

Article

Serum Prolactin, Glycemic Control, and Insuline Resistance in Type 2 Diabetes in Iraq: A Sex-Stratified Cross-Sectional Comparative Studay

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Abstract: Type 2 diabetes mellitus (T2DM) represents an increasing health burden in Iraq. Prolactin (PRL) is involved in the regulation of glucose metabolism since high PRL serum levels are associated with low incidence of T2DM. This study evaluated the relationship between serum prolactin levels and key indicators of glycemic control and insulin resistance in T2DM patients, with a dedicated sex disaggregated analysis. A comparative cross-sectional study was conducted in Salahaddin Governorate, Iraq. The study included 60 participants: 30 patients with T2DM and 30 healthy individuals of the same age group (15 males and 15 females) aged between 20 and 60 years. All participants underwent baseline assessment (age and Body mass index (BMI)) and five vital signs (Fasting blood glucose (FBG), fasting insulin, glycated hemoglobin, insulin resistance index, and prolactin). All statistical analyses were performed using IBM SPSS Statistics software for Windows. The level of statistical significance was set at $p < 0.05$. Body mass index did not differ between the groups ($P > 0.05$). However, the patients were significantly older than the control group overall ($p = 0.002$ and $p = 0.006$, respectively). The patient group recorded higher fasting blood glucose and glycated hemoglobin (HbA1c) values compared to the control group in the overall sample ($P < 0.05$). At the correlation level, prolactin was associated with fasting blood glucose ($r = 0.31$, $P = 0.013$) and HbA1c ($r = 0.35$, $P = 0.005$) in the overall sample; while a non-statistically significant correlation was observed with the insulin resistance index ($r = 0.24$, $P = 0.059$), and no statistically significant correlation was found with fasting insulin. None of the sex-specific subgroup correlations were statistically significant. Prolactin shows a statistically significant positive association with palm-expressed FBG and HbA1c at the aggregate level when controlling for age difference between groups. Importantly, however, this association did not reach significance in the sex stratified subanalyses. Although this observation is a preliminary one, it should be confirmed in larger, broader powered studies specifically designed to explore sex dependent metabolic effects.

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1. Introduction

Type 2 diabetes mellitus (T2DM) is one of the most common and problematic chronic diseases on a global level. According to the IDF Diabetes Atlas, 589 million people aged 20~79 years were living with diabetes (worldwide prevalence =11.1%) and will increase to 852 million (13.0%) by the year of 2030 due largely to continued urbanization, changing lifestyles and increasing obesity rates. The Middle East and North Africa region has the

greatest integrated regional burden, with an age adjusted prevalence of 19.9% [1]. For Iraq nationally, an age standardised prevalence of 19.7% was reported by a large population based survey from Basra (n = 5,445) [2] this finding was subsequently confirmed by the Iraqi National Consensus Document on the Treatment of Type 2 Diabetes, which also noted the local prevalence of the disease [3]. In addition, a study conducted in Mosul within the country reported that the prevalence of the disease among adults was 11.46% (14.77% among males versus 9.58% among females) and particularly high rates of undiagnosed diabetes were reported even among the general population aged 40 years and over living in Zakho [4].

T2DM is pathophysiologically based on two main pillars: peripheral insulin resistance and a progressive pancreatic β cell dysfunction, resulting in chronic hyperglycaemia and its microvascular complications [5]. Glycated haemoglobin (HbA1c) is currently the key marker for both diagnostic and monitoring long term glycaemic control in accordance with recent update of ADA standards of Care [6] In conjunction with this, Homeostatic Model Assessment for Insulin Resistance (HOMA IR) serves as a well validated, simple non invasive surrogate measure of insulin resistance based on fasting blood glucose (FBG) and fasting insulin measurements, although more complex clamp methods are avoided [7].

Biological sex contributes an additional layer of complexity to the pathophysiology of T2DM and clinical heterogeneity, similarly, The finding by [8] noted that compared to men our patients are diagnosed at a lower body weight and younger age but have a greater burden of metabolic risk factors present at the time of diagnosis an observation consistent with their former broader review in Endocrine Reviews [9]. Likewise, other author found that Glucose and energy homeostasis to T2DM in a sex-specific manner [10].

Over the past two decades, Prolactin (PRL) is a pituitary hormone essential for various physiological functions in the human body. It is not only important for the initiation and maintenance of lactation, but seems to be also involved in reproduction, growth and development, and metabolism. These different functions of PRL can only be fulfilled due to the fact that the PRL receptor is expressed in different tissues and cells such as lymphoid cells, endometrium, prostate, adipocytes, and β -cell of the pancreas [11]. Into the aspect, PRL is involved in the regulation of glucose metabolism through regulation the function of pancreatic β -cell [12]. The research by [13] where its diverse roles in health and disease were reinforced. More recently, the study by [14] or Prolifetime Metabolic roles of prolactin further corroborates [15].

In spite of the growing body of evidence linking increased prolactin concentrations to impaired glycaemic control, the vast majority of studies performed to date have treated their cohorts as effectively homogeneous entities neglecting the fact that there are profound sex dependent physiological variations in the regulation and secretion of prolactin, accompanied by significant differences in insulin sensitivity. As far as we know, neither Iraqi nor regional study has yet integrated prolactin and all four indices (FBG, fasting insulin, HbA1c and HOMA IR) into one clinical comparative framework that performs well-established quantifiable stratification of men and women for each variable. Local studies conducted so far have only focused on sex-specific interrelations among one or two of these biomarkers in a piecemeal fashion. Thus, the objective of the present study is to fill this integrative gap and contribute towards improved mechanisms-informed understanding of T2DM pathophysiology through an informed sex lens.

2. Materials and Methods

2.1. Study Design and Ethical Approval

A cross-sectional comparative experimental design was conducted, in which all clinical and laboratory assessments were performed for each participant. Participants were selected from outpatient clinic visitors, and data collection continued for four months

(from 1 January to 31 April 2026). All patients and enrolled individuals gave informed verbal consent for their participation in this study. This study was permitted by Scientific Ethical Committee in College of Basic Education / Shirqat , Tikrit University, Iraq, under ethical permission number (ref. TU BE 0004) accordance with the Declaration of Helsinki

2.2. Participants and Exclusion Criteria

This study involved 60 individuals from Saladin Governorate, Iraq divided into four groups (n= 15 each) males with T2DM, females with T2DM, healthy male (control), and healthy female(control). Had ages from 35 to 60 years The diagnosis of T2DM was established via official medical records after referral by specialist physicians in the outpatient setting based on the standard clinical protocol at our institution. Individuals using insulin therapy, with history of chronic diseases (liver, renal or cardiovascular disease), other diagnosed endocrinopathies and pregnancy/lactation were strictly excluded to validate HOMA IR and hormone estimates except if they suffered from hypertension. Patients were on different oral antidiabetic therapies (either metformin-based as in those on glimepiride or gliclazide, or sitagliptin/metformin combination). Controls were subjected to the same laboratory panel to define normoglycaemia and had no previous history of diabetes or significant illness.

2.3. Sample Size Justification

As this investigation was exploratory and the collection window was restricted to four months, we structured our study based on convenience rather than performing a statistical power calculation in advance. This initial work should serve as exploratory groundwork, enabling future larger studies with prospectively determined sample sizes.

2.4. Clinical and Anthropometric Measurements

Age and other demographic data were validated against official clinical records during the actual visit. Weight was measured in kg using a medical scale (precision ± 0.1 kg). Subsequently, body mass index (BMI) was calculated using the standard formula: weight in kilograms divided by height in metres squared (kg/m^2).

2.5. Biochemical and Hormonal Assays

A volume of 10 mL of venous blood was taken after overnight fasting from recruited patients and individuals. Fasting blood glucose was measured using the GOD PAP (glucose-phenol oxidase and 4-aminoantipyrine) method (Randox, UK) by absorbance using a PD 303 spectrophotometer at 505 nm. Glycated hemoglobin was measured using fluorescence immunoassay (FIA) with a Finecare™ FIA Meter III Plus, Guangzhou Wondfo Biotech, China. Serum was separated prior to insulin and prolactin analysis by centrifugation at $3000 \times g$ for 10 minutes at 4°C and then stored at -80°C . Serum levels for both assays were then determined using CLIA on a Mindray CL 900 platform (Shenzhen Mindray Bio Medical Electronics, China) according to the manufacturer's instructions.

2.6. Insulin Resistance Calculation

Insulin Resistance Index (HOMA IR index), as originally described by [7] to calculate insulin resistance, applying the standard formula:

$$\text{HOMA IR} = \text{Fasting Insulin } (\mu\text{IU/mL}) * \text{Fasting Glucose (mg/dL)} / 405$$

Higher HOMA IR values indicate more severe insulin resistance.

2.7. Statistical Analysis

Quantitative variables (FBG, fasting insulin, HbA1c, HOMA IR and prolactin) were quoted in means $\pm$ SD. Independent samples t-tests were used to evaluate differences between T2DM patients and controls in the total sample, followed by separate sex analyses. Pearson correlation coefficient was used to explore the association of prolactin with the other variables in total, as well as by stratifying patients between male and female subgroups. Analysis of covariance (ANCOVA) used with age entered as a covariate to examine differences in the core study variables above and beyond this baseline age

difference, because there was a statistically significant age difference between two main groups. All data were analyzed using SPSS (IBM SPSS Statistics for Windows version 20.0, 2014 Armonk, NY, USA: IBM Corp). Statistical significance was defined as $P < 0.05$.

3. Results

3.1. Sample Description and Baseline Characteristics

The total sample consisted of 60 participants (30 with T2DM, 30 controls), and was composed of 15 males and 15 females per study group. In the overall cohort and in each sex specific subgroup, baseline BMI was well matched between patients and controls ($P \geq 0.05$ for all comparisons). However, at the aggregate level a statistically relevant difference was noted in age between both groups (51.17 ± 6.36 vs. 45.70 ± 6.80 years; $P = 0.002$). This difference was particularly pronounced in males (52.13 ± 6.36 vs. 45.80 ± 5.33 years; $P = 0.006$); this age difference approached but did not reach significance among females (50.20 ± 6.43 vs. 45.60 ± 8.21 years; $P = 0.099$) (Table 1).

Table 1. Comparison of baseline characteristics (age and body mass index) between T2DM patients and controls—total sample, males, and females.

Parameters	Patients	Controls	P-Value	Patients	Controls	P-Value	Patients	Controls	P-Value
	Males and Females	Males and Females		Males	Males		Females	Females	
	Mean + SD	Mean + SD		Mean + SD	Mean + SD		Mean + SD	Mean + SD	
Age(year)	51.17±6.36	45.70±6.80	0.002**	52.13±6.36	45.80±5.33	0.006**	50.20±6.43	45.60±8.21	0.099
BMI (Kg/m2)	30.09±4.75	31.14±5.37	0.424	27.71±4.30	28.61±3.05	0.514	32.47±4.01	33.67±6.06	0.525

SD= Standard Deviation; BMI=Body Mass Index (kg/m2) P-Value calculated using independent samples t-test ;

* Significant at $P \leq 0.05$; **Significant at $P \leq 0.01$

3.2. Comparison of Study Variable Means

FBG and HbA1c values were found to be significantly higher in patients than controls for the total sample and in males and females ($P < 0.001$ for all). Compared to HOMA IR, the difference in patients was statistically significantly elevated in the total population ($P = 0.010$) and women ($P = 0.023$), but not men ($P = 0.233$). The total sample indicated a significantly higher serum prolactin among patients (23.98 ± 9.38 vs. 17.88 ± 8.74 , $P = 0.009$). However, on sex stratified analysis, this effect decreased: there was no significant difference between males ($P = 0.074$) and females ($P = 0.051$) as the difference approached but fell short of conventional significance (Table 2; Figures 1–3).

Table 2. Comparison of the five study variables between T2DM patients and healthy controls—total sample, males, and females.

Parameters	Patients	Controls	P-Value	Patients	Controls	P-Value	Patients	Controls	P-Value
	Males and Females	Males and Females		Males	Males		Females	Females	
	Mean + SD	Mean + SD		Mean + SD	Mean + SD		Mean + SD	Mean + SD	
FBG (mg/dL)	157.0±41.0	91.4±8.8	<0.001**	146.6±42.5	90.3±6.3	<0.001**	167.4±38.1	92.4±10.8	<0.001**
Fasting Insulin (µIU/mL)	13.715±8.677	15.123±6.297	0.478	12.298±5.31	15.582±6.291	0.133	15.131±11.111	14.665±6.489	0.889

HbA1c (%)	7.5433±1.109	5.3600±0.356	<0.001**	7.1933±1.19	5.3267±0.3595	<0.001**	7.8933±0.9323	5.3933±0.3615	0.001**
HOMA-IR	5.2593±3.516	3.4143±1.455	0.010**	4.5013±2.67	3.5240±1.5928	0.233	6.0173±4.1522	3.3047±1.351	0.023*
Prolactin	23.9837±9.38	17.8777±8.74	0.009**	20.4887±7.4	16.2533±4.897	0.074	27.4787±10.01	19.5020±11.3407	0.051

SD=Standard Deviation; FBG= Fasting Blood Glucose; HbA1c=Glycated Hemoglobin (%); HOMA-IR=Homeostasis Model Assessment of Insulin Resistance; P-Value calculated using independent samples t-test; * Significant at $P \leq 0.05$; **Significant at $P \leq 0.01$.

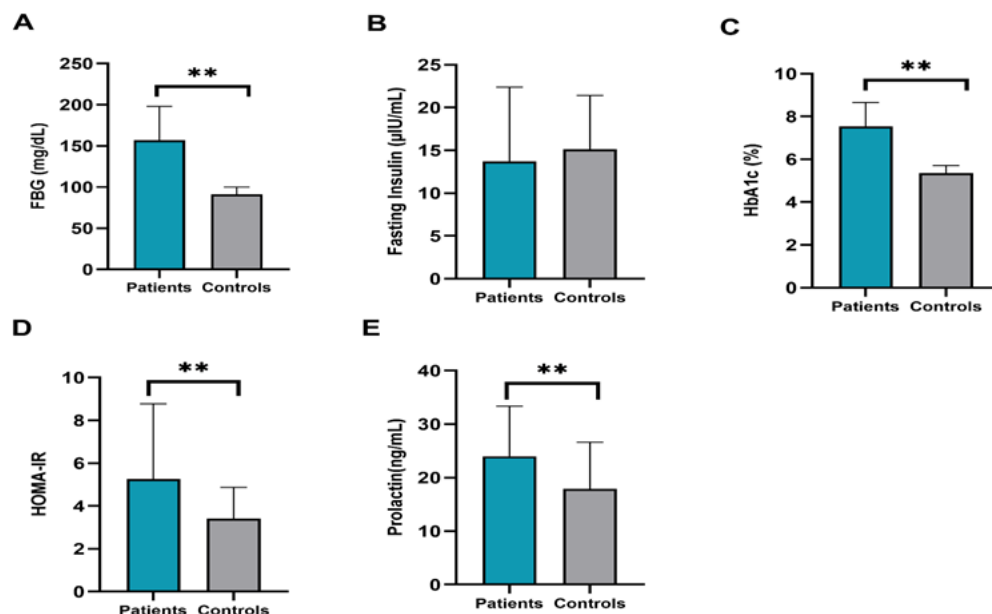


Figure 1. Mean comparison of the study variables between type 2 diabetes patients and healthy controls (total sample)

The figure illustrates mean $\pm$ standard deviation of the five study variables among type 2 diabetes patients ($n=30$) compared with healthy controls (30): (A) FBG; (B) Fasting insulin; (C) HbA1c; (D) HOMA-IR; (E) Prolactin. * Significant at $P \leq 0.05$; **Significant at $P \leq 0.01$.

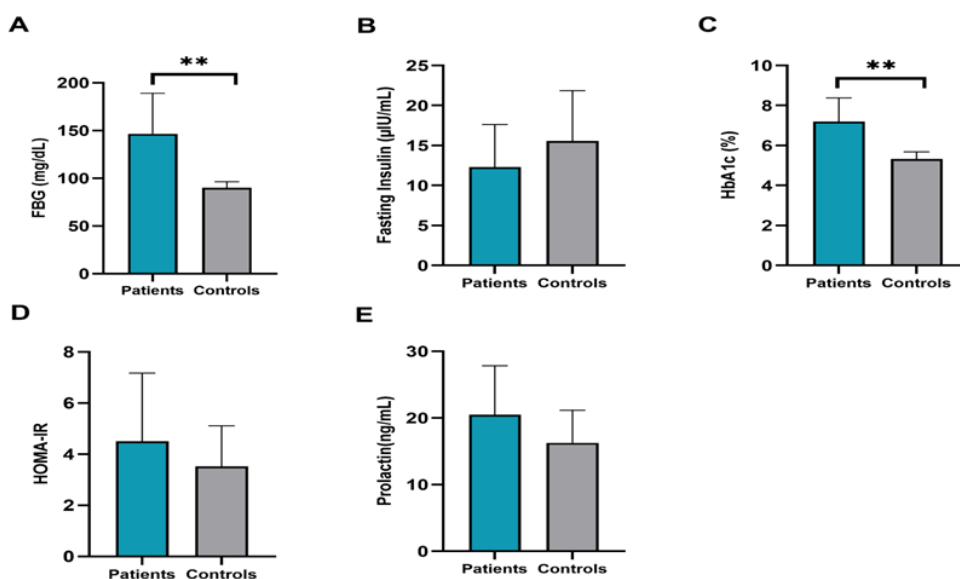


Figure 2. Mean comparison of the study variables between type 2 diabetes patients and healthy controls (males).

The figure illustrates mean $\pm$ standard deviation of the five study variables among male type 2 diabetes patients (n=15) compared with male healthy controls (15): (A) FBG; (B) Fasting insulin; (C) HbA1c; (D) HOMA-IR; (E) Prolactin. * Significant at $P \leq 0.05$; **Significant at $P \leq 0.01$.

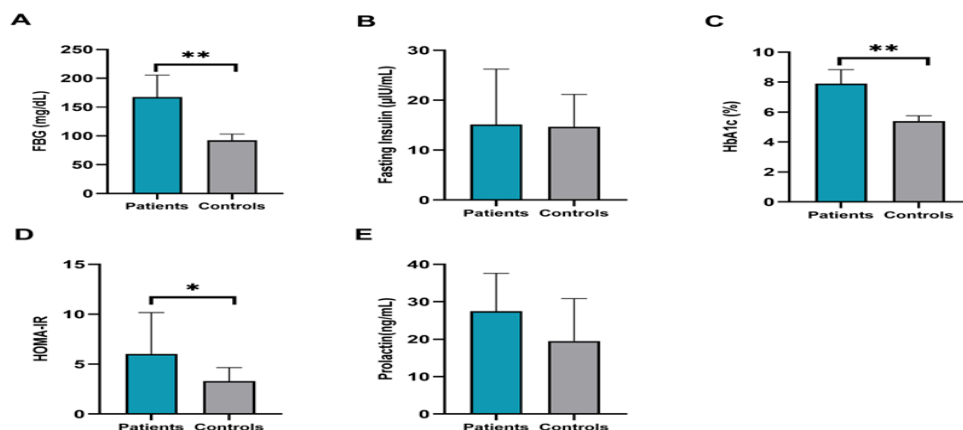


Figure 3. Mean comparison of the study variables between type 2 diabetes patients and healthy controls (females)

The figure illustrates mean $\pm$ standard deviation of the five study variables among female type 2 diabetes patients (n=15) compared with female healthy controls (15): (A) FBG; (B) Fasting insulin; (C) HbA1c; (D) HOMA-IR; (E) Prolactin. * Significant at $P \leq 0.05$; **Significant at $P \leq 0.01$.

3.3. Analysis of Covariance (ANCOVA)

Given the statistically significant age discrepancy between the two groups, we performed an analysis of covariance with age entered as a covariate, to adjust for its potential confounding influence on the five study variables. The findings validated the main differences seen for FBG, HbA1c and HOMA IR remained significant overall even after this adjustment. By contrast, the effect of age adjustment on prolactin significance showed a marked difference between men and women. In men, the already weak P value (0.074) dropped significantly to 0.362. In contrast, the evidence for females was actually attenuated with adjustment ($P=0.052$ to 0.030) (Table 3).

Table 3. Comparison of study variables between T2DM patients and controls, before and after adjusting for age using analysis of covariance (ANCOVA).

Parameters	Group	Patients (Mean + SD)	Controls (Mean + SD)	P- (unadjusted)	P- (adjusted)
FBG (mg/dL)	Overall (n=60)	157.0 $\pm$ 41.0	8.8 $\pm$ 91.4	<0.001**	<0.001**
	Males (n=30)	146.6 $\pm$ 42.5	90.3 $\pm$ 6.3	<0.001**	<0.001**
	Females (n=30)	38.1 $\pm$ 167.4	92.4 $\pm$ 10.8	<0.001**	<0.001**
Fasting Insulin (μ IU/mL)	Overall (n=60)	13.715 $\pm$ 8.677	15.123 $\pm$ 6.297	0.478	0.625
	Males (n=30)	12.298 $\pm$ 5.312	15.582 $\pm$ 6.291	0.133	0.094
	Females (n=30)	15.131 $\pm$ 11.111	14.665 $\pm$ 6.489	0.889	0.717
HbA1c (%)	Overall (n=60)	1.1088 $\pm$ 7.5433	5.3600 $\pm$ 0.3558	<0.001**	<0.001**

HOMA-IR	Males (n=30)	7.1933±1.1895	5.3267±0.3595	<0.001**	<0.001**
	Females (n=30)	7.8933±0.9323	0.3615±5.3933	<0.001**	<0.001**
	Overall (n=60)	5.2593±3.5164	3.4143±1.4554	0.010**	0.010**
	Males (n=30)	4.5013±2.6724	3.5240±1.5928	0.233	0.298
Prolactin	Females (n=30)	6.0173±4.1522	3.3047±1.351	0.023*	0.024*
	Overall (n=60)	23.9837±9.3821	17.8777±8.7403	0.009**	0.011*
	Males (n=30)	20.4887±7.3606	16.2533±4.8968	0.074	0.362
	Females (n=30)	27.4787±10.0986	19.5020±11.3407	0.051	0.030*

SD=standard Deviation ; P-(unadjusted)= independent samples t-test ; P(adjusted)=Analysis of Covariance (ANCOVA) with age as covariate ; *significant at $P \leq 0.05$; ** significant at $P \leq 0.01$.

3.4. Correlation Analysis between Prolactin and Study Variables

Pearson correlation analysis showed a positive correlation between prolactin and both FBG ($r = 0.31$, $P = 0.013$) and HbA1c ($r = 0.35$, $P = 0.005$). There was a nonsignificant association with HOMA IR ($r = 0.24$, $P = 0.059$) and no significant relationship with fasting insulin. However, none of the correlations reached full statistical significance when analyzing the data by sex. The correlation coefficients in males ranged from 0.06 (for fasting blood glucose) to 0.31 (for the HOMA-IR insulin resistance index). In females, the range was from $r = 0.07$ (fasting insulin) to $r = 0.35$ (HbA1c), with the latter being the strongest unadjusted correlation in females and approaching the traditional significance threshold ($P = 0.052$; Table 4; Figure 4).

Table 4. Pearson correlation coefficients between prolactin and study variables in T2DM patients—total sample, males, and females.

Parameters	Males and Females	Males	Females
FBG (mg/dL)	$r=0.31$, $p=0.013^*$	$r=0.06$, $p=0.165$	$r=0.32$, $p=0.081$
Fasting Insulin (μIU/mL)	$r=0.09$, $p=0.465$	$r=0.10$, $p=0.566$	$r=0.07$, $p=0.705$
HbA1c (%)	$r=0.35$, $p=0.005^{**}$	$r=0.29$, $p=0.112$	$r=0.35$, $p=0.052$
HOMA-IR	$r=0.24$, $p=0.059$	$r=0.31$, $p=0.088$	$r=0.18$, $p=0.317$

r =Person Correlation Coefficient; FBG= Fasting Blood Glucose; HbA1c=Glycated Hemoglobin; HOMA-IR= Homeostasis Model Assessment of Insulin Resistance; * Significant at $P \leq 0.05$; **Significant at $P \leq 0.01$.

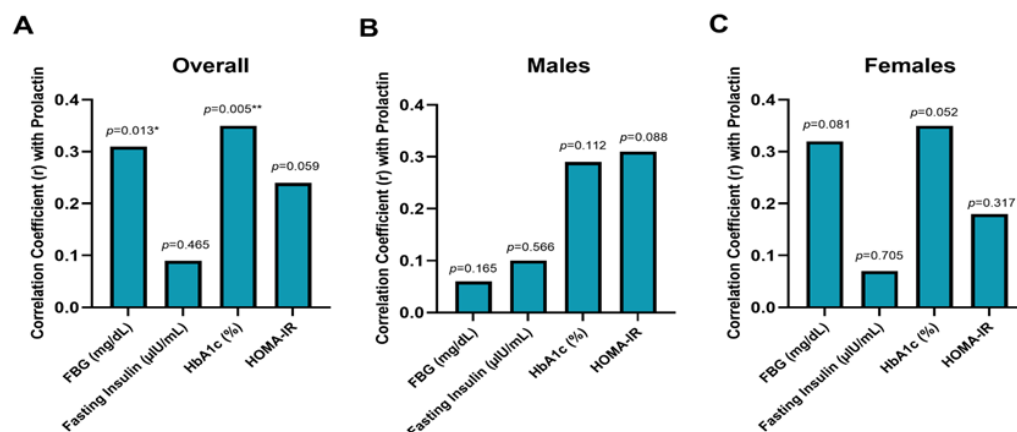


Figure 4. Scatter plot (or graphical representation) of the correlation between prolactin and study variables in T2DM patients

The figure illustrates Person correlation coefficients (r) between prolactin and FBG, fasting insulin, HbA1c, and HOMA-IR among type 2 diabetes patients> (A) Overall sample (n=30); (B) Males (n=15); (C) Females (n=15). * Significant at $P \leq 0.05$; **Significant at $P \leq 0.01$.

4. Discussion

The current study investigated the relationship between serum prolactin, glycaemic control and insulin resistance in patients with type 2 diabetes mellitus considering sex differences among the participants. Body mass index was similarly well matched between the patient and control groups, both in the overall cohort and within the each sex specific subgroup ($P \geq 0.05$). But there was a statistically significant difference between groups at the aggregate level for age, due mainly to the male subgroup none of these differences reached significance among females. Because this age difference potentially confounds our results, we conducted an analysis of covariance including age as a covariate. After adjustment, it was confirmed that the differences in FBG, HbA1c, and HOMA IR remained statistically significant (Table 4). In the case of prolactin, age adjustment had a noticeably different influence on males (further limited significance) than on females (signal increased): in males from $P = 0.074$ to 0.362 ; and in females from $P = 0.051$ to $P = 0.030$.

Overall, all patients had higher levels of prolactin than controls ($P = 0.060325$); however, this was not statistically significant. This trend of effect too (high level of prolactin in patients) similar to Iraqi study from Baghdad who found significant increase of the mean levels of prolactin in T2DM group compared to control group, with $P < 0.01$ (Rashid et al., 2019). This is also in line with an Ethiopian study that included only 330 males (165 with diabetes and 156 in the control group) which reported male patients had much higher prolactin levels (7.79 ± 2.9 vs. 6.81 ± 3.1 , $P = 0.004$; male: female ratio was not defined [16]. These results are in line with the theoretical model put forward by Macotela et al., which showed a U-shaped relationship between prolactin disorder and metabolism: both subphysiological (high) and pathologically elevated levels of prolactin are correlated with poor glycemic control, while intermediate-range prolactin levels appear metabolically favorable. . This U shaped model needs to be better understood and this may, at least in part, explain why our finding (raised prolactin in subjects) appears contradictory to the Indian comparative study [17], which found much lower prolactin in diabetic patients than controls. Variations in population characteristics, sample sizes or inclusion/exclusion criteria are possibly to blame for such discrepancies across studies. At the mechanistic level by author, [18] that showed that prolactin receptors, located on pancreatic beta cells and adipose tissue, directly modulate insulin secretion and sensitivity; a dual role confirmed by [19] in their recent review, which emphasized prolactin's effect

on glucose and insulin homeostasis through the inhibition of physiological dopaminergic tone.

The sex specific difference is HOMA IR significance significant for females but not males and in the large scale Korean population based study (KNHANES), The author [20] found that women at diagnosis of T2DM were more insulin resistant than men even being diagnosed at an older age and higher BMI. That mechanism is consistent with the overall physical basis proposed by [21]. In a systematic review of observational studies state that the circadian fluctuations of oestrogen in premenopausal women seems to have an advantage which protects against insulin resistance and elevated levels of androgens lead men to be more susceptible to insulin resistance [21].

As [22], illustrated, this is mechanistically linked to the basic protective mechanism of 17β oestradiol via the Foxa1 transcription factor pathway to enhance insulin sensitivity and inhibit hepatic gluconeogenesis. Hence, women have a more profound underlying physiological advantage against the development of insulin resistance, meaning that T2DM in females is only established after they encounter enough perturbation to their metabolism to overcome this protective advantage

Pearson's correlation coefficient showed a clear positive pattern for prolactin with fasting blood glucose and glycated hemoglobin (HbA1c), while the insulin resistance index (HOMA-IR) approached but did not reach statistical significance. These results are consistent with a previous Iraqi study by Al-Nami et al. on patients with type 2 diabetes, which indicated very strong positive correlations between prolactin and fasting blood glucose ($r = 0.84$, $P < 0.0001$), glycated hemoglobin (HbA1c) ($r = 0.81$, $P < 0.0001$), insulin ($r = 0.99$, $P < 0.000001$), and the insulin resistance index (HOMA-IR), as well as a statistically significant correlation between elevated serum prolactin levels and impaired insulin sensitivity in patients with type 2 diabetes. The weaker correlation coefficients in our cohort likely reflect differences in sample size or characteristics.

However, this positive directional trend contrasts with the protective association reported in non diabetic populations within the normal physiological range. The author [23] proves that prolactin was positively associated with sensitivity ($P = 0.001$) in 1,883 participants [24, 25]. A study by [26] Using the biphasic (non linear) framework of [27], these apparently opposite directions can be reconciled in which the effect of prolactin on glucose metabolism is contextualized according to ones position on the dose response curve there is no singular invariant direction. Hence, whereas prolactin may be protective in its normal range in healthy individuals, its increased level in diabetes patients as shown here, could just be the compensatory accompaniment of the ongoing metabolic derangement rather than a causative factor.

Analyses stratified by sex showed that these correlations were of differing stability. In men, this relationship between prolactin and fasting blood glucose (FBG) significantly weakened after multiple adjustments, while the relationships with HbA1c and HOMA-IR still presented a generally positive trend. Results of study at hand are parallel to those of [28], showed that hyperprolactinemia in obese men was well correlated with elevated HOMA-IR compared to age- and BMI-matched controls, and negatively correlated apn testosterone ($p < 0.01$) A common mechanism, for which the details were carefully reviewed by [29] who has shown that hyperprolactinemia raises insulin resistance in tissues by stimulating glucose-dependent expression of the insulin gene and modulating adipose tissue lipogenesis (insulin sensitivity and metabolic homeostasis).

In females, however, a more consistent positive pattern was evident for prolactin across all variables: FBG: $r = 0.32$; fasting insulin: $r = 0.07$; HbA1c: $r = 0.35$; HOMA IR: $r = 0.18$.) These are similar with the study of [30], who claimed high prolactin to be a risk factor for insulin resistances, overweight, or prediabetes in women with polycystic ovary syndrome. This also echoes the idea of [31] note a J shaped non linear relationship between prolactin and metabolic complication observed in female T2DM. One feasible direction relies on the previous works [30-34]. This is in accordance with the study of [30], which

found high free testosterone to be associated with increased insulin resistance ($r=0.47$, $P < 0.05$) in hyperprolactinaemic women. Clinically, these findings have potentially substantial implications at the population level: the replication of a positive association between prolactin FBG and HbA1c p-values suggest that prolactin could be viewed as an adjunctive marker.

4.1 Limitations

The study has several limitations, most notably its small overall sample size ($n = 60$), which becomes even smaller after being divided by sex ($n = 15$ per category). This necessitates careful interpretation of the observed high correlation patterns between the sexes until these results are replicated in larger studies, especially given the lack of statistical correction for multiple comparisons. Secondly, the cross-sectional design prevents any causal inferences; the correlations we observed represent only a single moment of shared statistical variance. Third, the single-center study design limits the generalizability of the results to populations with different sociodemographic or ethnic characteristics. Fourth, our use of a convenience sample without prior accounting for study power (although justified by the exploratory nature of this study) reduces the impact of our findings. Fifth, we did not account for the effect of duration of diabetes or smoking status, two other potential confounding factors. Sixth, oral diabetes regimens were heterogeneous among participants and were not controlled for as concomitant variables, and we did not exclude patients with concomitant hypertension, leaving open the possibility that these factors could have differentially affected prolactin or glycemic indices.

5. Conclusion

The results of the current study indicate a statistically significant direct association between serum prolactin and fasting blood glucose/glycated hemoglobin (HbA1c) levels at the population level in patients with type 2 diabetes in general. This association remained strong after age adjustment analyses but was not conclusive in sex-disaggregated analyses due to the small sample size. This initial observation calls for further studies on larger populations with direct measurements of sex hormones to explore potential mechanisms and determine the clinical feasibility of including patient sex in prolactin-based metabolic risk assessment.

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