



Importance of testosterone and cortisol in prediabetic and diabetic male patients in Diyala Governorate (Iraq)

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Article info

Received 14.03.2025

Received in revised form

17.04.2025

Accepted 21.05.2025

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Arif, A. I., Rmaidh, A. Y., Qaddoori, H. T., & Mohammad, S. Q. (2025). Importance of testosterone and cortisol in male patients with prediabetic and diabetic in Diyala Governorate (Iraq). *Regulatory Mechanisms in Biosystems*, 16(2), e25070. doi:10.15421/0225070

This study aimed to investigate the predictive role of biochemical and hormonal indicators in screening patients with prediabetes and diabetes. This research was carried out in Diyala province from March–June 2024. 60 samples were collected from patients (30 prediabetic and 30 diabetic) who visited the consultation clinic at Baqabi Teaching Hospital. 30 samples were collected from healthy subjects as a control group. All indicators were quantified by a Biorex machine. The results show differences in glucose with prediabetic and diabetic individuals mostly within the groups 31–50 and >50. Prediabetic and diabetic patients were often overweight or obese. They had higher levels of FBS, HbA1C, and cortisol than control, while testosterone levels were lower. The ROC curve indicated that FBS and HbA1C were more sensitive and specific than cortisol and testosterone for predicting prediabetes and diabetes. Cortisol was more effective than testosterone for prediabetes screening, while testosterone was better for diabetes. In conclusion, elevated indicators (except testosterone) were observed compared to normal glucose levels. HbA1C and FBS were most effective for screening. Cortisol was better for prediabetic screening, while testosterone was better for diabetes. BMI had no significant effect on indicators in diabetics.

Keywords: HbA1c; cortisol; testosterone; prediabetes; diabetes.

Introduction

A dangerous condition threatening diabetes and its related macro- and microvascular consequences is prediabetes. Meta-analyses indicate that between 5% and 10% of those with prediabetes develop diabetes every year (Echouffo-Tcheugui et al., 2023). Individuals with prediabetes have a significant chance of developing diabetes; amongst middle-aged people with prediabetes, 5–10% will develop the disease annually, totaling 70% over their lifetimes (Hu et al., 2023). Hyperglycemia over standard but below the diabetic criterion is the standard definition of prediabetes (Rooney et al., 2023). According to Aldossari et al. (2018), the American Diabetes Association's current criteria for diagnosing prediabetes involve fasting blood sugar (FBS) ranging from 100–125 mg/dL or impaired glucose tolerance (IGT) of 140–199 mg/dL after two hours of a 75 mg glucose load, or HbA1c of 5.7–6.4 mmol/mol (Aldossari et al., 2018). Ten percent of adults worldwide suffer from prediabetes, a major health problem. 319 million people (6.2% of the world's adult population) were expected to have impaired fasting glucose (IFG) in 2021, whereas 541 million persons (10.6% of the world's adult population) had impaired glucose tolerance (IGT) (Pourat et al., 2023). Over ninety percent of all instances of diabetes that are diagnosed are type 2 diabetes (DM2), but only five to ten percent are type 1 diabetes. Numerous risk factors that can be changed or eliminated impact the onset and course of diabetes mellitus type 2.

Potential danger signs include smoking, elevated blood pressure, poor nutrition, being overweight, and lack of exercise. In contrast, age, genealogy, race, and genetic susceptibility are examples of non-modifiable risk variables (Alshaikh et al., 2024). The American Diabetes Association has advised against utilizing glucose tolerance screening in the twenty-first century in favor of glycated hemoglobin (HbA1c) for the diagnosis and follow-up of diabetes and prediabetes. Hemoglobin types that show an average level of plasma glucose during the previous three months are called HbA1c. Because HbA1c

values gauge the stability of glycemic control and forecast the likelihood of problems, they are essential in the regular care of diabetes. HbA1c values are being utilized more often in the diagnosis of diabetes because of the test's increased accuracy (Patel & Anuradha, 2023). One kind of glucocorticoid hormone that is crucial to several processes related to metabolism is cortisol. The cortisol regulatory and effector mechanisms are capable of being disrupted by environmental variables and some common not transmissible disorders, such as obesity, type 2 diabetes, high blood pressure, dyslipidemia, osteoporosis, artery disease, and cardiovascular disease, are associated with hypercortisolism (Araujo-Castro et al., 2023; Malika et al., 2023).

Compared to the rest of the population, people with diabetes have a greater prevalence of hypercortisolism (Felix et al., 2024). Deveci et al. (2023) discovered a favorable correlation between cortisol levels and glycated hemoglobin (HbA1c), which held true even in the absence of diabetic medication usage (Deveci et al., 2023). There is abundant evidence from recent studies that hypergonadism and type 2 diabetes (T2DM) are related. This is due to the fact that obesity raises the risk of testosterone deficiency (TD), which exacerbates glycemic regulation and promotes insulin resistance and fat accumulation (Caliber & Saad, 2021). There is a growing body of evidence that raises doubts about the appropriate use of testosterone in the normal clinical care of type 2 diabetes, an issue on which there are conflicting opinions. In males with type 2 diabetes, testosterone treatment has been shown in several trials to improve a number of parameters, including systolic and diastolic blood pressure, lipids profiles, insulin sensibility, inflammatory conditions, fasting plasma glucose (FPG), and glycated hemoglobin (HbA1c) levels (Mody & Covinsky, 2024). Most previous studies showed a relationship between cortisol and testosterone levels with type 2 diabetes but not prediabetes. Therefore, the aim of our study is to investigate the predictive significance of fasting blood sugar (FBS), HbA1c, cortisol, and testosterone levels in screening patients with prediabetes and diabetes.

Materials and methods

Ethical approval was obtained from those accredited in this study for the purpose of using their blood samples. The current investigation was studied in Baquba city / Diyala province / Iraq from March–June 2024. The total numbers of participants giving blood samples was 100. We collected 60 blood samples (30 prediabetic and 30 diabetic) from peoples who visited the consultation clinic at Baqabi Teaching Hospital and these people were screened by the consultant doctor in this establishment. Additionally, we collected 30 blood samples from normoglycemia people, whom we considered as the control group. Age and body mass index of participants were entered in the questionnaire. The inclusion criteria required that all patients had pre-diabetic and diabetic diseases, but no other chronic disease, that they did not have reproductive disorders and that they were at least 20 years old.

We collected five ml of blood from all participants in the current study and separated it in EDTA (to calculate HbA1C) and gel tubes (to calculate FBS, HbA1C, cortisol and testosterone). The collected blood in gel tubes was centrifuged in a centrifuge machine at 3000 rpm for 15 minutes to obtain serum. All indicators were quantified by a Biorex machine (Denmark) based on kit packing that was supplied from manufacturer company.

FBS, HbA1C, cortisol and testosterone indicators were expressed such as mean \pm SD. ANOVA was utilized to discover the differences among study groups according to the Duncan test, which detects variation among mean levels of indicators. The relation of age groups and body mass index to the study groups were assessed by the Pearson Chi-square test. Area under the curve (AUC), cut off, sensitivity, and specificity of biochemical indicators were measured by Receiver Operating Characteristic (ROC) curve. The differences among indicators were assessed at significance level $P < 0.05$. SPSS v. 20.0 with prism v.6 programs were used to programme our results.

Results

The findings of our research reveal no significant differences ($P > 0.05$) between age groups and study groups. In contrast, there is significant variation ($P < 0.05$) among age groups for prediabetic, diabetic and normal glycemia, where it was found all participants came within the age groups 31–50 and >50 years respectively (prediabetic 56.7% and 30.0%, diabetic 33.3% and 56.7%, and normal glycemia was 46.7% and 30.0%). According to body mass index (BMI), the current investigation showed most prediabetic and diabetic patients were overweight (53.3% and 60.0%) and obese (36.7% and 26.7%), while the most normoglycemia people were of normal weight (43.3%) with significant differences ($P < 0.05$) among BMI levels for each group. In contrast, we did not find a statistical difference ($P > 0.05$) between the BMI level and the study group (Table 1).

Table 1

Comparative age groups and BMI levels with study groups

Group	Groups			Total	P-value		
	prediabetic	diabetic	normoglycemia				
Age groups, years	≤ 30	n	4	3	7	>0.05	
		%	13.3	10.0	23.3		
	31–50	n	17	10	14	41	>0.05
		%	56.7	33.3	46.7		
	>50	n	9	17	9	35	>0.05
		%	30.0	56.7	30.0		
P-value		<0.05	<0.05	>0.05	<0.001	–	
Body mass index, kg/m ²	normal weight	n	3	4	10	17	>0.05
		%	10.0	13.3	43.3		
	overweight	n	16	18	13	47	>0.05
		%	53.3	60.0	33.3		
	obese	n	11	8	7	26	>0.05
		%	36.7	26.7	23.3		
P-value		<0.05	<0.001	>0.05	<0.001	–	

Outcomes of the current research mentioned the highest levels of FBS, HbA1C, and cortisol in diabetic (194.7 ± 29.8 , 12.1 ± 3.9 , and 15.2 ± 3.3) and then prediabetic patients (116.4 ± 7.8 , 6.2 ± 0.3 , and 9.1 ± 1.1) compared to normoglycemia (82.5 ± 6.29 , 5.1 ± 0.6 , and 7.9 ± 1.2) respectively, with statistical significance ($P < 0.05$). By contrast, our outcomes reveal the greatest decrease of testosterone in diabetic (4.2 ± 0.9) and then a smaller decrease in prediabetic patients (8.1 ± 0.9) compared to normoglycemia subjects (12.6 ± 3.8) with statistical significance ($P < 0.05$) (Table 2 and Figure 1).

Table 2

Comparative concentrations average of biochemical indicators within the study groups

Biochemical indicators	n	Mean	Standard deviation	P-value
FBS, mg/dL	prediabetic	30	116.37 ^b	7.75
	diabetic	30	194.70 ^a	29.82
	normoglycemia	30	82.53 ^c	6.29
HbA1C, %	prediabetic	30	6.22 ^b	0.32
	diabetic	30	12.10 ^a	3.90
	normoglycemia	30	5.11 ^c	0.57
Cortisol, μ g/dL	prediabetic	30	9.07 ^b	1.08
	diabetic	30	15.20 ^a	3.25
	normoglycemia	30	7.90 ^b	1.18
Testosterone, nmol/L	prediabetic	30	8.10 ^b	0.88
	diabetic	30	4.20 ^c	0.92
	normoglycemia	30	12.57 ^a	3.78

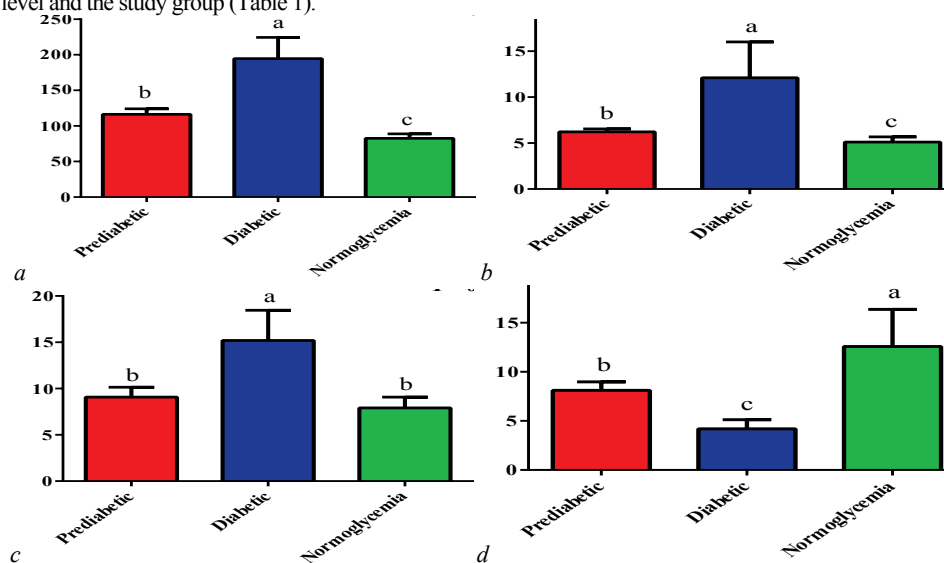


Fig. 1. Average levels of biochemical indicators within the study groups (mean \pm SD): a – FBG (mg/dL), b – HbA1C (%), c – cortisol (μ g/dL), d – testosterone (nmol/L)

ROC curve results showed that FBS scored highest sensitivity and specificity (93% and 100%), followed by HbA1C (97% and 82%), cortisol (77% and 70%) and testosterone (76% and 57%) at cut off (>100, >5.60, >8.50 and < 9.50) respectively, in screening patients with prediabetes with significant variation ($P < 0.05$) (Table 3 and Fig. 2). ROC curve findings showed that the FBS scored highest sensitivity and specificity (98% and 100%), followed by HbA1C (93% and 96%), testosterone (93% and 83%) and cortisol (80% and 78%) at cut off (>130.50, >6.21, >10.70 and <6.49) respectively, in screening patients with diabetes with significant variation ($P < 0.05$) (Table 4 and Fig. 3).

Table 3
Receiver Operating Characteristic curve analysis of FBS, HbA1C, cortisol and testosterone in prediabetes

Variables	Area under curve	P-value	Cut off	Sensitivity, %	Specificity, %
FBS,mg/dL	1.000	<0.05	>100	93	100
HbA1C, %	0.984	<0.05	>5.60	97	82
Cortisol, $\mu\text{g/dL}$	0.750	<0.05	>8.50	77	70
Testosterone, nmol/L	0.821	<0.05	< 9.50	76	57

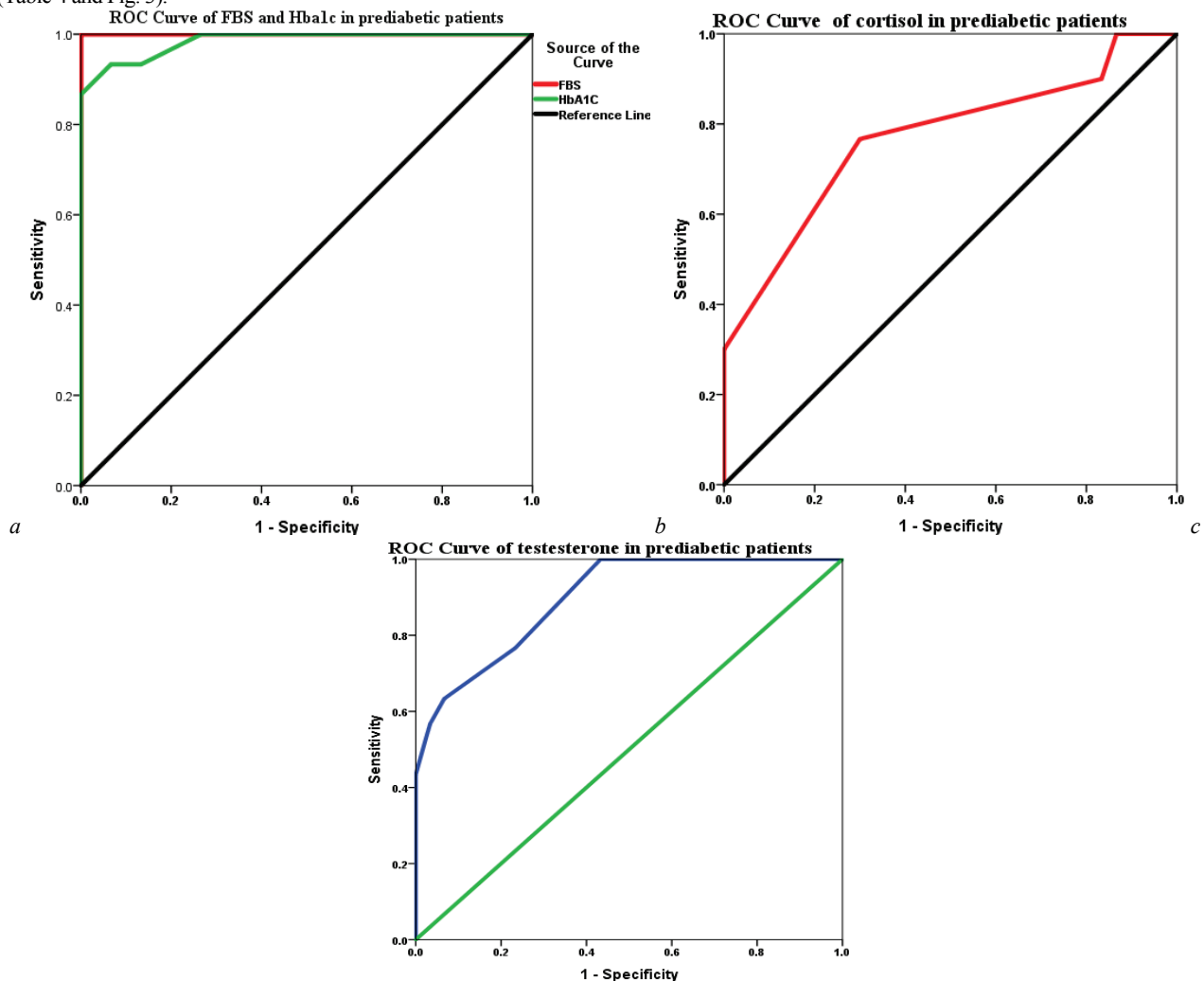


Fig. 2. Receiver Operating Characteristic curve analysis of FBS, HbA1C, Cortisol and testosterone in prediabetes

Table 4
Receiver Operating Characteristic curve analysis of FBS, HbA1C, cortisol and testosterone in diabetic patients

Variables	Area under curve	P-value	Cut off	Sensitivity, %	Specificity, %
FBS, mg/dL	0.97	<0.05	>130.50	98	100
HbA1C, %	0.96	<0.05	>6.21	93	96
Cortisol, $\mu\text{g/dL}$	0.87	<0.05	>10.70	80	78
Testosterone, nmol/L	0.93	<0.05	<6.49	93	83

Results of the present investigation showed that HbA1C scored the highest level with prediabetic patients with overweight and obesity (6.35 ± 0.29 and 6.23 ± 0.26), while cortisol scored the highest level with prediabetic patients with normal weight (11.30 ± 0.98) and the lowest level with obese patients (8.09 ± 0.83) with statistically significant differences ($P < 0.05$) for HbA1C and cortisol. On the other hand, the present findings do not reveal important differences ($P > 0.05$) for FBS and testosterone among BMI levels in prediabetic patients (Table 5). The results of the conducted study showed no impor-

tant variations ($P > 0.05$) between levels of biochemical indicators and BMI levels of diabetic patients (Table 6).

Table 5
Comparative mean levels of biochemical indicators with BMI in prediabetic patients

	BMI	N	Mean	Standard deviation	P-value
FBS, mg/dL	normal weight	3	118.33	6.35	>0.05
	overweight	16	115.50	7.39	
	obese	11	117.09	9.01	
HbA1C, %	normal weight	3	5.30 ^b	0.20	<0.05
	overweight	16	6.23 ^a	0.26	
	obese	11	6.35 ^a	0.29	
Cortisol, $\mu\text{g/dL}$	normal weight	3	11.30 ^a	0.98	<0.05
	overweight	16	9.38 ^b	0.50	
	obese	11	8.09 ^b	0.83	
Testosterone, nmol/L	normal weight	3	7.67	0.58	>0.05
	overweight	16	8.13	0.81	
	obese	11	8.18	1.08	

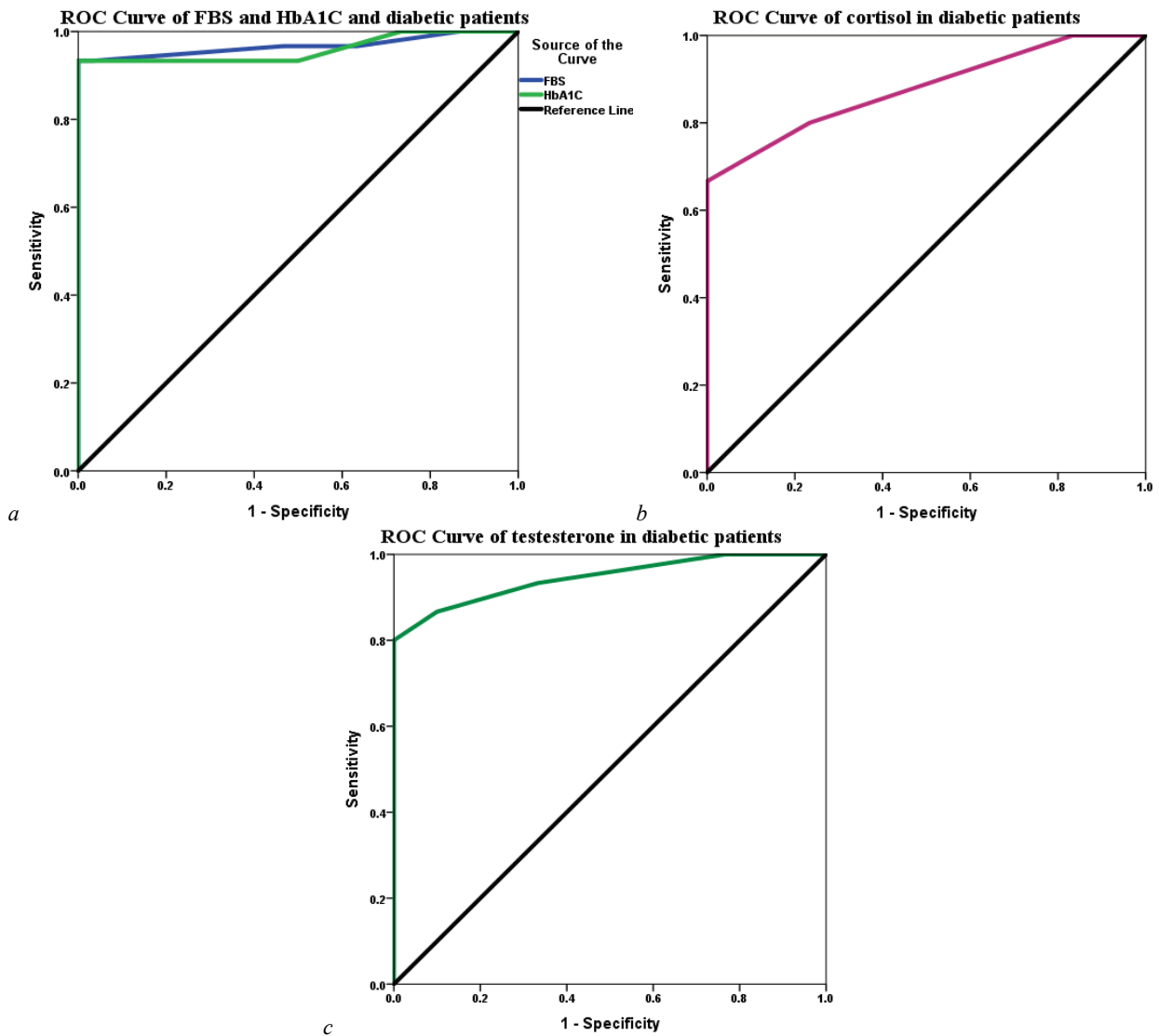


Fig. 3. Receiver Operating Characteristic curve analysis of FBS, HbA1C, cortisol and testosterone in diabetic patients

Table 6
Comparative mean levels of biochemical indicators with BMI in diabetic patients

Biochemical indicators	N	Mean	Standard deviation	P-value
FBS, mg/dL	normal weight	4	188.50	>0.05
	overweight	18	196.00	
	obese	8	194.88	
HbA1C, %	normal weight	4	8.00	>0.05
	overweight	18	12.72	
	obese	8	12.75	
Cortisol, $\mu\text{g/dL}$	normal weight	4	14.75	>0.05
	overweight	18	14.89	
	obese	8	16.13	
Testosterone, nmol/L	normal weight	4	3.00	>0.05
	overweight	18	4.61	
	obese	8	3.88	

Discussion

Insulin resistance and β -cell dysfunction occur together in prediabetes, which is characterized by problems that begin before glucose alterations become noticeable. According to observational data, prediabetes is linked to a greater risk of macrovascular illness, chronic renal failure, diabetic retinopathy, as well as early kinds of nephropathy. According to Shi & Wen (2023), those with prediabetes are more likely to acquire diabetes than people with normoglycemia (Shi &

Wen, 2023). In line with earlier national and international research, age plays a significant role in a higher likelihood of prediabetes and diabetes. The present investigation contradicted earlier findings that revealed that the elderly had a greater prevalence of prediabetes and diabetes than middle-aged individuals (Wang et al., 2021). The results we obtained were consistent with those of Chandrasekaran & Weiskirchen (2024), who demonstrated that those over 30 have a higher prevalence of diabetes and prediabetes compared to the entire population.

The possibility of dementia is linked to prediabetes; however, the risk can be attributed to an onset of diabetes later on. Diabetes that develops earlier in life significantly raises the chance of dementia. According to the BMI, being overweight or obese increases the chance of developing prediabetes and diabetes (Maliszewska et al., 2019). According to earlier research of Yan et al. (2023), having a high BMI raises the risk of type 2 diabetes in older adults, which is in line with the findings of our investigation. The majority of individuals with prediabetes and diabetes, according to Alshaikh et al. (2024), are overweight and in age groups older than thirty. These results aligned with the current study. Furthermore, older adults have a higher chance of developing sarcopenic obesity and greater insulin resistance than middle-aged adults due to aging, changing hormones, and an unhealthy diet (Cao et al., 2022; Han et al., 2023).

In Chinese individuals with prediabetes, a prior investigation showed a positive, non-linear connection between the triglyceride glucose-body mass index (TyG-BMI) and the likelihood of developing diabetes. According to Han et al. (2023), there was a statistically significant positive correlation between TyG-BMI and the probability of developing diabetes when the BMI was less than 231.66 (Cao et al.,

2022). The most recent sensitivity analysis revealed that the central obesity category had a 59% and 44% greater chance of developing diabetes mellitus compared to the non-central obesity category. Diabetes risk was shown to be independently correlated with centrally obese status. Subjects with centrally obese bodies had a 72% greater chance of developing diabetes than those without central obesity, even after controlling for confounding variables (Yazdanpanah et al., 2022) (Table 1).

The current study was consistent with the findings of Yazdanpanah et al. (2022), which indicated higher levels of FBS and HbA1C in prediabetic and diabetic patients compared to controls. These elevated levels might be linked to insufficient insulin production or to an inability of the body to withstand the rise in blood sugar (Zhang et al., 2020). According to previous research, patients who have poorly controlled blood glucose levels are more likely to get diabetic nephropathy because elevated serum urea concentrations are a result (Wu et al., 2023). The most reliable test for identifying and treating diabetes, especially type 2, is glycated hemoglobin (HbA1c). When it comes to those without diabetes, the normal range for HbA1c readings is 4.0 to 5.6%. Pre-diabetic persons range in HbA1c readings from 5.7% to 6.4%. Yet, diabetes is identified in people with HbA1c values of 6.4% or above. The results of the investigation showed that, in comparison to the control population, the total HbA1C of those with diabetes jumped considerably. These results are consistent with the research of Jabbar & Majeed (2020), who found higher HbA1c values in those with diabetes. A slight correlation between HbA1c and fasting blood glucose yield was discovered in prior research. Apart from fasting blood glucose tests, HbA1C is still employed as an indicator to detect prediabetes, notwithstanding its poor connection. This is because the average lifespan of a red blood cell, which is approximately 120 days, and the amount of glycated hemoglobin (HbA1C) are related. Therefore, the relative amount of HbA1C at any given moment is determined by the mean circulating blood glucose level across that three-month period (Kwok et al., 2020). The current study found that patients with prediabetes and diabetes had more cortisol in their blood than controls, and the results were consistent with those of (Sun & Wang, 2023). Cortisol activates lipolysis and releases free fatty acids, which increases resistance to insulin and causes diabetes (Boswell et al., 2024). It is premature to regard serum cortisol as a significant and important cause of prediabetes, but a prior investigation showing a higher level of cortisol in participants with prediabetes validates the concept that high cortisol will eventually result in prediabetes (Yao et al., 2018).

Numerous investigations have demonstrated that following breakfast and low-dose dexamethasone testing, diabetic participants had considerably greater levels of blood cortisone and late-night salivary cortisol (Ho et al., 2013). However, other research revealed that salivary cortisol was gender-related and that cortisol was not linked to the risk of diabetes in Mendel's genetic predictions (Leutner et al., 2021). Thus, there remained a debate over the link between the hypothalamus-pituitary-adrenal axis and the probability of diabetes. A prior study demonstrated a substantial correlation between high cortisol levels and the likelihood of diabetic microangiopathy. Microvascular problems might be more likely to occur among individuals with type 2 diabetes if their levels of cortisol are 272.8–297.0 nmol/L or higher. Thus, according to Sun and Wang (Bhasin et al., 2024), cortisol might be a possible metabolic marker for diabetic microangiopathy. The authors found that among patients who had undergone simultaneous pancreas-kidney transplants (SPKT), reduced nighttime cortisol was linked to decreasing baseline systolic blood pressure, improved anti-hypertensive medication one year following the transplant, and a greater incidence of diabetic neuropathy. A recent investigation found that, preferably in men or subjects with mild to serious obstructive sleep apnea (OSA), a greater diurnal cortisol slope (DCS) and greater early hours level of cortisol were linked with lower and greater T2D dangers for individuals with high blood pressure and OSA, accordingly. In this cohort, diurnal cortisol characteristics could be an objective for initial prevention of diabetes (Kumari et al., 2023). Previous research indicates that in individuals with T2DM and prediabetes, microalbuminuria is positively correlated with blood cortisol production.

Within the normal range of values, elevated levels of cortisol may be linked to a rise of microalbuminuria (Kumari et al., 2023). The results of this research, which were consistent with those of Yao et al. (2018), revealed a reverse association between testosterone levels and the development of prediabetes to diabetes. Men who have low testosterone have a higher chance of developing type 2 diabetes as well as prediabetes. Elevated body obesity, insulin resistance, and type 2 diabetes are linked to males who are intentionally or therapeutically induced to have low testosterone levels (Kumari et al., 2023). A prior investigation demonstrated that, irrespective of obesity and metabolic syndrome (MetS), prediabetes is linked to an elevated likelihood of testosterone insufficiency. Following (MetS) adjustment, the probability is equivalent to that of diabetic. According to these findings, men who have prediabetes should have regular testosterone tests (Yassin et al., 2019).

In contrast, testosterone did not appear to be associated with the breakdown of glucose in prediabetic females. Another research investigation found that higher testosterone levels in men were linked to better utilization of glucose, which involves decrease in HbA1c, reduced stimulated glucose levels, and much greater insulin sensitivity (Belkacem, 2021). The researchers found that newly identified male individuals with early-onset T2DM exhibited less testosterone compared to those with a late-onset T2DM. This difference in testosterone concentrations may be related to the participants' higher levels of metabolic conditions and lowered 3 β -HSD levels prior to their diagnosis of T2DM. Men with early-onset T2DM should receive vigorous treatment for their poor glycemic control, obesity, lipid problem, and testosterone deficit (Swamy et al., 2021). According to a new study, in men with hypogonadism and prediabetes there was no substantial variation between those who received testosterone treatment and those who received a placebo in the likelihood of moving from prediabetes to diabetes. Men following hypogonadism, prediabetes, or diabetes failed to observe an improvement in controlling their blood sugar with testosterone replacement therapy (TRT). These results imply that in males with hypogonadism, TRT alone cannot be used as a treatment strategy to stop or cure diabetes (Hami et al., 2023). Glycosylated hemoglobin (HbA1c) is lowered with testosterone replacement treatment, according to observational data. Furthermore, it has been discovered that testosterone replacement therapy stops prediabetes from developing into diabetes and brings on glycemic remission in men (45–80 years of age) who have hypogonadism (Dehghan et al., 2023). Previous findings show that individuals with hypogonadal type 2 diabetes who received long-term testosterone replacement treatment had a long-lasting improvement in their diabetes. This treatment lowered triglycerides, total cholesterol, HDL levels, and the measurement of the waist in addition to improving glycemic control. Researchers suggest that for these individuals, this therapy be administered in addition to anti-diabetes drugs (Bakr et al., 2021).

A prior investigation demonstrated that over time testosterone treatment (TTh) improves glycemia, lipids, and the Aging Males' Symptoms (AMS) Scale in men with hypogonadism and entirely prevents the development of prediabetes to type 2 diabetes. For the sizable and expanding community of men with hypogonadism and prediabetes, TTh offers enormous promise (Bakr et al., 2021) (Table 2). According to Hashim et al. (2020), the HbA1C sensitivity and specificity in prediabetes were (80% and 66%), respectively. Compared to our investigation, which showed great sensitivity and specificity (97% and 82%), their results were lower. HbA1C's sensitivity and specificity in prediabetes were demonstrated in different research to be (77% and 81%), respectively (Steffensen et al., 2016). A prior study showed that the rate of prediabetes detected when coupled with FBS and HbA1c is greater than when done alone. HbA1c is a far more sensitive metric than FBS in identifying prediabetes, despite the fact that FBS is a well-established indicator of prediabetes (Mei et al., 2022). Previous investigation mentioned the sensitivity and specificity of testosterone in diagnosed prediabetes were (51% and 85%) (Mei et al., 2022). These outcomes do not agree with the present research, which showed (76% and 57%) (Table 3). In people with type 2 diabetes, sugar levels in the blood are a significant predictor of HbA1c levels. Because FBS and Post-prandial Blood Sugar (PPBS) have high

her sensitivity and specificity than RBS, they may be more reliable indicators than RBS. According to earlier research, controlling blood sugar and lowering the likelihood of consequences from diabetes need regular monitoring of glucose levels, especially FBS and PPBS. Furthermore, while forecasting HbA1c values, age and the duration of diabetes should be taken into account (Hara et al., 2024). According to Belkacem (2021), HbA1C's sensitivity and specificity in DM patients were (77% and 81%), respectively. In comparison to our study, which showed excellent sensitivity and specificity (93% and 96%), their results were lower (Boye et al., 2021).

Although the FBS test was shown to be acceptable, it proved to have lower precision of diagnosis than each of the other tests for pregnancy-related diabetes. The HbA1c and the glucose challenge test (GCT) were found to be accurate assays for this condition. Additionally, it was discovered that the HbA1c test was very significant for determining the presence of gestational diabetes and that, when applied to pregnant women who had diabetes detected by both the GCT and the oral glucose tolerance test (OGTT), the HbA1c test yielded more positive findings than the FBS test (Boye et al., 2021). According to an earlier investigation (Kharroubi et al., 2014), the sensitivity and specificity of HbA1c in testing for prediabetes were 57% and 83%, while for DM, they were 67% and 81%. Although only around 50% of the diabetes participants were recognized by both HbA1c and FPG, HbA1c, when compared with FPG, appeared to be useful for identifying diabetes instead of prediabetes in Palestinian Arabs (Boye et al., 2021; Khan et al., 2022). These results were almost identical to ours, which showed that HbA1c was more important in the diagnosis of DM than prediabetes. Our results, which are consistent with those used by Bakr (2021), suggested using HbA1c with a percentage of >6.20% in the diagnosis of diabetes mellitus. Steffensen et al showed that the sensitivity and specificity of salivary cortisol in screening patients with diabetes were (85% and 14%). These findings did not match the present research. Additionally, Mohan et al. (2021) showed that the sensitivity and specificity of cortisol in screening patients with diabetic retinopathy were (83% and 81%) (Kunin-Batson et al., 2023).

Prior research revealed that the sensitivity and specificity of testosterone in diagnosis of diabetes were (51% and 55%). These data were lower than our findings, which showed (93% and 83%). Mei et al., (2022) showed that the sensitivity and specificity of testosterone in diagnosis of diabetes with coronary diseases were (75% and 45%) (Table 4) (Corona et al., 2023). According to current data, people with diabetes mellitus who are overweight or obese have higher HbA1c values. These findings are consistent with those of Hara et al. (2024). Inadequate glycemic control (HbA1c \geq 7%) was seen in over half of T2D patients who belonged to obesity class I–IV or central obesity, particularly in the 18–44 age range. This emphasizes the necessity of controlling body weight in relatively young Japanese individuals with T2D and adiposity in order to improve glycemic control (Hara et al., 2024). Therapies that lower BMI and HbA1c may have a substantial effect on the treatment of T2D, considering the rise in BMI and declining proportion of persons with T2D who achieved glycemic control during the research period (Boye et al., 2021). Keeping appropriate levels of cortisol is linked to testosterone, particularly in those with T2DM. Because T2DM has so many negative health implications, it might aggravate other illnesses.

Whether the levels of cortisol were elevated or decreased, the majority of T2DM patients had low testosterone levels, according to a previous investigation. These levels were also considerably lower in T2DM patients than in non-diabetic individuals, and they are strongly linked with both cortisone and BMI (Khan et al., 2022). The current research revealed higher levels of cortisol in prediabetic individuals with a typical weight, which contrasted with observations by Kunin-Batson et al. (2023), that indicated elevated cortisol levels were associated with increasing weight. Although elevated cortisol levels can seem to be more prevalent, low cortisol might also have negative effects that should be considered. In certain cases, low levels of cortisol can result in weight reduction, while persistently high cortisol levels might encourage snacking and weight gain (Kunin-Batson et al., 2023).

A new study found that increasing physical activity and losing weight can enhance testosterone levels and metabolism profile. In in-

dicative hypogonadal men with prediabetes, a combination of testosterone replacement therapy and changes in lifestyle may be recommended to encourage patients to engage in sport, which can ultimately lead to weight loss as well as improvements in their metabolism and genital health. Further research is necessary to see whether these strategies may stop type 2 diabetes mellitus from developing from pre-clinical circumstances (Corona et al., 2023) (Table 5).

Conclusions

Most prediabetic and diabetic patients were in the age group >30 years and had overweight BMI. All levels of indicators were increased in pre and diabetic patients compared to normoglycemia, with the exception that testosterone was decreased. HbA1C and FBS scored the highest sensitivity and specificity in screening pre and diabetic patients compared to cortisol and testosterone. Cortisol is better than testosterone in screening prediabetics, while testosterone is better than cortisol in screening diabetic patients. In prediabetic patients, HbA1C and cortisol scored the highest level in obese and normal weight respectively. Finally, we did not find a significant effect of BMI on all indicators in diabetic patients.

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