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Serum Adiponectin and Indian Diabetes Risk Score: Association with Glycosylated Hemoglobin in Undiagnosed Diabetes and Prediabetes in Uttarakhand Adults

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Abstract

Background:
Diabetes and prediabetes are significant public health issues, particularly in India, where their prevalence is rising due to lifestyle changes and genetic factors. The Indian Diabetes Risk Score (IDRS) is a practical screening tool that identifies individuals at high risk for diabetes through a simple assessment of key risk factors. Serum adiponectin, an important biomarker, inversely correlates with insulin resistance and obesity, serving as a valuable indicator of metabolic disturbances. Glycosylated hemoglobin (HbA1c) measures long-term glycemic control, aiding in the diagnosis of diabetes and prediabetes. Keeping this prospective in mind, a recent study was conducted to assess the association of serum adiponectin and IDRS with HbA1c levels to improve the detection of undiagnosed diabetes and prediabetes, enhancing public health strategies and individual health outcomes.

Materials and Methodology:
This cross-sectional study evaluated the association of serum adiponectin and the Indian Diabetes Risk Score (IDRS) with HbA1c in adults (≥18 years) at the Veer Chandra Singh Garhwali Government Institute of Medical Science and Research, Uttarakhand. Data were collected via a structured questionnaire. IDRS was derived from age, abdominal obesity, family history, and physical activity. Serum adiponectin and HbA1c levels were measured using standard laboratory methods. Statistical analyses included Pearson correlation and logistic regression to assess associations.

Result:
Our findings revealed a significant negative correlation between serum adiponectin levels and HbA1c ($r = -0.148$, $p = 0.001$), indicating that lower adiponectin is associated with poorer glycemic control. Additionally, higher IDRS scores were significantly correlated with elevated HbA1c levels ($p < 0.005$), highlighting the IDRS's effectiveness in identifying individuals at risk for diabetes. The prevalence of undiagnosed diabetes was notably higher in participants with elevated IDRS scores, emphasizing the importance of both serum adiponectin and IDRS in early diabetes detection and intervention strategies.

Conclusion:
In summary, this study establishes a significant association between serum adiponectin levels, the Indian Diabetes Risk Score (IDRS), and HbA1c in identifying undiagnosed diabetes and prediabetes. Lower adiponectin concentrations correlate with higher HbA1c levels, indicating impaired glycemic control. The IDRS effectively stratifies individuals by diabetes risk, highlighting its utility in early detection. These findings suggest that integrating serum

adiponectin and IDRS into screening protocols can enhance the identification of at-risk populations, facilitating timely interventions to improve metabolic health and prevent diabetes progression.

Key words: Serum adiponectin (ADP), Indian Diabetes Risk Score (IDRS) Glycosylated Hemoglobin (HbA1c)

Introduction:

Diabetes mellitus (DM) is a long-term metabolic condition characterized by consistently high blood sugar levels resulting from inadequate insulin secretion, resistance to insulin's effects in the body, or a combination of both[1]. Diabetes has emerged as a major global health concern, with its prevalence rising sharply across all regions and income levels. As of 2021, approximately 537 million adults aged 20-79 were living with diabetes, accounting for about 10.5% of the global adult population[2]. This alarming trend is projected to escalate, with estimates suggesting that the number of individuals affected could reach 643 million by 2030 and 783 million by 2045[2]. The burden of diabetes is particularly pronounced in low- and middle-income countries, where the incidence has increased more rapidly compared to high-income regions. The World Health Organization's Eastern Mediterranean Region has reported the highest prevalence globally, at 13.7%[3]. Type 2 diabetes constitutes about 90% of all diabetes cases and is a leading cause of mortality, contributing to over 1.5 million deaths annually[4]. The rising incidence of diabetes not only poses significant challenges to public health systems but also leads to increased healthcare expenditures, projected to exceed $1,054 billion by 2045[2]. Addressing this global diabetes epidemic requires coordinated public health strategies focused on prevention, treatment, and management of risk factors, such as obesity and sedentary lifestyles, to mitigate its growing impact on population health and global economies[5].

The burden of diabetes in India is a pressing public health issue, with the country experiencing a significant rise in the prevalence of the disease. Currently, approximately 77 million Indians aged 20-79 are living with diabetes, and projections indicate that this number could soar to 134.2 million by 2045[2]. This alarming trend is driven by rapid socioeconomic changes, urbanization, sedentary lifestyles, and dietary transitions, which have collectively contributed to an increase in diabetes cases[6]. The prevalence of diabetes is particularly concerning in rural areas, where awareness and healthcare access are limited. Studies show that only 36.8% of rural residents are aware of their diabetes status, compared to 58.4% in urban areas[7]. Furthermore, the ICMR-INDIAB study highlights that over 50% of diabetes cases in rural areas and 30% in urban areas remain undiagnosed, indicating a significant gap in healthcare infrastructure and awareness[1]. The combination of genetic predisposition, environmental factors, and lifestyle changes has led to a high susceptibility to type 2 diabetes among the Indian population. As the incidence of diabetes continues to rise, it poses substantial challenges not only to individual health but also to the healthcare system, necessitating urgent interventions and improved healthcare strategies to manage and prevent the disease effectively[8].

Early detection of diabetes, especially in undiagnosed cases, is essential for preventing serious health complications and improving overall health outcomes. Many individuals with diabetes remain asymptomatic in the early stages, which can lead to a lack of awareness until complications such as cardiovascular disease, kidney failure, and neuropathy develop[9]. Timely identification of the disease allows for prompt intervention, enabling individuals to implement necessary lifestyle modifications and receive appropriate medical management to control blood sugar levels. This proactive approach not only enhances individual health but also alleviates the burden on healthcare systems by reducing the need for more intensive treatments associated with advanced diabetes complications. Furthermore, early diagnosis empowers individuals with knowledge about their health, facilitating informed decision-making regarding lifestyle and treatment options. Overall, the importance of early detection lies in its potential to prevent

complications, improve health outcomes, and lower healthcare costs related to the management of advanced diabetes[10].

The Indian Diabetes Risk Score (IDRS) serves as a highly relevant and effective screening tool for identifying individuals at risk of developing diabetes, particularly in resource-limited settings. Its simplicity and ease of use make it accessible for community health workers and healthcare providers, allowing for rapid assessment of diabetes risk without the need for complex laboratory tests[11]. The IDRS incorporates key risk factors such as age, body mass index, waist circumference, physical activity, and family history of diabetes, enabling a comprehensive evaluation of an individual's risk profile. This straightforward scoring system categorizes individuals into high, moderate, and low-risk groups, facilitating targeted interventions for those most in need[12]. By promoting early detection and timely management of diabetes, the IDRS not only helps in reducing the prevalence of the disease but also empowers individuals to make informed lifestyle choices[13]. Its applicability across diverse populations in India further enhances its relevance, as it can be tailored to reflect local demographic and lifestyle characteristics, ultimately contributing to more effective public health strategies in combating the diabetes epidemic[14].

Serum adiponectin plays a crucial role in metabolic regulation and is significantly associated with diabetes particularly type 2 diabetes mellitus (T2DM). As a hormone secreted by adipose tissue, adiponectin enhances insulin sensitivity, promotes glucose uptake, and facilitates fatty acid oxidation in various tissues, including the liver, muscle, and adipose tissue[15]. Higher levels of adiponectin are linked to improved insulin sensitivity and a reduced risk of developing T2DM, while lower levels are commonly observed in individuals with obesity, insulin resistance, and metabolic syndrome[16]. This inverse relationship highlights adiponectin's potential as a biomarker for assessing diabetes risk. Additionally, adiponectin possesses anti-inflammatory properties, which further contribute to its protective effects against metabolic disorders[17]. Research suggests that strategies aimed at increasing adiponectin levels, such as lifestyle modifications and pharmacological interventions, can improve insulin sensitivity and glycemic control. Understanding the dynamics of serum adiponectin is essential for developing effective strategies for diabetes management and prevention, making it a valuable target for therapeutic interventions in metabolic disorders[18'19].

HbA1c, or glycosylated hemoglobin, is a reliable biomarker for assessing glycemic control and diagnosing diabetes. It reflects average blood glucose levels over the previous two to three months, providing a stable measure that is less influenced by daily fluctuations in blood sugar[20]. This characteristic makes HbA1c particularly valuable for monitoring long-term glycemic control in individuals with diabetes. The standardization of HbA1c testing, established by initiatives like the National Glycohemoglobin Standardization Program (NGSP), has further enhanced its reliability across different laboratories[21]. According to the American Diabetes Association (ADA), an HbA1c level of 6.5% or higher indicates diabetes, while levels between 5.7% and 6.4% suggest prediabetes[22]. This diagnostic capability allows for early identification of individuals at risk, enabling timely interventions to prevent the progression to diabetes. Additionally, HbA1c is instrumental in evaluating the effectiveness of diabetes management strategies, guiding treatment adjustments to minimize the risk of complications[23]. Despite its limitations, such as the inability to capture short-term glucose fluctuations, HbA1c remains a cornerstone in diabetes diagnosis and management, particularly when used in conjunction with other monitoring methods for a comprehensive assessment of glycemic control[24].

Our earlier publication[25] investigated diabetes risk in undiagnosed prediabetic and diabetic individuals using the diabetes risk assessment tool (IDRS) and a biochemical indicator of long-termglycemic control (HbA1c) in the adult population of Uttarakhand., and the current study extends this work by examining the association of serum adiponectin and IDRS with HbA1c in detecting undiagnosed diabetes and prediabetes in the adult population of Uttarakhand.

Material and Methods:

The study was conducted in Uttarakhand, India, to evaluate the association of serum adiponectin and the Indian Diabetic Risk Score (IDRS) with HbA1c in undiagnosed diabetes and prediabetes. This facility-based cross-sectional study included adult participants aged 18 years or older who had not been previously diagnosed with diabetes mellitus and who consented to participate. The research was conducted over three years, from December 2021 to December 2024. The IDRS and glycated hemoglobin (HbA1c) were used to assess the risk of diabetes in the population, and their association with serum adiponectin levels was further analyzed.

Participants were categorized into three groups based on their IDRS: low-risk, moderate-risk, and high-risk. The IDRS questionnaire included four components: age, family history of diabetes, physical activity, and waist circumference. HbA1c levels were estimated using a latex agglutination inhibition technique certified by the National Glycohemoglobin Standardization Program (NGSP) and standardized to the Diabetes Control and Complications Trial (DCCT). Serum adiponectin levels were measured using a sandwich ELISA method, where specific antibodies pre-coated onto a microplate captured adiponectin, which was then detected using an HRP-conjugated antibody. The resulting color development was directly proportional to the concentration of adiponectin.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 20. One-way analysis of variance (ANOVA) was employed for continuous data, while chi-square tests were applied for categorical data. However, the study had certain limitations, including the absence of blood sugar levels and other biochemical or hematological parameters, which might have led to an underestimation of diabetes prevalence in the study area. Additionally, the cross-sectional design of the study did not permit causal inference, and the results may not be generalizable to other regions or populations. The reliance on self-reported data also introduced potential recall bias. Despite these limitations, the study provided valuable insights into the potential risk factors associated with elevated HbA1c levels indicative of prediabetes or diabetes in the adult population of Uttarakhand, India.

Results:

In this study, we aimed to assess the association of serum adiponectin and the Indian Diabetes Risk Score (IDRS) with glycosylated hemoglobin (HbA1c) levels in detecting undiagnosed diabetes and prediabetes. A total of 513 participants were evaluated, with serum adiponectin levels measured alongside HbA1c and IDRS scores.

The results indicated a significant negative correlation between serum adiponectin levels and HbA1c, with a correlation coefficient of $r = -0.148$ ($p = 0.001$). This suggests that lower serum adiponectin levels are associated with higher HbA1c levels, indicating poorer glycemic control. Specifically, individuals classified as diabetic exhibited significantly lower serum adiponectin levels (mean of 5.68 ng/ml ± 1.37) compared to non-diabetics (mean of 9.93 ng/ml ± 3.33), with a p-value of <0.001. This finding underscores the potential of serum adiponectin as a biomarker for identifying individuals at risk of diabetes.

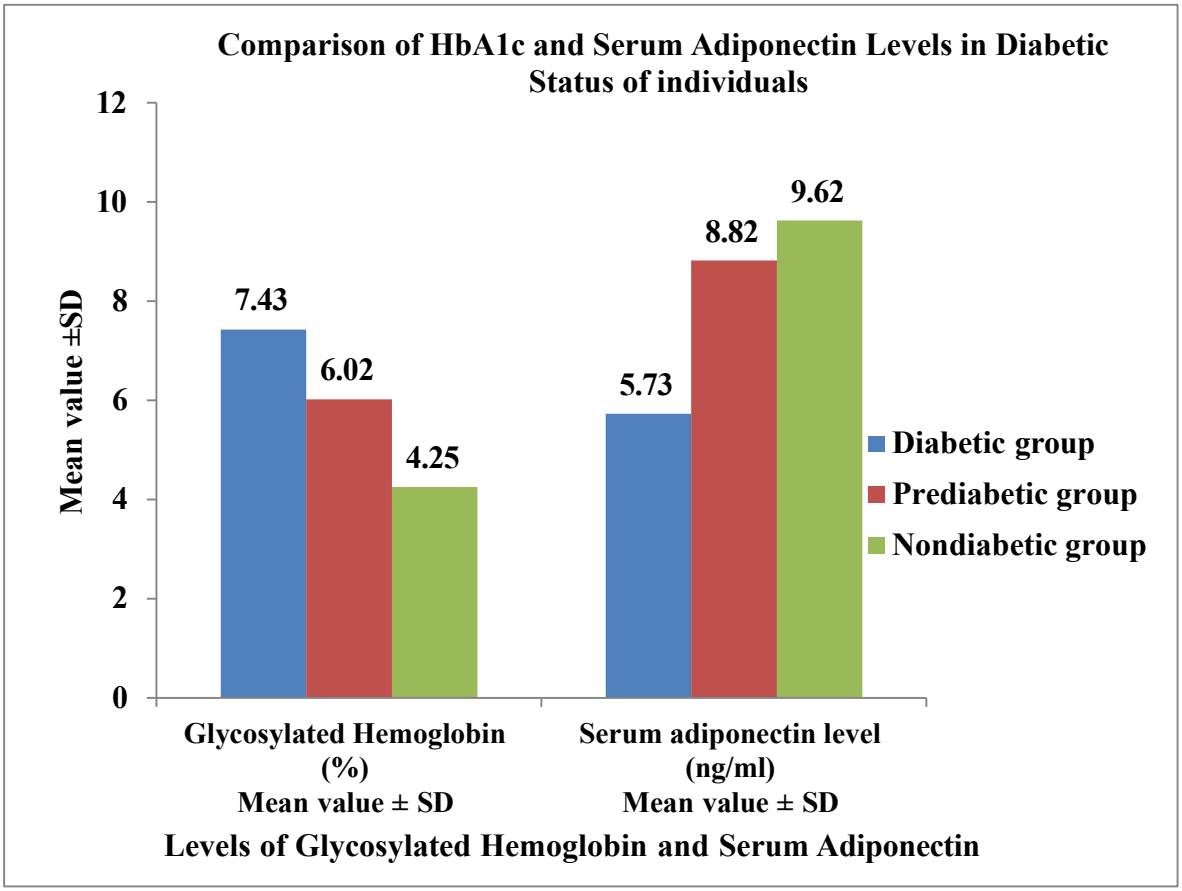

Figure: 1 Comparison of hbA1c and Serum Adiponectin Levels in Diabetic Status of Individuals

Additionally, the analysis of IDRS scores revealed that participants with higher IDRS scores were more likely to have elevated HbA1c levels, indicating a higher risk of undiagnosed diabetes and prediabetes. The prevalence of undiagnosed diabetes was significantly associated with IDRS categories, with 5.85% of participants classified as diabetic, 11.90% as prediabetic, and 82.26% as non-diabetic.

Table: 1 Association of Serum Adiponectin and IDRS with HbA1c Levels in Detecting Undiagnosed Diabetes and Prediabetes

Parameter	Diabetic Group (n=30)	Prediabetic Group (n=61)	Non-Diabetic Group (n=422)	Total (n=513)	p-Value
Mean Serum Adiponectin**(ng/ml)** (Mean value ± SD)	5.68±1.38	9.26±2.59	9.93±3.33	-	<0.001
Mean HbA1c (%) (Mean value ± SD)	7.46±0.49	6.03±0.23	4.42±0.94	-	<0.001

IDRS Score (Mean value ± SD)	62.00±10.00	45.00±5.00	25.00±5.00	-	<0.001
Prevalence of Undiagnosed diabetes (%)	5.85%	11.90%	82.26%	-	<0.005

Values are expressed as Mean ± SD; the comparison of variables between groups was performed using the chi-square test; *p<0.05 is statistically significant among groups.

Furthermore, the study found that serum adiponectin levels did not significantly differ across IDRS risk categories (p-values ranging from 0.611 to 0.714), suggesting that while adiponectin is associated with glycemic control, it may not effectively differentiate between risk categories in this population.

In conclusion, our findings highlight the significant association between serum adiponectin and HbA1c levels, suggesting that adiponectin could serve as a valuable biomarker in the detection of undiagnosed diabetes and prediabetes. The IDRS also proved to be a useful tool in identifying individuals at risk, although its relationship with serum adiponectin levels requires further investigation to clarify its role in diabetes risk assessment.

Discussion:

The objective of this study was to investigate the association of serum adiponectin levels and the Indian Diabetes Risk Score (IDRS) with HbA1c in detecting undiagnosed diabetes and prediabetes among the adult population of Uttarakhand. Our findings reveal significant correlations that underscore the potential of these biomarkers and risk assessment tools in identifying individuals at risk for diabetes.
The relationship between adiponectin levels and diabetes, particularly type 2 diabetes mellitus (T2DM), has garnered significant attention in recently because of its implications on metabolic health and cardiovascular risk[26, 27]. Adiponectin, an adipocyte-derived hormone, plays a crucial role in regulating glucose levels and fatty acid breakdown[28, 29]. The levels of lipids are inversely correlated with body fat percentage, making them a potential biomarker for metabolic disorders. The reviewed studies provide compelling evidence that lower adiponectin levels are associated with higher glycosylated hemoglobin (HbA1c) levels, indicating poor glycemic control and an increased risk of diabetes[30, 31].

Our results indicate a negative correlation between serum adiponectin levels and HbA1c, suggesting that lower adiponectin levels are associated with higher HbA1c values. This finding is consistent with existing literature that highlights the role of adiponectin as an insulin-sensitizing hormone[32,33]. Adiponectin is known to enhance insulin sensitivity and has anti-inflammatory properties, which may contribute to its protective role against the development of type 2 diabetes. The observed decrease in adiponectin levels among individuals with elevated HbA1c levels aligns with studies that have reported lower adiponectin concentrations in individuals with insulin resistance and metabolic syndrome[34,35].

The IDRS has proven to be an effective screening tool for identifying individuals at risk of developing diabetes. Our study found that participants classified in the high-risk category (IDRS ≥ 60) exhibited significantly higher HbA1c levels compared to those in the moderate and low-risk categories. This finding supports the utility of the IDRS in early identification of individuals who may benefit from lifestyle modifications and medical interventions. The IDRS incorporates key risk factors such as age, waist circumference, physical activity, and family history of diabetes, which are critical in assessing diabetes risk.

The implications of our findings are significant for public health strategies aimed at diabetes prevention. By integrating serum adiponectin measurements with IDRS assessments, healthcare providers can enhance the accuracy of diabetes risk stratification. This approach allows for targeted interventions that focus on lifestyle modifications, such as increased physical activity and dietary changes, which are essential for improving insulin sensitivity and overall metabolic health.

While our study provides valuable insights, it is important to acknowledge certain limitations. The cross-sectional design limits causal inferences, and the sample size, although adequate, may not fully represent the diverse population of Uttarakhand. Future longitudinal studies are warranted to further explore the temporal relationships between adiponectin levels, IDRS, and HbA1c changes over time. Additionally, investigating the underlying mechanisms linking adiponectin and diabetes risk could provide deeper insights into potential therapeutic targets.

Conclusion:

The study successfully demonstrates a significant association between serum adiponectin levels, the Indian Diabetes Risk Score (IDRS), and HbA1c levels in detecting undiagnosed diabetes and prediabetes. The findings reveal that lower adiponectin concentrations correlate with elevated HbA1c levels, indicating poorer glycemic control and a heightened risk of diabetes. Additionally, the IDRS effectively identifies individuals at increased risk of developing diabetes, as those with higher IDRS scores tend to exhibit lower adiponectin levels and higher HbA1c values.

These results underscore the potential of using serum adiponectin and IDRS as valuable biomarkers in clinical settings for early detection of undiagnosed diabetes and prediabetes. By integrating these measures into routine screening protocols, healthcare providers can enhance the identification of at-risk individuals, facilitating timely interventions aimed at improving glycemic control and preventing the progression of diabetes-related complications. Furthermore, the study advocates for public health initiatives that focus on lifestyle modifications and increased awareness of diabetes risk factors, ultimately contributing to better health outcomes in the population. Regular monitoring of HbA1c levels, alongside adiponectin assessments and IDRS evaluations, is essential for effective diabetes management and prevention strategies moving forward.

In conclusion, our study highlights the significant association of serum adiponectin and IDRS with HbA1c in detecting undiagnosed diabetes and prediabetes in the adult population of Uttarakhand. These findings underscore the importance of early screening and intervention strategies to mitigate the rising burden of diabetes in this region. By leveraging both biochemical markers and risk assessment tools, healthcare providers can better identify at-risk individuals and implement effective preventive measures.

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Author contributions:

All authors contributed equally to the conceptualization,methodology, validation, writing, and supervision of this study, and they made a joint decision to publish the manuscript.

Ethical approval:

Institutional Ethics Committee (IEC) of Veer Chandra Singh Garhwali Government Institute of Medical Science and Research Srinagar (Garhwal) Uttarakhand and the University Ethical Committee Hemwati Nandan Bahuguna Uttarakhand Medical Education University Dehradun Uttarakhand approved this study.

Informed Consent Statement:

Before the final enrollment in the study, all participants were given an explanation of the study procedure and their role in it in their native language, and written informed consent was obtained from them.

Conflict of Interest:

The authors declare that there are no conflicts of interestassociated with this study.

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