Original Research

Evaluation of the non-HDL cholesterol, AIP and other cardiac indices as CVD risk in diabetic patients

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ABSTRACT:

Background: Diabetic type 2 dyslipidemia is recognized as a risk factor for the onset of cardiovascular disease, constituting a significant contributor to morbidity and mortality in individuals with diabetes. While LDL-cholesterol is conventionally employed as a marker for cardiovascular disease risk, alternative indicators such as lipid ratios, atherogenic index of plasma (AIP), and atherogenic coefficient have been identified as more effective predictors of cardiovascular disease. The objective of the current study is to assess non-HDL cholesterol, AIP, and other cardiac indices as indicators of cardiovascular disease risk in diabetic patients.

Methods: A cross-sectional investigation was conducted within the Department of Biochemistry, involving a total of 120 participants. Among them, 60 were individuals with diabetes, and the remaining 60 constituted a control group comprising healthy individuals of both genders. Various anthropometric parameters such as age, weight, height, and blood pressure, along with biochemical parameters including fasting blood sugar, lipid profiles, cardiac risk ratio, atherogenic index of plasma, atherogenic coefficient, and non-HDL cholesterol, were meticulously measured.

Results: The investigation revealed significant increases in fasting blood glucose, HbA1c, total cholesterol, triglycerides, and LDL-cholesterol, accompanied by a noteworthy decrease in HDL-cholesterol among diabetic patients compared to the normal healthy control group. Furthermore, cardiac indices such as Cardiac Risk Ratio (CRR), Atherogenic Index of Plasma (AIP), Atherogenic Coefficient (AC), and non-HDL cholesterol were observed to be significantly elevated in diabetic patients when compared to their counterparts in the normal healthy population.

Conclusion: The current study draws the conclusion that lipid ratios offer greater clinical convenience and can serve as valuable indicators for evaluating cardiovascular complications in diabetic patients, surpassing the utility of relying solely on lipid profiles.

Keywords: Anthropometric, cardiovascular,biochemical.

INTRODUCTION:

The escalating prevalence of Type 2 diabetes (T2DM) signals a future surge in diabetes-related complications. This trend underscores the imperative for healthcare professionals to adeptly administer suitable treatments for individuals with (T2DM), aiming to achieve optimal glycemic control.[1] The intricate interplay between glycemic control and the lipid profile accentuates the need for diligent monitoring of both aspects, a critical measure to avert the onset of diabetes-related macrovascular and microvascular complications. Despite its limitations in patients with hemoglobinopathies, glycosylated hemoglobin (HbA1c) remains the foremost criterion for evaluating glycemic control in (T2DM) patients.[2] This widely accepted metric serves as a reliable indicator, even though challenges may arise in individuals with certain hemoglobin disorders. Consistently elevated and variable HbA1c levels emerge as robust predictors, signifying an increased risk for cardiovascular disorders and heightened overall mortality in the diabetic population. Thus, healthcare providers must navigate these challenges and focus on maintaining a delicate balance in glycemic control to mitigate the risks associated with diabetes-related complications effectively. Managing lipid profiles in individuals with coronary artery disease (CAD) or its risk factors, such as diabetes, is a critical aspect of cardiovascular health.[3] This is emphasized by both the National Cholesterol Education Program Treatment for Adults Panel III (NCEP ATP III) and the European Society of

Cardiology, with a particular focus on low-density lipoprotein cholesterol (LDL-C). However, the intricate relationship between diabetes and LDL-C levels introduces complexity, as elevated LDL-C may not always be evident, leaving uncertainties about cardiovascular risk. Addressing this challenge, recent guidelines, including those from NCEP ATP III, and various studies have underscored the importance of non-high-density lipoprotein (non-HDL) cholesterol as a valuable predictor of cardiovascular risk, especially when triglyceride levels are high. Computed as the difference between total cholesterol and high-density lipoprotein (HDL) cholesterol, non-HDL cholesterol provides a comprehensive measure by encapsulating the total cholesterol carried by potentially prothrombotic apolipoprotein B-containing particles.[4,5] This metric stands out as a practical, reliable, and cost-effective alternative, particularly in routine clinical practice where direct measurement of apolipoprotein B (apo B) may not be readily available. Apolipoproteins, including apoA, apoB, apoC, apoD, apoE, and apoM, are integral components of plasma lipoproteins. These apolipoproteins play crucial roles in lipid transport and maintaining the structural integrity of lipoproteins. Within this framework, non-HDL cholesterol and apolipoproteins collectively offer a more nuanced and comprehensive understanding of cardiovascular risk in patients with diabetes or CAD risk factors. This multifaceted approach enhances the precision of cardiovascular risk assessment, providing healthcare professionals with valuable insights for more effective patient management.[6]Non-HDL cholesterol, derived by subtracting HDL cholesterol from total cholesterol, has emerged as a significant marker for predicting cardiovascular disease (CVD). The rationale behind calculating non-HDL-C and various lipid ratios lies in their effectiveness, often surpassing the predictive power of individual lipoproteins. Lipid ratios, in particular, have proven to be instrumental in indicating atherogenic risk, presenting as more robust predictors of cardiovascular diseases compared to focusing solely on individual lipid components. Notably, when evaluating the severity and prevalence of Coronary Artery Disease (CAD), heightened lipoprotein ratios demonstrate a more pronounced and statistically robust association.[7,8]In the realm of diabetes, a condition inherently linked to an elevated cardiovascular disease risk, lipid abnormalities play a pivotal role. Recognizing this, early identification and management of cardiovascular risk factors in patients with Type 2 Diabetes Mellitus (T2DM) become paramount, yielding positive outcomes by mitigating the risk of CVD and mortality, and concurrently improving overall prognoses. Recent research has redirected attention towards a novel lipid index known as the Atherogenic Index of Plasma (AIP), with the aim of offering a more comprehensive reflection of the intricate balance between atherogenic and anti-atherogenic factors. Numerous studies have underscored the superiority of AIP as a marker for predicting the risk of Coronary Artery Disease (CAD). For instance, research conducted in Iran establishes positive associations between AIP, waist circumference, body mass index, and conversely, negative associations with physical activity. The Atherogenic Index of Plasma (AIP), calculated as log (TG/HDL-C), has garnered attention for its role as a predictive measure for atherosclerosis and a surrogate for small low-density lipoprotein particle size.[9] Consequently, the current study aims to delve into the assessment of the Atherogenic Coefficient, Atherogenic Index of Plasma, and other cardiac indices, specifically in the context of evaluating cardiovascular risk in diabetic patients. These calculated fractions not only offer a more nuanced approach but also contribute to the evolving landscape of cardiovascular risk assessment and management, providing valuable insights for clinicians and researchers alike.

MATERIALS AND METHODS:

This investigative study, spanning a duration of one year, was conducted within the Department of Biochemistry, emphasizing the importance of ethical considerations and participant consent. The determination of the sample size was meticulously carried out, utilizing the prevalence rate of Diabetes Mellitus (7.03%) as a guiding parameter. Ethical approval was sought and obtained from the relevant committee, and informed consent was diligently obtained from each participant, underlining the commitment to ethical standards in research. Inclusion Criteria: A comprehensive total of 120 subjects, encompassing both genders, were actively recruited for the study. Within this cohort, 60 individuals were identified with Diabetes Mellitus, (T2DM) diagnosed according to the criteria established by the International Diabetes Federation (IDF). The remaining 60 participants were carefully selected as a control group, representing individuals without diabetes, thus serving as a valuable point of comparison in the study. Exclusion Criteria: To ensure the specificity and relevance of the study, a set of exclusion criteria was applied. Participants with pre-existing hepatic disease, cardiovascular disease, any chronic or acute inflammatory illness, various types of cancer, pulmonary tuberculosis, addiction to alcohol, individuals who smoked, and those grappling with prolonged illnesses were intentionally excluded from the study. This meticulous screening process aimed to create a focused and representative study group, ensuring that the investigation could isolate and examine the impact of diabetes and related risk factors more precisely.

By employing these rigorous inclusion and exclusion criteria, the study sought to enhance the validity and reliability of its findings, providing a solid foundation for exploring the intricate relationships between diabetes, its associated risk factors, and the broader

implications for health and well-being.In this study, aseptic precautions were strictly adhered to as approximately 5 ml of blood was drawn from both clinically diagnosed type 2 diabetes mellitus (T2DM) patients and control subjects following an overnight fast. The collected blood samples were processed using an automated analyzer, employing enzymatic methods to measure fasting plasma glucose levels and various lipid parameters.

To further assess cardiovascular risk, several derived indices were calculated:

- **Cardiac Risk Ratio (CRR):** Formula: Total Cholesterol / HDL-Cholesterol
- **Atherogenic Coefficient (AC):** Formula: (Total Cholesterol - HDL cholesterol) / HDL-cholesterol
- **Atherogenic Index of Plasma (AIP):** Formula: Log (Triglyceride / HDL-cholesterol) (mg/dL)
- **Non-HDL Cholesterol:** Formula: Total Cholesterol – HDL-cholesterol

These calculated indices provide valuable insights into the cardiovascular risk profile of the participants. The Cardiac Risk Ratio (CRR) assesses the relationship between total cholesterol and HDL-cholesterol, providing a metric for potential cardiac risk. The Atherogenic Coefficient (AC) offers a measure of the atherogenic potential by considering the balance between total cholesterol and HDL-cholesterol.[10] The Atherogenic Index of Plasma (AIP) incorporates the logarithm of the ratio of triglyceride to HDL-cholesterol, offering a more nuanced assessment of atherogenicity. Finally, Non-HDL Cholesterol provides an indicator of cholesterol carried by non-HDL lipoproteins, which are considered atherogenic.This meticulous approach to blood sample collection, coupled with the computation of these indices, enables a comprehensive evaluation of cardiovascular risk factors in both type 2 diabetes mellitus (T2DM) patients and controls, contributing valuable data to the understanding of lipid metabolism and its implications for cardiovascular health in the studied populations.

RESULTS:

In this comprehensive study, a total of 120 participants were carefully enrolled, with an equal distribution of 60 individuals diagnosed with diabetes and 60 normal healthy individuals, spanning both sexes. The detailed analysis of demographic parameters, as presented in Table 1, provides crucial insights into the distinct characteristics of both groups. Notably, the mean values for key anthropometric indicators, including weight and BMI, exhibited a significant increase in the diabetic cohort compared to the healthy control group.

This heightened weight and BMI in individuals with diabetes underscore the potential impact of the condition on body composition and metabolic health.Furthermore, the observed statistically significant increase in both systolic and diastolic blood pressure among diabetic patients raises important considerations regarding the cardiovascular implications of diabetes. These findings highlight the intricate relationship between diabetes and cardiovascular health, emphasizing the need for a comprehensive approach to understanding and managing these interconnected health factors. The data presented in this study contribute significantly to our understanding of the physiological differences between diabetic and non-diabetic individuals, shedding light on potential avenues for intervention and emphasizing the importance of tailored healthcare strategies. These insights are invaluable for healthcare professionals working towards optimizing health outcomes for individuals with diabetes and guiding preventive measures for those at risk.

Table 1: Showing Demographic parameters in diabetic and normal healthy individual

S.No.	Variables	Diabetics	Healthy Controls
1	Age (years)	38.72	37.17
2	Weight (Kg)	54.27	76.17
3	Height (Meter)	1.59	1.67
4	BMI (Kg/Meter2)	23.38	27.39
5	Systolic Blood pressure (mm of Hg)	119.47	129.57
6	Diastolic Blood Pressure (mm of Hg)	78.58	84.30

Figure 1: Showing Demographic parameters in diabetic and normal healthy individual

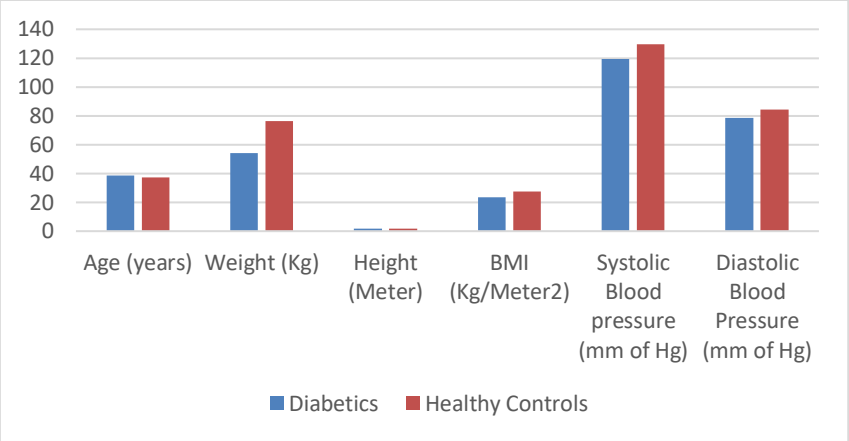
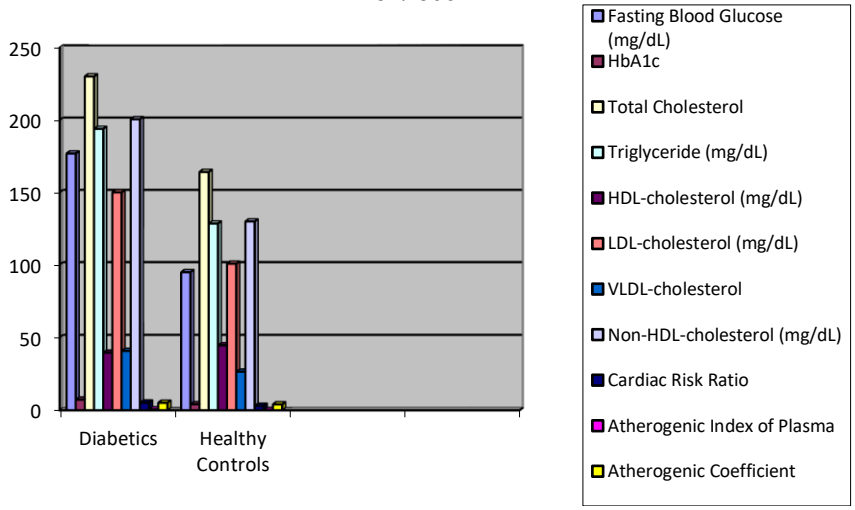


Table 2: Showing biochemical parameters and cardiac indices in diabetic and normal healthy individual

S.No.	Variables	Diabetics	Healthy Controls	p-Value
1	Fasting Blood Glucose (mg/dL)	176.74	94.66	<0.001
2	HbA1c	7.28	4.16	<0.001
3	Total Cholesterol	230.08	164.00	<0.001
4	Triglyceride (mg/dL)	193.81	128.32	<0.001
5	HDL-cholesterol (mg/dL)	39.44	44.47	<0.001
6	LDL-cholesterol (mg/dL)	149.86	100.55	<0.001
7	VLDL-cholesterol	40.62	26.45	<0.001
8	Non-HDL-cholesterol (mg/dL)	200.48	129.77	<0.001
9	Cardiac Risk Ratio	5.23	3.03	<0.001
10	Atherogenic Index of Plasma	0.61	0.124	<0.001
11	Atherogenic Coefficient	5.13	4.03	<0.001

Figure 2: Bar graph showing biochemical parameters and cardiac indices in diabetic and normal healthy individual



DISCUSSION:

Maintaining optimal glycemic control in individuals with Diabetes Mellitus (T2DM) is paramount for reducing the risk of diabetes-related complications and enhancing overall health outcomes. The current study underscores the challenges in achieving this goal, revealing that a substantial 84.5% of the participants exhibited poor glycemic control.[11] This concerning trend mirrors findings from a previous study in Iraq, where an equally high rate of 86.2% was reported.Global investigations into glycemic control among T2DM patients have unveiled a spectrum of rates in different regions. In Saudi Arabia, for instance, the reported rate stood at 74.9%, while in Yazd, Iran, it was noted at 58.3%. Ethiopia documented a rate of 72.7%. Intriguingly, T2DM patients in the United States demonstrated a comparatively better rate of glycemic control, hovering around 50%, indicating potential variations in healthcare practices and management

approaches.The disparities in glycemic control rates across nations may be influenced by a myriad of factors, including variations in healthcare infrastructure, accessibility to medical resources, cultural nuances, and differences in healthcare management strategies. Recognizing these distinctions is crucial for tailoring interventions that address the unique challenges faced by T2DM patients globally.[12,13]The higher prevalence of poor glycemic control in certain regions highlights the urgent need for targeted and culturally sensitive interventions. Healthcare policies and strategies aimed at enhancing diabetes management, patient education, and access to healthcare resources are imperative. Understanding these regional differences not only contributes to a more nuanced global perspective on diabetes but also lays the foundation for more effective and targeted public health initiatives, ultimately working towards reducing the burden of diabetes-related complications and improving the overall well-being of individuals with T2DM.

In a study conducted by S. Bhardwaj et al., significant findings were observed in key cardiovascular indices—Atherogenic Index of Plasma (AIP), CRI 1, CRI II, and Atherogenic Coefficient (AC)—among angiographically confirmed cases of Coronary Artery Disease (CAD).[14] These indices played a substantial role in contributing to the overall CAD risk, with AIP being the most influential at 31%, followed by CRI 1 at 20%, AC at 17%, and CRI II. This underscores the importance of these cardiovascular markers in assessing and understanding the risk of CAD.It is not unexpected to find elevated levels of these cardiovascular indices in individuals with Type 2 Diabetes (T2D) in the present study. Diabetes is known to carry a significantly heightened risk of coronary heart disease. The study reveals a noteworthy correlation between AIP and other indices such as CRI I, CRI II, and AC. These indices collectively indicate a higher plaque density in the coronary arteries, suggesting an increased risk of CAD among the participants.The observed elevation in these cardiovascular indices among individuals with Type 2 Diabetes in the study underscores the urgency of addressing the heightened CAD risk in this specific population. The findings highlight the importance of early intervention and management strategies to mitigate the risk factors associated with cardiovascular diseases in individuals with Type 2 Diabetes. The correlation between these indices and plaque density further emphasizes the need for targeted approaches to tackle CAD risk in this specific setting.[15] This knowledge is crucial for informing healthcare practices and policies to enhance the cardiovascular health of individuals with Type 2 Diabetes.The persistent increase in the prevalence of diabetes mellitus has elevated it to the status of one of the most prevalent and impactful health conditions globally. Significantly, this rise in diabetes has brought forth a profound connection between diabetes and cardiovascular disease, which now stands as the foremost cause of morbidity and mortality in individuals with diabetes. Notably, common cardiovascular risk factors such as hypertension, obesity, and dyslipidemia are frequently intertwined with diabetes, collectively heightening the risk for adverse cardiac events.[16,17] One compelling study has even reported that the incidence of cardiovascular disease in diabetic patients is three times higher than in their non-diabetic counterparts, establishing cardiovascular complications as a major contributor to the morbidity and mortality associated with diabetes.The present study contributes to this growing body of knowledge by shedding light on the Atherogenic Index of Plasma (AIP), which was found to be significantly elevated in diabetic patients compared to healthy individuals. This observation aligns with the findings of numerous researchers, supporting the notion that AIP, representing a simple relationship between triglycerides and high-density lipoprotein cholesterol, serves as a robust predictor of atherosclerosis. Atherosclerosis, a key pathological process underlying cardiovascular diseases, emphasizes the clinical relevance of AIP in assessing cardiovascular risk in diabetic populations.Furthermore, the study delves into the assessment of the Cardiac Risk Ratio and Atherogenic Coefficient, both of which were found to be significantly increased in diabetic patients compared to their healthy counterparts. These metrics provide valuable insights into the cardiovascular risk profile of diabetic individuals, reinforcing the urgency of comprehensive monitoring and intervention strategies to mitigate the heightened risk of atherosclerosis and subsequent cardiovascular events.In conclusion, the findings from this study underscore the imperative of understanding and addressing cardiovascular risk factors in the context of diabetes.[18,19] The elevated levels of AIP, Cardiac Risk Ratio, and Atherogenic Coefficient emphasize the need for a multidimensional approach to healthcare for individuals with diabetes, encompassing proactive monitoring, lifestyle interventions, and targeted medical management to effectively mitigate the risk of cardiovascular complications and improve overall health outcomes.In individuals with diabetes, insulin deficiency can play a pivotal role in disrupting lipid metabolism and triggering various pathways that contribute to cardiovascular disease. The deficiency of insulin can lead to increased metabolization of free fatty acids, resulting in a disorder in lipid metabolism and activation of the protein kinase-C pathway. These disruptions collectively impair vasodilatory responses, creating an environment that predicts cardiovascular disease. The elevation in triacylglycerol levels observed in diabetes may be attributed to the accumulation of triacylglycerol, increased lipogenesis, and decreased fatty acid oxidation.[20]Insulin resistance, a hallmark of type 2 diabetes, exacerbates the dysregulation of lipid metabolism. This resistance

leads to heightened catabolism of high-density lipoprotein (HDL) particles and the formation of low-density lipoprotein (LDL) particles, contributing to an increase in LDL levels and a decrease in HDL levels.[21] These alterations in lipid profiles are significant contributors to the heightened cardiovascular risk associated with type 2 diabetes.Lipid ratios and Atherogenic Index of Plasma (AIP) have emerged as valuable indicators of atherogenic dyslipidemia in diabetic individuals. The imbalance in these lipid and lipoprotein fractions has been documented in diabetes, both with and without complications. Researchers conducting studies in this domain have observed that atherogenic index and the ratio of total cholesterol to HDL cholesterol (TC/HDL-C) levels are significantly elevated in diabetic patients compared to controls. Notably, these indices were found to be lower in patients undergoing insulin treatment.[22]These findings underscore the importance of lipid ratios in identifying cardiovascular risk, emphasizing that evaluating lipid profiles in isolation may not provide a comprehensive understanding of the cardiovascular risk landscape in diabetes. The role of insulin, lipid ratios, and AIP collectively highlights the intricate interplay between metabolic factors and cardiovascular health in individuals with diabetes, contributing valuable insights for both clinical management and further research in this field.

CONCLUSION:

In the context of diabetes, there is a notable disruption in the utilization of lipids and lipoproteins, leading to the development of atherogenic dyslipidemia. This condition, characterized by an unfavorable lipid profile, stands out as one of the most common risk factors for the initiation and progression of atherosclerosis—the underlying pathology of cardiovascular disease. While low-density lipoprotein cholesterol (LDL-C) is traditionally employed as a marker of cardiovascular risk in diabetes, additional parameters such as lipid ratios, atherogenic coefficient, and atherogenic index of plasma have garnered attention for their ability to provide a more comprehensive assessment of atherogenic risk.The significance of lipid ratios, atherogenic coefficient, and atherogenic index of plasma lies in their capacity to indicate the propensity for atherogenic changes in the vascular system. These parameters have demonstrated their superiority as predictors of cardiovascular risk compared to assessing individual lipid components alone. As a result, there is a growing consensus on the inclusion of these comprehensive lipid indices in routine cardiac profiles for individuals with diabetes. This approach aims to enhance the predictive accuracy of atherosclerotic damage and better inform clinicians about the cardiovascular risk landscape in diabetic patients.By incorporating these advanced lipid parameters into routine cardiac assessments, healthcare practitioners can gain a more nuanced understanding of the cardiovascular risk profile in diabetes. This proactive approach enables timely interventions and personalized management strategies, ultimately contributing to the prevention or early treatment of cardiovascular complications in individuals with diabetes. The recognition of the multifaceted nature of atherogenic dyslipidemia emphasizes the importance of a holistic evaluation that extends beyond individual lipid markers for a more robust assessment of cardiovascular risk in diabetic populations.

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