

Evaluation of Fructosamine and Biochemical Markers for Enhanced Diagnosis of Type 2 Diabetes Mellitus

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ABSTRACT

Background: Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia and alterations in carbohydrate, lipid, and protein metabolism due to impaired insulin secretion or action. Fructosamine, a glycation product, is a valuable marker for assessing short-term glycemic control and predicting the risk of microvascular complications in diabetic patients. Glycated albumin (GA) also serves as a crucial marker for blood glucose regulation over approximately three weeks, aiding in screening, predicting, preventing, diagnosing, and monitoring diabetes. **Objective:** This study aims to evaluate the association of fructosamine, glycated albumin, and other biochemical markers with the diagnosis and management of type 2 diabetes mellitus (T2DM). **Materials and Methods:** Between January 12, 2023, and February 30, 2024, 120 blood samples were collected from T2DM patients at Baquba Teaching Hospital, Diyala Governorate. Patients were categorized into two groups: irregularly managed diabetes patients (n=60, aged 35–77 years) and regularly managed diabetes patients (n=20, aged 34–75 years). A control group (n=40) was also included. Blood samples were collected in EDTA and gel tubes for analysis. Body Mass Index (BMI) was calculated, and statistical analyses were performed using SPSS version 25.0 and GraphPad Prism version 6. T-tests and one-way ANOVA were used for group comparisons, with p-values < 0.05 considered statistically significant. **Results:** The mean age of T2DM patients was significantly higher than that of the control group, although no significant age difference was observed between the diabetic and diabetic control groups. T2DM patients exhibited elevated levels of insulin, HbA1c, and insulin resistance (HOMA-IR) compared to non-diabetic controls. A significant positive correlation was observed between glycated albumin and HbA1c% in the diabetic group. Furthermore, HOMA-IR demonstrated high sensitivity (93%) and specificity (95%) with an AUC of 0.9797. Age also showed high sensitivity (90%) and specificity (92%) with an AUC of 0.9473. **Conclusion:** The findings underscore the utility of fructosamine, glycated albumin, and HOMA-IR as robust markers for assessing glycemic control and insulin resistance in T2DM. These markers, along with demographic factors such as age, offer valuable insights into the diagnosis and management of T2DM, highlighting the escalating health risks associated with obesity and diabetes-related complications.

Keywords: Diabetes Mellitus, Fructosamine, Glycated albumin, HbA1c%, HOMA-IR

INTRODUCTION

Hyperglycemia and changes in glucose, lipid, and protein metabolism as a result of inadequate insulin production, diminished insulin action, or both define diabetes mellitus (DM), a chronic hormonal and metabolic disease [1]. This is a major concern in global health because of the correlation between diabetes mellitus and the rise in the prevalence of complications such as peripheral vascular disease and macrovascular disease. Serious sickness or death can occur as a result of three of these outcomes: nephropathy, neuropathy, and retinopathy [2, 3]. Gestational diabetes is the second most frequent sort of diabetes, right after type 2 diabetes mellitus (T2DM) and type 1 diabetes mellitus (T1DM) [3].

Decreased insulin production or insulin sensitivity is a hallmark of type 2 diabetes mellitus (T2DM). These characteristics are widely believed to be the main risk factors for type 2 diabetes [4]. Approximately 95% of all instances of diabetes are type 2 diabetes. Insulin resistance in peripheral tissues is highly related to inadequate insulin response, or low insulin sensitivity [5–7]. A chemical known as fructosamine is generated when blood sugar levels are continuously high. Sugar and protein are the two main components of this substance. The presence of high fructosamine levels is indicative of albumin glycation, since albumin is the most common protein in the blood. Quick, easy, cheap, and accurate—that is the measurement. Factors that affect albumin and serum protein metabolism can also affect fructosamine levels. Reason being: total protein and albumin

concentrations are strongly correlated with fructosamine levels [8, 9]. Serum fructosamine can be used to assess the effectiveness of short-term glycemic control, even in cancer patients. Fructosamine is underutilised in both clinical practice and research, which is a major concern. Fructosamine may also be useful as a standalone biomarker for the prediction of diabetic microvascular complications such as nephropathy and diabetic retinopathy [10]. When measured over a three-week period, glycated albumin (GA) can provide valuable insight into the maintenance of stable blood sugar levels. Metabolic disorder screening, prediction, prevention, diagnosis, and monitoring all rely on genetic analysis (glycated albumin) [11]. Whenever glycemic compensation cannot be accurately assessed by glycated haemoglobin (HbA1c) tests, the study demonstrated that GA can function as a valuable biomarker.

Some of the medical issues that can arise include hemolytic anaemia, changes in haemoglobin, chronic renal failure, gestational diabetes, haemorrhage, difficulty with dialysis, and recent blood transfusions [12]. Postprandial monitoring allows people with hyperglycemia or uncontrolled diabetes to track their blood sugar levels in the near term. The efficacy of diabetic treatment can be assessed by closely monitoring individuals. Recognising prediabetes in those whose blood sugar levels are usually within the normal range is vital since early care is critical in preventing the development of diabetes [13].

MATERIAL AND METHODS

From January 12, 2023, to February 30, 2024, a total of one hundred twenty-two blood samples were taken from diabetes patients who had been diagnosed by a specialist at Baquba Teaching Hospital in Diyala Governorate. Two categories were established from the 80 samples that were considered: Group (A) comprises 60 patients, 24 men and 36 females, ranging in age from 35 to 77 years; Group (B) comprises 20 patients, 11 men and 9 females, ranging in age from 34 to 75 years; and Group (A) is the group of irregular patients. As a control group, we also took 40 samples from a healthy group of people, which included 14 men and 26 females ranging in age from 31 to 49. There were no acute or chronic diseases in the control group when the samples were taken. Five millilitres of blood was extracted from the veins using disposable medical syringes to create the samples. In order to perform various blood tests, the collected blood was placed in a set of tubes containing EDTA and gel. After the serums were centrifuged for five minutes at 3000 rpm, they were split into 250 microliters each and kept at (20°C) degrees Celsius until needed. The formula for calculating body mass index (BMI) is weight divided by square of height, which is the basic equation. The weight status is then divided by the BMI number. Statistical analysis: All the statistical analyses were performed using SPSS version 25.0 and Graph pad prism version 6. Depending on the data being investigated, different analysis strategies were used. T-test was used when comparing two sets of data depending

on the normal or skewed distribution of the data. A one-way ANOVA (or non-parametric equivalent) was used for the comparison of three or more groups. P values of < 0.05 were considered to be statistically significant and illustrated in tables as $* = p < 0.05$, $= p < 0.01$, $* = p < 0.001$.

Results

In this study, we used the homeostasis model assessment (HOMA-IR) index to look for a correlation between insulin resistance and elevated serum HbA1c levels in obese adults. Comparison research was conducted to investigate any possible differences between the control and diabetic individuals with type 2 diabetes groups. A correlation between all components was attempted. Identify any possible differences in levels across the research population's subgroups and how they relate to obesity. The type 2 diabetes patients' age ranged from 34 to 55 years old, with a standard deviation of 9.574. Group 1's ages ranged from twenty-five to sixty-five, with the mean age being 56.38 and the age range of the T2DM Control group being 35 to seventy years old, as shown in table (1) (2). Mean = 38.65, standard deviation = 6.036 in the control group. Table 1 and Figure 1 show the results of the statistical analysis. It was found that the average age of the patients was significantly higher than that of the diabetic control group ($P < 0.05$), but there was no significant difference between the diabetic and non-diabetic control groups. This result shown in figure 1.

Table 1: Mean and SD of Clinical Demographic Study (Age, BMI,) with HbA1c%, Fasting Insulin Index and HOMA-IR in Studied Groups

Groups		Age Years	BMI kg/m ²	FSG mg/dL	HbA1c%	FSI μ IU/mL	HOMA-IR
T2DM Patients (1)	Mean	55.00	30.78	184.35	8.620	16.863	7.772
	SD	9.574	4.56	52.05	1.656	13.264	8.155
	Median	52.00	30.08	172.50	8.000	13.650	5.363
T2DM Control (2)	Mean	56.38	26.54	130.75	6.110	24.258	16.739
	SD	12.67	3.15	45.29	1.083	26.318	17.678
	Median	53.00	26.70	110.50	5.800	19.000	7.229
Controls Group (3)	Mean	38.65	24.97	87.95	5.028	4.656	1.004
	SD	6.036	2.01	5.144	0.276	3.066	0.638
	Median	40.00	25.06	88.00	5.000	3.995	0.879

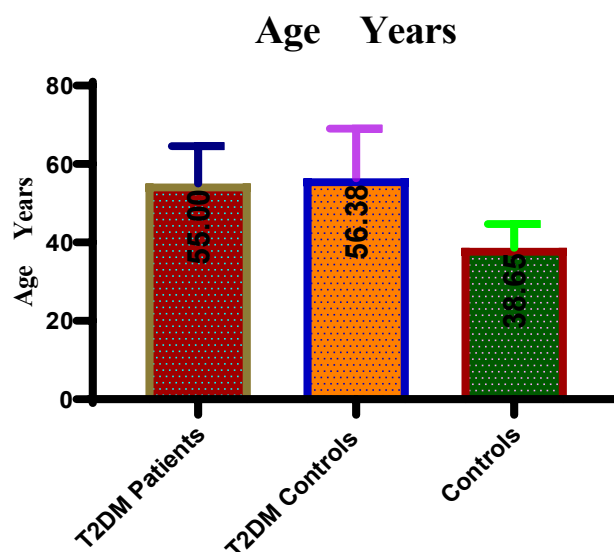


Figure 1: Mean and SD of Age in Patients and Control Groups

Each group's average and standard deviation of body mass index (BMI) was calculated. Table 1 and Figure 2 display these statistics. Results showed that individuals in the diabetic typ2 group had a significantly higher body mass index (BMI; 30.78 kg/m²) than those

in the diabetic control group (26.54 kg/m²). This difference was statistically significant ($P < 0.05$). These results shown was significant difference between studied groups in fasting blood glucose as shown in table 1 and figure 3.

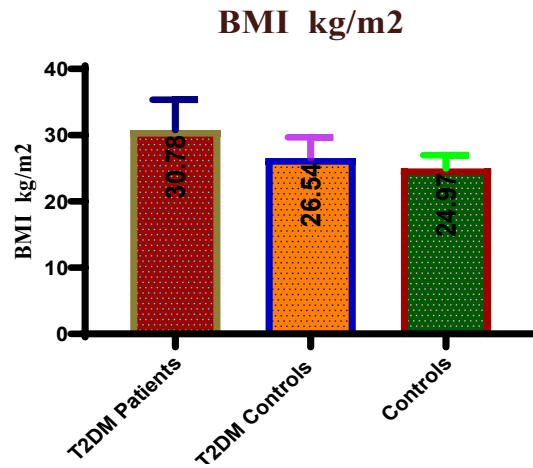


FIGURE 2: Mean and SD in Patients and Control Groups

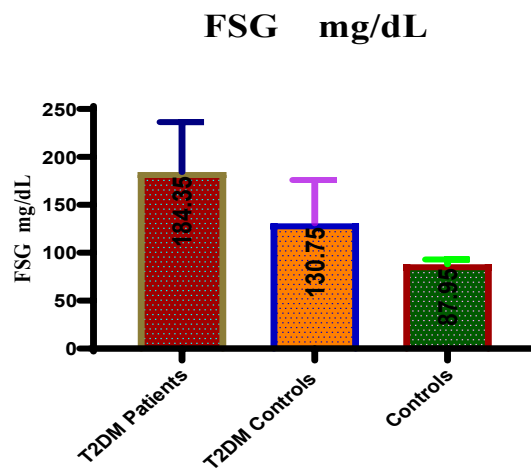


FIGURE 3: Mean and SD in Patient and Control Group.

When comparing the diabetic and non-diabetic groups, statistical analysis revealed that the former had higher levels of insulin, HbA1c, and HOMA-IR. Between the groups, there was also a noticeable statistical difference ($P < 0.05$).

Table 1's worth of numbers. An emergency is quickly developing due to the increasing prevalence of obesity globally. It is associated

with a number of diseases and disorders. Numerous studies have demonstrated that diabetes is associated with an increased risk of cardiovascular disease, dyslipidemia, hypertension, and mortality (figures 4,5, 6). These results observed a highly significant between parameters especially in HOMA-IR, insulin, HbA1c% and blood glucose as shown in table 2.

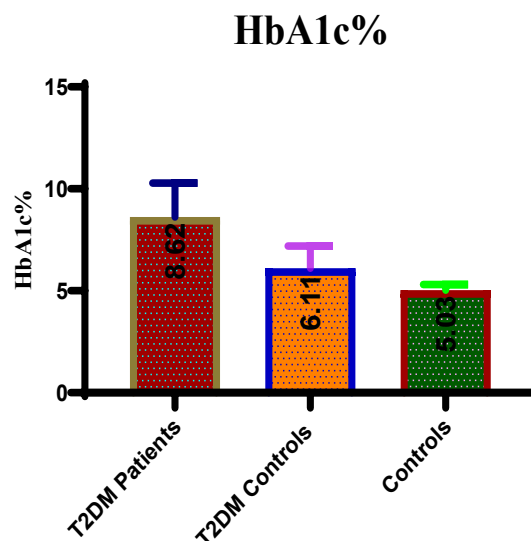


FIGURE 4: Mean and SD for HbA1c% in Patients and Control Groups

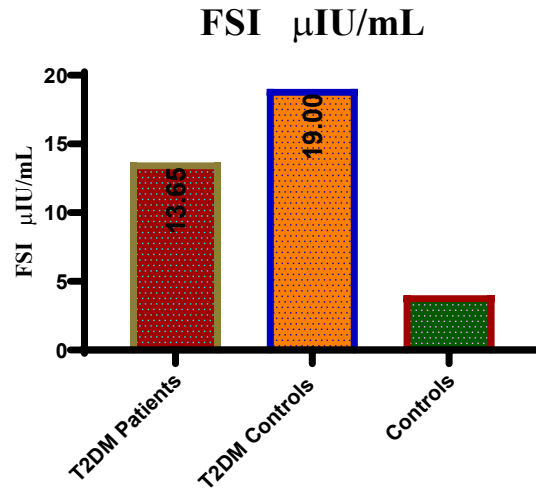


Figure 5: Median of FSI in Patients and Control Groups

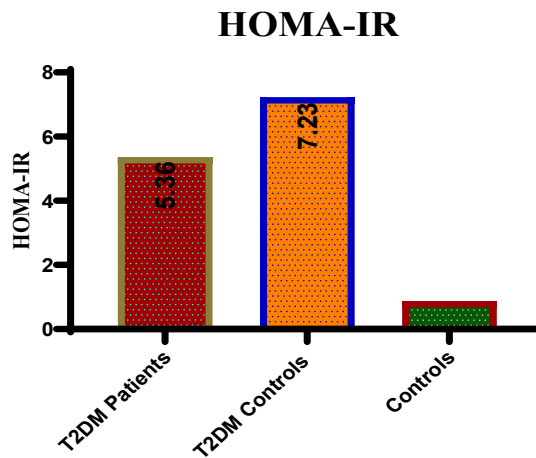


Figure 6: Median of HOMA -IR in Patients and Control Groups

Table 2: Mean difference between Parameters of Study and Clinical Demographic between Groups

Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	P-Value
Age Years	1	2	-1.38	2.34	0.557
	1	3	16.35*	1.89	0.000
	2	1	1.38	2.34	0.557
BMI kg/m ²	1	3	17.73*	2.49	0.000
	1	2	4.24*	0.93	0.000
	2	3	5.81*	0.75	0.000
FSG mg/dL	1	1	-4.24*	0.93	0.000
	2	3	1.57	0.98	0.113
	1	2	53.60*	10.6	0.000
HbA1c%	1	3	96.40*	8.57	0.000
	2	1	-53.60*	10.62	0.000
	3	2	42.80*	10.86	0.000
FSI μIU/mL	1	2	2.51*	0.33	0.000
	1	3	3.59*	0.24	0.000
	2	1	-2.51*	0.33	0.000
HOMA-IR	1	3	1.08*	0.34	0.002
	1	2	-7.40	3.74	0.051
	2	3	12.21*	2.91	0.000
	1	1	7.40	3.74	0.051
	2	3	19.60*	3.95	0.000
	1	2	-8.97*	2.8	0.002
	1	3	6.77*	1.66	0.000
	2	1	8.97*	2.81	0.002
	3	2	15.74*	2.86	0.000

From table 3 shown a significant positive correlation between glycated albumin with HbA1c%, there's ($r = 0.562$, p -value < 0.001) in diabetic group, while the current study did not indicate any significant

changes between glycated albumin and the rest of the variables, as shown in Table 3 and figure 7. ($r = 0.283$ p -value = 0.004) for HOMA-IR.

Table 3: Correlation Coefficient between Glycated Albumin (GA) with Studied Parameters

Parameter	R (GA mmol/L)	P-Value
GA mmol/L	1.000	0.000
HOMA-IR	0.283	0.004
FSI μ IU/mL	0.313	0.0005
HbA1c%	0.562	<0.0001
Age Years	0.465	<0.0001
BMI kg/m ²	0.442	<0.0001
FSG mg/dL	0.526	<0.0001

From table 4 shown a significant positive correlation between HOMA-IR with FSI, and FSG theres (r= 0.977, p -value <0.0001, r 0.566, p<0.0001) respectively in diabetic group, while While the

current study did not indicate any significant changes between glycated albumin and the rest of the variables, as shown in Table 4. (r=0.342 p-value = 0.07) for HBA1c%.

Table 4: Correlation Coefficient between Homa-IR with Studied Parameters

Parameter	R (HOMA-IR)	P-Value
HOMA-IR	1.000	0.000
GA mmol/L	0.283	0.06
FS μ IU/mL	0.977	<0.0001
HbA1c%	0.342	0.07
Age Years	0.298	0.07
BMI kg/m ²	0.288	0.066
FSG mg/dL	0.566	<0.0001

From table 5 shown a significant positive correlation between FSI, and FSG with HOMA-IRtheres (r= 0.873, p -value <0.0001, r 0.977, p<0.0001) respectively in diabetic group, while the current study did not indicate any significant changes between glycated albumin and the rest of the variables, as shown in Table 5 (r=0.300 p-

value = 0.07) for HBA1c%. Moreover, our results shown a highly Specificity and sensitivity HOMA-IR (Sensitivity% 93% and Specificity% 95 % with AUC= 0.9797) ALSO Age have a highly sensitivity and specificity (90 and 92 %) resistively and AUC= 0.9473. this result illustrates in table 6 and figure (7,8,9,10,11,12)

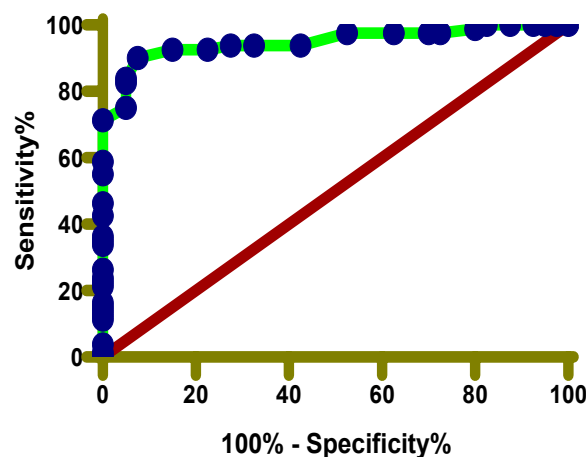
Table 5: Correlation Coefficient between FSI with Studied Parameters

Parameter	R (FSI μ IU/mL)	P-Value
FSI μ IU/mL	1.000	0.000
HOMA-IR	0.977	<0.0001
GA mmol/L	0.313	0.05
HbA1c%	0.300	0.07
Age Years	0.357	0.077
BMI kg/m ²	0.333	0.066
FSG mg/dL	0.873	<0.0001

Table 6: Roc Curve Analysis for Parameters in Diabetic Patients with Control Groups.

Parameter	AUC	Positive if COV	Sensitivity%	Specificity%	Likelihood Ratio
Age Years	0.9473	> 45.50	90.00	92.50	12.00
BMI kg/m ²	0.8372	> 26.53	75.00	75.00	3.000
FSG mg/dL	1.000	> 101.0	100.0	100.0	
HbA1c%	0.9831	> 5.450	96.92	92.50	12.92
FSI μ IU/mL	0.9231	> 6.665	82.28	82.50	4.702
HOMA-IR	0.9797	> 2.161	93.22	95.00	18.64

ROC curve of Age Years

**Figure 7:** Roc Curve for Age in Studied Groups

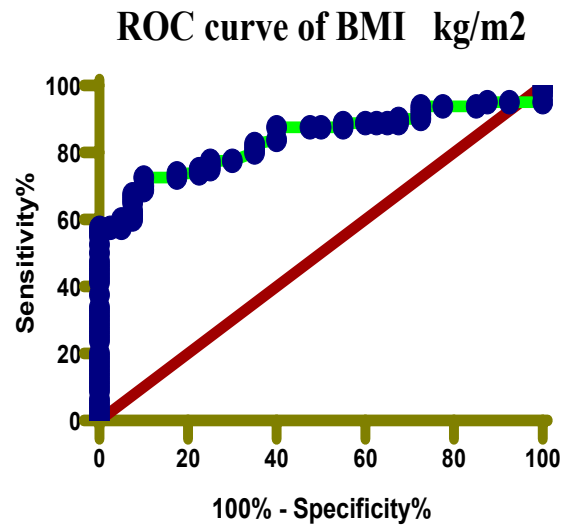


FIGURE 8: Roc Curve for BMI in Studied Groups

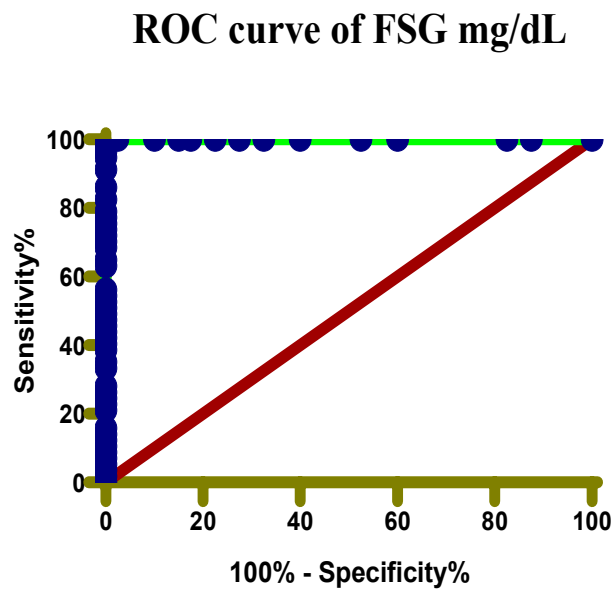


FIGURE 9: Roc Curve for FSG in Studied Groups

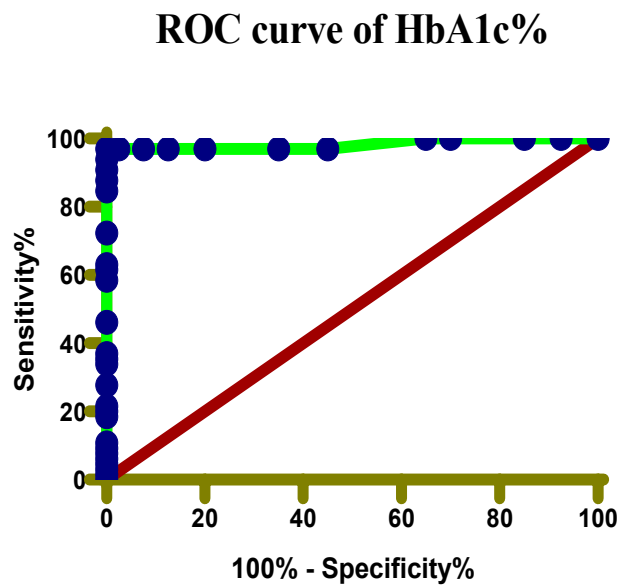


FIGURE 10: Roc Curve for HbA1c% in Studied Groups

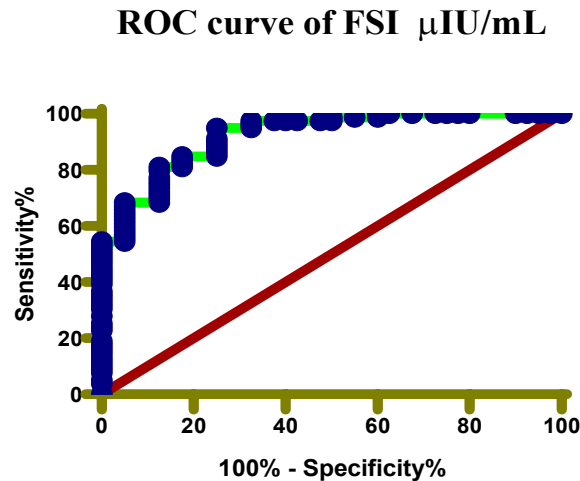


FIGURE 11: Roc Curve for FSI in Studied Groups

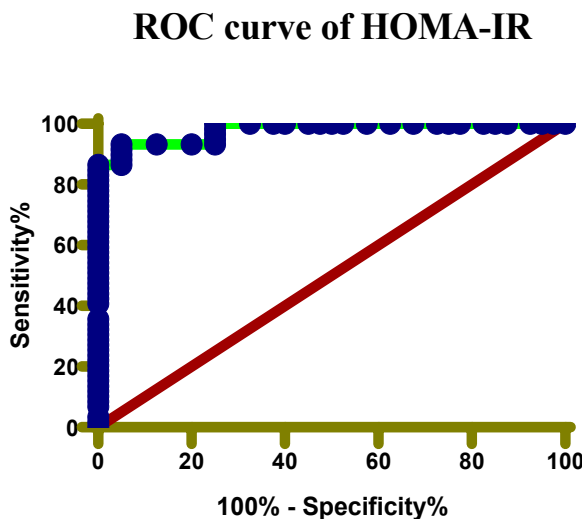


FIGURE 12: Roc Curve for HOMA-IR in Studied Groups

Discussion

According to Grandy, M., et al. (2018), the incidence of obesity in adults and children in the United States has been climbing over the past few decades [14]. The results of the National Health and Nutrition Examination Survey, which included measurements of height and weight, led to this conclusion. If a person's body mass index (BMI) is 30 or higher, 39% of adults are considered obese; if a youth's BMI is at or above the 95th percentile for their gender and age, 18.5% are obese. The years 2015 and 2016 are the sources for these figures. Over the same time period (from 1980 to 2013), Ng, M. et al. (2014) also found comparable results.[15] The findings revealed that the highest frequency of overweight and obesity was observed in men aged 55 to 59. Obesity affects about 25% of women and 75% of men in industrialised countries. Ng et al. found that between 1980 and 2013, the percentage of boys with a body mass index (BMI) of 25 kg/m² or more rose from 28.8% to 36.9% [15]. An astonishing 1.9 billion people on Earth were overweight in 2016 (those aged 18 and over), making it a very common health problem. In this category, obesity affects almost 650 million people. In 2020, scientists from the World Health Organisation (WHO) found that being overweight or obese is linked to a greater risk of death globally, compared to being underweight. On a global scale, there are more individuals who are obese than

underweight. In 2019, Chume et al.[16] Glycated albumin (GA) can serve as a suitable alternative to haemoglobin A1c when haemoglobin A1c is unable to provide a clear enough picture of blood glucose levels, according to this study. This study set out to determine whether GA is clinically useful for the diagnosis of DM. Compared to those identified by HbA1c, genetic analysis (GA) distinguished between separate people with diabetes mellitus (DM). Having said that, GA showed diagnostic accuracy in DM that was on par with HbA1c in the aggregate. That is why GA is better used in addition to HbA1c and OGTT tests, not in instead of them. In addition, using GA as the only diagnostic tool for DM should be approached with caution. In 2020, Giglio et al. revealed [17]. When diagnosing type 2 diabetes, who investigated the role of fructosamine and HbA1c levels? One hundred and ten persons with type 2 diabetes, ranging in age from thirty to sixty, comprising both sexes, were the subjects of the study. The Bio-Rad Variant II TURBO Haemoglobin Test System uses a photometric technique to measure HbA1c. In contrast, a fructosamine (NBT) kit made by Biosystems is used to test fructosamine. The results of this study show that fructosamine can be used to measure blood sugar levels in a shorter amount of time (2-3 weeks) than HbA1c (2-3 months). To overcome the limitations of oral glucose tolerance tests (OGTTs), Peer, N., et al.,[18] studied the associations between fructosamine (FA) and glycated albumin (GA) as alternative diagnostic tests for diabetes

screening in South Africans. The results of oral glucose tolerance tests (OGTTs) can be grouped into three types of glycaemic status: There are three types of blood sugar levels: 1) normal, 2) dysglycemia (which includes impaired glucose tolerance, impaired fasting glucose, and newly diagnosed diabetes), and 3) known diabetes. Alternative ways to assess dysglycemia in clinical settings among Africans could involve employing GA and/or FA.

A study was conducted by Li, G. Y., et al.[19] to assess the diagnostic accuracy of GA in detecting diabetes mellitus and to determine how well GA identifies people with diabetes in northeast China. A total of 1935 people who were considered to be at high risk for diabetes or who had diabetes suspicions were included in this investigation. The results of this study showed that GA was a reliable marker for the diagnosis of diabetes [20].

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