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Evaluation of the serum fasting insulin and HOMA-IR in diabetic and FDR patients

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Abstract

Background: Diabetes mellitus is an endocrine disorder. It is one of the leading causes of morbidity and mortality due to its role in the development of microvascular and macrovascular complications. The main pathophysiological features of type 2 diabetes mellitus are impaired insulin secretion and increased insulin resistance (IR). There is a relationship between fasting serum insulin, IR, and beta-cell dysfunction. Familial aggregation is a significant risk factor for early-onset type 2 diabetes mellitus. First-degree relatives not only share genetic predispositions but also socio-environmental risk factors like obesity and hyperglycemia, forming a high-risk group.

Methods: The study population consists of 60 people, including healthy controls (n = 20), first-degree relatives (n = 20), and diabetes patients (n = 20). The level of serum fasting insulin was measured by the chemiluminescence immunoassay method. IR was calculated using mathematical formulas such as HOMA-IR and HOMA-B.

Results: The results showed that the level of serum insulin increased in the FDR group (8.5 ± 5.6) compared to the diabetic and control groups ($p < 0.001$). HOMA-IR was significantly increased in individuals with diabetes (2.10 ± 1.10) and the FDR group (1.81 ± 1.25) compared to controls ($p < 0.0001$). We also noted a strong positive correlation between fasting serum insulin and HOMA-IR in the FDR group ($r = +0.98$) and in diabetic patients ($r = +0.79$).

Conclusion: Serum fasting insulin is an excellent and dependable marker for diagnosing IR in individuals at risk of developing diabetes, including FDR.

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Highlights

What is current knowledge?

HOMA-IR and serum fasting insulin suggest that serum fasting insulin is a reliable marker for diagnosing IR in populations susceptible to developing diabetes, including FDR.

What is new here?

Fasting insulin is an indicator of developing type 2 diabetes mellitus in first-degree relative patients.

Introduction

Diabetes Mellitus is a chronic and progressive endocrine disorder characterized by hyperglycemia, polyuria, polyphagia, and polydipsia, affecting millions worldwide (1). As a leading cause of morbidity and mortality, it contributes to the development of microvascular and macrovascular complications (2). According to the International Diabetes Federation, approximately 40.9 million individuals have diabetes, with a projected increase to 69.9 million by 2025 (3). Familial aggregation is a significant risk factor for early-onset type 2 diabetes mellitus (4). First-degree relatives (FDR) not only share genetic predispositions but also socio-environmental risk factors like obesity and hyperglycemia, forming a high-risk group (5).

Notably, 35-40% of FDR of type 2 diabetic individuals are asymptomatic and unaware of their condition. Among newly diagnosed cases, one-third are younger patients and individuals over 45 with a positive family history (6).

Type 2 diabetes mellitus results from a combination of genetic factors, including impaired insulin secretion and insulin resistance (IR), and environmental factors like obesity, overeating, lack of exercise, stress, and aging. The primary pathophysiological features are impaired insulin secretion and increased IR (7). IR, defined as the decreased ability of insulin to stimulate glucose uptake in target cells, often precedes type 2 diabetes development (8). This occurs due to inadequate insulin production by pancreatic beta cells or ineffective insulin utilization (7). While IR and impaired beta-cell function are well-established features of type 2 diabetes, the primary abnormality remains unclear (8).

The hyperinsulinemic-euglycemic glucose clamp technique is the gold standard for measuring IR and pancreatic beta-cell dysfunction (9). However, its impracticality in clinical practice and population-based research has led to alternative indices like QUICKI, HOMA, and McAuley (10-13). HOMA has demonstrated a significant correlation with IR as measured by the clamp method and is utilized in this study to evaluate IR. The clustering of glucose dysregulation and obesity among FDR of diabetic patients makes these individuals ideal candidates for lifestyle modifications and pharmacological interventions aimed at preventing type 2 diabetes and its complications (14). Therefore, this study aimed to evaluate the correlation between serum insulin and IR in diabetic, non-diabetic, and FDR, potentially identifying diagnostic and prognostic markers to assess disease control and delay or prevent complications.

Methods

This study was conducted after obtaining clearance from the Institutional Ethical Review Committee at D. Y. Patil Medical College. Informed consent was obtained from all participants. The study included 60 subjects who attended D. Y. Patil Medical College and Hospital, Kolhapur, between 2016 and 2017. The subjects were divided into three groups:

A. Group I (Controls): 20 non-diabetic individuals without a family history of diabetes
B. Group II: 20 non-diabetic FDR of diabetic patients
C. Group III: 20 diabetic patients with a disease duration of 5-10 years

The present study assessed the biochemical parameters of these three groups, including fasting blood sugar, post-prandial blood sugar, and fasting insulin levels.

Study design:

In the present study, 20 diabetic patients and 20 FDR were compared with 20 age-matched control subjects. The age range of the subjects was 20-65 years.

Inclusion criteria: -

1) Patients with known type 2 diabetes mellitus (And a disease duration of 5 years were included.
2) Non-diabetic FDR of diabetic patients were also included in the study.
3) In this study, we only included patients taking metformin, a standard drug approved for type 2 diabetes mellitus in India, to ensure uniformity in IR measurements and avoid the influence of other medications (14).
4) Participants who provided informed, written consent and were willing to participate were included in the study.

Exclusion criteria:

1) Insulin-dependent diabetic patients (IDDM).
2) Patients with chronic illness, pregnancy, and diabetic complications were excluded.

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Sample collection:

The whole blood was collected after fasting to estimate fasting blood sugar and insulin. Similarly, for the estimation of post-prandial blood sugar, 0.5 ml of blood was collected from the patients 2 hours after eating.

Clinical methods for the following biochemical parameters:

1) Estimation of blood sugar by GOD-POD method
2) Estimation of insulin by CLIA method.
3) IR can be calculated by the homeostasis model assessment (HOMA-IR): HOMA-IR = Fasting serum insulin / 22.5

In the present study, we calculated beta-cell dysfunction using Usgaonkar et al. According to this method, the homeostasis model assessment (HOMA-B) can calculate beta-cell dysfunction (2).

HOMA-B=360×FPI/(FPG-63).

Results

Various parameters in studied groups.

The results showed that the level of serum insulin increased in the FDR group (8.5 ± 5.6) compared to the diabetic and control groups ($p < 0.001$) (Table1).

Table 1. Various parameters in diabetic, non-diabetic (FDR), and control subjects

Parameters	Group	No. of subjects (n)	Mean ± Standard deviation
BMI	I	20	18.2±2.49
	II	20	24.07 ±2.93
	III	20	25.65±4.87
FBSL	I	20	89.88 ±13.02
	II	20	91.029±9.32
	III	20	162.275±54.48
PPBSL	I	20	111.18±13.68
	II	20	108.39±14.52
	III	20	232.91±95.69
Serum insulin	I	20	4±1.97
	II	20	8.5±5.6
	III	20	5.73±3.18
HOMA-IR	I	20	0.86±0.47
	II	20	1.81±1.25
	III	20	2.108±1.105
HOMA-B	I	20	69.35±46.73
	II	20	125.02±93.42
	III	20	32.58±33.38

Values were expressed as Mean±SD.
Group I= Control Group
II= FDR Group
III= Diabetic

Fasting insulin

The results showed that the level of fasting insulin significantly increased in the diabetic and FDR groups compared to the control groups (Table 2).

Table 2. The fasting insulin level in different groups

Sr. No.	Study subjects	Number of subjects (N)	Serum fasting insulin (µgm/dl)	P-value
1	Control	20	4 ± 1.97	-
2	Diabetic	20	5.73±3.18	< 0.05
3	FDR	20	8.5±5.60	< 0.001

Values were expressed as Mean±SD.
P<0.05 – Significant
P<0.001 – Highly significant

HOMA-IR Level

HOMA-IR was significantly increased in individuals with diabetes (2.10 ± 1.10) and the FDR group (1.81 ± 1.25) compared to control ($p < 0.0001$) (Table3).

Table 3. The HOMA-IR level in healthy control and fdr diabetic patients

Sr. No.	Study subjects	Number of subjects (N)	HOMA-IR	P-value
1	Control	20	0.86±0.47	-
2	Diabetic	20	2.108±1.105	0.0001
3	FDR	20	1.81±1.25	0.0001

Values were expressed as Mean ±SD.
P<0.05 – Significant
P<0.001 – Highly significant

Correlation between fasting serum insulin and HOMA-IR

We also noted a strong positive correlation between fasting serum insulin and HOMA-IR in the FDR group (r = +0.98; Figure 1) and in diabetic patients (r = +0.79; Figure 2).

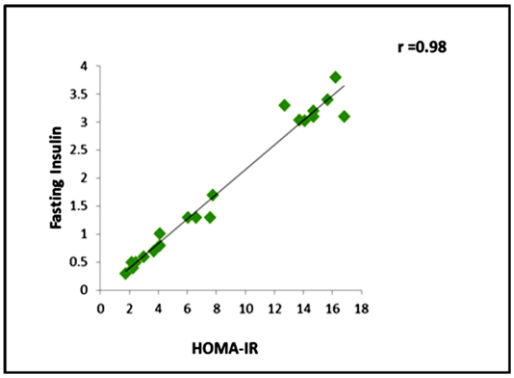

Figure 1. Positive correlation between HOMA-IR and fasting serum insulin in FDR patients

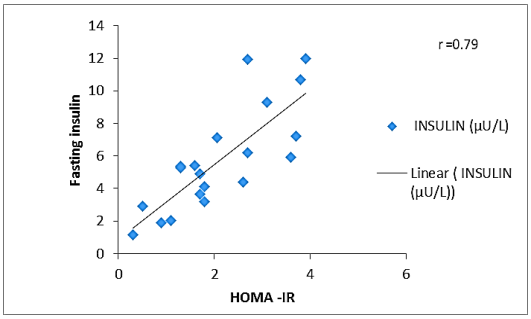

Figure 2. Positive correlation between HOMA-IR and fasting serum insulin in diabetic patients

Discussion

Extensive research on the pathophysiology of type 2 diabetes mellitus has identified two key endocrine dysfunctions: IR and deficiency. Despite agreement on their presence in most patients with established type 2 diabetes, debate surrounds the primary cause. To address this, healthy individuals at increased risk of developing diabetes, such as FDR of type 2 diabetic patients, have been studied to assess early metabolic abnormalities preceding type 2 diabetes development. Few studies have investigated IR among Indian populations with a family history of diabetes, and even fewer have examined beta-cell secretory defects. Therefore, we aimed to study these parameters in FDR and known diabetic patients.

In this study, 20 non-diabetic FDR, 20 diabetic patients, and 20 non-diabetic healthy subjects were included. Table 1 shows the BMI, FBS, and PPBS levels in the different groups. BMI levels were significantly higher in the FDR and diabetic groups compared to controls, and higher in diabetic patients compared to FDR. BMI has a strong relationship with diabetes mellitus, and obesity is more prevalent in diabetic patients due to NEFA secretion from adipose tissue. FBS and PPBS levels were significantly higher in diabetic patients compared to controls, consistent with findings by Tripathi et al. (16).

Table 2 indicates that serum fasting insulin levels were significantly higher in diabetic patients compared to controls and higher in FDR than in diabetic patients. This suggests that individuals with a familial predisposition to diabetes are hyperinsulinemic despite normal blood sugar levels. Fasting hyperinsulinemia may be an early defect in glucose metabolism, preceding IR. It also reflects decreased insulin sensitivity and increased resistance, constituting the strongest independent predictor of type 2 diabetes mellitus (17).

Our findings showed (Table 3) that HOMA-IR levels were significantly higher in the diabetic and FDR groups than in controls. A strong positive correlation was observed between fasting serum insulin and HOMA-IR in FDR (r = +0.98) and diabetic patients (r = +0.79). These results suggest that IR precedes beta-cell dysfunction in high-risk individuals. HOMA-B analysis revealed altered pancreatic beta-cell function in diabetic patients compared to controls and FDR subjects, indicating progressive beta-cell dysfunction with increasing diabetes duration (18,19).

Conclusion

This study concludes that IR is highly prevalent in FDR of type 2 diabetes mellitus patients and increases with disease progression. The positive correlation between HOMA-IR and serum fasting insulin suggests that serum fasting insulin is a reliable marker for diagnosing IR in populations susceptible to developing diabetes, including FDR.

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None.

Ethical statement

This study was approved by the university, D.Y. Patil Medical College, and the hospital's Institutional Ethics Committee.
Signed informed consent was obtained from all patients.

Conflicts of interest

None.

Author contributions

We performed the conception and design of the study, analyzed and interpreted the patient data, and contributed to writing the manuscript.

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