Association of Serum Prolactin Levels with Glycemic Control in Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: As per estimates of IDF in 2015, 415 million adults (20-79 years) were affected by diabetes, by 2040 this figure is expected to rise to 642 million. The present study was conducted to establish the relationship between serum prolactin level with glycemic control in Type 2 DM .

Material and methods: A cross sectional study was conducted on 100 diabetic patients presenting at OPD/IPD in SRN Hospital Prayagraj between july 2021 and august 2022. Blood samples were taken to estimate CBC, HbA1C, FPG, 2HR PG, S. Prolactin, S creatinine, UACR, USG whole abdomen, urine R/M and lipid profile. Data was collected, entered in MS Excel Spreadsheet and analysed.

Result: Among diabetic patients with no diabetic nephropathy, S. prolactin levels of patients with Good glycemic control was significantly higher than that of Poor control for all the above glycemic parameters i.e. HbA1c (19.48±5.29 vs. 11.23±7.56 ng/ml), Fasting BS (21.88±7.23 vs. 9.53±5.13 ng/ml) and PP BS (21.86±6.45 vs. 8.39±3.60 ng/ml).

Keywords: T2DM, Prolactin, Glycaemic Control

INTRODUCTION

Diabetes mellitus is a global health threat affecting the functional capacity and quality of life on the one hand while on the other hand is a major cause of morbidities and premature mortality[1]. Diabetes mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycemia[2]. It may be due to impaired insulin secretion, resistance to peripheral actions of insulin, or both. As per estimates of International Diabetes Federation in 2015, 415 million adults (20-79 years) were affected by diabetes, by 2040 this figure is expected to rise to 642 million[3].

Major biological function of prolactin is to initiate and maintain lactation[4],[5] but additional 300 functions of prolactin have been demonstrated in various studies[6,7,8].

Role of prolactin in Food intake, weight gain, insulin resistance via inhibiting adiponectin and IL-6 production in adipose tissue leading to T2DM had been found to be associated in experimental studies[9,10,11].

Several studies have found decreased PRL levels among diabetic as compared to healthy, prediabetics and diabetic nephropathy cases they also found that higher prolactin level were associated with lower HbA1c and fasting plasma glucose.[12,13,14].

MATERIAL AND METHODS

Study Site

Department of Medicine, Swaroop Rani Nehru (SRN) Hospital associated with MLN Medical College, Prayagraj. MLN Medical College is a state run medical college by Government of Uttar Pradesh, having state of the art-infrastructure and multi-speciality facilities.

Study Design

Cross-sectional Observational Study.

Study Duration

Twelve months

Study Population

Type 2 Diabetes mellitus patients (both male & female) aged >18 years attending the Department of Medicine, MLN Medical College, Prayagraj were included in the study.

Inclusion Criteria

- Type 2 DM (newly diagnosed or on treatment) patients
- Age >18 years

Exclusion Criteria

Known cases of

- Type 1 Diabetes mellitus
- Thyroid disorder.
- Prolactinoma
- Drugs causing hyperprolactinemia
- Pregnancy

Methodology

- After obtaining informed consent all the patients were clinically examined and demographic details, clinical history was collected.
- Patients were subjected to following investigations
  - Haemoglobin
  - S Cholesterol, S. Triglyceride
  - HbA_1c
  - Fasting plasma glucose (FPG)
  - Post prandial plasma glucose (2h PG)
  - Kidney function test
  - Serum prolactin

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- Urine R,M
- UACR
- eGFR
- USG Whole Abdomen With KUB

- Type 2 diabetes mellitus patients were divided into two subgroups:
  Type 2 DM patients with good glycaemic control.
  Type 2 DM patients with poor glycaemic control.
- Good glycemic control[15] was defined as:
  HbA_1c <7.0
  FPG ≤130 mg/dl
  2h PG <180 mg/dl
- Normal range of Serum prolactin was considered to be 5-25 in the present study and also the same range of prolactin levels considered normal in our SRN pathology lab.[33]

Ethical Considerations

The study was approved by Institutional Ethical Committee. Informed consent was obtained from the patients/their attendants. The participation in the study was entirely voluntary giving the patient right to withdraw from study whenever he/she wishes to do so.

Data Collection Method

The data was collected on a semi-structured questionnaire. Records of all the test reports were maintained. All observations were made under direct supervision of the supervisor.

The data so collected was fed into computer using MS Excel 2013 or compatible software.

Statistical Tools Employed

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 21.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD.

The following Statistical formulas were used:

1. Mean: To obtain the mean, the individual observations were first added together and then divided by the number of observation. The operation of adding together or summation is denoted by the sign Σ.

The individual observation is denoted by the sign X, number of observation denoted by n, and the mean by $\overline{X}$.

$$\overline{X} = \frac{\Sigma X}{\text{No. of observations (n)}}$$

2. Standard Deviation: It is denoted by the Greek letter σ. If a sample is more than 30 then.

$$\sigma = \sqrt{\frac{\Sigma (X - \overline{X})^2}{n}}$$

When sample in less than 30 then.

$$\sigma = \sqrt{\frac{\Sigma (X - \overline{X})^2}{n-1}}$$

3. **Chi square test:**

$$\chi^2 = \sum \frac{(O-E)^2}{E}$$

Where O = Observed frequency,
E = Expected frequency

4. **Student 't' test**: To test the significance of two means the student 't' test was used

$$t = \frac{\overline{X}_1 - \overline{X}_2}{S\sqrt{\frac{1}{n_1} + \frac{1}{n_2}}}$$

where $S^2 = \frac{(N_1 - 1)SD_1^2 + (N_2 - 1)SD_2^2}{N_1 + N_2 - 2}$

where $\overline{X}_1$, $\overline{X}_2$ are means of group 1 and group 2
N_1, N_2 are number of observation group1 and group 2
SD_1, SD_2 are standard deviation in group1 and group 2

5. Level of significance: "p" is level of significance
p > 0.05 Not significant
p <0.05 Significant
p <0.01 Highly significant
p <0.001 Very highly significant

RESULT

The present study was conducted at Department of Medicine, MLN Medical College & S.R.N. Hospital, Prayagraj to measure serum prolactin levels of Type 2 diabetes mellitus patients and to explore the association of serum prolactin levels with glycemic control among type 2 diabetes mellitus patients.

All the adult type 2 diabetes mellitus patients attending the department were invited to participate in the study, of these 100 consecutive patients fulfilling the inclusion criteria were enrolled in the study after obtaining their informed consent. Following table shows demographic profile of study population.

Age of type 2 DM patients enrolled in the study ranged between 35 to 85 years, mean age was 57.23±11.81 years. Only 21.0% patients were aged ≤45 years and 21.0% were aged ≥66 years. Majority of the patients were aged 46-65 years (58.0%).

Out of 100 patients enrolled in the study 59 (59.0%) were males and rest 41 (41.0%) were females.

Blood samples of all the patients were collected and glycemic levels were assessed.

HbA_1c levels of study population ranged between 6.7 & 16.5. Mean HbA_1c level of patients was 9.17±2.00.

Range of fasting blood sugar levels of patients enrolled in the study lied between 26.0 and 312.0 mg/dl. Mean fasting blood sugar level was 173.93±62.20 mg/dl.

Post-prandial blood sugar levels of patients enrolled in the study ranged from 73.0 to 626.0 mg/dl. Mean PP blood sugar level was 252.21±95.83 mg/dl.

Based on the above glycemic levels, Glycemic control of

SN	Demographic Variables	Number of Type 2 DM cases	Percentage
1-	Age Group (years)		
	≤45 years	21	21.0
	46-55 years	31	31.0
	56-65 years	27	27.0
	66-75 years	15	15.0
	76-85 years	6	6.0
	Mean age±SD (Range)	57.23±11.81 (35-85) years	
2-	Gender		
	Female	41	41.0
	Male	59	59.0

Table-1: Demographic Profile of Study Population (N=100)

Glycemic parameters	No. of patients	Min.	Max.	Mean	S.D.
HbA_1c	100	6.7	16.5	9.17	2.00
Fasting BS (mg/dl)	100	26.0	312.0	173.93	62.20
PP BS (mg/dl)	100	73.0	626.0	252.21	95.83

Table-2: Glycemic Levels of Study Population

SN	Glycemic levels	Number of cases	Percentage
1-	HbA_1c <7.0	16	16.0
2-	Fasting BS ≤130 mg/dl	31	31.0
3-	PP BS <180 mg/dl	35	35.0

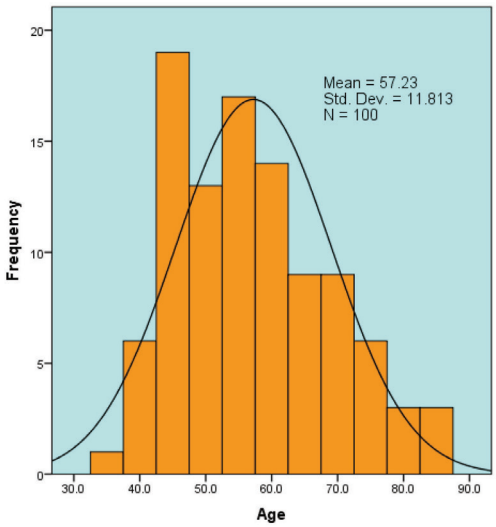
Table-3: Distribution of Study population according to diabetic control

No. of patients	Min.	Max	Mean	S.D.
100	4.55	95.37	27.72	22.23

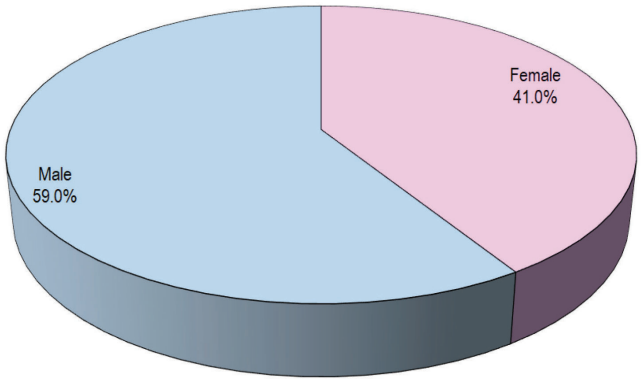
Table-5: Serum Prolactin level (ng/ml) of Study Population (Type 2 DM patients)

SN	Parameter	Good Control			Poor Control			Statistical significance	
		n	Mean	SD	n	Mean	SD	't'	'p'
1-	HbA1c	16	29.76	16.64	84	27.34	23.20	0.398	0.692
2-	Fasting BS	31	36.78	17.99	69	23.65	22.86	2.825	0.006
3-	PP BS	35	34.07	16.66	65	24.30	24.15	2.133	0.035

Table-9: Association of S. Prolactin with Glycemic control



Graph-1.1: Histogram Showing dispersion of Age of Study Population

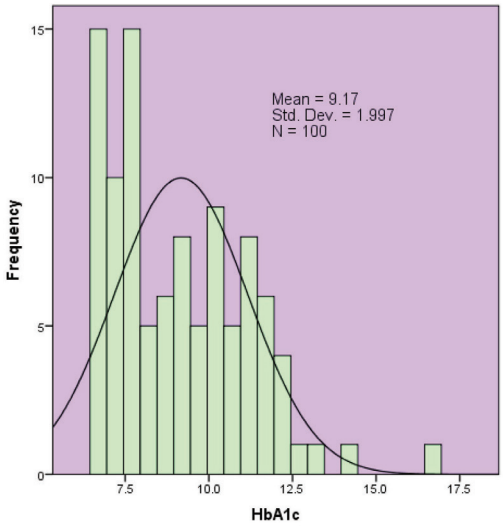


Graph-1.2: Gender wise Distribution of Study Population

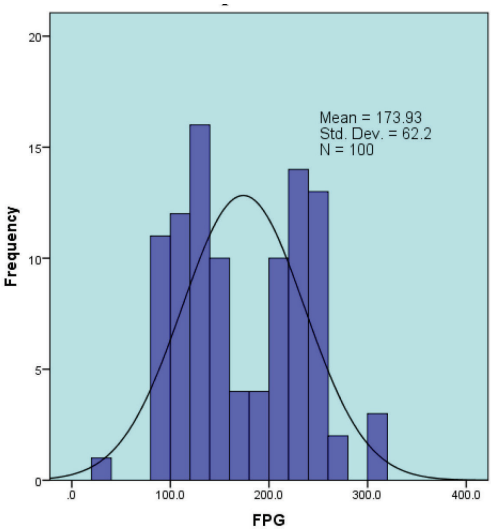
patients was assessed.

Only 16 (16.0%) patients had HbA_1c levels <7.0%.

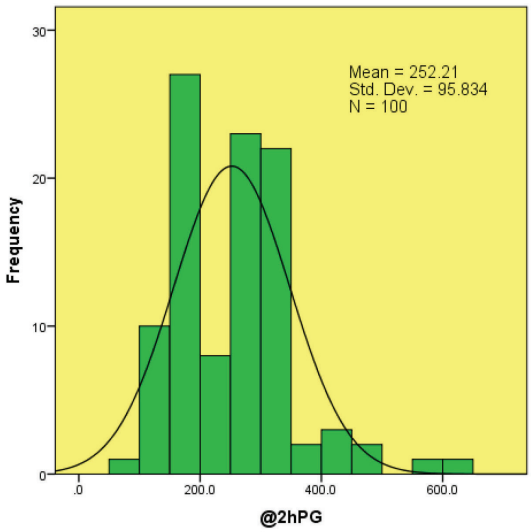
Fasting blood sugar of 31 (31.0%) patients was found to be ≤130 mg/dl.



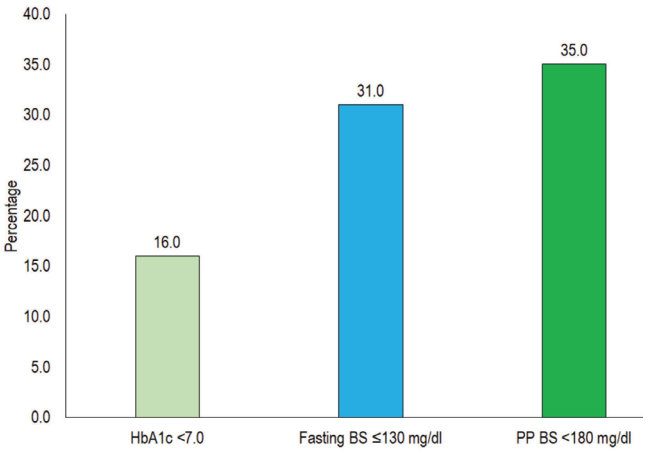
Graph-2.1: Histogram showing Dispersion of HbA1c level of Study Population



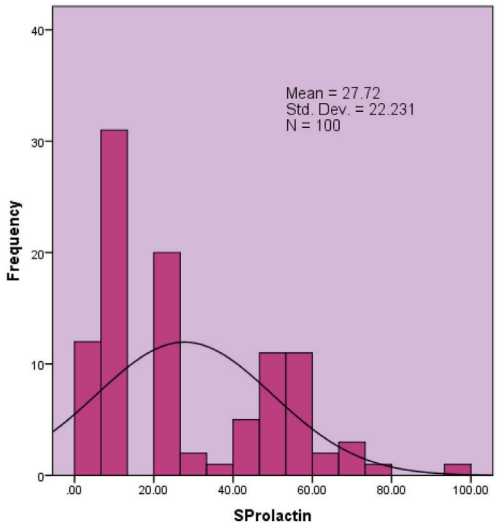
Graph-2.2: Histogram showing Dispersion of Fasting Blood Sugar levels of Study Population



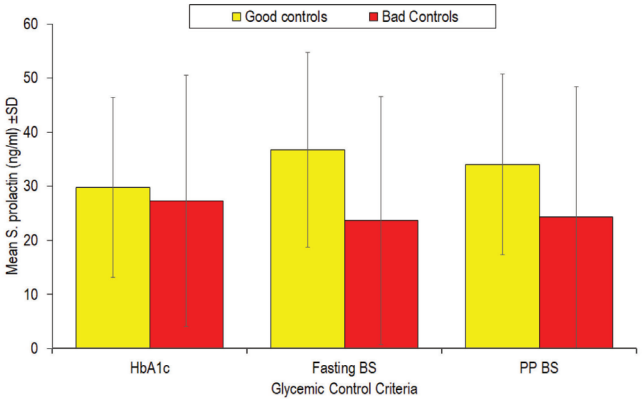
Graph-2.3: Histogram showing Dispersion of Post-prandial Blood Sugar levels of Study Population



Graph-3: Good Glycemic Control of patients based on different glycemic parameters



Graph-5: Histogram showing Dispersion of Serum Prolactin levels of Study Population



Graph-9: Association of S. Prolactin with Glycemic control

Post-prandial blood sugar levels of 35 (35.0%) patients were <180 mg/dl.

According to HbA1c, Fasting BS and PP BS levels, good glycemic control was observed in 16%, 31% and 35% patients respectively.

Range of Serum prolactin levels of type 2 diabetes mellitus

patients enrolled in the study was 4.55 to 95.37 ng/ml. Mean serum prolactin levels of study population was 27.72±22.23 ng/ml.

S. prolactin levels of patients with Good HbA_1c (<7.0) was higher than that of Poor HbA_1c (≥7.0) (29.75±16.64 ng/ml vs. 27.34±23.20 ng/ml) but this difference was not found to be significant statistically.

S. prolactin levels of patients with Good fasting blood sugar (≤130 mg/dl) was found to be significantly higher than those with Poor fasting blood sugar levels (>130 mg/dl) (36.78±17.99 ng/ml vs. 23.65±22.86 ng/ml).

S. prolactin levels patients with Good Post-prandial blood sugar (<180 mg/dl) was significantly higher as compared to those with Poor PP blood sugar (>180 mg/dl) (34.07±16.66 ng/ml vs. 24.30±24.15 ng/ml).

DISCUSSION

Diabetes mellitus is a metabolic disease defined by its characteristic excessive glucose in blood. It is a resultant of poor sugar absorption by the organs and/or under-secretion of insulin. The growing prevalence of diabetes has been compared to pandemics and with the ever-increasing burden of the disease, it has been an important topic of research over the past decades. The efforts to study diabetes on a macro scale have resulted in various associations of diabetes being studied with various comorbidities, especially micro- & macro-vascular diseases like dyslipidemia, obesity, bone related disorders including osteoporosis, kidney related diseases like nephropathy and ocular diseases like retinopathy.

India has one of the highest number of diabetics in the world and challenges like poor education, necessity of adherence to glycemic control, disease awareness and lack of health care infrastructure pose threat to health care ergonomics and disrupt the chain of quick and efficient treatment goals.

Contemporary experimental studies have reported association of prolactin and regulation of metabolic activities including insulin resistance, weight gain, food intake and others[21-27]. This has led to developing hypothesises to access association and estimate correlation of prolactin levels in diabetic patients with and without good glycaemic control.

With the similar aim, the present study was conducted to measure serum prolactin in T2DM patients and to find association of serum prolactin level with glycemic control in T2DM patients. For this purpose, 100 diabetic individuals fulfilling the inclusion and exclusion criteria were included in the study. Mean age of the study population was 57.23±11.81 years and a majority of the patients (58.0%) were aged through 46 to 65 years. Male preponderance was observed in the study, 59% of the study population consisted of males. In the present study diabetics were included and glycemic parameters were evaluated. HbA_{1c} ranged from 6.7% to 16.5% (Mean HbA_{1c}: 9.17±2.00%), Fasting BS ranged through 26.0 to 312 mg/dl (Mean FBS: 173.93±62.20 mg/dl) and PP BS ranged between 73 to 626 mg/dl (Mean PP BS:252.21±95.83 mg/dl).

In the present study, only a few patients had good diabetic control as measured by HbA_{1c} <7% (16%), fasting BS ≤130 mg/dl (31.0%) and PP BS <180 mg/dl (35.0%). Mean serum prolactin was 27.72±22.23 ng/ml (Range: 4.55-95.37 ng/ml). Among all T2DM patients serum prolactin levels was similar between patients with- and without-good diabetic control with respect to HbA_{1c} (29.76±16.64 *vs.* 27.34±23.20 ng/ml), while prolactin levels were significantly increased in patients with good glycemic control as compared to poor glycemic control with respect to Fasting BS (36.78±17.99 *vs.* 23.65±22.86 ng/ml) and Post-Prandial BS (34.07±16.66 *vs.* 24.30±24.15 ng/ml).

There seems to be a lot of contradicting literature with respect to the prolactin levels among different populations like diabetics, non-diabetics, with- & without-renal dysfunction, and between male and females, and interestingly this dispersion seems to broaden with the increasing researches in this regard. The pathophysiology of the prolactin and diabetes is complex and not well-established and similarly, paucity of literature exists with respect to levels of serum prolactin and their association with diabetes or diabetes related complications.

The findings of the present study, present a rather novel and unique insight to the prolactin levels and diabetics and diabetes related complications. While, the study presented with some unique findings like comparison of prolactin levels between tight- or poor- glycemic controls. However, one of the limitations of the study was that, unlike some of the contemporary studies, prolactin levels were not evaluated stratified between genders.

Limitation

1. The sample size of the study population was limited.
2. The study was confined to a particular geographical area only.

CONCLUSION

The present study was conducted to assess the serum prolactin levels in Type-2 diabetes mellitus patients and associate the same with glycemic control . A total of 100 T2DM patients fulfilling the inclusion criteria were included in the study, age of patients ranged from 35 to 85 years (mean age: 57.23±11.81 years) with slight dominance of males (59%). Following were the major findings of the present study:

1. Good glycemic control in terms of HbA_1c (<7.0), Fasting BS (≤130 mg/dl) and PP BS <180 mg/dl was observed in only 16.0%, 31.0% and 35.0% patients respectively.
2. Serum prolactin levels of T2DM patients enrolled in the study ranged between 4.55 and 95.37 ng/ml, mean S. prolactin level was 27.72±22.23 ng/ml.
3. Among all T2DM patients serum prolactin levels was similar between patients with- and without-good diabetic control with respect to HbA_{1c} (29.76±16.64 *vs.* 27.34±23.20 ng/ml).
4. Among all T2DM patients, prolactin levels were significantly increased in patients with good glycemic control as compared to poor glycemic control with respect to Fasting BS (36.78±17.99 *vs.* 23.65±22.86 ng/ml) and Post-Prandial BS (34.07±16.66 *vs.* 24.30±24.15

ng/ml).

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