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Original Article

A cross-sectional study of type -2 diabetic females at a higher CVD risk owing to a strong correlation of Systolic hypertension to CVD risk factors

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ABSTRACT

Aim - We aimed at evaluating the CVD risk in the female type 2 diabetic patients as compared to the type – 2 diabetic males at diagnosis. Background - India faces dual epidemic of diabetes and CVDs. Hypertension affects approximately 70% of patients with diabetes and is approximately twice as common in persons with diabetes as in those without.The hypertensive diabetic women with coronary heart disease appeared to be under-diagnosed. Materials & Methods – The study included 280 subjects (healthy controls – 50 males & females, 180 DM -2 – 98 females, 82 males). The patients were selected on the basis of symptomatology & a FBS > 126 mg/dl and were analysed for BMI, BP, serum Insulin, HOMA – IR, C – peptide, Lipid profile &apo –B & A1. CVD risk was assessed using T.chol/HDL and apo – B/apo A1 ratios.Statistical analysis was done using the students -'t' test and spearman's coefficient of correlation. Results – The DM -2 patients presented with raised BMI, hypertension, dyslipidaemia, hyperinsulinemia, HOMA - IR & raised serum C – peptide ($p<0.0001$, HS) as compared to the healthy controls. Hypertension was observed in 39.79% female & 40.24% male diabetics. But the SBP was significantly raised in the diabetic females as compared to the males ($p = 0.04$). However, DBP had a NS difference ($p = 0.47$). The female & male diabetics had comparable biochemical parameters. Correlative analysis showed a strong association of SBP in the female type – 2 diabetics with potential CVD risk biochemical markers& CVD risk ratio T.Chol./HDLc but a NS association was observed in male diabetics. Conclusion – The type two diabetic females have a higher CVD risk as compared to males at comparable levels of biochemical parameters, probably due to a greater mean systolic hypertension in them, which in turn is strongly associated to potential CVD risk markers (insulin, HOMA –IR, C –peptide &T.Chol/HDL ratio).

1. Introduction

Type – 2 diabetes mellitus, one of the top five causes for mortality, affected more than 170 million individuals worldwide. [1] More than 80% of the deaths in diabetic subjects are attributed to CVDs. [2] There are more than 35 million diabetics in India, making it 'the diabetic capital of the world. [1]Indians also tend to develop CVDs about a decade earlier than Europeans. [3] Thus India faces dual epidemic of diabetes and CVDs and the pathogenesis of the two conditions maybe similar. Hypertension affects approximately 70% of patients with diabetes and is approximately twice as common in persons with diabetes as in those without. [4]

Arterial hypertension has been estimated to occur in about 50% of type – 2 diabetic populations. [4, 5]According to the American Diabetes Association, the optimal blood pressure goal for patients with diabetes is less than 130/80 mm Hg, in part because the Hypertension Optimal Treatment trial showed a 51% reduction in cardiovascular events with a target diastolic blood pressure of less than 80 mm Hg compared with 90 mm Hg. [6]The prevalence of coexistent hypertension and diabetes varies across different ethnic, racial, and social groups. There have been few nationwide epidemiological studies in India on hypertension. However, the sporadic studies from different regions suggest a rising prevalence of hypertension. [7] Hypertension has been reported to be higher in the urban populations as compared to the rural populations. [8] A recent study from Jaipur reported a 36.9% prevalence of hypertension in the urban population of Jaipur, the capital city of Rajasthan. [8] Western Rajasthan is in a developmental transitional zone & the rapid urbanisation is taking its toll on the

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health of general masses, with such populations showing an alarming rise in the rates of non – communicable chronic diseases like DM. The females of this region (especially the urban population) frequently present with raised BMI, owing to their sedentary lifestyle and a traditionally high fat – high calorie meal consumption. The majority of women with type 2 diabetes are also obese. There have been reports of the pre – menopausal women being at a risk of CVD owing to the abolishment of the protective female gender effect. [9] Thus the current study was undertaken with an aim of screening the adult obese population for the prevalence of type – 2 DM and to assess their CVD risk based on the correlative analysis of the biochemical parameters and blood pressure, to find out correlation if any.

2.Materials and Methods:

The current study was conducted in the Dept. of Biochemistry, Dr S.N. Medical College & associated group of hospitals, Jodhpur, as part of three year Ph. D research program. In the current study we planned to screen the adult obese population attending our OPDs with biochemical parameters that are important contributors to CVD risk & to find out a correlation with SBP & DBP, to predict the possible risk of CVD in these patients.

The study included 280 subjects (100 healthy controls – 50 each males & females, 180 DM -2 – 98 females; 82 males). The patients were selected based on the criteria –

I. Should be age matched (mean age 42.34±3.2 years)

II. Should have a raised BMI (>25 kg/m2)

III. Should have a FBS > 126 mg/dl.

IV. Should not be pre diagnosed diabetic to rule out the effect of drugs.

V. Should not be taking OHG/anti-hypertensive / diuretics/ hypolipidemic drugs.

VI. Should not have any other secondary cause of hypertension.

VII. Should be non – smoker & non tobacco chewer.

The subjects were analysed anthropometrically for calculating BMI. Clinical examination of patients was done & SBP – DBP recorded by auscultatory method. Biochemical analysis of fasting blood samples was done using fully automated analyser. The biochemical analysis included –

- FBS [enzymatic]
- Insulin [ELISA]
- HOMA – IR
- C –peptide [ELISA]
- Lipid profile [enzymatic]
- Apo proteins apo – B &apo –A1 [Immunoturbidimetrically]

Statistical analysis of all observations was done using the graph pad software for finding out correlation by Pearson's coefficient.

3.Result

Figure No – 1 Body Mass Index (kg/m^2) of Healthy controls and type – 2 diabetics

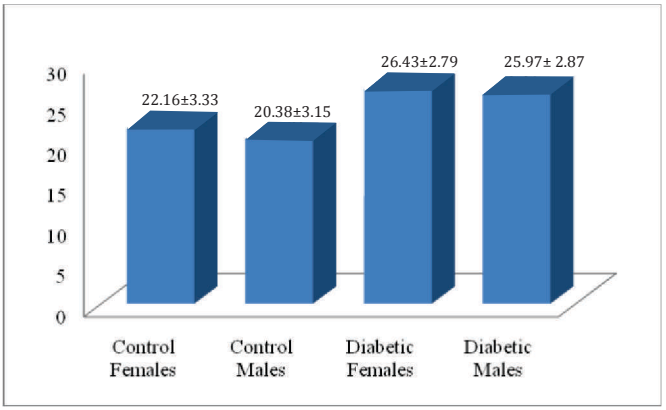


Figure No – 2 Prevalence of Hypertension in Type – 2 Diabetic adults

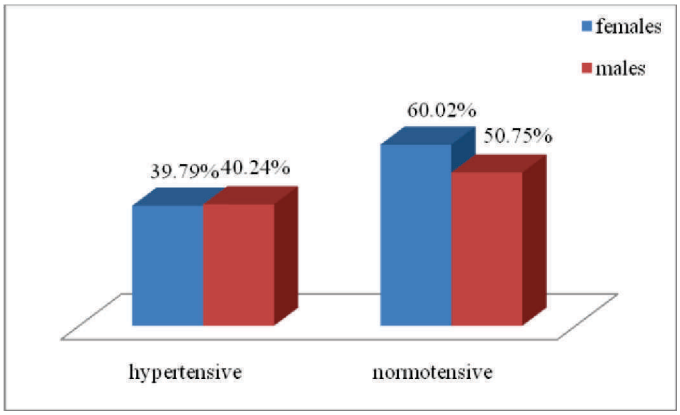
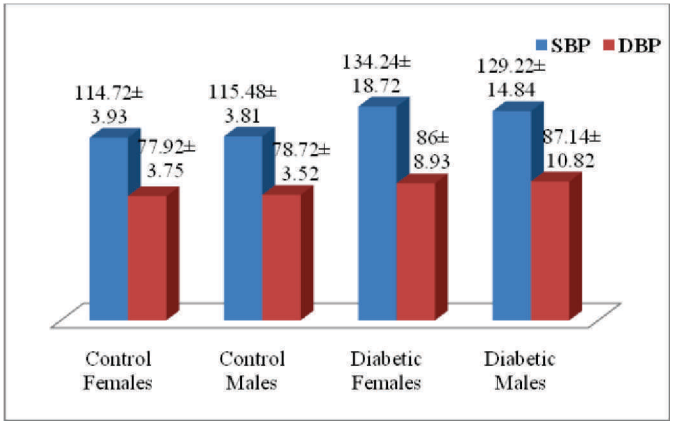


Figure No – 3 Hypertension in Diabetic females as compared to healthy controls and diabetic males



DM – 2 Female v/s Male - SBP p = 0.04 [S]; DBP p = 0.47 [NS]

Table No – 1 Biochemical parameters in controls and type – 2 diabetics

	Controls	p - value	Type – 2 Diabetics
FBS (mg/dl)	83.53±11.23	p<0.0001,HS	213.63±54.61
Insulin (µIu/ml)	16.73±4.24	p<0.0001,HS	55.72±17.91
HOMA – IR	3.33±0.78	p<0.0001,HS	30.63±16.18
C – peptide (ng/ml)	1.46±1.08	p<0.0001,HS	4.62±1.59
T.chol (mg/dl)	177.99±17.57	p<0.0001,HS	231.15±22.19
TG (mg/dl)	128.32±22.42	p<0.0001,HS	197.35±35.31
HDL (mg/dl)	41.43±5.29	p<0.0001,HS	33.56±2.67
TC/HDL	4.34±0.54	p<0.0001,HS	6.93±0.90
apo –A1 (mg/dl)	140.75±10.20	p<0.0001,HS	96.94±8.55
apo – B (mg/dl)	82.90±10.94	p<0.0001,HS	154.47±12.87
apo – B/ apo –A1	0.59±0.08	p<0.0001,HS	1.6±0.20

Table No – 2 . Comparison of the biochemical parameters of Female and Male type – 2 Diabetics

	Females	p - value	Males
FBS (mg/dl)	215.19±53.76	p=0.67, NS	211.77±55.87
Insulin (µIu/ml)	55.56±17.63	p=1, NS	55.56±18.35
HOMA – IR	31.14±16.7	p=0.64, NS	30.02±15.5
C – peptide (ng/ml)	4.62±1.69	p=0.96, NS	4.61±1.47
T.chol (mg/dl)	231.26±20.84	p=0.94, NS	231.01±23.84
TG (mg/dl)	196.18±37.25	p=0.62, NS	198.75±33.02
HDL (mg/dl)	33.43±2.58	p=0.46, NS	33.72±2.78
TC/HDL	6.94±0.85	p=0.82, NS	6.91±0.95
apo –B (mg/dl)	153.90±12.83	p=0.32, NS	155.08±12.90
apo – A1 (mg/dl)	97.00±9.70	p=0.91, NS	96.87±6.99
apo – B/ apo –A1	1.60±0.20	p=1.0, NS	1.60±0.19

Table No – 3. Correlation of the biochemical parameters of Female and Male type – 2 Diabetics with Blood Pressure

	SBP		DBP	
	Females	Males	Females	Males
Insulin (µIu/ml)	r = 0.31 p = 0.0014 VS	r = -0.18 p=0.09 NS	r= 0.311 p =0.0017 VS	r = -0.171 p = 0.122 NS
HOMA – IR	r = 0.25 p = 0.012 S	r = -0.16 p=0.14 NS	r = 0.257 p =0.01 S	r = -0.150 p = 0.17 NS
C – peptide (ng/ml)	r = 0.34 p = 0.001 VS	r = -0.25 p= 02 S	r = 0.304 p =0.001 VS	r = -0.201 p =0.06 NS
TC/HDL	r = -0.28 p =0.005 VS	r=0.02 p=0.85 NS	r = -0.195 p=0.05 S	r = -0.0101 p = 0.92 NS
apo – B/ apo –A1	r = -0.14 p = 0.16 NS	r = -0.047 p = 0.67 NS	r = -0.090 p =0.37 NS	r = -0.074 p = 0.50 NS

4.Discussion

Over the last few decades there has been increasing interest in the clinical association between hypertension and diabetes. The current study reports of a significantly raised blood pressure (both SBP & DBP) in the type 2 diabetics than healthy controls. (Figure no 3) Besides, there were 39% diabetic hypertensive females and 40.24% diabetic males. (NS difference) [Figure no 2] Both hypertension and diabetes predisposes to the development of cardiovascular disease (CVD). [10]When hypertension coexists with diabetes, the risk of CVD is increased by 75%, which further contributes to the overall morbidity and mortality of an already high risk population. [11, 12]Indians are at a higher risk of CVDs as compared to their European counterparts, as has been reported by Beckeles et al [3]. In the current study the females had a higher BMI than the males in both the categories of subjects – controls and type – 2 diabetics. (Fig no – 1)We also observed the type – 2 diabetic patients to have significantly raised FBS, insulin, HOMA – IR and C – peptide as compared with the healthy controls (Table No – 1)[13, 14, 15, 16]and dyslipidaemia in the type – 2 diabetics as compared with the healthy controls. (Table No – 1) The diabetic patients appear to have a higher risk of CVDs owing to the hyperinsulinemia, IR, atherogenic dyslipidaemia characterised by raised T. Chol., TG, apo –B, and a reduced cardio protective HDLc and apo – A1. Hyperinsulinemia is in – itself an independent cause of atherosclerosis as it promotes atherogenic dyslipidaemia [17]hinting an enhanced CVD risk in such individuals. There are reports of increased risk of hypertension in women with deteriorating glycaemic control. [18]But, the hypertensive diabetic women with coronary heart disease appeared to be under-diagnosed.[19] The diabetic females of the current study presented with comparable levels of CVD risk factors with male counterparts like – BMI, SBP, FBS, Insulin, HOMA – IR, TC:HDL, apo – B, apo –A1, and CVD risk ratios. (Table No 2) However, the SBP in the female diabetics was significantly higher than in the male diabetics & the systolic blood pressure has been considered as the superior predictor of all the complications we attribute to hypertension. Moreover, the correlative analysis of blood pressure with biochemical parameters (Table No – 4) shows that the female diabetics had a strong association of SBP with serum insulin, IR, C – peptide and T.Chol / HDLc ratio, but NS association to apo –B /apo –A1. The association of apo –B / apo A1 though [NS], was still a negative one with SBP suggesting weak association of the CVD risk ratio with SBP. The strong positive association of SBP with serum insulin, HOMA – IR & C – peptide suggests that the hypertensive diabetic females would show further deterioration in their blood pressures with the with hyperinsulinemia, increased IR & loss of glycemic control (shown by C – peptide). Our observations are consistent with the reports of a strong association between hypertension, diabetes and insulin resistance. [20]Furthermore,a strong association between up regulation of Renin Angiotensin Aldosterone System (RAAS), hypertension and diabetes results in an enhanced generation of reactive oxygen specie (ROS) and may explain impaired glucose utilisation as well as hypertension associated with insulin resistance and type 2 diabetes.[21, 22, 23, 24]Besides, there is some evidence that insulin resistance precedes the onset of established hypertension in high risk individuals, just as it precedes type – 2 DM.[25] Sari &Balki [26] reported that serum c–peptide level was higher in patients with dyslipidemia (p = 0.045), hypertension (p = 0.001), CAD (p = 0.001) indicating a relationship between c–peptide and macro vascular complications with NIDDM. [24] Thus further validating the strong association we observed between hypertension & C – peptide of type – 2 diabetics in current study.

5.Conclusion

The type two diabetic females are at a higher CVD risk as compared to the type two diabetic males at comparable levels of biochemical parameters, probably due to a greater mean systolic hypertension in them, which in turn is strongly associated to potential CVD risk factors (insulin, HOMA –IR, C –peptide &T.Chol/HDL ratio). The coexisting hypertension & type – 2 DM should be thus aggressively managed specially in female diabetics, which otherwise are ignored in view of the female gender factor.

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