

Diagnostic Performance of Serum HDL-Cholesterol for Identifying Insulin Resistance in Adults

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Abstract

Background: Insulin resistance is seen as an important metabolic condition. This condition has to do with problems with glucose metabolism and fat metabolism and may be detected even before onset of type 2 diabetes. Being able to identify convenient and frequently available markers of IR is important for the early detection of the population that may be at risk of developing metabolic complications. This study evaluated the discriminatory performance of serum HDL-C for identifying IR in non-diabetic adults.

Methods: This case control study incorporated 75 non-diabetic individuals aged between 18 and 65 years originating from Al-Samawah, Iraq, with 50 subjects having IR and 25 as controls. FBG, fasting insulin, TG, HDL-C, waist circumference, weight, height, and BMI were studied. Insulin resistance was computed using the (HOMA-IR. Independent-samples t-test was carried out to determine the differences between the groups, whereas ROC curve analysis was utilized to assess the discriminatory capabilities of the various parameters used.

Results: People in the IR group had much lower HDL-C levels than those in the control group (40.82 ± 9.31 vs. 57.18 ± 11.86 mg/dL, $P < 0.001$). The IR group had significantly higher levels of TG, FBG, fasting insulin, HOMA-IR, and waist circumference compared to the control group. However, there was no significant difference in BMI levels between the two groups ($P = 0.49$). According to the analysis carried out with the help of the ROC curve, HDL-C has yielded the best results in terms of its ability to differentiate populations with the AUC equal to 0.879 (95% CI: 0.822–0.936; $P < 0.001$). It was followed by TG with the AUC value of 0.842, and FBG with AUC equal to 0.786, as well as fasting insulin with AUC of 0.758 and waist circumference with AUC of 0.681.

Conclusion: Serum HDL-C levels were significantly low in non-diabetic subjects with IR and it displayed the best distinguishing ability among the routine biochemical tests and anthropometric measurements. Hence, HDL-C can be considered as an easily accessible marker of elevated risk of IR. More future studies with larger sample size and validation should be done to prove the clinical value of this marker.

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Introduction

Insulin resistance (IR) is a metabolic condition leading to low response to insulin in different tissues such as muscle, adipose tissue, and liver [1]. R is one of the key factors in various metabolic disorders associated with type 2 diabetes, obesity, atherogenic dyslipidemia and a higher chance of cardiovascular diseases [2]. Crucial to note is the fact that insulin resistance may happen

before the development of true hyperglycemia, in light of the fact that compensatory rises in insulin secretion can initially keep glucose levels within or near normal limits. Hence, recognizing insulin resistance prior to any serious metabolic disorder has the potential of providing a chance for early identification of people exposed to a higher metabolic risk [3]. While it is important to know the amount of IR, it is still not easy to assess the IR level in everyday practice. The hyperinsulinemic–euglycemic clamp is usually considered as the criterion of availability of insulin sensitivity assessment. However, the methodology underlying this technique is too complex and expensive, making it possible to carry out the research only in specialized clinics. As a result, simpler surrogate markers have been developed specifically for epidemiological and clinical studies [4]. One of the best-known alternatives is the HOMA-IR, a method based on the concentrations of both insulin and glucose during fasting. Unfortunately, HOMA-IR necessitates determining insulin levels, and its interpretation may vary based on the features of the population, their metabolic state, and analytical methods [5]. Such limitations prompted scientists to look for simpler indicators that can more easily be applied and are available on a regular basis thus reflecting the existence of IR.

Alterations in lipid metabolism characterize the state of insulin resistance. Defective action of insulin increases the release of FFA from fat cells into the liver, resulting in increased synthesis of triglyceride-loaded very-low-density lipoproteins in the liver [6]. Meanwhile, disturbances within the metabolism and excretion of circulating lipoproteins pave the way for the establishment of the certain dyslipidemia pattern characterized by increased levels of TG and diminished high-density HDL-C. The decline of HDL-C is mechanistically associated with the rise of triglyceride-rich lipoproteins within the body [7]. Increased lipid transfer by cholesteryl ester transfer protein leads to the generation of HDL particles that are rich in triglycerides and more vulnerable to hydrolysis by liver lipase, which in turn causes smaller HDL to be produced, greater HDL metabolism to occur, and lower circulating HDL-calculated concentrations. It has been suggested that the interactions between HDL and insulin metabolism are not only due to changes in circulating lipid levels. HDL itself and its major apolipoprotein (ApoA-I) are regarded as players in different phases of glucose homeostasis, such as pancreatic β-cell functioning, insulin secretory activity, glucose utilization by tissues, and insulin sensitivity [8]. In contrast, insulin resistant and diabetic metabolic conditions can modify HDL concentration, composition, particle distribution and biological function [9]. There is therefore a potential biological mechanism linking the decline in HDL-C to a decrease in insulin sensitivity. Nevertheless, the commonly assessed concentration of HDL-C indicates the amount of cholesterol in circulating HDL particles rather than their number, composition or ability to function and the capability of this biomarker to tell apart individuals with abnormal insulin sensitivity requires a direct clinical study to be done.

Various biochemical and anthropometric metrics have been assessed as useful indicators of IR, including FBS, fasting insulin levels, TG, WC, BMI, and lipid-derived indicators. Much focus has also been placed on composite indicators such as the TG: HDL-C ratio and the triglyceride-glucose index. These methods are likely to help in assessing metabolic risk, but they are not adequate and need the two or more measurements. On the other hand, HDL-C is inexpensive and standardized, available widely and processed just as part of the normal lipid profile. Consequently, it would be beneficial to establish the clinical relevance of whether HDL-C alone offers suitable discriminative insights pertaining to IR; particularly as an easily accessible device to recognize patients requiring further metabolic tests.

Consequently, the intention of this research study was to evaluate the diagnostic performance of serum HDL-C in identifying insulin-resistant adults and compare it with the traditional metabolic and anthropometric measurements.

Materials and Methods

Study Design and Participants

A case-control study took place in the region of Al-Muthanna in Al-Samawah, Iraq. The total number of adults surveyed was 75, among which were certain individuals assigned to both an insulin-resistant group and a control group, and thus represented 50 and 25 individuals respectively. The selection of prospective participants was first carried out in consideration of clinical and anthropometric conditions indicative of metabolic disorder, such as waist circumference, obesity, and neck hyperpigmentation suggesting acanthosis nigricans. Each participant had no history of diabetes. The study excluded female participants who were pregnant and also subjects under lipid-lowering therapy. HOMA-IR, a homeostatic assessment tool, was used to measure the insulin resistance and categorized the participants depending on the cutoff for HOMA-IR.

Anthropometric Measurements

Body weight and height were examined for each participant and BMI calculated as kg/m². WC was also examined and expressed in centimeters as an indicator of central obesity.

Blood Sampling and Biochemical Measurements

Taking advantage of all the volunteers had a fasting time of overnight limit, venous blood samples were collected. Serum was utilized for determining FBG, TG, HDL-C as well as fasting insulin levels. Serum triglycerides and HDL-C levels were analyzed with the help of Biolabo's given reagents. The levels of blood-glucose were measured with the help of reagents supplied by Randox, while the serum insulin levels were measured through Roche's provided product. The operations were performed based on the specifications of the producers.

Assessment of Insulin Resistance

Subsequently, the homeostatic model assessment for evaluating insulin resistance (HOMA-IR) was applied. The HOMA-IR was computed as a result of determing fasting levels of glucose and fasting levels of insulin:

HOMA-IR = [Fasting glucose (mg/dL) × Fasting insulin (μIU/mL)] / 405

Participants were subsequently categorized as insulin resistant or controls according to the predefined HOMA-IR criterion.

Statistical Analysis

Statistical analysis was carried out using the IBM SPSS Statistics programme version 26. Numerical variables are

reported as mean ± standard deviation (SD). A t-test for independent samples was used to compare the biochemical and anthropometric parameters in subjects with insulin resistance and control subjects. ROC curve analysis was carried out to assess the validity of the tested parameters in detecting insulin resistance. The area under the curve (AUC), standard error (SE), and 95% confidence interval (CI) were reported. A two-sided P value < 0.05 was considered statistically significant.

Ethical Considerations

All participants were informed about the study objectives, and informed consent was obtained prior to participation. Confidentiality of participants' information was maintained throughout the study.

Results

Biochemical and Anthropometric Characteristics of the Study Groups

There were 75 people in all who took part in the study, out of which there were 50 people having IR and 25 control subjects. There were highly significant differences between the two groups in comparison with most of the parameters assessed (Table 1).

Participants with insulin resistance demonstrated considerably elevated amounts of triglycerides (TG), FBG, fasting insulin, and HOMA-IR as compared to the control group (all P < 0.001). Waist circumference was also significantly greater in participants with insulin resistance (P = 0.002). On the other hand, HDL-C was significantly reduced in IR compared with control (40.82 ± 9.31 vs. 57.18 ± 11.86 mg/dL, P < 0.001). No substantial disparity was found in BMI between the two groups (P = 0.49).

Table 1: Biochemical and anthropometric characteristics of the insulin-resistant and control groups

Parameter	IR group (n=50)	Control group (n=25)	P-value
TG (mg/dL)	184.62 ± 72.35	109.73 ± 30.14	<0.001
HDL-C (mg/dL)	40.82 ± 9.31	57.18 ± 11.86	<0.001
FBG (mg/dL)	103.76 ± 12.42	89.24 ± 11.18	<0.001
Fasting insulin (µIU/mL)	18.37 ± 10.26	9.68 ± 4.51	<0.001
HOMA-IR	4.68 ± 2.73	1.83 ± 1.08	<0.001
Waist circumference (cm)	104.92 ± 12.76	96.84 ± 10.17	0.002
BMI (kg/m²)	31.63 ± 6.21	30.94 ± 5.46	0.49

Data are presented as mean ± standard deviation (SD). Differences between groups were assessed using the independent-samples t-test. P < 0.05 was considered statistically significant.

Discriminatory Performance of HDL-C and Other Parameters for Insulin Resistance

The use of ROC curve analysis was employed to determine the effectiveness of the different parameters examined to identify the presence of insulin resistance. Among the studied parameters, HDL-C had the greatest efficacy, recording an AUC of 0.879 (95% CI: 0.822–0.936; P < 0.001). In the second place, ranked was TG with an AUC of 0.842 (95% CI: 0.773–0.911; P < 0.001). The AUC values of FBG and fasting insulin were found to be 0.786 and 0.758, respectively, while waist circumference had the lowest discriminatory power, with an AUC of 0.681. HDL-C, thus, was shown to have the highest discriminatory power in separating insulin-resistant participants from the control ones in all of the routine biochemistry and anthropometry methods used.

Table 2: ROC Analysis of Biochemical and Anthropometric Parameters for Identifying Insulin Resistance

Parameter	AUC	SE	P-value	95% CI
HDL-C	**0.879**	**0.029**	**<0.001**	**0.822–0.936**
TG	0.842	0.035	<0.001	0.773–0.911
FBG	0.786	0.042	<0.001	0.703–0.869
Fasting insulin	0.758	0.045	<0.001	0.670–0.846
Waist circumference	0.681	0.050	<0.001	0.583–0.779

Discussion

Research was conducted to assess the effectiveness of serum HDL-C and other standard metabolic and anthropometric parameters in determining insulin resistance in non-diabetic individuals. The significant finding of the study was the decrease of serum HDL-C in the insulin-resistant group when compared with a controlling group (40.82 ± 9.31 vs. 57.18 ± 11.86 mg/dL, P < 0.001). Additionally, HDL-C was found to have the best discriminatory performance among the studied parameters with an AUC of 0.879 (95% CI: 0.822–0.936), followed by triglycerides (AUC=0.842). The above-mentioned results support the idea that HDL-C can provide additional discriminatory information regarding insulin resistance in this population.

It is biologically reasonable that insulin resistant individuals will have low levels of HDL-C due to lipid abnormalities that accompany the improper use of insulin. One of the consequences of insulin resistance is adipose tissue lipolysis and the consequent flow of free fatty acids to the liver that causes more triglyceride-rich VLDL to be produced [10]. Thus, the expansion of triglyceride-rich lipoproteins enables the transfer of triglycerides and cholesteryl esters between them and HDL mediated by cholesteryl ester transfer protein. In the end, HDL enriched with triglycerides is considered the substrate of choice for hepatic lipase, which is responsible for HDL remodeling and increased apolipoprotein A-I breakdown with resulting decreased HDL-C levels in circulation [11]. Therefore, decreased HDL-C can be seen as an indicator of the disturbance of lipid metabolism in patients with insulin resistance [12].

HDL-C's impressive discriminatory ability, as observed in the study at hand, is especially surprising as most previous studies have focused on lipid ratios instead of HDL-C alone. For example, the triglyceride-to-HDL-C ratio has been studied extensively as a surrogate marker of insulin resistance (IR), with a systematic review recently finding that it could be used as an affordable and practical marker of IR [13], although its efficacy and best thresholds depend on the population being studied, as well as the sex and ethnic group they belong to. The results of the current study contribute to this body of knowledge by indicating that the HDL-C component itself may have a lot of discriminating power.

However, doing direct comparisons with studies investigating composite lipid indices should be done with caution because differences in populations, definition of insulin resistance, and statistical techniques might greatly affect the ROC calculations [14].

The triglycerides in the present study also showed strong discriminatory ability (AUC = 0.842), and their levels were significantly higher in the insulin-resistant than in the control subjects. This result is consistent with the observed decrease in HDL-C, which is typical of insulin-resistant persons where a well-known atherogenic dyslipidemic pattern is apparent [15]. Elevated production of hepatic VLDL, reduced clearance of lipoproteins rich in triglycerides, and abnormal remodeling of lipoproteins cause hypertriglyceridemia in insulin-resistant states. Consequently, the combined increase of TG together with decrease of HDL-C is the result of a variety of metabolic dysfunctions rather than only lipid changes [16].

Individuals showing IR also had elevated levels of fasting blood glucose and fasting insulin; however, the results for these two variables were markedly inferior in terms of their predictive performance in the current study when compared to that of HDL-C and TG. These outcomes were anticipated in view of the central importance of glucose and insulin homeostasis in the phenomenon of IR. In the initial stage of the development of insulin resistance, the compensatory phenomenon of hyperinsulinemia could save the glucose level from dropping before the manifestation of clear diabetes. The current study is pertinent in that all participants were nondiabetic, indicating that something may be wrong with lipid metabolism among those experiencing insulin resistance prior to developing diabetes.

Waist circumference was much higher among people in the IR group, indicating moderate flexibility (AUC = 0.681). Meanwhile, no appreciable differences were found in BMI between the groups. The contradiction demonstrates the difference between body size and fat distribution. The waist circumference indicates a person's central obesity and has a stronger correlation with insulin resistance than a person's weight does. A recent study conducted among Iraqis showed that the anthropometric measurements correlate with HOMA-IR and thereby confirm the role of central obesity in the diagnosis of insulin resistance. It is important to note that the lack of important BMI differences in this study does not prove that BMI is not connected to insulin resistance; it simply means that within this sample, BMI did not discriminate between the two groups (17).

Generally speaking, HDL-C exhibits a number of practical benefits as a possible marker of metabolic disorder from a medical point of view. It is relatively cheap, universal, included in standard lipid profiles, and does not need to undergo special investigations for insulin levels. An AUC of 0.879 found in the current study shows that this sample has a good degree of discrimination capability. However, HDL-C should not be regarded as a substitute for other methods of assessment of insulin resistance. Numerous biological and lifestyle factors contribute to HDL-C levels, but the HDL cholesterol is not an accurate indicator of the HDL particles' number, structure, or function. Therefore, HDL-C may be used as an easily available parameter in determining people that need additional metabolic evaluation.

Several restrictions of the findings should be recognized. To begin with, the small sample size and case-control approach limit the applicability of the study. In addition, since participants were chosen based on some anthropometric and clinical features indicative of metabolic dysfunctions, this might have had an effect on the results obtained because the results may not correspond to the results expected in a random general population. The third limitation is that the data cannot be used for an external validation of the ROC results as well as to find out if the correlation of the HDL-C with the insulin resistance persists in case some confounding variables are taken into account. Additionally, there was a lack of access to HDL-C cutoff values with their corresponding levels of sensitivity and specificity for analysis. Accordingly, there is a necessity for wider cohort studies with more heterogeneous populations and independent validation cohorts to develop clinically relevant HDL-C cut-off values and determine whether the discriminative capability stays intact after adjusting for appropriate metabolic and demographic characteristics.

To conclude, the findings of this study reveal a significant decrease in HDL-C levels in healthy non-diabetic individuals having insulin resistance as compared to the controls and the promising discriminatory capability of the HDL-C among all studied variables, making a case for further examination of its suitability as an accessible marker for insulin resistance.

Conclusion

In patients with insulin resistance who do not have diabetes, serum HDL-C levels were found to be substantially lower than in the sample, yielding the most favorable results among the biochemical and anthropometric indices analyzed. The results imply that HDL-C can be used as a simple and accessible marker for detecting people with a higher risk of insulin resistance in clinical practice. Nonetheless, HDL-C must be used as a possible marker for the screening process but not as an alternative to generally recognized markers of insulin resistance. Therefore, bigger prospective studies with predetermined diagnostic cutoffs and external validation are needed to establish its utility in practice.

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