ORIGINAL ARTICLE

Metabolic Syndrome in the Middle Age: Insights from the Hemoglobin Glycation Index

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ABSTRACT

Background: Metabolic syndrome (MetS) is a global health issue linked to obesity, hypertension, dyslipidemia, and insulin resistance, increasing the risk of type 2 diabetes and cardiovascular diseases. In Bangladesh, MetS prevalence is high, especially among middle-aged individuals. The hemoglobin glycation index (HGI) has emerged as a potential marker for glycemic control, offering insights beyond traditional HbA1c by accounting for individual variations in glucose metabolism. However, its association with MetS remains underexplored. ***Objective:*** *To* investigate the relationship between HGI and MetS components, as well as assess HGI's potential as a metabolic risk biomarker. ***Methods:*** This cross-sectional study was conducted at the Department of Biochemistry, Sir Salimullah Medical College, Dhaka, Bangladesh, between March 2023 and February 2024. A total of 200 purposively selected middle-aged residents of old region of Dhaka city, Bangladesh, were enrolled. Data on demographics, medical history, physical examination, and lab findings were collected and analyzed. ***Results:*** Among 200 participants (46.5% male, 53.5% female), MetS prevalence was 27.5%, higher in the high HGI group (50.5%) than the low HGI group (5%). High HGI was significantly associated with waist circumference, systolic blood pressure, and triglycerides ($p<0.05$), while HDL was lower. Logistic regression showed a higher MetS risk in the high HGI group (OR= 17.878, 95% Cl: 6.119~52.232), as linking high HGI to abdominal obesity, hypertension, hypertriglyceridemia, and MetS ($p<0.05$). ***Conclusion:*** High HGI may serve as an independent marker of MetS, identifying individuals at higher risk, though large-scale studies are needed for validation.

Keywords: Hemoglobin glycation index, metabolic syndrome.

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INTRODUCTION

Metabolic syndrome (MetS) is a worldwide issue with rising prevalence (ie.an emerging epidemic). It pertains to a grouping of interrelated biochemical and anthropometric traits, including abdominal obesity, raised blood pressure, high blood glucose, dyslipidemia, as well as a proinflammatory and hypercoagulable state[1]. This condition not only increases the risk of developing type 2 diabetes mellitus (T2DM) and cardiovascular diseases (CVDs) but also contributes to the growing burden on healthcare systems worldwide[2]. Bangladesh, a South Asian country, is at high risk for developing Mets with a prevalence rate of 37.38% [3]. It is more prevalent in female (32%) than male (27%)[4]. The prevalence of MetS is rising steadily, particularly among middle-aged individuals, a group especially vulnerable to the long-term complications associated with these metabolic imbalances[5].

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In recent years, the hemoglobin glycation index (HGI) has emerged as a valuable tool for assessing individual variations in glycemic control and metabolic health. HGI measures the difference between observed HbA1c levels and those predicted from average blood glucose levels, providing a unique perspective on the interplay between glucose regulation and hemoglobin glycation[6]. Unlike traditional HbA1c measurements, which may be influenced by factors such as genetics or red cell turnover etc[7], HGI offers deeper insights into the metabolic risks associated with glycemic variability and insulin resistance, the central mechanism underlying MetS[8].

This study focuses on the critical middle-age period when the cumulative effects of metabolic risk factors often manifest[9]. Exploring the association between HGI and MetS in middle-aged populations can enhance our understanding of the syndrome's pathophysiology, improve risk stratification, and guide targeted interventions by investigating HGI's correlation with MetS components and its potential as a biomarker for metabolic health.

METHODS

This cross-sectional study was conducted in the Department of Biochemistry of Sir Salimullah Medical College, Dhaka, Bangladesh, from March 2023 to February 2024, including 200 seemingly healthy middle-aged (30-64 years) permanent residents of old Dhaka city, Bangladesh. Individuals classified as underweight (BMI <18.5 kg/m2) or morbidly obese (BMI >40 kg/m^2), as well as pregnant women, breastfeeding mothers, and those with a history of septicemia, systemic diseases, metabolic abnormalities, smoking, or drinking were excluded from this study. Individuals who denied to participate in the study were also excluded. Waist circumference (WC) was measured in centimeters using a measuring tape placed at the midpoint between the lower edge of the last palpable rib and the top of the iliac crest, with subjects standing upright, arms at their sides, feet close together, and weight evenly distributed. The participants calmed for 15 minutes prior to the measurement of their blood pressure, which was done using an aneroid sphygmomanometer and stethoscope. The mean of three measures, obtained at intervals of 10 to 15 minutes, was documented as the exact blood pressure value. Fasting plasma glucose (FPG), serum triglyceride (TG), and serum high-density lipoprotein cholesterol (HDL-C) were measured using the enzymatic colorimetric method. The quantitative assessment of HbA1c in whole blood was determined using an immunofluorescence technique. A linear regression equation was developed based on the scatter plot relationship between HbA1c and fasting plasma glucose (FPG) to estimate the predicted HbA1c value. The predicted HbA1c (%) was calculated using the equation:

Predicted HbA1c = 1.35 + 0.772 × FPG (mmol/L), $R^2 = 0.428$, ($p<0.001$) (Figure 1)

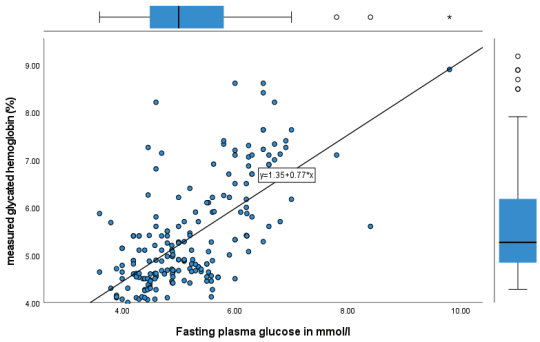

Figure 1. Regression of HbA1c vs FPG

The Hemoglobin Glycation Index (HGI) measures the variation in glycated hemoglobin levels. It represents the difference between an individual's actual HbA1c value and the predicted HbA1c value. The predicted HbA1c is computed by incorporating a date-matched fasting plasma glucose (FPG) level into a linear regression equation that quantifies the relationship between HbA1c and FPG in a reference population[10].

HGI = Measured HbA1c – Predicted HbA1c

The median HGI of the reference population serves as the cut-off point for categorizing individuals: High HGI group: HGI > median HGI and low HGI group: HGI ≤ median HGI[8].

MetS was defined based on the Modified National Cholesterol Education Program Adult Treatment Panel III (Modified NCEP-ATP III) criteria[11].

Data were analyzed using SPSS (Statistical Package for Social Sciences) version 27.0 for Windows. Continuous variables with an approximately normal distribution were presented as mean±standard deviation, and group comparisons were performed using the unpaired Student's t-test. Categorical variables were

expressed as percentages, with group comparisons conducted using the chi-square test. Pearson's correlation coefficient test was applied to assess the correlation between HGI groups and MetS, as well as its diagnostic components. Binary logistic regression was used to analyze risk factors for MetS and to evaluate the association between HGI and MetS. A p-value of <0.05 was considered statistically significant.

RESULTS

This study included 200 subjects (46.5% Males and 53.5% Females) with the mean age of 47.34±7.92 years. The mean±SD of fasting plasma glucose (FPG) in mmol/L was 5.24±0.56, glycated hemoglobin (HbA1c) in percent was 5.36±1.05, hemoglobin glycation index (HGI) was 0.0021±0.80 and median value of HGI was -0.15 respectively (Table 1). The prevalence of MetS was observed in 27.5% (55 cases) (Figure 2), and the median HGI was -0.15 (-0.53, 0.48). (Table 1). Among study population, abdominal obesity was found in 51%, while hypertriglyceridemia, low HDL-C, hypertension and hyperglycemia was evident in 33%, 5.5%, 24%, and 30% respectively (Figure 3). There were significant differences in age, WC, SBP, abdominal obesity between two HGI groups (p<0.05). No statistical differences were found in gender, DBP between the two groups (p>0.05) (Table 3). There were significant differences in TG between the two HGI groups (p<0.05) but no statistical differences were found in FPG and HDL-C (p>0.05) (Table 4). Table 5 shows the prevalence of MetS in study subjects between two HGI groups. Compared to the low HGI group, the prevalence of MetS was higher (50.5%) in the High HGI group that was statistically significant (p<0.001) (Table 5). Significant correlations of HGI was observed with abdominal obesity, hypertension, hyperglycemia and hypertriglyceridemia (p <0.05). except with HDL-C (p>0.05) (Table 6). We also found that age and HGI exhibited correlations with the prevalence of MetS. The high HGI group exhibited a 17.878-fold increase in the prevalence of MetS compared to the low HGI group (p<0.05) (Table 7). Elevated levels of HGI were significantly associated with components of abdominal obesity, hypertension, hyperglycemia, hypertriglyceridemia (p<0.05) except low HDL-C (p>0.05) (Table 8).

Table 1: Biochemical parameters of study subjects (n= 200)

Variables	Mean±SD
FPG (mmol/L)	5.24±0.56
HbA1c (%)	5.36±1.05
HGI	0.0021±0.80
Median of HGI	-0.15 (-0.53, 0.48)

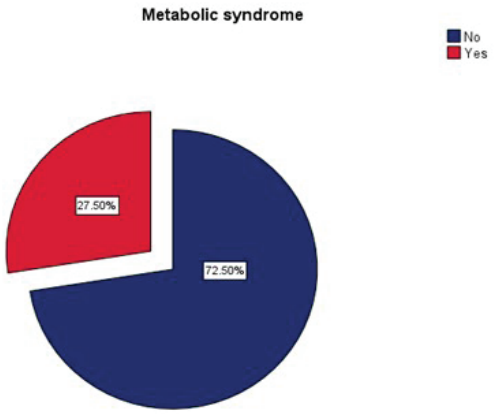

Figure 2: Pie diagram shows the percentage of metabolic syndrome present in the study population (n=200)

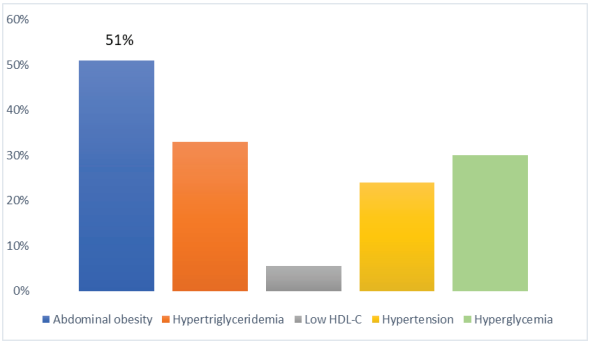

Figure 3. Bar diagram showing percentage of abdominal obesity, hypertriglyceridemia

low HDL-C hypertension and Hyperglycemia in study population (n=200)

Table 3: Baseline characteristics of study subjects in between HGI groups

	Low HGI (n=101)	High HGI (n=99)	p-value
Sex	Male (44,43.6%) Female (57,56.4%)	Male (49,49.5%) Female (50,50.5%)	0.400**
Age (years)	45.31±7.52	49.41±7.82	<0.001*
WC (cm)	84.46±6.72	88.37±8.07	<0.001*
SBP (mmHg)	120.09±8.48	127.84±14.04	<0.001*
DBP (mmHg)	69.06±7.23	70.35±7.15	0.205*

Data were expressed as mean±SD; p values were determined by Chi-square test** and Unpaired student t-test*.

Table 4: Comparison of biochemical parameters of study subjects in between Low and High HGI groups

Variables	Low HGI (n=101)	High HGI (n=99)	p-value
FPG (mmol/L)	5.15±0.80	5.25±1.04	0.448
TG (mg/dl)	116.77±34.20	154.93±52.01	<0.001
HDL-C (mg/dl)	51.18±6.50	49.77±6.58	0.129

Data were expressed as mean ± SD; p values were determined by Unpaired student t-test.

Table 5: Comparison of prevalence of metabolic syndrome between HGI groups

	Low HGI (n=101)	High HGI (n=99)	p-value
MetS	5(5%)	50(50.5%)	<0.001

p value was determined by Chi-square test

Table 6: Correlation Analysis of HGI Groups with MetS and Its Diagnostic Components

	r-value	p-value
MetS	0.637	<0.001
Abdominal obesity	0.279	<0.001
Hypertension	0.480	<0.001
Hyperglycemia	0.170	0.016
Hypertriglyceridemia	0.432	<0.001
Low HDL-C	0.132	0.062

Correlations were determined by Pearson's correlation coefficient test

Table 7: Logistic Regression Analysis of Risk Factors for MetS Prevalence

	OR (95%CI)	S. E	β	p-value
Age	1.216(1.132,1.306)	0.037	0.195	<0.001
HGI groups	17.878(6.119,52.232)	0.547	2.884	<0.001

Logistic regression analysis was done for adjusted odds ratio [OR (95%CI)]

Table 8: Logistic Regression Analysis showing association of MetS and its Components with HGI

	OR (95%CI)	S. E	β	p-value
Abdominal Obesity	2.349 (1.332,4.143)	0.289	0.854	0.003
Hypertension	6.644 (3.002,14.705)	0.405	1.894	<0.001
Hyperglycemia	2.237 (1.201,4.168)	0.318	0.805	0.011
Hypertriglyceridemia	7.799 (3.859,15.764)	0.359	2.054	<0.001
Low HDL-C	2.872 (0.739,11.158)	0.692	1.055	0.128

Binary logistic regression analysis was done for adjusted odds ratio [OR (95%CI)]

DISCUSSION

In this study, among 200 participants, 93 were male (46.5%) and 107 were female (53.5%). After anthropometric measurement and biochemical tests, 55 (27.50%) were diagnosed as MetS and remaining 145 (72.50%) were non-Mets. According to the median cut-off value of HGI (-0.15), 101 were found in low HGI group and 99 were in high HGI group. It was observed that low HGI group included half (50.5%) of the participants (Male 43.6%; Female 56.4%) with a mean age of 45.31±7.52 years and remaining (49.5%) were in high HGI group (male 49.5% and female 50.5%) with a mean age of 49.41±7.82 years. There were significant age differences ($p<0.05$) in between both groups but no statistical differences in gender distribution ($p>0.05$), which was consistent with the study of Marini et al.[11]

In this study, the prevalence of MetS in middle-aged individual was 27.5%, is similar to worldwide prevalence rate (25%) but lower than the value of 37% in Bangladesh[4,12] and higher in high HGI group (50.5%) compared to low HGI group (5%)[8]. The mean waist circumference (84.46±6.72 vs. 88.37±8.07) was significantly higher in subjects with high HGI and abdominal obesity showed statistically significant correlation with HGI ($P<0.05$). These findings are in accordance with the study carried out by Mi et al.[13]

It was evident that subjects with mean SBP (120.09±8.48 vs. 127.84±14.04), mean DBP (69.06±7.23 vs. 70.35±7.15) were higher in high HGI group. Hypertension had positive, statistically significant correlation ($p<0.05$) with

HGI in the patient with MetS. The findings of SBP were consistent with most of the studies observation whereas Nagayama et al.[14] observed decreased DBP with increasing HGI. Song et al.[15] did not find any association with DBP. In the current study DBP had also revealed no statistical differences in between two HGI groups ($p>0.05$).

We found that the mean TG (116.77±34.20 vs. 154.93±52.01) was higher in high HGI group than low HGI group and statistically significant ($p<0.05$). The mean HDL (51.18±6.50 vs. 49.77±6.58) was lower in high HGI group compared to low HGI group. Similar results were reported in studies done by Xie et al.[8] and Nagayama et al.[14]. There were also higher mean FPG (5.15±0.80 vs. 5.25±1.04) in high HGI group. Consistent findings were noted in the research conducted by van Steen et al.[16] The outcomes from several studies are not completely concordant. Lin et al.[17] and Nagayama et al.[14] reported the decreased levels of FPG and the significant association of high HGI with hyperglycemia but Marini et al.[11] observed the non-significant association between FPG and high HGI including significant association with hyperglycemia that is similar with the findings of this study.

The logistic regression analysis showed that the risk of MetS in the high HGI group was 17.878-fold for the risk of low HGI group and higher HGI was positively associated with the risk of abdominal obesity, hypertension, hypertriglyceridemia, hyperglycemia and MetS. The identical results were also noted in the studies conducted by Xie et al.[8] Marini et al.[11] and Lin et al.[18] However, there was no statistically significant association between HGI and low HDL-C in this study. The results of this study showed that high HGI is associated with multiple diagnostic factors of Mets. Therefore, high HGI is thought to be associated with MetS.

CONCLUSION

Correct recognition of the discrepancy between HbA1c and glycemic levels has important clinical implications for predicting the individuals with MetS. A high HGI identified individuals with increased susceptibility to components of MetS like abdominal obesity, hyperglycemia, hypertriglyceridemia, hypertension. Therefore, HGI can be considered as an independent predictor of MetS. Furthermore, large-scale research is required to reinforce this evidence before recommending its practical implementation.

Conflict of interest: None declared.

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Ethical clearance: Ethical clearance was issued by the Institutional Review Board (IRB) of Sir Salimullah Medical College, Dhaka, Bangladesh (IRB Ref No. 59.14.1100.031.18.001.23.5421).

Author's contribution: Concept and design: TRL; data collection, compilation and analysis: TRL, IAB, MKBRA; manuscript writing, editing, and final submission: TRL, IAB, MKBRA.

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