Serum insulin and C-peptide levels were estimated by Chemiluminescence immunoassay technique on *Autoplex^{TM} CLIA* (chemiluminescence immunoassay) *workstation* using *Acculite^{TM}* C-peptide and Insulin test kits (*Monobind ^{TM} Inc.*(US)) while fasting blood glucose was estimated by Trinders method (GOD-POD) on *Pace plus* ^{TM} semi auto analyser using *Erba glucose kit (Erba diagnostics Manheim, Germany.* (The serum samples were analysed for glucose levels within 2 hrs of sample collection.)

Statistical Analysis

Statistical analysis was performed using Microsoft Excel 2007 and IBM SPSS 16. Descriptive analysis was performed, followed by graphical representation of different parameters in terms of mean / median and standard deviation / range. Patients were grouped on basis of age into groups <30 years, 30-40 years, 40-50 years, 50-60 years and >60 years. On basis of BMI, patients were categorized as underweight (< 18.49), normal (18.5-24.49), pre obese (25-29.99), obese I (30-34.99), obese II (35-39.9) and obese III (>40). On basis of duration of DM, patients were grouped as duration < 5 years, 5-10 years, >10 years. The duration of diabetes was ascertained on basis of the age at which the patient was first diagnosed as a case of DM. Since many parameters like fasting blood glucose, insulin, C-peptide did not follow a Gaussian distribution, log transformation was performed on these parameters to normalize the distribution, as has been reported in several other studies (15,16,17). Pearson's coefficient was used to analyse the different parameters for correlation and student t test was performed to analyse the hypertensive and normotensive patients for association. P value <0.05 was considered significant

Ethical Justification

Ethical approval was obtained from Institutional Ethics Committee (IEC) of the institute. All procedures performed in the study were in accordance with the ethical standards of the institute.

RESULTS AND DISCUSSION

Results

In our study we found that 16% (16) patients were 30-39 years of age, 35% (35) of 40-49 years, 21% (21) of 50-59 years, 22% (22) of 60-69 years and 6% (6) of the patients were >70 years of age. The average age in our study was 50.55±11.28 years.

Out of the hundred patients enrolled in our study, 53% (53) had a history of diabetes for <5years, 22% (22) for 5-10 years and 25% (25) for >10 years. Average duration of diabetes in our study was 6.5 ± 7.2 years.

In our study, we observed that on basis of BMI, 5% (5) patients were underweight (BMI<18.49 kg/m^2), 48% (48) patients had normal BMI (18.5-24.99 kg/m^2), 35% (35) were pre obese (25-29.99 kg/m^2), 8% (8) patients were category 1 obese (30-34.99 kg/m^2), 4 were category 2 obese (35-39.99 kg/m^2) and none of the patients were category 3 obese (>40 kg/m^2). In our study we observed that the average BMI was 25.07±4.4 kg/m^2.

We found that serum insulin levels were raised in diabetic patients. Mean insulin levels were 11.24±10.57 µIU/ml (reference interval = 0-10 µIU/ml). Median, interquartile range and SEM were 7.1, 3.98-13.35 and 1.06µIU/ml respectively. Males had slightly higher insulin levels than females (11.67±10.72 µIU/ml as compared to 10.58 ± 10.42 µIU/ml), but the difference was not statistically significant (*P*=0.67).

In our study, we observed that serum C-peptide levels were also raised in diabetic patients 2.59 ± 1.45 ng/ml (reference interval = 0.78-1.89 ng/ml) Median, interquartile range and SEM were 2.00, 1.6-3.7 and 0.15 ng/ml respectively. Significant associations were found of duration of DM, BMI and fasting blood glucose with hypertension (Table 3).

Hypertensive patients had mean serum C-peptide levels of 2.72 ± 1.57 (median 1.9 interquartile range 2.4). Normotensive patients had serum C-peptide levels of 2.45±1.31 ng/ml

(median 2.1, interquartile range 1.2). The difference was statistically insignificant (*P*=0.449). Similar insignificant difference was seen in insulin levels in hypertensives and non hypertensives (*P*=0.212)

DISCUSSION

The demographic profile of our patients matched that of various other studies. Similar age distributions (Table 1) and BMI (Table 2) have been reported in many other studies on diabetic patients. Distribution on basis of duration of diabetes similar to ours has been reported in a study on 42 diabetic patients by Masood *et al* (2013) who found that 50.0% (21) patients had diabetes for < 5 years, 35.71% (15) for 5-10 years and 14.29% (6) for >10 years. (18)

Table 1 Age distribution of type 2 diabetic patients reported in various studies

Authors	Age (Mean±SD in years)
Zargar *et al* (19)	51.6±8.8
Sari *et al* (8)	55.5±8.4
Masood *et al* (20)	46.55± 9.67
Ko *et al* (21)	54.4±13.1
Kim *et al* (22)	56.75±14.28
Ohkura *et al* (23)	53.2 ± 12.7
Current study	50.55±11.28

Table 2 BMI of type 2 diabetic patients reported in different studies

Authors	BMI (mean ± SD in kg/m^2)
Zargar *et al* (19)	24.5 ±3.8
Sari *et al* (8)	27.1 ±9.8
Kim *et al* (22)	24.47 ± 4.17
Thunander *et al*(25)	28.8 ±5.4
Current study	25.07 ±4.4

Serum insulin levels were raised in our patients with mean levels of 11.24±10.57 µIU/ml (reference interval = 0-10 µIU/ml). Median, interquartile range and SEM were 7.1, 3.98-13.35 and 1.06µIU/ml respectively Similar results were reported by Gayoso-diz *et al* (2011), who found mean serum insulin levels of 11.4 ± 6.3 µIU/ml in diabetic patients(19) and Islam *et al* (2013), who reported insulin levels of 10.0, 6.8-17.6 µIU/ml (median, interquartile range) (20).

Table 3 Association of different patient parameters with hypertension

	H/O Hypertension	N	Mean	Std. Deviation	Std. Error of Mean	Independent t test (p value)
BMI	YES	50	26.3441	4.64355	.65670	0.003
	NO	50	23.7939	3.82514	.54096	
Insulin (Log)	YES	50	.9287	.36364	.05143	0.212
	NO	50	.8319	.40570	.05737	
C-peptide (Log)	YES	50	.3697	.23451	.03317	0.449
	NO	50	.3354	.21567	.03050	
Fasting blood glucose (Log)	YES	50	2.1156	.17006	.02405	0.003
	NO	50	2.2174	.16052	.02270	
Duration of diabetes mellitus (years)	YES	50	8.780	8.1063	1.1464	0.001
	NO	50	4.258	5.3705	.7595	
Age (years)	YES	50	52.70	9.941	1.406	0.056
	NO	50	48.40	12.199	1.725	

In our study, we observed that serum C-peptide levels were also raised in diabetic patients 2.59 ± 1.45 ng/ml (reference interval = 0.78-1.89 ng/ml) Median, interquartile range and SEM were 2.00, 1.6-3.7 and 0.15 ng/ml respectively Similar findings were reported by Kim *et al* (2011), who found mean C-peptide levels of 2.27± 1.51 ng/ml (21). Chowta *et al* (2010), also reported C-peptide levels of 2.91±0.15 ng/ml (0.97 ± 0.05 nmol/L) (mean ± SE of mean) (22).

Hypertensive patients had mean serum C-peptide levels of 2.72 ± 1.57 (median 1.9 interquartile range 2.4) while Normotensive patients had serum C-peptide levels of 2.45±1.31 ng/ml (median 2.1, interquartile range 1.2). The difference was statistically insignificant (*P*=0.449). This was similar to the findings of Kim *et al* (1995), who did not find any significant association between hypertension and C-peptide levels (10). Tomaschitz *et al* (2012), reported slightly elevated C-peptide levels of 3.1±2.7 ng/ml in hypertensive patients (12). The assumption that serum C-peptide and insulin levels may be effected by hypertensive status of the patient was made because of the possible roles of these markers in hypertension. C-peptide is known to up regulate the synthesis of nitric oxide synthase, thereby increasing the serum levels of the endogenous vasodilator nitric oxide (11). Alteration in the levels of C-peptide could thus result in altered blood pressure homeostasis. Also because of the growing evidence of the correlation between glucose intolerance and hypertension, as seen in metabolic syndrome, a possible interaction between insulin resistance and hypertension in diabetics was speculated.

In our study, however, we did not find any such association between serum C-peptide, insulin levels and hypertension. The role that these parameters play viz a viz hypertension remained obscure and no direct relationship could be elucidated. This could possibly be because beta cell activity tends to vary considerably in different populations. Probably, studies with a broader patient base could throw further light on the subject and are a need of the hour.

As with all other human experiments, our study too was not devoid of pitfalls. Because of financial constraints, HbA$_{1C}$ levels could not be estimated. HbA$_{1C}$ is now considered as a diagnostic as well as a prognostic marker for DM and its estimation could have been quite useful in further unraveling the interrelationships of these parameters. The population under study was mainly limited to north Indian population. Given the fact that insulin resistance and beta cell activity tend to vary considerably in different populations, studies with a broader patient base could further broaden our knowledge on the subject.

SUMMARY AND CONCLUSIONS

The current study was undertaken in the Departments of Biochemistry and General Medicine in Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala, Haryana, India on hundred type 2 diabetic patients admitted in the Department of General Medicine /attending the Medical OPD, out of which fifty were hypertensive and fifty normotensive. The study aimed at evaluating the relationship of hypertension with different parameters and patient characterictics in type 2 diabetic patients.

The salient findings of the study are as under

- The average age of patients in our study was 50.55±11.28 years, average duration of diabetes was

6.5 ± 7.2 years while average BMI was 25.07±4.4 kg/m^2.

- Serum insulin and c-peptide levels were raised in diabetic patients. Mean insulin levels were 11.24 ± 10.57 μIU/ml (reference interval = 0-10 μIU/ml) while mean c-peptide levels were (2.59 ± 1.45 ng/ml) (reference interval = 0.78-1.89 ng/ml).
- Hypertensive status of the patients was found be be significantly associated with duration of diabetes and BMI.
- We did not find any significant association of serum insulin and C-peptide levels with hypertension.

Although hypertension was found to be associated significantly with BMI and duration of diabetes, association with serum insulin, c-peptide levels could not be elucidated. The assumption that serum C-peptide, insulin levels and insulin resistance may be affected by hypertensive status of the patient was made because of the possible roles of these markers in hypertension. C-peptide is known to up regulate the synthesis of nitric oxide synthase, thereby increasing the serum levels of the endogenous vasodilator nitric oxide. Alteration in the levels of C-peptide could thus result in altered blood pressure homeostasis. In our study, however, we did not find any such association of insulin and c-peptide levels with hypertension. The role that these parameters play with regards hypertension remained obscure and no direct relationship could be elucidated. This could possibly be because beta cell activity tends to vary considerably in different populations. Probably, studies with a broader patient base could throw further light on the subject and are a need of the hour.

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