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Original Article

Correlation of Biochemical Parameters among Diabetes patients attending Medicine OPD of Janaki Medical College Teaching Hospital

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ABSTRACT

Background and objectives: With increasing incidence of diabetes mellitus, the cardiovascular and renal complications associated with it are emerging as major concern. The morbidity and mortality associated with diabetes can be reduced by timely assessment of those risk factors. Our study evaluated lipid profile and renal function test in male and female diabetic patients as well as the correlation among those biochemical parameters.

Materials and methods: Blood sugar, lipid profile and renal function test were assessed in 249 confirmed type 2 diabetic patients attending medicine OPD of Janaki medical college teaching hospital (JMCTH), Ramdaiya-Bhawadi, Dhanusha, Nepal. Independent 't' test was used to observe the gender difference in those parameters and Pierson correlation test was applied to look for correlation among different biochemical parameters.

Results: Significant difference was observed between male and female for FBS (p=0.05) and PPBS (p=0.003). Such significant difference between male and female was also noted for lipid profile parameters, TC (177.65±43.09 and 163.45±35.68 respectively, p=0.05), VLDL-C (33.47+16.51 and 28.83+14.00 respectively, p=0.018) and HDL-C (40.52+10.62 and 37.94+8.07 respectively, p=0.033). According to our study TC, TG, VLDL, LDL, HDL showed significant positive correlation with FBS and PPBS. Likewise, creatinine, urea, uric acid was also positively correlated with FBS and PPBS ($p<0.05$). Moreover, there was significantly high correlation of uric acid with TC, TG, VLDL, LDL ($p<0.05$). In addition, there was highly significant correlation between creatinine and sodium.

Conclusion: There was a significant difference for blood sugar and lipid profile among male and female diabetic patients. Correlation was seen between blood sugar and lipid profile; uric acid and lipid profile as well as creatinine and sodium.

Keywords: Diabetes mellitus, lipid profile, renal function test

INTRODUCTION

Diabetes mellitus (DM) is one of the most prevalent metabolic disorders characterized by hyperglycemia, variable degrees of insulin resistance and impaired insulin secretion. It can be divided into Type-1 also known as insulin-dependent diabetes mellitus and Type-2 also known as non-insulin-dependent diabetes mellitus [1]. The major hallmarks of type 2 DM (T2DM) are insulin resistance (IR) and β-cell dysfunction [2]. The risk factors associated with T2DM can be grouped as genetic, behavioral and environmental. Though the genetic basis of the disease has not been well established yet, obesity and physical inactivity are well established non-genetic determinants of T2DM [3]. Type-2 diabetes is more prevalent than type 1. The risk of cardiovascular disease (CVD) is significantly increased in patients with type 2 DM and it is the major cause of death in the diabetic population [4].

According to International Diabetes Federation, the number of adults between the age of 20–79 years living with diabetes was 463 million worldwide and is predicted to rise to 700 million by 2045 [5]. While type 2 diabetes is more prevalent in the older population, the number of cases in the younger population is also on the rise. The cases of type 2 DM in people of below 44 years constituted 8% of total cases in developed countries and 25% in developing countries [6]. In 2017, nearly 10,145 deaths were attributed to diabetes, which was also ranked as the 11th most common cause of disability-adjusted life years (DALYs) in Nepal (1226 DALYs per 10,000 population) [7].

If not diagnosed on time, diabetes may lead to various complications such as neuropathy, nephropathy, retinopathy, cardiovascular disease, and stroke [8]. Approximately 21% deaths from ischemic heart disease and 13% of the deaths from stroke were attributed to hyperglycemia [9]. The risk of developing CVD in patients with diabetes is closely associated with plasma lipid profile [10]. An abnormal lipid profile has a close relationship with IR which is a major component of type 2 DM. Evidence suggests that some of the factors associated with IR are high levels of very-low-density lipoprotein (VLDL), high concentrations of serum triglycerides (TG), and low serum high-density lipoprotein (HDL). This makes the lipid profile an essential component of all follow-up programs of T2DM and serves as an important prognostic factor [11]. Assessment of renal function is another important component of diabetes management as the life time risk of developing chronic kidney disease (CKD) is 25-40% in patients with T2DM [12]. Coexistence of CKD increases the risk of CVD, hypertension, obesity [13-15] and premature mortality in patients with T2DM [16].

South Asia is home to nearly two-thirds of all global diabetes cases [17]. As diabetes is becoming a major public health concern in South Asia, plenty of research is being conducted in this field. However, most of the diabetes literature in South Asia is from India. In Nepal, it still remains an area to be explored more [18]. Various public and private sectors are available in Nepal for diabetes care. However, the availability and quality of service is not uniform and referral system is not well structured. Since the country adopted a federal system of governance, there has been significant progress in healthcare facilities in the Madhesh Pradesh of Nepal. However, the management of T2DM still remains a daunting challenge for individual patients and

for public health in Terai region of Nepal. Particularly, there seems to be a lack of established mechanism for screening of diabetes and its complications, awareness, treatment and laboratory examinations in the province-specific new federal setup.

One important step in the diagnosis and management of patients with diabetes mellitus is to monitor different biochemical parameters and multiple laboratory tests. Therefore, this study was designed to study the correlation of different biochemical parameters among diabetes patients attending medicine OPD of Janaki Medical College Teaching Hospital to develop an appropriate strategy for curbing the diabetes epidemic in Nepal.

MATERIALS AND METHODS

Study design and Settings

A hospital based cross-sectional study was conducted in the department of biochemistry with collaboration of department of internal medicine from July to December 2017 at Janaki Medical College Teaching Hospital (JMCTH). JMCTH is a 450-bed referral hospital located in Ramdaiya-Bhawadi in Kshireshwarnath Municipality of Dhanusha district, Madhesh Pradesh, Nepal providing teaching programs of MBBS, MD and other paramedical courses. It is estimated to deliver health service for about more than 8,00,000 population in Dhanusha district.

Participants and procedures

A total of 249 consecutive patients attending medicine OPD on every third day of week diagnosed as T2DM or already taking treatment for T2DM during the study period were enrolled. World Health Organization (WHO) criteria were used for the diagnosis of type 2 DM [19]. A detailed clinical history was obtained from the patients. The detailed history suggestive of symptoms including polyuria, polydipsia, polyphagia and weight loss were recorded in a predesigned proforma. All the patients were sent for blood sugar, lipid profile and kidney profile assessment.

Inclusion and exclusion criteria

All T2DM patients >18 years old irrespective of duration of disease were included in this study. Patients having severe anemia, any metabolic instability, any type of cutaneous or systemic infection and pregnant females were excluded.

Blood sample collection and laboratory methods

Fasting and post-prandial venous blood sample was collected using serum separator test tube following aseptic procedure. Standard operating procedures were followed for estimating different blood parameters. Serum glucose, lipid profiles viz. TC, TG, HDL-C, LDL-C, VLDL-C, TC /HDL-C and kidney profiles (Potassium, Sodium, creatinine, urea and uric acid) were estimated from serum sample using Humalyzer 3500 semi-automatic biochemistry analyzer (Human Diagnostics Uganda, 84 Tufnell Drive, Uganda) by following standardized protocols of Human's clinical chemistry reagents.

Statistical analysis and data management

The data was entered to SPSS version 20 statistical package for analysis. Descriptive statistics were used to summarize the frequency distributions. Independent 't' test was applied to observe the difference between male and female. Pearson correlation test was applied to observe correlation between different biochemical parameters among diabetes patients. P-value <0.05 was considered to be significant.

Ethical consideration

Institutional review committee of JMCTH provided ethical approval towards this study (Ref: IRC/06/2074-075).

RESULTS

Table 1 show the age and sex distribution of diabetes patients. Out of total 249 patients, 131(52.6%) were male and 118(47.4%) were female. Among them, the highest number of 129(51.8%) diabetes patients was in the age above 50 years whereas lowest in below 30 years.

Table 1: Age and Sex distribution of diabetes patients

Characteristics Age Group	No	%
< 30 years	13	5.2
30-50 Years	107	43.0
>50 Years	129	51.8
Mean±SD	52.64 ± 14.05	-
Gender		
Male	131	52.6
Female	118	47.4

Table 2 depicts biochemical parameters by gender status among diabetes patients. The male and female population of our study was age matched (p =0.417). The FBS among male (127.58±59.56) was significantly higher (p=0.050) than that among female (115.02±39.84). PPBS was also significantly (p<0.003) higher in male (194.92±92.32) compared to female (163.95±69.38).

Among the lipid profile parameters, difference among male and female was significant for TC (p=0.05), VLDL-C (p=0.018) and HDL-C (p=0.033). On the other hand, the difference in male and female was not significant for TG (p=0.025) and TC/HDL-C

Table 2: Biochemical parameters by gender status among diabetes patients

Characteristics	Male Mean ± SD	Female Mean ± SD	P-Value*
Age (years)	53.35± 13.51	51.88±14.69	0.417
FBS (mg/dl)	127.58± 59.56	115.02±39.84	0.050
PPBS (mg/dl)	194.92±92.32	163.95±69.38	0.003
TC (mg/dl)	177.65±43.09	163.45±35.68	0.005
TG (mg/dl)	161.37±72.49	141.25±67.43	0.025
VLDL-C (mg/dl)	33.47±16.51	28.83±14.00	0.018
LDL-C (mg/dl)	111.11±87.54	96.82±29.02	0.092
HDL-C (mg/dl)	40.52±10.62	37.94±8.07	0.033
TC/HDL-C	5.98±16.77	5.68±13.90	0.880
Potassium (mEq/L)	4.15±0.56	4.07±0.55	0.253
Sodium (mEq/L)	141.47±5.03	141.58±4.24	0.851
Creatinine (mg/dl)	0.97±0.19	1.03±0.54	0.267
Urea (mg/dl)	28.88±12.19	27.74±15.33	0.518
Uric Acid (mg/dl)	5.50±1.77	5.33±1.60	0.449

*p-value for statistics t-test
(FBS-Fasting blood Sugar, PPBS-Post prandial blood sugar, TC-Total Cholesterol, TG-Triglycerides, VLDL-C-Very low-density lipoprotein cholesterol, LDL-C, Low density lipoprotein cholesterol, HDL-C- High density lipoprotein cholesterol, TC/HDL-C- Total Cholesterol/High density lipoprotein Cholesterol)

ratio (p=0.880). The kidney profile of male and female was almost similar. There was no significant difference among male and female for potassium (p=0.253), sodium (p=0.851), creatinine (p=0.267), urea (p=0.518) and uric acid (p=0.449).

Table 3 describes the correlation between different biochemical parameters among diabetes patients. For lipid profile, we observed significant positive correlation of TC, TG, VLDL-C, LDL-C, HDL-C with FBS and PPBS (p<0.05).

Table -3: Correlation between different biochemical parameters among diabetes patients

Parameters	FBS	PPBS	TC	TG	VLDL-C	LDL-C	HDL-C	TC/HDL-C	Potassium	Sodium	Creatinine	Urea	Uric Acid
FBS	1	-	-	-	-	-	-	-	-	-	-	-	-
PPBS	.805**	1	-	-	-	-	-	-	-	-	-	-	-
TC	.499**	.599**	1	-	-	-	-	-	-	-	-	-	-
TG	.521**	.592**	.384**	1	-	-	-	-	-	-	-	-	-
VLDL-C	.442**	.512**	.334**	.834**	1	-		-	-	-	-	-	-
LDL-C	.140*	.207**	.460**	.015	-.012	1	-	-	-	-	-	-	-
HDL-C	.137*	.127*	.353**	-.073	-.164**	.135*	1	-	-	-	-	-	-
TC/HDL-C	-.035	-.037	.041	.021	.013	.020	-.091	1	-	-	-	-	-
Potassium	.072	.106	.034	.089	.028	-.049	.132*	-.014	1	-	-	-	-
Sodium	.073	.026	.007	-.009	.003	.084	.055	.014	.050	1	-	-	-
Creatinine	.176**	.163*	.127*	.127*	.137*	.004	.045	-.032	.168**	-.164**	1	-	-
Urea	.281**	.195**	.120	.142*	.163*	.069	-.002	.026	.037	-.103	.694**	1	-
Uric Acid	0.445**	0.521**	0.469**	0.324**	0.306**	0.185**	0.158*	-0.101	0.005	0.019	0.093	0.069	1

*Correlation is significant at p<0.05; ** Correlation is significant at p<0.01
(FBS-Fasting blood Sugar, PPBS-Post prandial blood sugar, TC-Total Cholesterol, TG-Triglycerides, VLDL-C-Very low-density lipoprotein cholesterol, LDL-C, Low density lipoprotein cholesterol, HDL-C- High density lipoprotein cholesterol, TC/HDL-C- Total Cholesterol/High density lipoprotein Cholesterol)

Moreover, there was significantly high correlation with uric acid and TC, TG, VLDL-C, LDL-C ($p<0.05$). Also, creatinine and sodium showed highly significant correlation.

DISCUSSION

Gender distribution of diabetic cases in our study was 131(52.6%) and 118(47.4%) for male and female respectively. This distribution is in accordance with a cross-sectional study conducted at the University of Gondar Hospital, Ethiopia in which out of 384 participants, 232(60.4%) were male and 152(39.6%) females [20]. In another study, the prevalence of diabetes was found to be 1.6% and 1.1% in male and female respectively [21]. Findings analogous to our results were also noted in the database of the Endocrinology and Isfahan Diabetes Prevention Study [22]. However, some studies reported findings contradicting to ours. In a study conducted by Asiimwe et al. [23], among 139 elderly patients at Kanungu District, Uganda, 38(27.3%) were males and 101(72.7%) were female. Also, the prevalence of T2DM was found to be higher in female (4.3%) compared to male (2.6%) in general population of Iran [24].

Recent studies established a predominance of T2DM in male over female [25-27] but the reason for this difference is unclear. The insulin resistance due to fatty acid is also found to be prominent in male compared to female [28]. In recent years, male sex has been regarded as a risk factor for the development of T2DM [25,29-33]. However, the prevalence increases in females at older age [32].

The higher prevalence of T2DM in male might be related to central obesity associated with android obesity [34]. Central obesity has also been found to be a stronger risk factor for glucose intolerance, insulin resistance,

metabolic perturbations and hyperinsulinemia than BMI [35]. Even with similar BMIs, men seem to be at greater risk of developing T2DM than female [36]. These inconsistencies may be partly explained by limitation of body BMI in true estimation of adiposity [37,38]. Other research suggests that women are more likely to develop diabetes due to higher levels of estrogen and progesterone which reduce insulin sensitivity and because they have less total muscle mass to uptake additional glucose load [39]. To overcome these non-uniformity of risk factors, clinical manifestations, and therapeutic approaches in men and women; a woman specific recommendation has been endorsed by the American Heart Association [40].

In the present study, the mean (±SD) age of diabetes patients was 52.64±14.05 in line with 55.74±9.05 years noted by Woldeamlak et al. [20]. The, mean age for male and female was 53.35±13.51 and 51.88±14.69 respectively in our study. In a similar study conducted at B.P. Koirala Institute of Health Sciences, Dharan, Nepal among T2DM patients, the mean(±SD) age of male and female was 52.7±11.9 and 51.84±12.1 years respectively [41]. Almost parallel results were obtained by Salih et al. [42] and Shrestha et al. [43].

The age-related decline in function [44] and proliferative capacity of pancreatic islet cells [45] have previously been described. The increased risk of development of T2DM at older age may be associated with combined effect of increasing insulin resistance and impaired pancreatic islet function. Age-related insulin resistance appears to be primarily associated with adiposity, sarcopenia and physical inactivity [46] which partially explains the higher success of intensive lifestyle intervention among older participants in the diabetes prevention program [47]. Moreover, the complications like major lower-extremity amputation [48], myocardial infarction (MI), visual impairment, and end-stage renal disease in diabetic patients increases with age [49].

Glycemic control is the most important aspect in management of diabetes mellitus. In our study, there was a significant difference between FBS in male (127.58±59.56 mg/dl) and female (115.02±39.84 mg/dl). A study conducted in Pune, India reported higher FBS in male (157.4±48.98 mg/dl) than in female (157.4±48.98 mg/dl) similar to our study but the difference was not significant [50]. Similar observations have been made in other studies [51-55]. Our study also reported significantly higher PPBS in male compared to female. However, a study from India showed no significant difference in PPBS of male (224.72±41.36 mg/dl) and female (223.02±37.04 mg/dl) [50]. Genetic factors may play role in gender difference in blood sugar [56, 57] and glucose metabolism related risk factors [58] such as obesity.

Dyslipidemia is often characterized by high TC, TG, LDL and low HDL cholesterol [59]. It increases CVD risk independently as well as in combination with hyperglycemia by augmenting atherosclerosis-related inflammation [60, 61]. In addition to increasing the risk of macrovascular complications, [62]; dyslipidemia has also been associated with microvascular complications like diabetic retinopathy, diabetic nephropathy and diabetic neuropathy [63-65].

In our study, the difference of mean in male and female was found to be significant for TC, VLDL-C, HDL-C and insignificant for TG and

LDL-C. In coherence to our study, research from Iran reported TG (150.9±91.5; 154.3±81.7), TC (154.9±40.5; 168.9±38.5), HDL-C (41.8±8.8; 48.8±10.8), LDL-C (83.6±31.9; 89.9±31.3) in male and female diabetic patients respectively. The difference was significant for all parameters except TG [66]. Gilan et al. [67] also reported similar results for lipid profile in diabetic patients. Similarly, a cross-sectional study carried by Baranwal et al. [41] on diabetic patients at Dharan, Nepal noted means(±SD) among males and females for TC (176.3±42.4; 188.4±41), LDL-C (95.1±19.8; 94.7±20.3) and HDL-C (40.9±9.2; 42.1±6.9) respectively. Sadeghi et al. [18] reported lipid profile parameters viz. TG, TC, HDL-C, LDL-C, TC/HDL-C ratio in male and female T2DM patients were (159.01±93.74, 195.17±39.45, 45.35±11.58, 123.78±29.20 mg/dL and 4.53±1.31) respectively.

Diabetic dyslipidemia may be linked with role of insulin in liver apoprotein production, regulation of lipoprotein lipase, actions of cholesteryl ester transfer protein (CETP), as well as peripheral actions of insulin on adipose and muscle tissue [68]. Most patients with poorly controlled diabetes have increased TG [69] and VLDL [70]. Excess fatty acids in the liver are secreted in VLDL in the form of TG. This decreases the conversion of VLDL into LDL [68]. LDL level is generally unchanged in diabetes probably due to balancing effects of decreased LDL production and decreased number or sensitivity of LDL receptors. The lower level of HDL in diabetes can be attributed to exchange of cholesteryl ester in HDL with triglyceride in VLDL, a process mediated by CETP [68, 71].

Endothelial derived nitric oxide (NO) seems to contribute to vasodilation and generation of reactive oxygen species in diabetic patients leading to renal disease [72]. Except for creatinine, all the renal profile parameters viz. potassium, sodium, urea and uric acid were comparatively lower in females than males in our study. However, there was no significant difference for any parameter. Similar results were obtained in a study carried out at Biratnagar, Nepal [73]. Serum creatinine level is one of the basic markers for renal function examination and provides a good estimate for glomerular filtration rate (GFR) [74]. However, several factors can cause increase in creatinine level which may not be true representation of decline in GFR [75]. Nitromethane, flucytosine, acetone, acetoacetate and cefoxitin are some of the substances which are found to cause overestimation of serum creatinine [76-78].

In general, females are more insulin sensitive and are at lower risk of vascular disease than males [79]. The possible explanation for reduced cardiovascular risk in female could be due to protective effects of estrogen against vasoconstriction, lipid profile derangement, inflammation, oxidation and fibrosis [80,81]. These vasoprotective effects are compromised in female with T2DM as their estrogen production decreases [80,82]. Moreover, risk of atherosclerosis and endothelial dysfunction tend to increase in female with hyperglycemia [79,83], making them more vulnerable to vascular complications such as diabetic nephropathy [80].

We also observed significant positive correlation of TC, TG, VLDL-C, LDL-C, HDL-C with FBS and PPBS. Moreover, there was significantly high correlation of uric acid with TC, TG, VLDL-C, LDL-C and positive relationship with HDL. Likewise, creatinine, urea, and uric acid were also positively

correlated with FBS and PPBS. Moreover, there was significantly high correlation of uric acid with TC, TG, VLDL-C and LDL-C. Also, creatinine and sodium had highly significant correlation.

This shows that hyperglycemia strongly impairs lipid metabolism. A study carried out by Sapkota and Thapa in Central region of Nepal reported statistically significant positive correlation of FBS and PPBS with TC, TG, LDL-C and VLDL-C [84] analogous to our results. Our findings are also concomitant with Khan et al. [85], Mahato et al. [86], Ramona et al. [87] and Bhowmik et al. [88]. Many factors associated with dyslipidemia are affected by insulin. They include apolipoprotein synthesis by liver, regulation of enzymatic activity of lipoprotein lipase and cholesterol ester transport protein (CETP) [89-91]. Hence, insulin resistance plays a major role in pathogenesis of dyslipidemia in type 2 DM [92].

The positive correlation between plasma FBS and plasma uric acid levels could be associated with renal complications of diabetes. According to Bos et al. and Ectkel et al. [93,94], glycosuria secondary to hyperglycemia cause decrease in urine pH which influences uric acid reabsorption from renal tubules. Feig et al. [95] have also established an association of hyperuricemia with diabetes mellitus. Insulin resistance causes defective ammoniogenesis which also decreases urine pH [94]. On the other hand, hyperuricemia may itself increase the risk of by obesity and metabolic syndrome inducing adipose tissue inflammation and insulin resistance [96].

CONCLUSION

Our study concludes with a gender disparity in blood sugar, lipid profile and kidney profile in the routine management of diabetic patients. Female diabetic patients had lower biochemical parameters as compared to males except for serum creatinine. Significant positive correlation was observed among different biochemical parameters like TC, TG, VLDL-C, LDL-C, HDL-C, creatinine, urea, and uric acid with blood sugar.

Also, significantly high correlation with uric acid and TC, TG, VLDL, LDL was observed. Highly significant correlation was seen between creatinine and sodium too. Whether high creatinine is a true risk factor for increased progression of kidney disease among females in Nepalese population of Terai region is not known and new studies are needed to investigate this further. Finally, it is important to address the potential gender specific CVD risk factors during management of T2DM.

LIMITATIONS

The lack of information on pattern of drug use among diabetics may represent one of the limitations. Moreover, the study was limited to hospital setting only which may affect the generalization of our study.

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intellectual critical review of the final manuscript: ***BJ,SP,OPY,JKS.*** *All authors contributed to analysis, review and revision of the manuscript, and all have read and agreed with the contents of the final manuscript.*

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