



## Original Article

# Atherogenic index of plasma and its association with cardiovascular disease risk factors among postmenopausal rural women of Bangladesh

Lingkan Barua<sup>a,\*</sup>, Mithila Faruque<sup>a</sup>, Palash Chandra Banik<sup>a</sup>, Liaquat Ali<sup>b</sup>

<sup>a</sup> Department of Noncommunicable Diseases, Bangladesh University of Health Sciences (BUHS), 125/1 Darus Salam, Mirpur-1, Dhaka 1216, Bangladesh

<sup>b</sup> Department of Biochemistry and Cell Biology, Bangladesh University of Health Sciences (BUHS), 125/1 Darus Salam, Mirpur-1, Dhaka 1216, Bangladesh

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## ABSTRACT

**Objectives:** There is absolute lacking of evidences on atherogenic index of plasma (AIP) and its association with cardiovascular disease (CVD) risk factors among postmenopausal women of Bangladesh. This prompted us to investigate this association between AIP and CVD risk factors among postmenopausal women in a rural setting.

**Methods:** This cross-sectional study recruited 265 postmenopausal women aged 40–70 years who visited a primary health-care center of Bangladesh. We used modified STEP-wise approach for the Surveillance of Noncommunicable diseases risk factors questionnaire of the World Health Organization to collect data on sociodemographic and behavioral risk factors. Physical measurements were carried out following the method described in the ‘noncommunicable disease risk factors survey Bangladesh 2010’. AIP was determined by the logarithmic transformation of triglyceride to high-density lipoprotein ratio, and association with CVD risk factors were examined by multiple linear regression analysis.

**Results:** Overall 35.5% respondents had a high risk level of AIP with a mean of  $0.16 \pm 0.25$ . After adjusting the confounders, CVD risk factors including duration of menopause ( $\beta = 0.606$ ,  $p = 0.043$ ), waist–hip ratio ( $\beta = 0.165$ ,  $p = 0.003$ ), 2-h plasma glucose ( $\beta = 0.118$ ,  $p = 0.04$ ), total cholesterol ( $\beta = 1.082$ ,  $p < 0.001$ ), low-density lipoprotein cholesterol ( $\beta = -1.044$ ,  $p < 0.001$ ), and metabolic equivalent of tasks ( $\beta = -0.171$ ,  $p = 0.003$ ) showed a significant association with AIP.

**Conclusion:** High AIP and its significant association with CVD risk factors demand proper lifestyle intervention for postmenopausal women of Bangladesh.

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## 1. Introduction

Globally cardiovascular diseases (CVDs) mortality among women is gradually increasing, and the burden is already higher in women than in men.<sup>1</sup> There is evidence that the risk of coronary artery diseases is higher among postmenopausal women compared to premenopausal and greater than the men of same age.<sup>2,3</sup> This risk differences are probably due to menopause which is characterized by estrogen deficiency leading to certain physiological changes in vascular system, body fat distribution, blood pressure, and lipid profile.<sup>4</sup> Again, these changes are responsible for

emergence of intermediate risk factors such as dyslipidemia, overweight, diabetes, or hypertension that indirectly affects the risk of CVD during postmenopausal period.<sup>5</sup> It has been suggested that high prevalence of these parameters is also responsible for high prevalence of metabolic syndrome and further increase of CVD risk among them.<sup>6</sup>

Atherogenic dyslipidemia due to alteration of lipid profile during postmenopausal period is a common phenomenon and considered as a part of metabolic syndrome. It is characterized by increase of triglyceride (TG) and low density lipoprotein (LDL-C) and decrease of high density lipoprotein (HDL-C) in blood.<sup>7</sup> This lipid triad abnormality increases atherogenicity among postmenopausal women compared with their premenopausal counterpart and considered as a strong risk factor of atherosclerotic heart diseases.<sup>8,9</sup> This atherogenic dyslipidemia has emerged as an important marker of future CVD event, and hence, different

\* Corresponding author.

E-mail addresses: [lingkanbarua@gmail.com](mailto:lingkanbarua@gmail.com) (L. Barua), [mithilafaruque@gmail.com](mailto:mithilafaruque@gmail.com) (M. Faruque), [palashchbanik@gmail.com](mailto:palashchbanik@gmail.com) (P.C. Banik), [liaquat304@gmail.com](mailto:liaquat304@gmail.com) (L. Ali).

research tried to address this issue by using various indexes of lipid profile. Among them, the atherogenic index of plasma (AIP), which is the logarithmic transformation of TG to HDL-C ratio, has showed strong predictability of atherosclerosis and CVD.<sup>10</sup> Other than simply the ratio, the AIP also correlates with the size of the lipoprotein particles (HDL, LDL, VLDL) that acts as the most sensitive markers of CVD.<sup>11,12</sup>

In Bangladesh, cardiovascular risk of postmenopausal women is a neglected issue and merely addressed by the policymakers. As per our knowledge, still no study conducted in Bangladesh to investigate the association between AIP and CVD risk factors among postmenopausal women. Therefore, the primary objective of this study was to assess the AIP and its association with CVD risk factors among postmenopausal rural women of Bangladesh. In addition to this, distribution of different physical and biochemical parameters of CVD were assessed to measure the risk factors burden among the study population.

## 2. Materials and methods

### 2.1. Recruitment of study population

This was a cross-sectional study conducted in the year 2016 among postmenopausal women residing in a rural area of Bangladesh. Total 265 postmenopausal women who were 40–70 years old were selected using convenient sampling technique. The sample size was determined by using a CVD risk prevalence resulted from a study conducted among postmenopausal women of Nigeria.<sup>13</sup> The participants were confirmed as having no CVD based on self-reported statement, clinical history, and medical record review. Menopausal status of them was defined as no menstrual bleeding for a period of at least 12 months and no other clinical condition causing amenorrhea.<sup>14</sup> Postmenopausal women with acute illness or unwilling to participate were excluded from the study.

### 2.2. Data collection procedures

Data were collected in the outpatient department of a primary health-care center situated in the village Karamtola of Gazipur district using a semistructured pretested questionnaire after informed written consent. A modified STEP-wise approach to the Surveillance of Noncommunicable diseases (NCD) risk factors (STEPS) questionnaire of the World Health Organization (WHO) was used to collect sociodemographic and behavioral information of the respondents.<sup>15</sup> Their physical activity (PA) level was measured using a Microsoft Excel spreadsheet template that was based on the Estimated Energy Requirement equation of the Dietary Reference Intakes Committee. Details methodology of PA measurement has been described elsewhere.<sup>16,17</sup>

### 2.3. Physical measurement

Physical measurements (anthropometric and blood pressure) were carried out following the method described in the ‘non-communicable disease risk factors survey Bangladesh 2010’ and measured by a trained female assistant with maintaining adequate privacy.<sup>18</sup> Among the anthropometric parameters, generalized obesity was categorized as per the WHO guideline<sup>19</sup> and waist–hip ratio according to the cut-off value of the International Diabetic Federation for women.<sup>20</sup> Blood pressure was defined in accordance with the ‘Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7),’ or a person was a known hypertensive or on antihypertensive drug.<sup>21</sup> To assure quality of measurements, we

followed and maintained three criteria’s (1) use of standard measurement protocol, (2) training by an experience national level trainer, (3) application of robust equipment, and (4) pre-testing to evaluate the whole procedure.

### 2.4. Biochemical measurement

At the end of physical measurement, the participants of the study underwent recommended blood tests in the laboratory of selected primary health-care center. Blood sample was collected from those who came with 8–12 h overnight fasting state. For this purpose, 5 cc of venous blood was collected with aseptic precaution, and again 3 cc was collected after two hours of 75 g glucose intake. Oral glucose tolerance test was carried out for those who did not know their glycemic status. Diabetes was diagnosed based on WHO criteria<sup>22</sup> and self-statement of a person as known diabetic or on antidiabetic medication. Lipid profile including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) was also measured at fasting state. The low-density lipoprotein cholesterol (LDL-C) was calculated according to the Friedewald formula using TC, HDL-C, and TG.<sup>23</sup> To define lipid abnormality, Adult Treatment Panel III cut-off value was followed.<sup>24</sup> The AIP was calculated as the logarithmic transformation of TG to HDL-C ratio and categorized as low (<0.11), intermediate (0.11–0.24), and high (>0.24).<sup>10</sup> All the biochemical tests were performed by Olympus AU400 analyzer.

### 2.5. Cardiovascular risk factors analyzed

In this study, to assess the distribution of CVD risk factors and examine their association with AIP, we analyzed the CVD risk factors such as nonmodifiable risk factors: age, age at menarche, age at menopause, duration of menopause, and family history of NCD; behavioral risk factors: use of oral contraceptive pills (OCs), tobacco use, extra salt intake, and physical inactivity; and cardiometabolic risk factors: generalized obesity, central obesity, hypertension, diabetes (fasting plasma glucose and 2-h plasma glucose), hypercholesterolemia, low level of HDL-C, and high level of TG and LDL-C.

### 2.6. Ethical approval

Written ethical approval was taken from the Ethical Review Committee of Bangladesh University of Health Sciences.

## 3. Data processing and analysis

Data were analyzed using the Statistical Package for Social Science version 20.0. Categorical variables were presented using frequency and proportion at 95% confidence intervals. Continuous variables were presented as mean, standard deviation, median, and interquartile range. The multiple linear regression analysis was run between AIP and other CVD risk factors to show the association between them. In the adjusted model, several confounders (age of menarche, body mass index, systolic blood pressure, diastolic blood pressure, and fasting blood glucose) were controlled to examine the association. The value of standardized coefficient  $\beta$  was considered statistically significant at a threshold of  $p < 0.05$ .

## 4. Results

### 4.1. Characteristics of study population

Table 1 represents sociodemographic, reproductive, and behavioral characteristics of the study population. We recruited

**Table 1**  
Sociodemographic, reproductive, and behavioral characteristics of the study population,  $n = 265$ .

Characteristics	Mean $\pm$ SD	Median (IQR)	$n$ (%)
<b>Sociodemographic</b>			
Age	53.51 $\pm$ 7.5	52 (49–60)	
Education status			
Illiterate			161 (60.8)
Literate			104 (39.2)
Occupation			
Housewife			239 (90.2)
Service holder			26 (9.8)
Monthly income (BDT)	12,279.34 $\pm$ 7920.26	10,000 (7000–15,250)	
Monthly income groups (BDT) <sup>a</sup>			
<4906 (low income)			24 (9.1)
4907–19,488 (lower-middle income)			187 (70.6)
19,489–60,252 (upper-middle income)			53 (20)
>60,252 (high income)			1 (0.4)
<b>Reproductive</b>			
Age of menarche	13.54 $\pm$ 1.78	13 (12–15)	
Age of onset of menopause	44.83 $\pm$ 5.22	45 (40–48)	
Duration of menopause	8.79 $\pm$ 6.45	7 (3–13)	
<b>Behavioral</b>			
Current tobacco use <sup>b</sup>			
Smoking			4 (1.5)
Smokeless			119 (44.9)
Extra salt intake <sup>c</sup>			118 (44.5)
Physical activity levels			
Active			111 (41.9)
Inactive			154 (58.1)
Oral contraceptive pill use			91 (34.3)

SD, standard deviation; IQR, interquartile range; BDT, Bangladeshi Taka.

<sup>a</sup> According to the 2006 per-capita gross national income (GNI) and the World Bank calculation.

<sup>b</sup> Tobacco use in the past 30 days.

<sup>c</sup> Dietary salt intake  $\geq$  5 g per day.

265 postmenopausal women with a mean age of 53.51  $\pm$  7.5 years. Their mean age at menarche and menopause was 13.54  $\pm$  1.78 and 44.83  $\pm$  5.22 years, respectively. More than half of the respondents (60.8%) were illiterate, and nearly three fourth of them (70.6%) were from lower-middle income economic background. Among the CVD risk behaviors, nearly half of the respondents (44.9%) were smokeless tobacco users, and same proportion (44.5%) of postmenopausal women also used to take extra salt with their meal. Majority of the study population (90.2%) were housewives and physically inactive (58.1%). Overall 91 respondents (34.3%) gave the history of OCP use for birth spacing.

#### 4.2. Physical and biochemical risk factors of CVD

Table 2 depicts distribution of various physical and biochemical parameters among postmenopausal women. Among the indicators of obesity, although the mean body mass index (23.26  $\pm$  4.74) was within normal range, the mean waist–hip ratio (0.89  $\pm$  0.07) was higher than the cut-off value. In accordance with this finding, the proportion of central obesity (73.2%) was also found ten times higher than the generalized obesity (7.5%). A total of 111 (41.9%) participants were detected as hypertensive, and among them, the proportion of systolic hypertension was more than the diastolic hypertension (28.7% vs 21.5%). Among the biochemical parameters, mean AIP was 0.16  $\pm$  0.25, and more than half of the participants (52.7%) had elevated level of AIP. Again, among the participants with elevated AIP, majority (35.5%) had the ‘high-risk’ level of AIP compared with ‘intermediate-risk’ level (17.2%). The proportion of hypercholesterolemia, hypertriglyceridemia, high LDL-C, and low level of HDL-C were 25.7%, 52.3%, 20.8%, and 26.4%, respectively.

#### 4.3. Association between AIP and CVD risk factors

Multiple linear regression analysis was carried out to investigate the association between AIP and CVD risk factors. In the adjusted model, the CVD risk factors including duration of menopause ( $\beta = 0.606$ ,  $p = 0.043$ ), waist–hip ratio ( $\beta = 0.165$ ,  $p = 0.003$ ), 2-h plasma glucose ( $\beta = 0.118$ ,  $p = 0.04$ ), TC ( $\beta = 1.082$ ,  $p < 0.001$ ), LDL-C ( $\beta = -1.044$ ,  $p < 0.001$ ), and metabolic equivalent of tasks ( $\beta = -0.171$ ,  $p = 0.003$ ) were significantly associated with the AIP of the study subjects (Table 3).

### 5. Discussion

Findings of the present study revealed a greater proportion of Bangladeshi postmenopausal women had a ‘high-risk’ level of AIP and it was significantly associated with different CVD risk factors.

This study demonstrated high CVD risk factors burden among postmenopausal women including smokeless tobacco use, high dietary salt intake, and physical inactivity. Among these behavioral risk factors, proportion of smokeless tobacco use was eleven times higher (4% vs 45%), and physical inactivity was similar (55% vs 58.1%) when compared with an Indian study among postmenopausal women.<sup>25</sup> Our finding about high dietary salt intake among rural women is consistent with the findings of a previous study conducted in a rural community of Bangladesh.<sup>26</sup> Uncontrolled and untreated behavioral risk factors will contribute to develop intermediate risk factors of CVD including obesity, hypertension, diabetes, and abnormal lipid profile. In this study, these risk factors were highly proportionately distributed and showed similarity with other studies for central obesity,<sup>25,27,28</sup> hypertension,<sup>27,28</sup> diabetes,<sup>27,28</sup> hypercholesterolemia,<sup>27,28</sup> and hypertriglyceridemia<sup>27,29</sup> among postmenopausal

**Table 2**  
Physical and biochemical parameters of cardiovascular diseases among the study population,  $n = 265$ .

Parameters	Mean $\pm$ SD	Median (IQR)	$n$ (%)
BMI ( $\text{kg}/\text{m}^2$ )	23.26 $\pm$ 4.74	23.05 (20.13–26.02)	
Nonobese			245 (92.5)
Generalized obese ( $\geq 30 \text{ kg}/\text{m}^2$ )			20 (7.5)
WHR	0.89 $\pm$ 0.07	0.89 (0.85–0.94)	
Nonobese			71 (26.8)
Centrally obese ( $>0.85$ )			194 (73.2)
SBP (mmHg)	120.56 $\pm$ 20.17	120 (100–140)	
Normal to prehypertension			189 (71.3)
Hypertension ( $\geq 140 \text{ mmHg}$ )			76 (28.7)
DBP (mmHg)	76.72 $\pm$ 11.49	80 (70–85)	
Normal to prehypertension			189 (71.3)
Hypertension ( $\geq 90 \text{ mmHg}$ )			57 (21.5)
FPG (mmol/l)	5.91 $\pm$ 2.39	5 (5–6)	
Nondiabetic			217 (81.9)
Diabetic ( $\geq 7.0 \text{ mmol/l}$ )			48 (18.1)
2-h PG (mmol/l), $n = 223$	6.24 $\pm$ 1.97	6 (5–7)	
Nondiabetic			215 (96.4)
Diabetic ( $\geq 11.0 \text{ mmol/l}$ )			8 (3.6)
TC (mmol/l)	5.23 $\pm$ 1.3	5.12 (4.36–6.19)	
Desirable to borderline high			197 (74.3)
Hypercholesterolemia ( $\geq 6.2 \text{ mmol/l}$ )			68 (25.7)
HDL-C (mmol/l)	1.1 $\pm$ 0.3	1 (1–1)	
Low ( $<1.0 \text{ mmol/l}$ )			70 (26.4)
High			195 (73.6)
LDL-C (mmol/l)	3.19 $\pm$ 1.18	3 (2–4)	
Optimal to borderline high			210 (79.2)
High ( $>4.1 \text{ mmol/l}$ )			55 (20.8)
TG (mmol/l)	1.86 $\pm$ 1.13	2 (1–2)	
Normal to borderline high			153 (57.7)
High ( $>2.3 \text{ mmol/l}$ )			112 (52.3)
AIP	0.16 $\pm$ 0.25	0.13 (–0.03 to 0.32)	
Low risk ( $<0.11$ )			124 (47.3)
Intermediate risk (0.11–0.24)			45 (17.2)
High risk ( $>0.24$ )			93 (35.5)

SD, standard deviation; IQR, interquartile range; BMI, body mass index; WHR, waist–hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; 2-h PG, 2-h plasma glucose; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; AIP, atherogenic index of plasma.

**Table 3**  
Association between AIP and CVD risk factors among postmenopausal rural women,  $n = 265$ .

CVD risk factors	Standardized coefficient $\beta$	$p$ value
Age	0.601 (–0.003 to 0.04)	0.087
Age at menopause	–0.488 (–0.043 to 0.000)	0.053
Duration of menopause	–0.606 (–0.043 to –0.001)	0.043*
WHR	0.165 (0.195–0.977)	0.003*
2-h PG	0.118 (0.001–0.027)	0.04*
TC (mmol/l)	1.082 (0.148–0.247)	0.000*
LDL-C (mmol/l)	–1.044 (–0.254 to –0.149)	0.000*
MET	–0.171 (0.000–0.000)	0.003*

Multiple linear regression analysis was done (adjusted).

All the precisions are estimated at 95% confidence interval.

AIP, atherogenic index of plasma; CVD, cardiovascular diseases; WHR, waist–hip ratio; PG, plasma glucose; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; MET, metabolic equivalent of tasks.

\*The standardized coefficient  $\beta$  was statistically significant at a threshold of  $p < 0.05$ .

women. Like the present study, high mean level of TC, LDL-C, TG, and low level of HDL-C was also found among postmenopausal women of Nigeria and Bangladesh.<sup>30,31</sup> Several factors might contribute to high CVD risk factors burden among Bangladeshi postmenopausal women. The most important factor is estrogen deficiency which is thought to be responsible for a significant proportion of increased cardiometabolic risk factors among postmenopausal women.<sup>32</sup> Other than estrogen deficiency, low socioeconomic condition of rural areas with high proportion of illiterate respondents might be an underlying factor of higher CVD risk factors burden of the present study. This is because previous study reported that CVD risk factors

are highly distributed among the population with low education and low socioeconomic condition.<sup>33</sup>

The mean AIP of the present study was similar to that of the study of Nwagha et al<sup>30</sup> conducted among Nigerian postmenopausal women and less than that of the Nansseu et al<sup>34</sup> conducted among Cameroonian postmenopausal women. The possible cause of this variation of mean AIP might be the inclusion or exclusion of obese participants in the study. The Nigerian study excluded obese participants while the Cameroonian study included. The mean BMI of Cameroonian study was  $31.56 \pm 5.27 \text{ kg}/\text{m}^2$  which reflected the higher burden of generalized obesity among the study population. Compared with the study of Nansseu et al, the mean BMI of our study was much lower and within normal range. Evidence suggested that the BMI is the strongest predictor of AIP compared with other anthropometric measures.<sup>35</sup> Moreover, the Cameroonian study was conducted in an urban area, whereas we conducted our study in a rural area. Higher BMI among urban residents and significant urban–rural difference was also reported by a nationally representative study conducted among 38 lower-middle income countries.<sup>36</sup> Other than the fact of BMI, the component of AIP from which it derived (TG and HDL) had a possible role in lower level of mean AIP in the present study. This is because reduction in TG and/or an increase in HDL-C at population level would result in consequential reduction in AIP. In our study, three fourth of the postmenopausal women had increased level of HDL-C and more than half had increased level of TG; thus, the AIP became low compared with other aforementioned studies. However, although the mean AIP was less than the other studies, more than half of the respondents of the present study had elevated AIP

(>0.1). At this cut-off value, the proportion of elevated AIP of our study also showed agreement with other studies of Bangladesh<sup>31,37</sup> and Africa<sup>30,34</sup> for postmenopausal women. However, according to CVD risk classification based on AIP revealed that higher proportion of Bangladeshi women was at the 'high-risk' category (AIP > 0.24) compared with African postmenopausal women.

We obtained a significant association between AIP and certain CVD risk factors. Among the nonmodifiable risk factors, significant negative association was found for duration of menopause. In accordance with this finding, significant association of AIP with duration of menopause was previously reported by an aforementioned study.<sup>30</sup> But that Nigerian study found a positive association that concurs with our results. On the other hand, although they showed the significant increased of AIP with 10 years and 20 years duration of menopause, they did not demonstrate any significant difference between these two categories of postmenopausal duration ( $p = 0.116$ ). Again another study<sup>34</sup> reported no association between AIP and duration of menopause that contradicted with the present study and the study of Nigeria.<sup>30</sup>

Several modifiable CVD risk factors including waist–hip ratio, 2-h plasma glucose, and TC showed significant positive association with AIP. For TC, similar association was also reported by the aforementioned study for postmenopausal women of Cameroon.<sup>34</sup> Again, a score matching case–control study of China reported same association between AIP and TC ( $r = 0.092$ ,  $p < 0.001$ ) for postmenopausal women.<sup>38</sup> Evidences for association of AIP with waist–hip ratio and 2-h plasma glucose are currently lacking for postmenopausal women. However, a study among the Chinese men showed significant positive association between AIP and waist circumference, which is one of the precursors of waist–hip ratio. Another Bangladeshi study showed centrally obese (determined by waist–hip ratio) postmenopausal women had significant difference compared with nonobese for AIP.<sup>37</sup> Regarding the association of blood glucose and AIP, Nansseu et al measured fasting blood glucose as a tool to diagnose diabetes and found significant positive association with AIP. Although this finding was contradicted with our study, another case–control study among prediabetes subjects found significant positive association between AIP and 2-h plasma glucose ( $p = 0.001$ ).<sup>39</sup>

The present study detected significant negative association of AIP with LDL-C and metabolic equivalent of tasks of physical activity. Similar association between these two was also reported by other studies among general population for LDL-C and physical activity.<sup>40</sup> There is evidence that among the vital lifestyle changing issues, moderate to vigorous physical activity has more role than the dietary modification to reduce the AIP.<sup>41</sup> However, contradictory to the aforementioned findings, an Iranian randomized controlled trial reported that dietary modification could modulate the atherogenicity and reduce the AIP.<sup>42</sup> As per the equation of AIP, if we want to reduce it, we should have to either reduce the TG level and or increase the HDL-C. There is no direct implication of LDL-C in the AIP equation; however, it is known that the increase in TG levels increases the level of small dense LDL cholesterol, which finally causes an increased risk for the development of cardiovascular disease.<sup>43</sup>

The study had some limitations that might impact the findings. The most important one is the cross-sectional design that does not allow drawing inferences about causality. Another issue is the relatively small sample size that limits the implication of the results for all postmenopausal women. Again, the behavioral information of the study might be associated with recall bias.

Other than these few limitations, this is the first study of Bangladesh that attempted to evaluate the association between AIP and CVD risk factors in a high risk but neglected population. Lack of research and lack of data on their cardiovascular health make

difficulties for the policymakers to take an initiative. Hence, the findings of this study is an important one that provides baseline information and demands further large scale study to establish the fact among AIP, lipid parameters, and CVD.

### Key messages

#### What is already known?

Atherogenic index of plasma is a predictor of cardiovascular diseases.

#### What this study adds?

For the first time, atherogenic index of plasma and its association with CVD risk factors are assessed among postmenopausal women of Bangladesh in a rural setting.

## 6. Conclusion

The high proportion of elevated AIP among postmenopausal women is alarming us about the emerging burden of CVD among them. Again, significant association of AIP with CVD risk factors demand proper preventive approach related to reduction of AIP and subsequent CVD risk for Bangladeshi postmenopausal women.

## Contributors

L.B. conceptualized the research idea and prepared the manuscript; P.C.B. provided support to L.B. in designing the study and acquisition and analysis of data; M.F. interpreted the findings and helped in data presentation; L.A. critically revised the draft for final version and gave the intellectual input as supervisor to submit the manuscript.

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## Conflict of interest

All authors have none to declare.

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