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Prevalence and Correlates of Cardiometabolic Multimorbidity among Hypertensive Individuals: a Cross-Sectional Study in Rural South Asia- Bangladesh, Pakistan, and Sri Lanka

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Running head: **Cardiometabolic Multimorbidity in South Asians**

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Abstract

Objective: To determinate the prevalence and correlates of cardiometabolic multimorbidity (CMM), and their cross-country variation among individuals with hypertension residing in rural communities in South Asia..

Design: A cross-sectional study.

Setting: Rural communities in Bangladesh, Pakistan, and Sri Lanka.

Participants: A total of 2288 individuals with hypertension aged ≥ 40 years from the ongoing COBRA-BPS (Control of Blood Pressure and Risk Attenuation- Bangladesh, Pakistan, and Sri Lanka) clinical trial.

Main outcome measures: CMM was defined as the presence of ≥two of the conditions: diabetes, chronic kidney disease (CKD), heart disease, and stroke. Logistic regression was done to evaluate the correlates of CMM.

Results: About 25.4% (95% CI (23.6, 27.2)) of the hypertensive individuals had CMM. Factors positively associated with CMM included being Bangladeshi (OR=3.28,95% CI (2.41,4.47)) or Sri Lankan (4.98,(3.76,6.58)) versus Pakistani, advancing age (2.44,(1.67,3.58) for 70 years and over versus 40 to 49 years), higher waist circumference (2.20, (1.45,3.33) for Q2~Q3, and 2.21,(1.52,3.22) for Q3 and above), and higher levels of triglyceride (1.01, (1.01,1.02) per 1 mg/dL increase). A lower odds of CMM was associated with being physically active (0.73,(0.57,0.94)) and higher high- density lipoprotein levels (0.92,(0.87,0.98) per 1 mg/dL increase). An inverted J-shaped association between International Wealth Index and CMM was found (P for nonlinear=0.049), suggesting higher risk in the middle than higher or lower socioeconomic strata.

Conclusions: CMM is highly prevalent in rural South Asians affecting 1 in 4 individuals with hypertension. There is an urgent need for strategies to concomitantly manage hypertension, cardiometabolic comorbid conditions, and associated determinants in South Asia. (n=255)

Keywords: Cardiometabolic multimorbidity, South Asia, hypertension, obesity

Strengths and limitations of the study:

- This study is the first to evaluate the prevalence and correlates of cardiometabolic comorbidity (CMM) in a representative sample aged≥ 40 years with hypertension from rural communities in Bangladesh, Pakistan, and Sri Lanka.
- Our study used a uniform study design, door to door sampling of individuals, random selection of clusters, consistent definition of variables and outcomes (e.g. standardized measurements of serum creatinine), and standardized study procedures in all three countries.
- A causal relationship between covariates and cardiometabolic comorbidity (CMM) cannot be inferred due to the cross-sectional design of the study.
- We did not have data on covariates such as healthcare access, dietary habit, psychological stress, and physiological biomarkers, which may additionally explain cross-country variation in multimorbidity.
- Our findings may not be generalized to urban-residing individuals free of hypertension or younger than 40 years in each country.

Introduction

Cardiometabolic multimorbidity (CMM) defined as the coexistence of two or more of the following chronic conditions (diabetes, heart disease, stroke, chronic kidney disease (CKD)) is being increasingly recognized as a global public health challenge [1, 2]. Compared with a single cardiometabolic disease, multimorbidity from these conditions is associated with multiplicative risk of mortality and cognitive decline [1, 3].

Individuals from South Asia have been shown to be more susceptible to cardiometabolic and other chronic conditions compared to other ethnic groups[4, 5]. In part, this is postulated to be due to higher visceral fat mass as South Asians have been shown to have higher amounts of abdominal adipose than Caucasians[6, 7], and abdominal obesity is better predictors for cardiovascular diseases (CVD) risk and diabetes than body mass index (BMI)[8]. Furthermore, most of South Asia is still rural with significant disparities in access to healthcare, and mortality from CVD has shown to be higher than in urban areas[9]. However, the prevalence, and correlates of CMM in rural South Asian countries have not been reported.

Therefore, we analyzed baseline data from the ongoing COBRA-BPS (Control of Blood Pressure (BP) and Risk Attenuation- Bangladesh, Pakistan, and Sri Lanka) trial on 2288 hypertensive individuals in rural communities in Bangladesh, Pakistan, and Sri Lanka with the following objectives: 1) To examine the prevalence of CMM, 2) to determine the sociodemographic characteristics, lifestyle factors, and clinical risk factors associated with CMM. We also sought to determine whether BMI or waist circumference was a stronger determinant of CMM in this population.

We hypothesized that: 1) the prevalence of CMM is high, and varies among hypertensive individuals in rural communities across the three South Asian countries; 2) the cross-country variation in CMM will only partially be accounted for by differences in sociodemographic,

lifestyle, and clinical risk factors; 3) waist circumference will be more strongly associated with CMM than BMI.

Methods

Population

The present study was performed using baseline data from COBRA-BPS (Control of Blood Pressure (BP) and Risk Attenuation- Bangladesh, Pakistan, and Sri Lanka) full-scale study. The study methodology has been described early [10]. Briefly, COBRA-BPS full-scale study is an ongoing two-year cluster randomized controlled trial among 2643 hypertensive adults from 30 randomly selected rural clusters (communities), 10 clusters each, in Bangladesh, Pakistan, and Sri Lanka. In each country, clusters selection was stratified by distance (≤ 2.5km for near and >2.5 for far) from the government primary care clinics such that there were 6 near and 4 far clusters in each country. Individuals in each cluster were screened using door-to-door sampling method. The inclusion criteria for COBRA-BPS were age ≥40 years, hypertension (defined as sustained elevation of systolic blood pressure (SBP) to ≥140 mmHg, or diastolic blood pressure (DBP) to ≥90 mmHg based on two readings from 2 separate days, or receiving antihypertensive medications), and residents in the selected clusters. Individuals were excluded if they had severe physical incapacity, were pregnant, had advanced diseases (on dialysis, liver failure, and other systemic diseases), or were mentally comprised leading to the incapability of giving consent.

Supplemental Fig. S1 shows the study flow diagram. Of the 2977 hypertensive individuals from 30 randomly selected clusters in 3 countries, 2643 were enrolled in the clinical trial after excluding 334 individuals for various reasons (Supplemental Fig. S1). Of the 2643 hypertensives

recruited, 355 (13.4%) were excluded because they missed data on diabetes (n=217), CKD (n=289), and heart disease (n=64), leaving 2288 for the final analysis. The study protocol was approved by relevant Ethical Review Committee in Singapore, Bangladesh, Pakistan, Sri Lanka, and UK. All study participants provided written informed consent.

Measurements

Sociodemographic variables were age (40~49,50~59,60~69,70 and over years), gender, education (formal vs. informal education), and marital status (married vs. single, divorced, or widowed). Economic status was assessed by International Wealth Index (IWI) [11]. IWI is based on a household's ownership of selected assets, access to basic service, and characteristics of the house and is estimated by principal component analysis. The score of IWI ranges from 0 to 100 and, in the current study, was classified into four groups via its quartiles (IWI<43, 43≤IWI<60, 60≤IWI<73, IWI≥73). Lifestyle factors included smoking status (current smoker vs. noncurrent smoker) and physical activity. Physical activity was evaluated by the short version of the International Physical Activity Questionnaire (IPAQ)[12] and was classified as inactive, minimally active, and highly active. BMI was calculated as weight (in kilogram)/height (in meters)^2 and was categorized as underweight (BMI<18.5), normal (18.5≤BMI<23), overweight (23≤BMI<27.5), and obesity (BMI≥27.5)[13]. Waist circumference was grouped into four categories using gender-specific quartiles (for male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm). Heart disease was ascertained based on self-reported physician diagnosis and stroke was determined according to the WHO definition[14]. Family history of CVD was determined according to self-reported family history of heart disease or stroke.

An overnight fasting blood sample was collected to measure serum creatinine (measured on Beckman DU), lipids (measured on Roche Hitachi-912), and plasma glucose (measured on Beckman Synchron Cx-7/Delta) in each country. Serum creatinine measurements were calibrated to isotope dilution mass spectrometry (IDMS) traceable values. Urine albumin and creatinine excretion were measured on spot urine samples by nephelometry using the Array Systems method on a Beckman Coulter. All tests were done in an accredited laboratory in each country. Diabetes was defined as a fasting plasma glucose (FPG) ≥126 mg/dL or self-reported use of anti-diabetic medication. CKD was defined as the presence of estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73m^2 or urine albumin and creatinine ratio (UACR)≥30 mg/g. Glomerular filtration rate (GFR) was estimated using the original Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation[15]. UACR was determined by urine albumin divided by urine creatinine.

Statistical analysis

The outcome measurement of this study was the presence of CMM, defined as having two or more of the following cardiometabolic conditions: diabetes, CKD, heart disease, and stroke.

Comparison of characteristics between individuals with and without CMM was performed using independent sample t-test for continuous variables and Chi-Square test for categorical variables. When continuous variables were not normally distributed, Mann–Whitney U test was used. We used Cochran-Armitage trend test to measure the association of waist circumference categories with different measurements of cardiometabolic conditions - individual and multimorbid.

We fitted generalized estimating equation (GEE) logistic regression models with an exchangeable correlation matrix for CMM to account for the hierarchical nature of the data

within the villages (clusters) in each country. Odds ratios (OR) and 95 % confidence intervals (CI) were presented. Covariates considered clinically relevant or found to be associated with CMM in previous literature or in the current bivariate analysis at P<0.15 were included in the multivariate models. Three models were built by sequentially entering the covariates in three individual blocks. In model 1, only country was included; in model 2, we included age, gender, education, marital status, IWI, and BMI besides country; in the last model, we additionally added physical activity, smoking, waist circumference, family history of CVD, high-density lipoprotein (HDL), and triglyceride. Because adjusted analysis suggested possible nonlinear associations of CMM with IWI and waist circumference, we further examined their associations with restricted cubic splines by modeling the two covariates as continuous variables[16]. We used '%RCS_Reg' SAS macro[17] to perform adjusted analysis with 5 knots (5%, 25%,50%,75%, and 95% percentiles) specified.

We also investigated two-way interactions between country and other variables in the last model to assess the presence of a country-specific effect. Significant interactions were interpreted by the ratio of odds ratios (ROR)[18] and subgroup analysis by country.

All analyses were conducted using SAS version 9.4, and all hypothesis testing was 2-tailed with $P < 0.05$ set as statistically significant.

Patient and public involvement statement

Patients were not involved in the conception, design or interpretation of this study.

Results

Baseline characteristics

The baseline characteristics of 2288 individuals with hypertension are shown in Table 1. The overall prevalence of CMM was 25.3% (n=581). The mean (SD) age was 59.0 (11.3) years ; 64.3% (n=1471) were female. The mean (SD) BMI and waist circumference were 24.7 (5.0) Kg/m^2 and 88.2 (12.8) cm, respectively.

Individuals with CMM were older, better educated, less likely to be married, and had higher IWI scores than were those without. They also had lower levels of physical activity, higher BMI, higher waist circumference, and elevated levels of triglyceride, and were more likely to have a family history of CVD and to be Sri Lankan. In contrast, no other baseline characteristics were associated with CMM (Table 1).

Supplementary table S1 shows the characteristics of individuals included (n=2288) and excluded (n=355) from the current analysis. Compared with individuals excluded, those included had higher education, higher IWI score, higher levels of physical activity, and were more likely to have a family history of CVD and to reside in Bangladesh and Sri Lanka. Country-specific baseline characteristics are summarized in supplementary tables S2-S4.

Cardiometabolic multimorbid conditions

Table 2 shows bivariate associations between various measurements of cardiometabolic conditions and waist circumference quartiles. Hypertensive individuals with a single additional cardiometabolic condition, two or more (cardiometabolic comorbidity), and three or more cardiometabolic conditions accounted for 35.3% (95% CI:33.3%-37.3%), 25.4% (95%CI:23.6%-27.2%), and 5.6% (95% CI:4.7%-6.7%), respectively. CKD was the most prevalent cardiometabolic condition (38.3%,95% CI (36.3,40.3)).

CMM and waist circumference

The prevalence of CMM increased across the first 3 quartile groups of waist circumference, and slightly dropped in the highest quartile (P value for linear trend<0.001) (Table 2). We also observed a significant linear trend for three or more cardiometabolic conditions, diabetes, heart disease, and stroke, but not for CKD (Table 2). Corresponding country-specific results are reported in supplementary Table S5-S7. CMM was most prevalent among participants from Sri Lanka (36.3% (95%CI:33.0%-39.8%)), followed by those from Bangladesh (27.4% (95%CI:24.3%-30.5%)), and Pakistan (10.2% (95%CI:8.0%-12.7%)).

The bivariate associations between morbidity pairs and waist circumference are presented in Table S8. The most frequently observed pair was diabetes and CKD (10.1%, 95% CI:8.9%-11.4%), and least observed was diabetes and stroke (1.2%,95% CI:0.8%-1.7%). An increasing trend across the quartile groups of waist circumference was observed for coexisting diabetes and CKD (P for linear trend<0.001). Diabetes and CKD were also the most prevalent pair in all three countries, but the prevalence of other pairs in each country differed from that of the whole sample and each other (Supplementary tables S9-S11).

Factors associated with CMM

In multivariate-adjusted analysis, living in Bangladesh or Sri Lanka (versus Pakistan), older age, higher IWI, higher waist circumference, and elevated levels of triglyceride were significantly associated with a higher odds of CMM, while being physically active and higher levels of HDL were associated with a lower odds of CMM (Model 3 in Table 3). BMI was not significantly associated with CMM in model 3. Multivariable-adjusted restricted cubic spline analyses suggested no evidence of a nonlinear association between waist circumference and CMM (Fig1A, P for nonlinear trend=0.561) but a weak nonlinear association between IWI and CMM (Fig1B, inverted J-shaped, p for nonlinear trend=0.049). The analysis of interaction showed that

country significantly modified the associations between CMM and three other covariates: age (P for interaction <0.001), history of CVD (P for interaction=0.007), and HDL (P for interaction=0.002) (supplementary Tables S12 and S13).

Discussion

Data on multimorbidity are limited from South Asian countries[19-24]. This study is the first to evaluate the prevalence and correlates of CMM in a representative sample aged≥ 40 years with hypertension from rural communities in Bangladesh, Pakistan, and Sri Lanka. We observed an alarmingly high prevalence of CMM –up to 25%- in rural South Asians with hypertension, and it was higher in Sri Lanka than the other two countries. CKD was the most common comorbid condition, followed by diabetes, stroke, and heart disease. CKD and diabetes dominated all the morbidity pairs, and were found in 10% of the population with hypertension. Individuals residing in Bangladesh and Sri Lanka (vs. Pakistan) had higher odds of CMM regardless of sociodemographics, economic status, lifestyles, and clinical factors. Being older, lower levels of physical activity, higher waist circumference, lower levels of HDL, and higher levels of triglyceride, each, were independently associated with the presence of CMM. Waist circumference was a stronger correlate of CMM than BMI. An inverted J-shaped association was found between IWI and the odds of CMM. Our findings add to the current knowledge on the epidemiology of CMM in rural South Asians, and underscore the importance to develop prevention and treatment strategies to target individuals at risk of or with CMM.

There are very few reports on CMM from South Asia, and the types of conditions vary. In a study from urban areas of Delhi, Chennai, and Karachi, 9.4% of adults aged>=20 years had two

or more of hypertension, diabetes, heart disease, stroke, and CKD [24]. Our study in hypertensive community dwellers from rural areas in 3 South Asian countries indicated a higher prevalence with one in four individuals having two additional cardiometabolic co-morbid conditions. The implications of findings are significant as health systems are more fragmented in rural compared to urban areas, highlighting the urgency to provide comprehensive services for vascular disease prevention and management in rural South Asia.

It is interesting that we found an inverted J-shaped association between socioeconomic status and CMM, which is in contrast with studies in developed countries showing that lower economic status was a risk factor for multimorbidity [25-27]. Studies from low- and middle- income countries show a positive association of chronic non-communicable diseases with a socioeconomic gradient [21, 23, 28]. However, the non-linear relationship of CMM in our study suggested that cardiometabolic risk was highest in those in the middle socioeconomic strata (SES), compared to the highest and the lowest quartile of SES. The latter finding may be suggestive of an early reversal of social gradient for CMM and is consistent with our earlier finding of higher odds of uncontrolled hypertension in this population[29], and other studies showing more rich patients receive treatment including antihypertensive medications in India [30].

Our study demonstrated that waist circumference had a stronger association with CMM than BMI. Earlier studies have shown clear incremental association of abdominal obesity over BMI for non-fatal myocardial infarction, stroke, diabetes, and CKD [31-34]. Also, a strong association of renal function decline with central obesity and BMI has been reported in a recent meta-analysis of 39 general population cohorts from 40 countries [35]. Taken together, our findings suggest that central obesity should probably be included in multimorbidity indices in Asians, and especially underscore the same for adults with hypertension.[36].

Obesity leads to dyslipidemia and a state of chronic inflammation, which may underline the development of multimorbidity such as cardiovascular disease and diabetes [37, 38]. In our study, the association between waist circumference (central obesity) and multimorbidity persisted with adjustment for HDL and triglyceride. We were unable to evaluate if inflammation mediates the observed association between obesity and multimorbidity due to unavailability of data on inflammatory biomarkers. Given the limited research on inflammatory biomarkers associated with multimorbidity [39], future studies should focus on the potential mediating effects of inflammation.

Our findings also showed a remarkable variation in the prevalence of CMM among the three countries, with the highest in Sri Lanka and the lowest in Pakistan. Both CKD and diabetes were much more prevalent in Sri Lanka than the other two countries, which was the main reason for the higher prevalence of multimorbidity in Sri Lanka. Moreover, the variation in the prevalence could not be fully explained by sociodemographics, economic status, lifestyles, and clinical factors, suggestive of the presence of residual confoundings. CKD of unknown etiology (CKDu) is more prevalent in Sri Lanka [40] and could be caused by the interaction of multiple agents such as heavy metals, pesticides, native (ayuverdic) medications, or infections [40, 41].

Our alarmingly high rate of CMM in rural South Asia has major implications for public health at the national, regional, and global levels. Our findings call for urgent programs to institute preventive measures to address hypertension and associated multimorbidity in rural areas in

these countries where poor access to treatment and high CVD mortality rates have been reported [9, 42].

The major strengths of our study are that we used a uniform study design, door to door sampling of individuals, random selection of clusters, consistent definition of variables and outcomes (e.g. standardized measurements of serum creatinine), and standardized study procedures in all three countries. This study also has limitations. First, a causal relationship between covariates and CMM cannot be inferred due to the cross-sectional design of the study. Therefore, the observed association between obesity and CMM could be underestimated because multimorbidity can cause subsequent weight loss. Second, heart disease was ascertained based on self-reported physician diagnosis and may be subject to information bias. Third, we allocated equal weight to each chronic condition in terms of disease severity. In fact, the effects of multimorbidity on various domains of health are likely to depend on disease severity, the unique combination of diseases, and access to treatment and support [43]. Fourth, we did not have data on covariates such as healthcare access, dietary habit, psychological stress, and physiological biomarkers, which may additionally explain cross-country variation in multimorbidity. However, the main objective of our study was to determine the prevalence and pattern of cardiometabolic co-morbidity and key determinants, which was achieved. Finally, our sample consisted of hypertensive participants aged ≥40 years sampled in rural communities in each country. Thus, the findings may not be generalized to urban-residing individuals free of hypertension or younger than 40 years in each country.

In conclusion, our study shows an alarmingly high burden of CMM affecting 1 in 4 individuals with hypertension from rural communities in Bangladesh, Pakistan, and Sri Lanka. Central obesity had a graded, positive association with CMM. IWI showed an inverted J-shaped

relationship with CMM, with individuals in middle SES have a higher burden than those in the highest or lowest SES. Our findings suggest that the current single-disease paradigm in hypertension prevention and management needs to be broadened and incorporate the large and increasing burden of comorbidities in rural South Asia. The management strategies should be customized to individual countries. Strategies to manage central obesity may be relevant for the prevention and management of CMM in rural South Asia.

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Competing interests: No potential conflicts of interest relevant to this article were reported.

Authors' contributions: THJ conceived the conceptual design of COBRA-BPS study. FL performed the statistical analysis and wrote the first draft in consultation with THJ. IJ, AdeS, AN contributed equally to data. All authors reviewed, and provided comments on the paper, and approved final version. THJ is the guarantor.

Data Availability

The data will be available to the public upon the approval of Trial Steering Committee for COBRA-BPS full scale study.

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Table 1. Baseline Characteristics by Status of Cardio-metabolic Multimorbidity† (n=2288)

Characteristics	All	Cardiometabolic multimorbidity Yes (n=581)	No (n=1707)	P value
Age (y), n(%)				<.001
40~49	566 (24.7)	92 (15.8)	474 (27.8)	.
50~59	633 (27.7)	138 (23.8)	495 (29.0)	.
60~69	660 (28.8)	203 (34.9)	457 (26.8)	.
70 and over	429 (18.8)	148 (25.5)	281 (16.5)	.
Male, n(%)	817 (35.7)	217 (37.3)	600 (35.1)	0.34
Formal education (vs. informal), n(%)	1396 (61.0)	431 (74.2)	965 (56.5)	<.001
Married (vs. Others), n(%)	1679 (73.4)	399 (68.7)	1280 (75.0)	0.003
International Wealth Index score, n(%)				<.001
0~43	539 (23.6)	83 (14.3)	456 (26.8)	.
43~60	596 (26.1)	158 (27.2)	438 (25.7)	.
60~73	555 (24.3)	159 (27.4)	396 (23.3)	.
73 and above	591 (25.9)	180 (31.0)	411 (24.2)	.
Current smoker (vs. current non-smoker), n(%)	236 (10.3)	55 (9.5)	181 (10.6)	0.44
Physical activity level (MET-min/week), n(%)				<.001
Inactive	603 (26.7)	157 (27.5)	446 (26.4)	.
Minimally active	512 (22.7)	164 (28.7)	348 (20.6)	.
Highly active	1144 (50.6)	250 (43.8)	894 (53.0)	.
BMI (kg/m^2), n(%)				0.001
<18.5	204 (8.9)	29 (5.0)	175 (10.3)	.
18.5~23.0	656 (28.7)	166 (28.7)	490 (28.8)	.
23.0~27.5	849 (37.2)	231 (39.9)	618 (36.3)	.
27.5 and above	573 (25.1)	153 (26.4)	420 (24.7)	.
Waist circumference* (cm), n(%)				<.001
0~Q1	543 (23.8)	93 (16.0)	450 (26.4)	.
Q1~Q2	570 (24.9)	139 (24.0)	431 (25.3)	.
Q2~Q3	554 (24.2)	174 (30.0)	380 (22.3)	.
Q3 and above	619 (27.1)	174 (30.0)	445 (26.1)	.
Family history of CVD, n(%)	593 (26.5)	177 (31.3)	416 (24.9)	0.003
Country, n(%)				<.001
Bangladesh	819 (35.8)	224 (38.6)	595 (34.9)	.
Pakistan	679 (29.7)	70 (12.0)	609 (35.7)	.
Sri Lanka	790 (34.5)	287 (49.4)	503 (29.5)	.

HDL (mg/dL), Mean (SD)	45.3 (12.8)	45.3 (12.8)	45.3 (12.8)	0.98
Triglyceride(mg/dL), Median (IQR)	129 (94.0, 183)	133 (99.3, 192)	127 (91.8, 179)	<.001

MET, metabolic equivalent of task; BMI, body mass index; CVD, cardiovascular disease; HDL, high density lipoprotein; SD, standard deviation; IQR, inter-quartile range

†Cardio-metabolic Multimorbidity was defined as as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke.

*For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table 2. Prevalence of Cardiometabolic Conditions Stratified by Quartiles† of Waist Circumference among All Individuals with Hypertension (n=2286*)

Cardiometabolic conditions**, n[%(95%CI)]	Total (n=2286)	0~Q1 (n=543)	Q1~Q2 (n=570)	Q2~Q3 (n=554)	Q3 and over (n=619)	P trend
Cardiometabolic multimorbidity‡	580 [25.4 (23.6,27.2)]	93 [17.1 (14.1,20.6)]	139 [24.4 (20.9,28.1)]	174 [31.4 (27.6,35.5)]	174 [28.1 (24.6,31.8)]	<.001
Single cardiometabolic condition	807 [35.3 (33.3,37.3)]	198 [36.5 (32.4,40.7)]	199 [34.9 (31.0,39.0)]	196 [35.4 (31.4,39.5)]	214 [34.6 (30.8,38.5)]	0.56
Three or more cardiometabolic conditions	129 [5.6 (4.7, 6.7)]	15 [2.8 (1.6, 4.5)]	27 [4.7 (3.1, 6.8)]	44 [7.9 (5.8,10.5)]	43 [6.9 (5.1, 9.2)]	<.001
Chronic kidney disease (CKD) §	875 [38.3 (36.3,40.3)]	208 [38.3 (34.2,42.5)]	213 [37.4 (33.4,41.5)]	218 [39.4 (35.3,43.6)]	236 [38.1 (34.3,42.1)]	0.88
Diabetes¶	622 [27.2 (25.4,29.1)]	61 [11.2 (8.7,14.2)]	140 [24.6 (21.1,28.3)]	190 [34.3 (30.3,38.4)]	231 [37.3 (33.5,41.3)]	<.001
Heart disease&	317 [13.9 (12.5,15.4)]	45 [8.3 (6.1,10.9)]	84 [14.7 (11.9,17.9)]	105 [19.0 (15.8,22.5)]	83 [13.4 (10.8,16.3)]	0.005
Stroke&&	293 [12.8 (11.5,14.3)]	85 [15.7 (12.7,19.0)]	70 [12.3 (9.7,15.3)]	79 [14.3 (11.5,17.5)]	59 [9.5 (7.3,12.1)]	0.008

95%CI, 95% confidence interval

‡Cardiometabolic multimorbidity was defined as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke;

§CKD was defined as the presence of estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73m^2 or urine albumin and creatinine ratio (UACR)≥30 mg/g;

¶Diabetes was defined as a fasting plasma glucose (FPG) ≥126 mg/dL or self-reported use of anti-diabetic medication;

&Heart disease was acertained based on self-reported physician diagnosis;

&&Stroke was determined if an invidual ever had unconciousness or had both abnormal speech and paralyzed face.

Table 3. Multivariate Predictors of Cardiometabolic Multimorbidity among Hypertensive Individuals in Rural Bangladesh, Pakistan and Sri Lanka

Variables	Model 1 (n=2288) OR (95% CI)	p-value	Model 2 (n=2275) OR (95% CI)	p-value	Model 3 (n=2191) OR (95% CI)	p-value
Country		<.001		<.001		<.001
Pakistan	1.00	.	1.00	.	1.00	.
Bangladesh	3.28 (2.41,4.47)	<.001	3.22 (2.41,4.29)	<.001	3.26 (2.42,4.38)	<.001
Sri Lanka	4.98 (3.76,6.58)	<.001	3.40 (2.50,4.63)	<.001	5.20 (3.48,7.78)	<.001
Age (y)		.		<.001		<.001
40~49		.	1.00	.	1.00	.
50~59		.	1.35 (0.99,1.86)	0.060	1.35 (0.98,1.87)	0.068
60~69		.	2.08 (1.51,2.86)	<.001	1.95 (1.40,2.72)	<.001
70 and over		.	2.59 (1.81,3.70)	<.001	2.44 (1.67,3.58)	<.001
Gender		.		0.32		0.58
Male		.	1.00	.	1.00	.
Female		.	0.86 (0.63,1.16)	0.32	0.92 (0.68,1.24)	0.58
Education		.		0.046		0.20
Informal		.	1.00	.	1.00	.
Formal		.	1.29 (1.00,1.64)	0.046	1.19 (0.91,1.56)	0.20
Marital status		.		0.15		0.20
Others		.	1.00	.	1.00	.
Married		.	0.82 (0.63,1.08)	0.15	0.83 (0.62,1.11)	0.20
International Wealth Index score		.		0.025		0.020
0~43		.	1.00	.	1.00	.
43~60		.	1.60 (1.11,2.31)	0.012	1.62 (1.09,2.41)	0.017
60~73		.	1.64 (1.14,2.36)	0.008	1.71 (1.14,2.55)	0.009
73 and above		.	1.38 (0.93,2.04)	0.11	1.33 (0.86,2.07)	0.20
BMI (kg/m^2)		.		<.001		0.18
<18.5		.	1.00	.	1.00	.
18.5~23.0		.	1.85 (1.30,2.65)	<.001	1.19 (0.78,1.82)	0.42
23.0~27.5		.	2.13 (1.45,3.14)	<.001	0.88 (0.55,1.43)	0.62
27.5 and above		.	2.44 (1.62,3.66)	<.001	0.88 (0.54,1.42)	0.60
Smoking		.		.		0.98
Current non-smoker		.		.	1.00	.

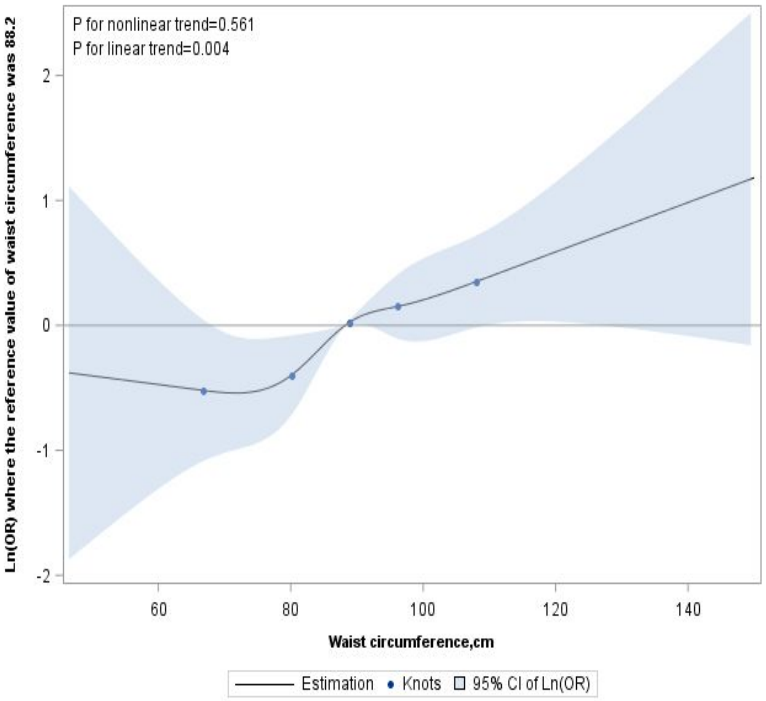
Variables	Model 1 (n=2288) OR (95% CI)	p-value	Model 2 (n=2275) OR (95% CI)	p-value	Model 3 (n=2191) OR (95% CI)	p-value
Current smoker	.	.	.	.	1.01 (0.64-1.57)	0.98
Physical activity level (MET-min/week)	.	.	.	.		0.003
Inactive	.	.	.	.	1.00	.
Minimally active	.	.	.	.	0.97 (0.72-1.29)	0.84
Highly active	.	.	.	.	0.73 (0.57-0.94)	0.013
Waist circumference† (cm)	.	.	.	.		<.001
0~Q1	.	.	.	.	1.00	.
Q1~Q2	.	.	.	.	1.42 (1.02-1.99)	0.041
Q2~Q3	.	.	.	.	2.20 (1.45-3.33)	<.001
Q3 and above	.	.	.	.	2.21 (1.52-3.22)	<.001
Family history of CVD	.	.	.	.		0.33
No	.	.	.	.	1.00	.
Yes	.	.	.	.	1.13 (0.88-1.45)	0.33
HDL (mg/dL,per 5 mg/dL increase)	.	.	.	.	0.92 (0.87-0.98)	0.010
Triglyceride (mg/dL,per 5 mg/dL increase	.	.	.	.	1.01 (1.01-1.02)	<.001

OR, odds ratio; 95% CI, 95% confidence interval; BMI, body mass index; MET, metabolic equivalent of task; CVD, cardiovascular disease; HDL, high density lipoprotein

† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Figure 1. Multiple-Adjusted Log (Odds Ratio) and 95% Confidence Intervals of Cardiometabolic Multimorbidity With Waist Circumference and International Wealth Index Score.

A. Waist circumference



B. International Wealth Index Score

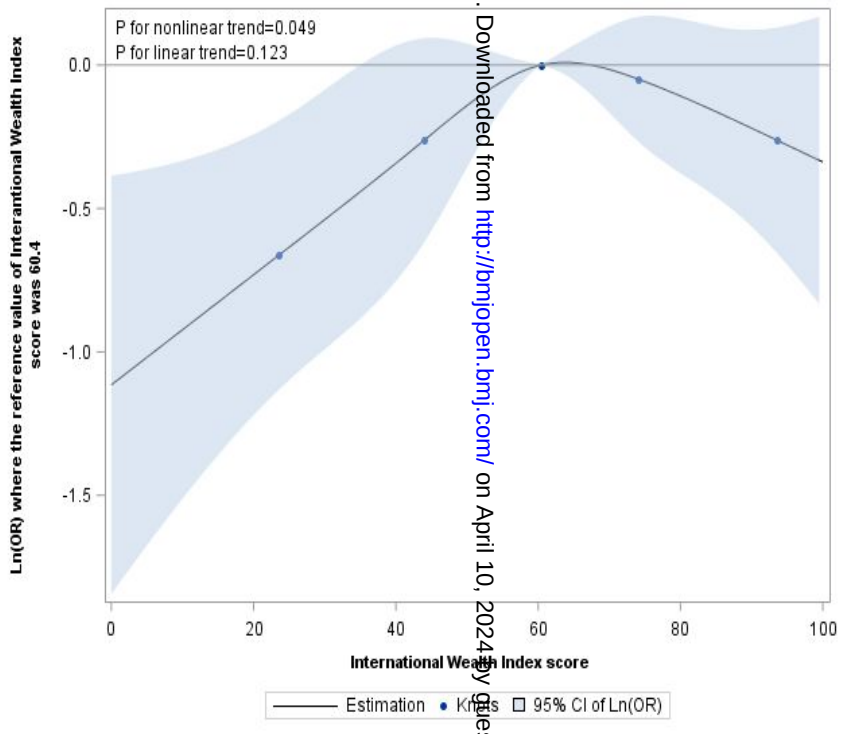


Table S1: Comparison of Baseline Characteristics between Hypertensive Individuals Included and Excluded from the Study

Characteristics	Excluded from analysis (n=355)	Included in analysis (n=2288)	P value
Age(y), n(%)			0.052
40~49	112 (31.5)	566 (24.7)	
50~59	89 (25.1)	633 (27.7)	
60~69	90 (25.4)	660 (28.8)	
70 and over	64 (18.0)	429 (18.8)	
Male, n(%)	126 (35.5)	817 (35.7)	0.94
Formal education(vs. informal), n(%)	161 (45.4)	1396 (61.0)	<.001
Married (vs. Others), n(%)	246 (69.3)	1679 (73.4)	0.11
International Wealth Index score, n(%)			<.001
0~43	121 (34.3)	539 (23.6)	
43~60	76 (21.5)	596 (26.1)	
60~73	84 (23.8)	555 (24.3)	
73 and above	72 (20.4)	591 (25.9)	
Current smoker (vs. current non-smoker), n(%)	38 (10.7)	236 (10.3)	0.82
Physical activity level(MET-min/week), n(%)			<.001
Highly active	148 (42.5)	1144 (50.6)	
Inactive	132 (37.9)	603 (26.7)	
Minimally active	68 (19.5)	512 (22.7)	
BMI(kg/m^2), n(%)			0.15
18.5~23.0	96 (31.4)	656 (28.7)	
23.0~27.5	95 (31.0)	849 (37.2)	
27.5 and above	80 (26.1)	573 (25.1)	
<18.5	35 (11.4)	204 (8.9)	
Waist circumference† (cm), n(%)			0.084
0~Q1	94 (27.1)	543 (23.8)	
Q1~Q2	93 (26.8)	570 (24.9)	
Q2~Q3	63 (18.2)	554 (24.2)	
Q3 and above	97 (28.0)	619 (27.1)	
Family history of CVD, n(%)	55 (16.1)	593 (26.5)	<.001
Country, n(%)			<.001
Bangladesh	76 (21.4)	819 (35.8)	
Pakistan	215 (60.6)	679 (29.7)	
Sri Lanka	64 (18.0)	790 (34.5)	

MET, metabolic equivalent of task; BMI, body mass index; CVD, cardiovascular disease
†For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table S2. Baseline Characteristics by Status of Cardiometabolic Multimorbidity† among Hypertensive Individuals in Bangaldesh (n=819)

Characteristics	All	Cardiometabolic multimorbidity		P value
		Yes (n=224)	No (n=595)	
Age(y), n(%)				0.038
40~49	259 (31.6)	63 (28.1)	196 (32.9)	.
50~59	254 (31.0)	60 (26.8)	194 (32.6)	.
60~69	178 (21.7)	56 (25.0)	122 (20.5)	.
70 and over	128 (15.6)	45 (20.1)	83 (13.9)	.
Male, n(%)	298 (36.4)	81 (36.2)	217 (36.5)	0.93
Formal education(vs. informal), n(%)	427 (52.1)	123 (54.9)	304 (51.1)	0.33
Married (vs. Others), n(%)	647 (79.0)	174 (77.7)	473 (79.5)	0.57
International wealth Index score, n(%)				0.038
0~43	258 (31.5)	54 (24.1)	204 (34.3)	.
43~60	300 (36.6)	87 (38.8)	213 (35.8)	.
60~73	207 (25.3)	65 (29.0)	142 (23.9)	.
73 and above	54 (6.6)	18 (8.0)	36 (6.1)	.
Current smoker (vs. current non-smoker), n(%)	99 (12.1)	28 (12.6)	71 (11.9)	0.81
Physical activity level(MET-min/week), n(%)				<.001
Inactive	152 (18.6)	49 (21.9)	103 (17.4)	.
Minimally active	202 (24.7)	76 (33.9)	126 (21.2)	.
Highly active	463 (56.7)	99 (44.2)	364 (61.4)	.
BMI(kg/m^2), n(%)				0.14
<18.5	59 (7.2)	10 (4.5)	49 (8.2)	.
18.5~23.0	264 (32.2)	66 (29.5)	198 (33.3)	.
23.0~27.5	340 (41.5)	102 (45.5)	238 (40.0)	.
27.5 and above	156 (19.0)	46 (20.5)	110 (18.5)	.
Waist circumference*(cm), n(%)				<.001
0~Q1	211 (25.8)	39 (17.4)	172 (28.9)	.
Q1~Q2	250 (30.5)	67 (29.9)	183 (30.8)	.
Q2~Q3	217 (26.5)	78 (34.8)	139 (23.4)	.
Q3 and above	141 (17.2)	40 (17.9)	101 (17.0)	.
Family history of CVD, n(%)	303 (38.8)	84 (39.4)	219 (38.6)	0.84
HDL (mg/dL), Mean (SD)	38.1 (10.3)	37.1 (10.3)	38.5 (10.2)	0.092
Triglyceride(mg/dL), Median (IQR)	146 (105, 208)	169 (122, 246)	141 (99.5, 193)	<.001

MET, metabolic equivalent of task; BMI, body mass index; CVD, cardiovascular disease; HDL, high density lipoprotein; SD, standard deviation; IQR, inter-quartile range

†Cardio-metabolic multimorbidity was defined as as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke.

*For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table S3. Baseline Characteristics by Status of Cardiometabolic Multimorbidity† among Hypertensive Individuals in Pakistan (n=679)

Chracteristics	All	Cardiometabolic multimorbidity		P value
		Yes (n=70)	No (n=609)	
Age(y), n(%)				0.81
40~49	209 (30.8)	19 (27.1)	190 (31.2)	.
50~59	193 (28.4)	23 (32.9)	170 (27.9)	.
60~69	172 (25.3)	18 (25.7)	154 (25.3)	.
70 and over	105 (15.5)	10 (14.3)	95 (15.6)	.
Male,n(%)	268 (39.5)	36 (51.4)	232 (38.1)	0.031
Formal education(vs. informal), n(%)	208 (30.6)	30 (42.9)	178 (29.2)	0.019
Married (vs. Others), n(%)	508 (74.8)	55 (78.6)	453 (74.4)	0.44
International wealth Index score, n(%)				0.12
0~43	240 (35.7)	16 (23.2)	224 (37.1)	.
43~60	173 (25.7)	21 (30.4)	152 (25.2)	.
60~73	148 (22.0)	20 (29.0)	128 (21.2)	.
73 and above	112 (16.6)	12 (17.4)	100 (16.6)	.
Current smoker (vs. current non-smoker), n(%)	95 (14.0)	12 (17.1)	83 (13.6)	0.42
Physical activity level(MET-min/week), n(%)				0.75
Inactive	264 (39.6)	29 (42.6)	235 (39.3)	.
Minimally active	109 (16.4)	12 (17.6)	97 (16.2)	.
Highly active	293 (44.0)	27 (39.7)	266 (44.5)	.
BMI(kg/m^2), n(%)				0.026
<18.5	91 (13.4)	4 (5.8)	87 (14.3)	.
18.5~23.0	179 (26.4)	12 (17.4)	167 (27.5)	.
23.0~27.5	210 (31.0)	27 (39.1)	183 (30.1)	.
27.5 and above	197 (29.1)	26 (37.7)	171 (28.1)	.
Waist circumference* (cm), n(%)				<.001
0~Q1	173 (25.6)	6 (8.7)	167 (27.5)	.
Q1~Q2	146 (21.6)	13 (18.8)	133 (21.9)	.
Q2~Q3	136 (20.1)	15 (21.7)	121 (19.9)	.
Q3 and above	222 (32.8)	35 (50.7)	187 (30.8)	.
Family history of CVD, n(%)	75 (11.1)	17 (24.3)	58 (9.6)	<.001
HDL (mg/dL), Mean (SD)	42.4 (11.8)	37.8 (9.8)	42.9 (11.9)	<.001
Triglyceride(mg/dL), Median (IQR)	137 (98.0, 197)	159 (117, 250)	135 (97.0, 192)	<.001

MET, metabolic equivalent of task; BMI, body mass index; CVD, cardiovascular disease; HDL, high density lipoprotein; SD, standard deviation; IQR, inter-quartile range

†Cardio-metabolic multimorbidity was defined as as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke.

*For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table S4 Baseline Characteristics by Status of Cardiometabolic Multimorbidity† among Hypertensive Individuals in Sri Lanka (n=790)

Chracteristics	All	Cardiometabolic multimorbidity		P value
		Yes (n=287)	No (n=503)	
Age(y), n(%)				<.001
40~49	98 (12.4)	10 (3.5)	88 (17.5)	.
50~59	186 (23.5)	55 (19.2)	131 (26.0)	.
60~69	310 (39.2)	129 (44.9)	181 (36.0)	.
70 and over	196 (24.8)	93 (32.4)	103 (20.5)	.
Male, n(%)	251 (31.8)	100 (34.8)	151 (30.0)	0.16
Formal education(vs. informal), n(%)	761 (96.3)	278 (96.9)	483 (96.0)	0.55
Married (vs. Others), n(%)	524 (66.3)	170 (59.2)	354 (70.4)	0.001
International wealth Index score, n(%)				0.66
0~43	41 (5.2)	13 (4.5)	28 (5.6)	.
43~60	123 (15.6)	50 (17.4)	73 (14.5)	.
60~73	200 (25.3)	74 (25.8)	126 (25.1)	.
73 and above	425 (53.9)	150 (52.3)	275 (54.8)	.
Current smoker (vs. current non-smoker), n(%)	42 (5.3)	15 (5.2)	27 (5.4)	0.93
Physical activity level (MET-min/week), n(%)				0.045
Inactive	187 (24.1)	79 (28.3)	108 (21.7)	.
Minimally active	201 (25.9)	76 (27.2)	125 (25.2)	.
Highly active	388 (50.0)	124 (44.4)	264 (53.1)	.
BMI(kg/m^2), n(%)				0.20
<18.5	54 (6.9)	15 (5.2)	39 (7.8)	.
18.5~23.0	213 (27.1)	88 (30.8)	125 (25.0)	.
23.0~27.5	299 (38.0)	102 (35.7)	197 (39.4)	.
27.5 and above	220 (28.0)	81 (28.3)	139 (27.8)	.
Waist circumference* (cm), n(%)				0.17
0~Q1	159 (20.1)	48 (16.7)	111 (22.1)	.
Q1~Q2	174 (22.0)	59 (20.6)	115 (22.9)	.
Q2~Q3	201 (25.4)	81 (28.2)	120 (23.9)	.
Q3 and above	256 (32.4)	99 (34.5)	157 (31.2)	.
Family history of CVD, n(%)	215 (27.6)	76 (26.9)	139 (28.0)	0.73
HDL (mg/dL), Mean (SD)	55.3 (9.3)	53.5 (9.6)	56.4 (9.0)	<.001
Triglyceride(mg/dL), Median (IQR)	109 (85.1, 143)	112 (89.3, 146)	106 (83.6, 143)	<.001

MET, metabolic equivalent of task; BMI, body mass index; CVD, cardiovascular disease; HDL, high density lipoprotein; SD, standard deviation; IQR, inter-quartile range

†Cardio-metabolic multimorbidity was defined as as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke.

Table S5. Prevalence of Cardiometabolic Conditions Stratified by Quartiles† of Waist Circumference among Individuals with Hypertension in **Bangladesh** (n=819)

Cardiometabolic conditions*, n[%(95% CI)]	Total (n=819)	0~Q1 (n=211)	Q1~Q2 (n=250)	Q2~Q3 (n=217)	Q3 and over (n=141)	P trend
Cardiometabolic multimorbidity‡	224 [27.4 (24.3,30.5)]	39 [18.5 (13.5,24.4)]	67 [26.8 (21.4,32.7)]	78 [35.9 (29.6,42.7)]	40 [28.4 (21.1,36.6)]	0.003
One cardiometabolic condition	297 [36.3 (33.0,39.7)]	83 [39.3 (32.7,46.3)]	87 [34.8 (28.9,41.1)]	75 [34.6 (28.3,41.3)]	52 [36.9 (28.9,45.4)]	0.56
Three or more cardiometabolic conditions	56 [6.8 (5.2, 8.8)]	5 [2.4 (0.8, 5.4)]	15 [6.0 (3.4, 9.7)]	22 [10.1 (6.5,14.9)]	14 [9.9 (5.5,16.1)]	<.001
Chronic kidney disease (CKD) §	298 [36.4 (33.1,39.8)]	77 [36.5 (30.0,43.4)]	90 [36.0 (30.0,42.3)]	81 [37.3 (30.9,44.1)]	50 [35.5 (27.6,44.0)]	0.96
Diabetes¶	188 [23.0 (20.1,26.0)]	14 [6.6 (3.7,10.9)]	52 [20.8 (15.9,26.4)]	70 [32.3 (26.1,38.9)]	52 [36.9 (28.9,45.4)]	<.001
Heart disease&	150 [18.3 (15.7,21.1)]	20 [9.5 (5.9,14.3)]	52 [20.8 (15.9,26.4)]	52 [24.0 (18.4,30.2)]	26 [18.4 (12.4,25.8)]	0.007
Stroke&&	173 [21.1 (18.4,24.1)]	55 [26.1 (20.3,32.5)]	44 [17.6 (13.1,22.9)]	53 [24.4 (18.9,30.7)]	21 [14.9 (9.5,21.9)]	0.087

95%CI, 95% confidence interval

† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

* Presence of any one of the following alone: diabetes, heart disease, CKD, and stroke

‡Cardiometabolic multimorbidity was defined as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke;

§CKD was defined as the presence of estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73m^2 or urine albumin and creatinine ratio (UACR)≥30 mg/g;

¶Diabetes was defined as a fasting plasma glucose (FPG) ≥126 mg/dL or self-reported use of anti-diabetic medication;

&Heart disease was acertained based on self-reported physician diagnosis;

&&Stroke was determined if an invidual ever had unconciousness or had both abnormal speech and paralyzed face.

Table S6. Prevalence of Cardiometabolic Conditions Stratified by Quartiles †of Waist Circumference among Individuals with Hypertension in **Pakistan** (n=677*)

Cardiometabolic conditions**, n[%(95% CI)]	Total (n=677)	0~Q1 (n=173)	Q1~Q2 (n=146)	Q2~Q3 (n=136)	Q3 and over (n=222)	P trend
Cardiometabolic multimorbidity‡	69 [10.2 (8.0,12.7)]	6 [3.5 (1.3, 7.4)]	13 [8.9 (4.8,14.7)]	15 [11.0 (6.3,19.5)]	35 [15.8 (11.2,21.2)]	<.001
One cardiometabolic condition	195 [28.8 (25.4,32.4)]	38 [22.0 (16.0,28.9)]	38 [26.0 (19.1,33.9)]	48 [35.3 (27.3,43.9)]	71 [32.0 (25.9,38.6)]	0.013
Three or more cardiometabolic conditions	10 [1.5 (0.7, 2.7)]	1 [0.6 (0.0, 3.2)]	2 [1.4 (0.2, 4.9)]	2 [1.5 (0.2, 5.2)]	5 [2.3 (0.7, 5.2)]	0.18
Chronic kidney disease(CKD) §	115 [17.0 (14.2,20.0)]	27 [15.6 (10.5,21.9)]	21 [14.4 (9.1,21.1)]	25 [18.4 (12.3,26.9)]	42 [18.9 (14.0,24.7)]	0.27
Diabetes¶	132 [19.5 (16.6,22.7)]	12 [6.9 (3.6,11.8)]	22 [15.1 (9.7,21.9)]	35 [25.7 (18.6,33.9)]	63 [28.4 (22.5,34.8)]	<.001
Heart disease&	49 [7.2 (5.4, 9.5)]	6 [3.5 (1.3, 7.4)]	11 [7.5 (3.8,13.1)]	9 [6.6 (3.1,12.2)]	23 [10.4 (6.7,15.1)]	0.015
Stroke&&	49 [7.2 (5.4, 9.5)]	6 [3.5 (1.3, 7.4)]	13 [8.9 (4.8,14.7)]	11 [8.1 (4.1,14.0)]	19 [8.6 (5.2,13.0)]	0.090

95%CI, 95% confidence interval

† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

* Two subjects had no data on waist circumference

** Presence of any one of the following alone: diabetes, heart disease, CKD, and stroke

‡Cardiometabolic multimorbidity was defined as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke;

§CKD was defined as the presence of estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73m^2 or urine albumin and creatinine ratio (UACR)≥30 mg/g;

¶Diabetes was defined as a fasting plasma glucose (FPG) ≥126 mg/dL or self-reported use of anti-diabetic medication;

&Heart disease was acertained based on self-reported physician diagnosis;

&&Stroke was determined if an invidual ever had unconciousness or had both abnormal speech and paralyzed face.

Table S7. Prevalence of **Cardiometabolic** Conditions Stratified by Quartiles† of Waist Circumference among Individuals with Hypertension in **Sri Lanka** (n=790)

Cardiometabolic conditions*, n[%(95% CI)]	Total (n=790)	0~Q1 (n=159)	Q1~Q2 (n=174)	Q2~Q3 (n=201)	Q3 and over (n=256)	P trend
Cardiometabolic multimorbidity‡	287 [36.3 (33.0,39.8)]	48 [30.2 (23.2,38.0)]	59 [33.9 (26.9,41.5)]	81 [40.3 (33.5,47.4)]	99 [38.7 (32.7,44.9)]	0.050
One Cardiometabolic condition	315 [39.9 (36.4,43.4)]	77 [48.4 (40.4,56.5)]	74 [42.5 (35.1,50.2)]	73 [36.3 (29.7,43.4)]	91 [35.5 (29.7,41.7)]	0.006
Three or more Cardiometabolic conditions	63 [8.0 (6.2,10.1)]	9 [5.7 (2.6,10.5)]	10 [5.7 (2.8,10.3)]	20 [10.0 (6.2,14.9)]	24 [9.4 (6.1,13.6)]	0.083
Chronic kidney disease(CKD) §	462 [58.5 (55.0,61.9)]	104 [65.4 (57.5,72.8)]	102 [58.6 (50.9,66.0)]	112 [55.7 (48.6,62.7)]	144 [56.3 (49.9,62.4)]	0.072
Diabetes¶	302 [38.2 (34.8,41.7)]	35 [22.0 (15.8,29.3)]	66 [37.9 (30.7,45.6)]	85 [42.3 (35.4,49.4)]	116 [45.3 (39.1,51.6)]	<.001
Heart disease&	118 [14.9 (12.5,17.6)]	19 [11.9 (7.4,18.0)]	21 [12.1 (7.6,17.9)]	44 [21.9 (16.4,28.3)]	34 [13.3 (9.4,18.1)]	0.36
Stroke&&	71 [9.0 (7.1,11.2)]	24 [15.1 (9.9,21.6)]	13 [7.5 (4.0,12.4)]	15 [7.5 (4.2,12.0)]	19 [7.4 (4.5,11.3)]	0.021

95%CI, 95% confidence interval

† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

* Presence of any one of the following alone: diabetes, heart disease, CKD, and stroke

‡Cardiometabolic multimorbidity was defined as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke;

§CKD was defined as the presence of estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73m^2 or urine albumin and creatinine ratio (UACR)≥30 mg/g;

¶Diabetes was defined as a fasting plasma glucose (FPG) ≥126 mg/dL or self-reported use of anti-diabetic medication;

&Heart disease was acertained based on self-reported physician diagnosis;

&&Stroke was determined if an invidual ever had unconciousness or had both abnormal speech and paralyzed face.

Table S8. Prevalence of Various Pairs of Conditions by Quartiles† of Waist Circumference (n=2286*)

Pairs, n[%(95%CI)]	Total (n=2286)	0~Q1 (n=543)	Q1~Q2 (n=570)	Q2~Q3 (n=554)	Q3 and over (n=619)	P trend
DM+CKD	230 [10.1 (8.9,11.4)]	26 [4.8 (3.2, 6.9)]	55 [9.6 (7.4,12.4)]	64 [11.6 (9.0,14.5)]	85 [13.7 (11.1,16.7)]	<.001
CKD+Stroke	67 [2.9 (2.3, 3.7)]	31 [5.7 (3.9, 8.0)]	15 [2.6 (1.5, 4.3)]	12 [2.2 (1.1, 3.8)]	9 [1.5 (0.7, 2.7)]	<.001
CKD+HD	55 [2.4 (1.8, 3.1)]	10 [1.8 (0.9, 3.4)]	14 [2.5 (1.3, 4.1)]	19 [3.4 (2.1, 5.3)]	12 [1.9 (1.0, 3.4)]	0.72
DM+HD	42 [1.8 (1.3, 2.5)]	2 [0.4 (0.0, 1.3)]	16 [2.8 (1.6, 4.5)]	11 [2.0 (1.0, 3.5)]	13 [2.1 (1.1, 3.6)]	0.095
HD+Stroke	30 [1.3 (0.9, 1.9)]	7 [1.3 (0.5, 2.6)]	7 [1.2 (0.5, 2.5)]	11 [2.0 (1.0, 3.5)]	5 [0.8 (0.3, 1.9)]	0.70
DM+Stroke	27 [1.2 (0.8, 1.7)]	2 [0.4 (0.0, 1.3)]	5 [0.9 (0.3, 2.0)]	13 [2.3 (1.3, 4.0)]	7 [1.1 (0.5, 2.3)]	0.078

The count of morbidity pairs was calculated for hypertensive individuals with only 2 other conditions.
95% CI, 95% confidence interval; DM, diabetes; CKD, chronic kidney disease; HD, heart disease

† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

* Two subjects had no data on waist circumference

Table S9. Prevalence of Various Pairs of Conditions by Quartiles† of Waist Circumference in **Bangladesh** (n=819)

Pairs, n[%(95%CI)]	Total (n=819)	0~Q1 (n=211)	Q1~Q2 (n=250)	Q2~Q3 (n=217)	Q3 and over (n=141)	P trend
DM+CKD	55 [6.7 (5.1, 8.7)]	5 [2.4 (0.8, 5.4)]	16 [6.4 (3.7,10.2)]	18 [8.3 (5.0,12.8)]	16 [11.3 (6.6,17.8)]	<.001
CKD+Stroke	42 [5.1 (3.7, 6.9)]	18 [8.5 (5.1,13.1)]	12 [4.8 (2.5, 8.2)]	9 [4.1 (1.9, 7.7)]	3 [2.1 (0.4, 6.1)]	0.007
HD+Stroke	22 [2.7 (1.7, 4.0)]	5 [2.4 (0.8, 5.4)]	7 [2.8 (1.1, 5.7)]	8 [3.7 (1.6, 7.1)]	2 [1.4 (0.2, 5.0)]	0.88
CKD+HD	19 [2.3 (1.4, 3.6)]	2 [0.9 (0.1, 3.4)]	8 [3.2 (1.4, 6.2)]	9 [4.1 (1.9, 7.7)]	0	0.94
DM+HD	18 [2.2 (1.3, 3.5)]	2 [0.9 (0.1, 3.4)]	8 [3.2 (1.4, 6.2)]	4 [1.8 (0.5, 4.7)]	4 [2.8 (0.8, 7.1)]	0.40
DM+Stroke	12 [1.5 (0.8, 2.5)]	2 [0.9 (0.1, 3.4)]	1 [0.4 (0.0, 2.2)]	8 [3.7 (1.6, 7.1)]	1 [0.7 (0.0, 3.9)]	0.29

The count of morbidity pairs was calculated for hypertensive individuals with only 2 other conditions.
95% CI, 95% confidence interval; DM, diabetes; CKD, chronic kidney disease; HD, heart disease
† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table S10. Prevalence of Various Pairs of Conditions by Quartiles† of Waist Circumference in **Pakistan** (n=677*)

Pairs, n[%(95%CI)]	Total (n=677)	0~Q1 (n=173)	Q1~Q2 (n=146)	Q2~Q3 (n=136)	Q3 and over (n=222)	P trend
DM+CKD	29 [4.3 (2.9, 6.1)]	2 [1.2 (0.1, 4.1)]	5 [3.4 (1.1, 7.8)]	7 [5.1 (2.1,10.3)]	15 [6.8 (3.8,10.9)]	0.005
DM+Stroke	12 [1.8 (0.9, 3.1)]	0	3 [2.1 (0.4, 5.9)]	4 [2.9 (0.8, 7.4)]	5 [2.3 (0.7, 5.2)]	0.096
DM+HD	7 [1.0 (0.4, 2.1)]	0	2 [1.4 (0.2, 4.9)]	1 [0.7 (0.0, 4.0)]	4 [1.8 (0.5, 4.5)]	0.12
HD+Stroke	5 [0.7 (0.2, 1.7)]	2 [1.2 (0.1, 4.1)]	0	0	3 [1.4 (0.3, 3.9)]	0.71
CKD+HD	4 [0.6 (0.2, 1.5)]	1 [0.6 (0.0, 3.2)]	1 [0.7 (0.0, 3.8)]		2 [0.9 (0.1, 3.2)]	0.80
CKD+Stroke	2 [0.3 (0.0, 1.1)]	0	0	1 [0.7 (0.0, 4.0)]	1 [0.5 (0.0, 2.5)]	0.28

The count of morbidity pairs was calculated for hypertensive individuals with only 2 other conditions.
95% CI, 95% confidence interval; DM, diabetes; CKD, chronic kidney disease; HD, heart disease
† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm
* Two subjects had no data on waist circumference

Table S11. Prevalence of Various Pairs of Conditions by Quartiles† of Waist Circumference in **Sri Lanka** (n=790)

Pairs, n[%(95%CI)]	Total (n=790)	0~Q1 (n=159)	Q1~Q2 (n=174)	Q2~Q3 (n=201)	Q3 and over (n=256)	P trend
DM+CKD	146 [18.5 (15.8,21.4)]	19 [11.9 (7.4,18.0)]	34 [19.5 (13.9,26.2)]	39 [19.4 (14.2,25.6)]	54 [21.1 (16.3,26.6)]	0.037
CKD+HD	32 [4.1 (2.8, 5.7)]	7 [4.4 (1.8, 8.9)]	5 [2.9 (0.9, 6.6)]	10 [5.0 (2.4, 9.0)]	10 [3.9 (1.9, 7.1)]	0.93
CKD+Stroke	23 [2.9 (1.9, 4.3)]	13 [8.2 (4.4,13.6)]	3 [1.7 (0.4, 5.0)]	2 [1.0 (0.1, 3.5)]	5 [2.0 (0.6, 4.5)]	0.001
DM+HD	17 [2.2 (1.3, 3.4)]	0	6 [3.4 (1.3, 7.4)]	6 [3.0 (1.1, 6.4)]	5 [2.0 (0.6, 4.5)]	0.37
DM+Stroke	3 [0.4 (0.1, 1.1)]	0	1 [0.6 (0.0, 3.2)]	1 [0.5 (0.0, 2.7)]	1 [0.4 (0.0, 2.2)]	0.64
HD+Stroke	3 [0.4 (0.1, 1.1)]	0	0	3 [1.5 (0.3, 4.3)]	0	0.64

The count of morbidity pairs was calculated for hypertensive individuals with only 2 other conditions.
95% CI, 95% confidence interval; DM, diabetes; CKD, chronic kidney disease; HD, heart disease
† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table S12. Ratio of Odds Rratios (RORs) and 95% Confidence Interval (CI) between Countries for Variables that Had Significant Interactions† with Country

	ROR (95%CI)(P value)		
Variables	**BD vs PK**	**BD vs SL**	**Pk Vs SL**
Age 50~59	0.63 (0.34 , 1.18) (0.15)	0.23 (0.1 , 0.53) (<.001)	0.37 (0.15 , 0.88) (0.025)
Age 60~69	1.29 (0.64 , 2.59) (0.47)	0.21 (0.09 , 0.48) (<.001)	0.16 (0.06 , 0.43) (<.001)
Age 70 and over	1.53 (0.7 , 3.34) (0.29)	0.18 (0.08 , 0.4) (<.001)	0.12 (0.04 , 0.31) (<.001)
Family history of CVD	0.34 (0.17 , 0.67) (0.002)	0.99 (0.61 , 1.61) (0.98)	2.92 (1.34 , 6.37) (0.007)
HDL	1.21 (1.03 , 1.43) (0.023)	1.18 (1.07 , 1.31) (0.001)	0.98 (0.83 , 1.15) (0.79)

BD, Bangladesh; PK,Pakistan; SL,Sri Lanka; CVD, cardiovascular disease; HDL, high density lipoprotein

†P values for interaction with country were <0.001 for age,0.007 for history of cardivarscular disease, and 0.002 for HDL, respectively

Table S13. Multivariate Predictors of Cardiometabolic Multimorbidity among Hypertensive Individuals in Each Country

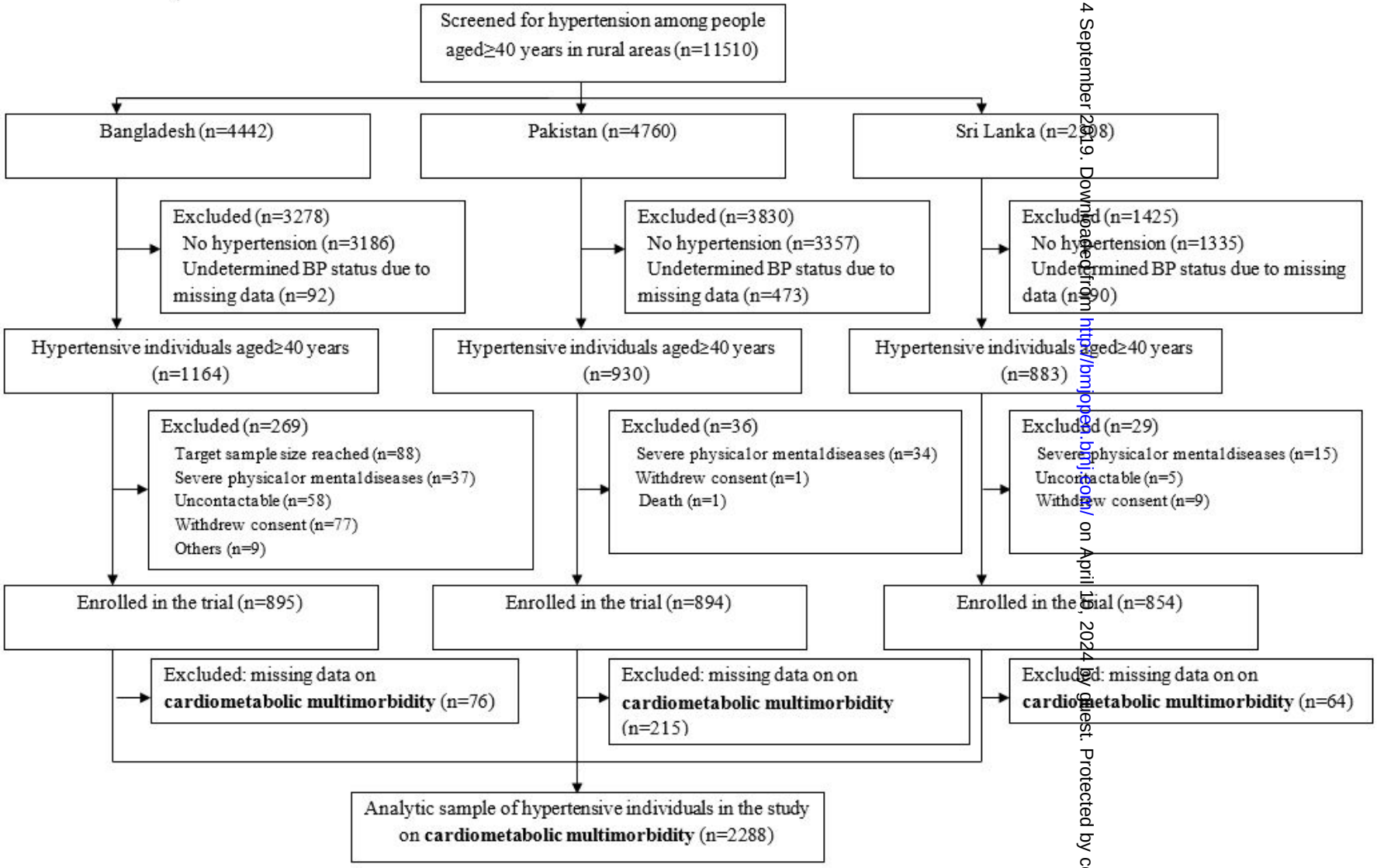
Variable	Bangladesh (n=776) OR (95% CI)	p-value	Pakistan (n=655) OR (95% CI)	p-value	Sri Lanka (n=760) OR (95% CI)	p-value
Age(y)		0.010		0.19		<.001
40~49	1.00		1.00		1.00	
50~59	0.94 (0.60,1.47)	0.78	1.58 (0.98,2.54)	0.063	4.27 (1.97,9.28)	<.001
60~69	1.41 (0.96,2.08)	0.079	1.08 (0.51,2.31)	0.83	6.64 (2.94,15.0)	<.001
70 and over	1.71 (1.17,2.50)	0.006	1.21 (0.55,2.70)	0.63	9.47 (3.72,24.1)	<.001
Gender		0.16		0.19		0.12
Male	1.00		1.00		1.00	
Female	1.38 (0.88,2.17)	0.16	0.67 (0.36,1.22)	0.19	0.69 (0.43,1.11)	0.12
Education		0.45		0.69		0.31
Informal	1.00		1.00		1.00	
Formal	1.13 (0.82,1.56)	0.45	1.17 (0.55,2.45)	0.69	1.54 (0.67,3.53)	0.31
Marital status		0.86		0.72		0.013
Others	1.00		1.00		1.00	
Married	1.06 (0.57,1.97)	0.86	0.82 (0.28,2.43)	0.72	0.73 (0.57,0.93)	0.013
International wealth Index score		0.19		0.18		0.021
0~43	1.00		1.00		1.00	
43~60	1.48 (0.88,2.49)	0.14	2.36 (1.07,5.20)	0.032	1.67 (0.71,3.94)	0.24
60~73	1.72 (0.96,3.06)	0.067	2.03 (0.61,6.76)	0.25	1.66 (0.96,2.89)	0.070
73 and above	1.76 (0.94,3.30)	0.080	1.81 (0.60,5.49)	0.29	1.15 (0.56,2.38)	0.70
BMI(kg/m^2)		0.70		0.92		<.001
<18.5	1.00		1.00		1.00	
18.5~23.0	1.00 (0.52,1.91)	0.99	0.73 (0.21,2.56)	0.62	1.64 (0.92,2.91)	0.091
23.0~27.5	0.83 (0.35,1.97)	0.67	0.72 (0.20,2.56)	0.61	0.81 (0.48,1.37)	0.44
27.5 and above	0.71 (0.37,1.37)	0.31	0.65 (0.19,2.27)	0.50	1.08 (0.53,2.19)	0.84
Smoking		0.59		0.91		0.80
Current non-smoker	1.00		1.00		1.00	
Current smoker	1.22 (0.58,2.57)	0.59	0.97 (0.55,1.69)	0.91	1.11 (0.51,2.41)	0.80
Physical activity level (MET-min/week)		<.001		0.98		0.095
Inactive	1.00		1.00		1.00	
Minimally active	1.13 (0.77,1.66)	0.54	0.96 (0.45,2.08)	0.93	0.87 (0.54,1.38)	0.54
Highly active	0.61 (0.46,0.82)	<.001	0.91 (0.37,2.27)	0.84	0.74 (0.53,1.04)	0.079

Waist circumference† (cm)		<.001		0.008		0.002
0~Q1	1.00		1.00		1.00	
Q1~Q2	1.32 (0.81,2.17)	0.27	2.28 (0.85,6.07)	0.10	1.71 (0.95,3.06)	0.072
Q2~Q3	2.24 (1.43,3.51)	<.001	2.70 (1.07,6.84)	0.036	2.70 (1.27,5.75)	0.010
Q3 and above	1.57 (0.84,2.91)	0.16	3.99 (1.77,9.01)	<.001	2.81 (1.56,5.07)	<.001
Family history of CVD		0.89		<.001		0.96
No	1.00		1.00		1.00	
Yes	0.99 (0.79,1.22)	0.89	3.13 (1.62,6.02)	<.001	1.01 (0.67,1.52)	0.96
HDL (mg/dL,per 5 mg/dL increase)	1.02 (0.93,1.12)	0.66	0.88 (0.76,1.01)	0.073	0.87 (0.81,0.94)	<.001
Triglyceride(mg/dL,per 5 mg/dL increase	1.01 (1.01,1.02)	<.001	1.01 (1.00,1.02)	0.038	1.01 (0.99,1.02)	0.28

OR, odds ratio; 95% CI, 95% confidence interval; BMI, body mass index; MET, metabolic equivalent of task; CVD, cardiovascular disease; HDL, high density lipoprotein

† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Figure S1: Study flow chart of hypertensive individuals included in the study on **cardiometabolic multimorbidity**



STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
3Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5,6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*7,8*
Bias	9	Describe any efforts to address potential sources of bias	7,8
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7,8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8,9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	NA
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	10
Outcome data	15*	Report numbers of outcome events or summary measures	10,11

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11,12
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13,14,15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prevalence and Correlates of Cardiometabolic Multimorbidity among Hypertensive Individuals: a Cross-Sectional Study in Rural South Asia- Bangladesh, Pakistan, and Sri Lanka

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Prevalence and Correlates of Cardiometabolic Multimorbidity among Hypertensive Individuals: a Cross-Sectional Study in Rural South Asia- Bangladesh, Pakistan, and Sri Lanka

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Running head: **Cardiometabolic Multimorbidity in South Asians**

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Abstract

Objective: To determinate the prevalence and correlates of cardiometabolic multimorbidity (CMM), and their cross-country variation among individuals with hypertension residing in rural communities in South Asia.

Design: A cross-sectional study.

Setting: Rural communities in Bangladesh, Pakistan, and Sri Lanka.

Participants: A total of 2288 individuals with hypertension aged ≥ 40 years from the ongoing COBRA-BPS (Control of Blood Pressure and Risk Attenuation- Bangladesh, Pakistan, and Sri Lanka) clinical trial.

Main outcome measures: CMM was defined as the presence of ≥two of the conditions: diabetes, chronic kidney disease (CKD), heart disease, and stroke. Logistic regression was done to evaluate the correlates of CMM.

Results: About 25.4% (95% CI (23.6, 27.2)) of the hypertensive individuals had CMM. Factors positively associated with CMM included residing in Bangladesh (OR=3.42,95% CI (2.52,4.65)) or Sri Lankan (3.73,(2.48,5.61)) versus in Pakistan, advancing age (2.33,(1.59,3.40) for 70 years and over versus 40 to 49 years), higher waist circumference (2.15, (1.42,3.25) for Q2~Q3, and 2.14,(1.50,3.06) for Q3 and above), statin use (2.43 (1.84,3.22)), and higher levels of triglyceride (1.01, (1.01,1.02) per 1 mg/dL increase). A lower odds of CMM was associated with being physically active (0.75,(0.57,0.97)). A weak inverted J-shaped association between International Wealth Index and CMM was found (P for nonlinear=0.058), suggesting higher risk in the middle than higher or lower socioeconomic strata.

Conclusions: CMM is highly prevalent in rural South Asians affecting 1 in 4 individuals with hypertension. There is an urgent need for strategies to concomitantly manage hypertension, cardiometabolic comorbid conditions, and associated determinants in South Asia.

Keywords: Cardiometabolic multimorbidity, South Asia, hypertension, obesity

Strengths and limitations of the study:

- This study is the first to evaluate the prevalence and correlates of cardiometabolic comorbidity (CMM) in a representative sample aged≥ 40 years with hypertension from rural communities in Bangladesh, Pakistan, and Sri Lanka.
- Our study used a uniform study design, door to door sampling of individuals, random selection of clusters, consistent definitions of variables and outcomes (e.g. standardized measurements of serum creatinine), and standardized study procedures in all three countries.
- A causal relationship between covariates and cardiometabolic comorbidity (CMM) cannot be inferred due to the cross-sectional design of the study.
- We did not have data on covariates such as healthcare access, dietary habit, psychological stress, and physiological biomarkers, which may additionally explain cross-country variation in multimorbidity.
- Our findings may not be generalized to all rural-residing hypertensive individuals aged 40 years and over in each country.

Introduction

Cardiometabolic multimorbidity (CMM) defined as the coexistence of two or more of the following chronic conditions (diabetes, heart disease, stroke, chronic kidney disease (CKD)) is being increasingly recognized as a global public health challenge [1, 2]. Compared with a single cardiometabolic disease, multimorbidity from these conditions is associated with multiplicative risk of mortality and cognitive decline [1, 3].

Individuals from South Asia have been shown to be more susceptible to cardiometabolic and other chronic conditions compared to other ethnic groups[4, 5]. In part, this is postulated to be due to higher visceral fat mass as South Asians have been shown to have higher amounts of abdominal adipose than Caucasians[6, 7], and abdominal obesity is better predictors for cardiovascular diseases (CVD) risk and diabetes than body mass index (BMI)[8]. Furthermore, most of South Asia is still rural with significant disparities in access to healthcare, and mortality from CVD has shown to be higher than in urban areas[9]. However, the prevalence, and correlates of CMM in rural South Asian countries have not been reported.

Therefore, we analyzed baseline data from the ongoing COBRA-BPS (Control of Blood Pressure (BP) and Risk Attenuation- Bangladesh, Pakistan, and Sri Lanka) trial on 2288 hypertensive individuals in rural communities in Bangladesh, Pakistan, and Sri Lanka with the following objectives: 1) To examine the prevalence of CMM, 2) to determine the sociodemographic characteristics, lifestyle factors, and clinical risk factors associated with CMM. We also sought to determine whether BMI or waist circumference was a stronger determinant of CMM in this population.

We hypothesized that: 1) the prevalence of CMM is high, and varies among hypertensive individuals in rural communities across the three South Asian countries; 2) the cross-country variation in CMM will only partially be accounted for by differences in sociodemographic,

lifestyle, and clinical risk factors; 3) waist circumference will be more strongly associated with CMM than BMI.

Methods

Population

The present study was performed using baseline data from COBRA-BPS (Control of Blood Pressure (BP) and Risk Attenuation- Bangladesh, Pakistan, and Sri Lanka) full-scale study. The study methodology has been described previously [10]. Briefly, COBRA-BPS full-scale study is an ongoing two-year cluster randomized controlled trial among 2643 hypertensive adults from 30 randomly selected rural clusters (communities), 10 clusters each, in Bangladesh, Pakistan, and Sri Lanka. In each country, clusters selection was stratified by distance (≤ 2.5km for near and >2.5 for far) from the government primary care clinics such that there were 6 near and 4 far clusters in each country. Individuals in each cluster were screened using door-to-door sampling method. The inclusion criteria for COBRA-BPS were age ≥40 years, hypertension (defined as a sustained elevation of systolic blood pressure (SBP) to ≥140 mmHg, or diastolic blood pressure (DBP) to ≥90 mmHg based on two readings from 2 separate days, or receiving antihypertensive medications), and residents in the selected clusters. Individuals were excluded if they had severe physical incapacity, were pregnant, had advanced diseases (on dialysis, liver failure, and other systemic diseases), or were mentally comprised leading to the incapability of giving consent.

Supplemental Fig. S1 shows the study flow diagram. Of the 2977 hypertensive individuals from 30 randomly selected clusters in 3 countries, 2643 were enrolled in the clinical trial after excluding 334 individuals for various reasons (Supplemental Fig. S1). Of the 2643 hypertensives

recruited, 355 (13.4%) were excluded because they missed data on diabetes (n=217), CKD (n=289), and heart disease (n=64), leaving 2288 for the final analysis. The study protocol was approved by the relevant Ethical Review Committee in Singapore, Bangladesh, Pakistan, Sri Lanka, and the UK. All study participants provided written informed consent.

Measurements

Sociodemographic variables were age (40~49,50~59,60~69,70 and over years), gender, education (formal vs. informal education), and marital status (married vs. single, divorced, or widowed). Economic status was assessed by International Wealth Index (IWI) [11]. IWI is based on a household's ownership of selected assets, access to basic service, and characteristics of the house and is estimated by principal component analysis. The score of IWI ranges from 0 to 100 and, in the current study, was classified into four groups via its quartiles (IWI<43, 43≤IWI<60, 60≤IWI<73, IWI≥73). Lifestyle factors included smoking status (current smoker vs. noncurrent smoker) and physical activity. Physical activity was evaluated by the short version of the International Physical Activity Questionnaire (IPAQ)[12] and was classified as inactive, minimally active, and highly active. BMI was calculated as weight (in kilogram)/height (in meters)^2 and was categorized as underweight (BMI<18.5), normal (18.5≤BMI<23), overweight (23≤BMI<27.5), and obesity (BMI≥27.5)[13]. Waist circumference was grouped into four categories using gender-specific quartiles (for male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm). Heart disease was ascertained based on self-reported physician diagnosis of angina, heart attack, and heart failure. Stroke was determined according to the WHO definition[14]. Family history of CVD was determined according to self-reported family history of heart disease or stroke.

An overnight fasting blood sample was collected to measure serum creatinine (measured on Beckman DU), lipids (measured on Roche Hitachi-912), and plasma glucose (measured on Beckman Synchron Cx-7/Delta) in each country. Serum creatinine measurements were calibrated to isotope dilution mass spectrometry (IDMS) traceable values. Urine albumin and creatinine excretion were measured on spot urine samples by nephelometry using the Array Systems method on a Beckman Coulter. All tests were done in an accredited laboratory in each country. Although no variability study was done for the tests, all three laboratories conformed to international standards for diagnostics. Diabetes was defined as a fasting plasma glucose (FPG) ≥126 mg/dL or self-reported use of anti-diabetic medication. CKD was defined as the presence of estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73m^2 or urine albumin and creatinine ratio (UACR)≥30 mg/g. Glomerular filtration rate (GFR) was estimated using the original Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation[15]. UACR was determined by urine albumin divided by urine creatinine.

Statistical analysis

The outcome measurement of this study was the presence of CMM, defined as having two or more of the following cardiometabolic conditions: diabetes, CKD, heart disease, and stroke. CKD was included in the definition because it has a strong association with CVD due to not only traditional cardiovascular risk factors (e.g. hypertension and diabetes), but also kidney-specific risk factors (e.g. dyslipidemia, anemia, and low-grade inflammation)[16].

Comparison of characteristics between individuals with and without CMM was performed using independent sample t-test for continuous variables and Chi-Square test for categorical variables. When continuous variables were not normally distributed, Mann–Whitney U test was used. We

used Cochran-Armitage trend test to measure the association of waist circumference categories with different measurements of cardiometabolic conditions - individual and multimorbid.

We fitted generalized estimating equation (GEE) logistic regression models with an exchangeable correlation matrix for CMM to account for the hierarchical nature of the data within the villages (clusters) in each country. Odds ratios (OR) and 95 % confidence intervals (CI) were presented. Covariates considered clinically relevant or found to be associated with CMM in previous literature or in the current bivariate analysis at $P<0.15$ were included in the multivariate models. Three models were built by sequentially entering the covariates in three individual blocks. In model 1, only country was included; in model 2, we included age, gender, education, marital status, IWI, and BMI besides country; in the last model, we additionally added physical activity, smoking, waist circumference, family history of CVD, statin use, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglyceride. Total cholesterol was not included in the model due to its strong correlation with LDL (Pearson correlation coefficient=0.90). Because adjusted analysis suggested possible nonlinear associations of CMM with IWI and waist circumference, we further examined their associations with restricted cubic splines by modeling the two covariates as continuous variables[17]. We used '%RCS_Reg' SAS macro[18] to perform adjusted analysis with 5 knots (5%, 25%,50%,75%, and 95% percentiles) specified.

We also investigated two-way interactions between country and other variables in the last model to assess the presence of a country-specific effect. Significant interactions were interpreted by the ratio of odds ratios (ROR)[19] and subgroup analysis by country.

All analyses were conducted using SAS version 9.4, and all hypothesis testing was 2-tailed with $P < 0.05$ set as statistically significant.

Patient and public involvement statement

Patients were not involved in the conception, design or interpretation of this study.

Results

Baseline characteristics

The baseline characteristics of 2288 individuals with hypertension are shown in Table 1. The overall prevalence of CMM was 25.3% (n=581). The mean (SD) age was 59.0 (11.3) years ; 64.3% (n=1471) were female. The mean (SD) BMI and waist circumference were 24.7 (5.0) Kg/m^2 and 88.2 (12.8) cm, respectively.

Individuals with CMM were older, better educated, less likely to be married, and had higher IWI scores than were those without. They also had lower levels of physical activity, higher BMI, higher waist circumference, and elevated levels of triglyceride, and were more likely to have a family history of CVD, to be Sri Lankan and statin users. In contrast, no other baseline characteristics were associated with CMM (Table 1).

Supplementary table S1 shows the characteristics of individuals included (n=2288) and excluded (n=355) from the current analysis. Compared with individuals excluded, those included had higher education, higher IWI score, higher levels of physical activity, and were more likely to have a family history of CVD, reside in Bangladesh and Sri Lanka, and use statin. Country-specific baseline characteristics are summarized in supplementary tables S2-S4.

Cardiometabolic multimorbid conditions

Table 2 shows bivariate associations between various measurements of cardiometabolic conditions and waist circumference quartiles. Hypertensive individuals with a single additional cardiometabolic condition, two or more (cardiometabolic comorbidity), and three or more cardiometabolic conditions accounted for 35.3% (95% CI:33.3%-37.3%), 25.4% (95%CI:23.6%-27.2%), and 5.6% (95% CI:4.7%-6.7%), respectively. CKD was the most prevalent cardiometabolic condition (38.3%,95% CI (36.3,40.3)).

CMM and waist circumference

The prevalence of CMM increased across the first 3 quartile groups of waist circumference, and slightly dropped in the highest quartile (P value for linear trend<0.001) (Table 2). We also observed a significant linear trend for three or more cardiometabolic conditions, diabetes, heart disease, and stroke, but not for CKD (Table 2). Corresponding country-specific results are reported in Supplementary Table S5-S7. CMM was most prevalent among participants from Sri Lanka (36.3% (95%CI:33.0%-39.8%)), followed by those from Bangladesh (27.4% (95%CI:24.3%-30.5%)), and Pakistan (10.2% (95%CI:8.0%-12.7%)).

The bivariate associations between morbidity pairs and waist circumference are presented in Table S8. The most frequently observed pair was diabetes and CKD (10.1%, 95% CI:8.9%-11.4%), and least observed was diabetes and stroke (1.2%,95% CI:0.8%-1.7%). An increasing trend across the quartile groups of waist circumference was observed for coexisting diabetes and CKD (P for linear trend<0.001). Diabetes and CKD were also the most prevalent pair in all three countries, but the prevalence of other pairs in each country differed from that of the whole sample and each other (Supplementary tables S9-S11).

Factors associated with CMM

In multivariate-adjusted analysis, living in Bangladesh or Sri Lanka (versus Pakistan), older age, higher IWI, higher waist circumference, statin use, and elevated levels of triglyceride were significantly associated with a higher odds of CMM, while being physically active was associated with a lower odds of CMM (Model 3 in Table 3). BMI was not significantly associated with CMM in model 3. The evaluation for interaction showed that country significantly modified the associations between CMM and four other covariates: age (P for interaction <0.001), history of CVD (P for interaction=0.012), HDL (P for interaction=0.008) and statin use (P for interaction=0.006) (Supplementary Tables S12 and S13). These assocations varied in strength but not direction across the three countries. Multivariable-adjusted restricted cubic spline analyses suggested no evidence of a nonlinear association between waist circumference and CMM (P for nonlinear trend=0.59 based on model3) but a weak nonlinear association between IWI and CMM (Fig1A, inverted J-shaped, p for nonlinear trend=0.058 based on model 3, and Fig1B, p for nonlinear trend=0.026 based on the model adjusted for only age and gender .

Discussion

Data on multimorbidity are limited from South Asian countries[20-25]. This study is the first to evaluate the prevalence and correlates of CMM in a representative sample aged≥ 40 years with hypertension from rural communities in Bangladesh, Pakistan, and Sri Lanka. We observed an alarmingly high prevalence of CMM –up to 25%- in rural South Asians with hypertension, and it was higher in Sri Lanka than the other two countries. CKD was the most common comorbid condition, followed by diabetes, stroke, and heart disease. CKD and diabetes dominated all the morbidity pairs, and were found in 10% of the population with hypertension. Individuals residing in Bangladesh and Sri Lanka (vs. Pakistan) had higher odds of CMM regardless of

sociodemographics, economic status, lifestyles, and clinical factors. Being older, lower levels of physical activity, higher waist circumference, lower levels of HDL, and higher levels of triglyceride, each, were independently associated with the presence of CMM. Waist circumference was a stronger correlate of CMM than BMI. An inverted J-shaped association was found between IWI and the odds of CMM. Our findings add to the current knowledge on the epidemiology of CMM in rural South Asians, and underscore the importance to develop prevention and treatment strategies to target individuals at risk of or with CMM.

There are very few reports on CMM from South Asia, and the types of conditions vary. In a study from urban areas of Delhi, Chennai, and Karachi, 9.4% of adults aged>=20 years had two or more of hypertension, diabetes, heart disease, stroke, and CKD [25]. Our study in hypertensive community dwellers from rural areas in 3 South Asian countries indicated a higher prevalence with one in four individuals having two additional cardiometabolic co-morbid conditions. CKD was the most prevalent comorbid condition, partially attributable to the high prevalence of diabetes and other factors[26], which deserves further study. The implications of findings are significant as health systems are more fragmented in rural compared to urban areas, highlighting the urgency to provide comprehensive services for vascular disease prevention and management in rural South Asia.

It is interesting that we found an inverted J-shaped association between socioeconomic status and CMM, which is in contrast with studies in developed countries showing that lower economic status was a risk factor for multimorbidity [27-29]. Studies from low- and middle- income countries show a positive association of chronic non-communicable diseases with a socioeconomic gradient [22, 24, 30]. However, the non-linear relationship of CMM in our study suggested that cardiometabolic risk was highest in those in the middle socioeconomic strata (SES), compared to

the highest and the lowest quartile of SES. The latter finding may be suggestive of an early reversal of social gradient for CMM and is consistent with our earlier finding of higher odds of uncontrolled hypertension in this population[31], and other studies showing more rich patients receive treatment including antihypertensive medications in India [32].

Our study demonstrated that waist circumference had a stronger association with CMM than BMI because waist circumference but not BMI was statistically significant in the fully adjusted model (model 3 in Table 3) Earlier studies have shown a clear incremental association of abdominal obesity over BMI for non-fatal myocardial infarction, stroke, diabetes, and CKD [33-36]. Also, a strong association of renal function decline with central obesity and BMI has been reported in a recent meta-analysis of 39 general population cohorts from 40 countries [37]. Taken together, our findings suggest that central obesity should probably be included in multimorbidity indices in Asians, and especially underscore the same for adults with hypertension.[38].

Our findings also showed a remarkable variation in the prevalence of CMM among the three countries, with the highest in Sri Lanka and the lowest in Pakistan. Both CKD and diabetes were much more prevalent in Sri Lanka than the other two countries, which was the main reason for the higher prevalence of multimorbidity in Sri Lanka. Moreover, the variation in the prevalence could not be fully explained by sociodemographics, economic status, lifestyles, and clinical factors, suggestive of the presence of residual confoundings. CKD of unknown etiology (CKDu) is more prevalent in Sri Lanka [39] and could be caused by the interaction of multiple agents such as heavy metals, pesticides, native (ayurvedic) medications, or infections [39, 40].

Our alarmingly high rate of CMM in rural South Asia has major implications for public health at the national, regional, and global levels. Our findings call for urgent programs to institute preventive measures to address hypertension and associated multimorbidity in rural areas in these countries where poor access to treatment and high CVD mortality rates have been reported [9, 41].

The major strengths of our study are that we used a uniform study design, door to door sampling of individuals, random selection of clusters, consistent definitions of variables and outcomes (e.g. standardized measurements of serum creatinine), and standardized study procedures in all three countries. This study also has limitations. First, a causal relationship between covariates and CMM cannot be inferred due to the cross-sectional design of the study. Therefore, the observed association between obesity and CMM could be underestimated because multimorbidity can cause subsequent weight loss. Second, heart disease was ascertained based on self-reported physician diagnosis and stroke based on self-reported signs and symptoms of stroke, which may be subject to information bias. Third, we allocated equal weight to each chronic condition in terms of disease severity. In fact, the effects of multimorbidity on various domains of health are likely to depend on disease severity, the unique combination of diseases, and access to treatment and support [42]. Fourth, we did not have data on covariates such as healthcare access, dietary habit, psychological stress, and physiological biomarkers, which may additionally explain cross-country variation in multimorbidity. However, the main objective of our study was to determine the prevalence and pattern of cardiometabolic co-morbidity and key determinants, which was achieved. Finally, our study was not conducted in a nationally representative sample of hypertensive individuals in rural areas, and the findings may not be generalized to all rural-residing hypertensive individuals aged ≥40 years in each country.

In conclusion, our study shows an alarmingly high burden of CMM affecting 1 in 4 individuals with hypertension from rural communities in Bangladesh, Pakistan, and Sri Lanka. Central obesity had a graded, positive association with CMM. IWI showed an inverted J-shaped relationship with CMM, with individuals in middle SES have a higher burden than those in the highest or lowest SES. Our findings suggest that the current single-disease paradigm in hypertension prevention and management needs to be broadened and incorporate the large and increasing burden of comorbidities in rural South Asia. The management strategies should be customized to individual countries. Strategies to manage central obesity may be relevant to the prevention and management of CMM in rural South Asia.

Figure Legend

Figure 1. Multiple-adjusted log (Odds Ratio) and 95% confidence intervals of cardiometabolic multimorbidity with International Wealth Index Score. Figure 1 A was based on model 3 in table 3, while figure 1 B was derived based on the model adjusted for only age and gender.

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Authors' contributions: THJ conceived the conceptual design of COBRA-BPS study. LF performed the statistical analysis and wrote the first draft in consultation with THJ. IJ, AdeS, AN contributed equally to data. All authors including LF, IJ, AdeS, AN, HF, SH,AK, CDR, MdTI, ATS, THJ reviewed, and provided comments on the paper, and approved final version. THJ is the guarantor.

Data Availability

The data will be available to the public upon the approval of Trial Steering Committee for COBRA-BPS full-scale study.

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Table 1. Baseline Characteristics by Status of Cardio-metabolic Multimorbidity† (n=2288)

Characteristics	All	Cardiometabolic multimorbidity		P value
		Yes (n=581)	No (n=1707)	
Age (y), n(%)				<.001
40~49	566 (24.7)	92 (15.8)	474 (27.8)	.
50~59	633 (27.7)	138 (23.8)	495 (29.0)	.
60~69	660 (28.8)	203 (34.9)	457 (26.8)	.
70 and over	429 (18.8)	148 (25.5)	281 (16.5)	.
Male, n(%)	817 (35.7)	217 (37.3)	600 (35.1)	0.34
Formal education (vs. informal), n(%)	1396 (61.0)	431 (74.2)	965 (56.5)	<.001
Married (vs. Others), n(%)	1679 (73.4)	399 (68.7)	1280 (75.0)	0.003
International Wealth Index score, n(%)				<.001
0~43	539 (23.6)	83 (14.3)	456 (26.8)	.
43~60	596 (26.1)	158 (27.2)	438 (25.7)	.
60~73	555 (24.3)	159 (27.4)	396 (23.3)	.
73 and above	591 (25.9)	180 (31.0)	411 (24.2)	.
Current smoker (vs. current non-smoker), n(%)	236 (10.3)	55 (9.5)	181 (10.6)	0.44
Physical activity level (MET-min/week), n(%)				<.001
Inactive	603 (26.7)	157 (27.5)	446 (26.4)	.
Minimally active	512 (22.7)	164 (28.7)	348 (20.6)	.
Highly active	1144 (50.6)	250 (43.8)	894 (53.0)	.
BMI (kg/m^2), n(%)				0.001
<18.5	204 (8.9)	29 (5.0)	175 (10.3)	.
18.5~23.0	656 (28.7)	166 (28.7)	490 (28.8)	.
23.0~27.5	849 (37.2)	231 (39.9)	618 (36.3)	.
27.5 and above	573 (25.1)	153 (26.4)	420 (24.7)	.
Waist circumference* (cm), n(%)				<.001
0~Q1	543 (23.8)	93 (16.0)	450 (26.4)	.
Q1~Q2	570 (24.9)	139 (24.0)	431 (25.3)	.
Q2~Q3	554 (24.2)	174 (30.0)	380 (22.3)	.
Q3 and above	619 (27.1)	174 (30.0)	445 (26.1)	.
Family history of CVD, n(%)	593 (26.5)	177 (31.3)	416 (24.9)	0.003

Characteristics	All	Cardiometabolic multimorbidity		P value
		Yes (n=581)	No (n=1707)	
Country, n(%)				<.001
Bangladesh	819 (35.8)	224 (38.6)	595 (34.9)	.
Pakistan	679 (29.7)	70 (12.0)	609 (35.7)	.
Sri Lanka	790 (34.5)	287 (49.4)	503 (29.5)	.
HDL (mg/dL), Mean (SD)	45.3 (12.8)	45.3 (12.8)	45.3 (12.8)	0.98
Triglyceride(mg/dL), Median (IQR)	128.7 (94.0,183.0)	132.8 (99.3,192.0)	127.0 (91.8,179.1)	<.001
Total cholestrol (mg/dL),Mean (SD)	194.6 (48.5)	197.4 (52.0)	193.6 (47.2)	0.12
LDL (mg/dL),Mean (SD)	124.4 (40.6)	124.0 (43.8)	124.5 (39.4)	0.82
Statin use,n(%)	315 (13.8)	156 (26.9)	159 (9.3)	<.001

MET, metabolic equivalent of task; BMI, body mass index; CVD, cardiovascular disease; HDL, high density lipoprotein; SD, standard deviation; IQR, inter-quartile range; LDL, low density lipoprotein.

†Cardio-metabolic Multimorbidity was defined as as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke.

*For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table 2. Prevalence of Cardiometabolic Conditions Stratified by Quartiles† of Waist Circumference among All Individuals with Hypertension (n=2286*)

Cardiometabolic conditions**, n[%(95%CI)]	Total (n=2286)	0~Q1 (n=543)	Q1~Q2 (n=570)	Q2~Q3 (n=554)	Q3 and over (n=619)	P trend
Cardiometabolic multimorbidity‡	580 [25.4 (23.6,27.2)]	93 [17.1 (14.1,20.6)]	139 [24.4 (20.9,28.1)]	174 [31.4 (27.6,35.5)]	174 [28.1 (24.6,31.8)]	<.001
Single cardiometabolic condition	807 [35.3 (33.3,37.3)]	198 [36.5 (32.4,40.7)]	199 [34.9 (31.0,39.0)]	196 [35.4 (31.4,39.5)]	214 [34.6 (30.8,38.5)]	0.56
Three or more cardiometabolic conditions	129 [5.6 (4.7, 6.7)]	15 [2.8 (1.6, 4.5)]	27 [4.7 (3.1, 6.8)]	44 [7.9 (5.8,10.5)]	43 [6.9 (5.1, 9.2)]	<.001
Chronic kidney disease (CKD) §	875 [38.3 (36.3,40.3)]	208 [38.3 (34.2,42.5)]	213 [37.4 (33.4,41.5)]	218 [39.4 (35.3,43.6)]	236 [38.1 (34.3,42.1)]	0.88
Diabetes¶	622 [27.2 (25.4,29.1)]	61 [11.2 (8.7,14.2)]	140 [24.6 (21.1,28.3)]	190 [34.3 (30.3,38.4)]	231 [37.3 (33.5,41.3)]	<.001
Heart disease&	317 [13.9 (12.5,15.4)]	45 [8.3 (6.1,10.9)]	84 [14.7 (11.9,17.9)]	105 [19.0 (15.8,22.5)]	83 [13.4 (10.8,16.3)]	0.005
Stroke&&	293 [12.8 (11.5,14.3)]	85 [15.7 (12.7,19.0)]	70 [12.3 (9.7,15.3)]	79 [14.3 (11.5,17.5)]	59 [9.5 (7.3,12.1)]	0.008

95%CI, 95% confidence interval

‡Cardiometabolic multimorbidity was defined as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke;

§CKD was defined as the presence of estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73m^2 or urine albumin and creatinine ratio (UACR)≥30 mg/g;

¶Diabetes was defined as a fasting plasma glucose (FPG) ≥126 mg/dL or self-reported use of anti-diabetic medication;

&Heart disease was acertained based on self-reported physician diagnosis;

&&Stroke was determined if an invidual ever had unconciousness or had both abnormal speech and paralyzed face.

Table 3. Multivariate Predictors of Cardiometabolic Multimorbidity among Hypertensive Individuals in Rural Bangladesh, Pakistan and Sri Lanka

Variables	Model1 (n=2288) OR (95% CI)	p-value	Model2 (n=2275) OR (95% CI)	p-value	Model3(n=2191) OR (95% CI)	p-value
Country		<.001		<.001		<.001
Pakistan	1.00		1.00		1.00	
Bangladesh	3.28 (2.41,4.47)	<.001	3.22 (2.41,4.29)	<.001	3.42 (2.52,4.65)	<.001
Sri Lanka	4.98 (3.76,6.58)	<.001	3.40 (2.50,4.63)	<.001	3.73 (2.48,5.61)	<.001
Age(y)				<.001		<.001
40~49			1.00		1.00	
50~59			1.35 (0.99,1.86)	0.060	1.29 (0.94,1.77)	0.12
60~69			2.08 (1.51,2.86)	<.001	1.82 (1.31,2.53)	<.001
70 and over			2.59 (1.81,3.70)	<.001	2.33 (1.59,3.40)	<.001
Gender				0.32		0.58
Male			1.00		1.00	
Female			0.86 (0.63,1.16)	0.32	0.92 (0.67,1.25)	0.58
Education				0.046		0.17
Informal			1.00		1.00	
Formal			1.29 (1.00,1.64)	0.046	1.20 (0.93,1.56)	0.17
Marrital status				0.15		0.18
Single or widowed or divorced			1.00		1.00	
Married			0.82 (0.63,1.08)	0.15	0.82 (0.62,1.10)	0.18
International wealth Index score				0.025		0.014
0~43			1.00		1.00	
43~60			1.60 (1.11,2.31)	0.012	1.63 (1.09,2.44)	0.018
60~73			1.64 (1.14,2.36)	0.008	1.69 (1.12,2.55)	0.013
73 and above			1.38 (0.93,2.04)	0.11	1.29 (0.84,1.97)	0.25
BMI(kg/m^2)				<.001		0.24
<18.5			1.00		1.00	
18.5~23.0			1.85 (1.30,2.65)	<.001	1.17 (0.78,1.76)	0.45
23.0~27.5			2.13 (1.45,3.14)	<.001	0.90 (0.57,1.42)	0.65
27.5 and above			2.44 (1.62,3.66)	<.001	0.89 (0.56,1.41)	0.61
Smoking						0.87
Non current smoker					1.00	
Current smoker					1.04 (0.66,1.64)	0.87

Variables	Model1 (n=2288) OR (95% CI)	p-value	Model2 (n=2275) OR (95% CI)	p-value	Model3(n=2191) OR (95% CI)	p-value
Physical activity level(MET-min/week)						0.010
Inactive					1.00	
Minimally active					0.97 (0.71-1.30)	0.82
Highly active					0.75 (0.57-0.97)	0.029
Waist circumference† (cm)						<.001
0~Q1					1.00	
Q1~Q2					1.43 (1.03-1.99)	0.033
Q2~Q3					2.15 (1.42-3.25)	<.001
Q3 and above					2.14 (1.50-3.06)	<.001
Family history of CVD						0.55
No					1.00	
Yes					1.08 (0.84-1.37)	0.55
Statin use						<.001
Nonuser					1.00	
User					2.43 (1.84-3.22)	<.001
HDL (mg/dL,per 5 mg/dL increase)					0.96 (0.89-1.02)	0.17
Triglyceride(mg/dL,per 5 mg/dL increase					1.01 (1.01-1.02)	<.001
LDL (mg/dL,per 5 mg/dL increase)					1.00 (0.98-1.01)	0.57

OR, odds ratio; 95% CI, 95% confidence interval; BMI, body mass index; MET, metabolic equivalent of task; CVD, cardiovascular disease; HDL, high density lipoprotein; LDL, low density lipoprotein.

† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

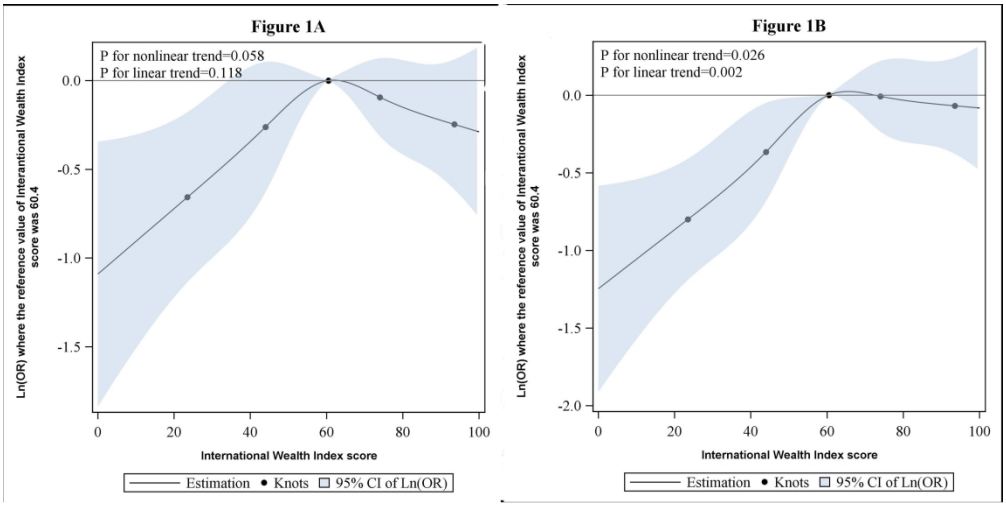

Figure 1. Multiple-adjusted log (Odds Ratio) and 95% confidence intervals of cardiometabolic multimorbidity with International Wealth Index Score. Figure 1 A was based on model 3 in table 3, while figure 1 B was derived based on the model adjusted for only age and gender.

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Table S1: Comparison of Baseline Characteristics between Hypertensive Individuals Included and Excluded from the Study

Characteristics	Excluded from analysis (n=355)	Included in analysis (n=2288)	P value
Age(y), n(%)			0.052
40~49	112 (31.5)	566 (24.7)	
50~59	89 (25.1)	633 (27.7)	
60~69	90 (25.4)	660 (28.8)	
70 and over	64 (18.0)	429 (18.8)	
Male, n(%)	126 (35.5)	817 (35.7)	0.94
Formal education(vs. informal), n(%)	161 (45.4)	1396 (61.0)	<.001
Married (vs. Others), n(%)	246 (69.3)	1679 (73.4)	0.11
International Wealth Index score, n(%)			<.001
0~43	121 (34.3)	539 (23.6)	
43~60	76 (21.5)	596 (26.1)	
60~73	84 (23.8)	555 (24.3)	
73 and above	72 (20.4)	591 (25.9)	
Current smoker (vs. current non-smoker), n(%)	38 (10.7)	236 (10.3)	0.82
Physical activity level(MET-min/week), n(%)			<.001
Highly active	148 (42.5)	1144 (50.6)	
Inactive	132 (37.9)	603 (26.7)	
Minimally active	68 (19.5)	512 (22.7)	
BMI(kg/m^2), n(%)			0.15
18.5~23.0	96 (31.4)	656 (28.7)	
23.0~27.5	95 (31.0)	849 (37.2)	
27.5 and above	80 (26.1)	573 (25.1)	
<18.5	35 (11.4)	204 (8.9)	
Waist circumference† (cm), n(%)			0.084
0~Q1	94 (27.1)	543 (23.8)	
Q1~Q2	93 (26.8)	570 (24.9)	
Q2~Q3	63 (18.2)	554 (24.2)	
Q3 and above	97 (28.0)	619 (27.1)	
Family history of CVD, n(%)	55 (16.1)	593 (26.5)	<.001
Country, n(%)			<.001
Bangladesh	76 (21.4)	819 (35.8)	
Pakistan	215 (60.6)	679 (29.7)	
Sri Lanka	64 (18.0)	790 (34.5)	
Statin use, n(%)	29 (8.2)	315 (13.8)	0.004

MET, metabolic equivalent of task; BMI, body mass index; CVD, cardiovascular disease
†For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table S2. Baseline Characteristics by Status of Cardiometabolic Multimorbidity† among Hypertensive Individuals in Bangaldesh (n=819)

Characteristics	All (n=819)	Cardiometabolic multimorbidity		P value
		Yes (n=224)	No (n=595)	
Age(y), n(%)				0.038
40~49	259 (31.6)	63 (28.1)	196 (32.9)	.
50~59	254 (31.0)	60 (26.8)	194 (32.6)	.
60~69	178 (21.7)	56 (25.0)	122 (20.5)	.
70 and over	128 (15.6)	45 (20.1)	83 (13.9)	.
Male, n(%)	298 (36.4)	81 (36.2)	217 (36.5)	0.93
Formal education(vs. informal), n(%)	427 (52.1)	123 (54.9)	304 (51.1)	0.33
Married (vs. Others), n(%)	647 (79.0)	174 (77.7)	473 (79.5)	0.57
International wealth Index score, n(%)				0.038
0~43	258 (31.5)	54 (24.1)	204 (34.3)	.
43~60	300 (36.6)	87 (38.8)	213 (35.8)	.
60~73	207 (25.3)	65 (29.0)	142 (23.9)	.
73 and above	54 (6.6)	18 (8.0)	36 (6.1)	.
Current smoker (vs. current non-smoker), n(%)	99 (12.1)	28 (12.6)	71 (11.9)	0.81
Physical activity level(MET-min/week), n(%)				<.001
Inactive	152 (18.6)	49 (21.9)	103 (17.4)	.
Minimally active	202 (24.7)	76 (33.9)	126 (21.2)	.
Highly active	463 (56.7)	99 (44.2)	364 (61.4)	.
BMI(kg/m^2), n(%)				0.14
<18.5	59 (7.2)	10 (4.5)	49 (8.2)	.
18.5~23.0	264 (32.2)	66 (29.5)	198 (33.3)	.
23.0~27.5	340 (41.5)	102 (45.5)	238 (40.0)	.
27.5 and above	156 (19.0)	46 (20.5)	110 (18.5)	.
Waist circumference*(cm), n(%)				<.001
0~Q1	211 (25.8)	39 (17.4)	172 (28.9)	.
Q1~Q2	250 (30.5)	67 (29.9)	183 (30.8)	.
Q2~Q3	217 (26.5)	78 (34.8)	139 (23.4)	.
Q3 and above	141 (17.2)	40 (17.9)	101 (17.0)	.
Family history of CVD, n(%)	303 (38.8)	84 (39.4)	219 (38.6)	0.84
HDL (mg/dL), Mean (SD)	38.1 (10.3)	37.1 (10.3)	38.5 (10.2)	0.092
Triglyceride(mg/dL), Median (IQR)	146.1 (105.4,208.0)	169.2 (122.4,246.2)	140.6 (99.5,193.4)	<.001
Total cholestrol (mg/dL),Mean (SD)	196.8 (46.9)	200.4 (50.8)	195.5 (45.3)	0.20
LDL (mg/dL),Mean (SD)	133.1 (40.3)	131.7 (42.6)	133.6 (39.5)	0.55
Statin use, n(%)	22 (2.7)	17 (7.6)	5 (0.8)	<.001

MET, metabolic equivalent of task; BMI, body mass index; CVD, cardiovascular disease; HDL, high density lipoprotein; SD, standard deviation; IQR, inter-quartile range; LDL, low density lipoprotein.
†Cardio-metabolic multimorbidity was defined as as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke.
*For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table S3. Baseline Characteristics by Status of Cardiometabolic Multimorbidity† among Hypertensive Individuals in Pakistan (n=679)

Chracteristics	All (n=679)	Cardiometabolic multimorbidity		P value
		Yes (n=70)	No (n=609)	
Age(y), n(%)				0.81
40~49	209 (30.8)	19 (27.1)	190 (31.2)	.
50~59	193 (28.4)	23 (32.9)	170 (27.9)	.
60~69	172 (25.3)	18 (25.7)	154 (25.3)	.
70 and over	105 (15.5)	10 (14.3)	95 (15.6)	.
Male,n(%)	268 (39.5)	36 (51.4)	232 (38.1)	0.031
Formal education(vs. informal), n(%)	208 (30.6)	30 (42.9)	178 (29.2)	0.019
Married (vs. Others), n(%)	508 (74.8)	55 (78.6)	453 (74.4)	0.44
International wealth Index score, n(%)				0.12
0~43	240 (35.7)	16 (23.2)	224 (37.1)	.
43~60	173 (25.7)	21 (30.4)	152 (25.2)	.
60~73	148 (22.0)	20 (29.0)	128 (21.2)	.
73 and above	112 (16.6)	12 (17.4)	100 (16.6)	.
Current smoker (vs. current non-smoker), n(%)	95 (14.0)	12 (17.1)	83 (13.6)	0.42
Physical activity level(MET-min/week), n(%)				0.75
Inactive	264 (39.6)	29 (42.6)	235 (39.3)	.
Minimally active	109 (16.4)	12 (17.6)	97 (16.2)	.
Highly active	293 (44.0)	27 (39.7)	266 (44.5)	.
BMI(kg/m^2), n(%)				0.026
<18.5	91 (13.4)	4 (5.8)	87 (14.3)	.
18.5~23.0	179 (26.4)	12 (17.4)	167 (27.5)	.
23.0~27.5	210 (31.0)	27 (39.1)	183 (30.1)	.
27.5 and above	197 (29.1)	26 (37.7)	171 (28.1)	.
Waist circumference* (cm), n(%)				<.001
0~Q1	173 (25.6)	6 (8.7)	167 (27.5)	.
Q1~Q2	146 (21.6)	13 (18.8)	133 (21.9)	.
Q2~Q3	136 (20.1)	15 (21.7)	121 (19.9)	.
Q3 and above	222 (32.8)	35 (50.7)	187 (30.8)	.
Family history of CVD, n(%)	75 (11.1)	17 (24.3)	58 (9.6)	<.001
HDL (mg/dL), Mean (SD)	42.4 (11.8)	37.8 (9.8)	42.9 (11.9)	<.001
Triglyceride(mg/dL), Median (IQR)	137.0 (98.0,197.0)	159.0 (117.0,250.0)	135.0 (97.0,192.0)	<.001
Total cholestrol (mg/dL),Mean (SD)	174.9 (42.5)	170.6 (47.9)	175.4 (41.8)	0.37
LDL (mg/dL),Mean (SD)	108.7 (34.1)	105.3 (40.9)	109.1 (33.2)	0.46
Statin use,n(%)	21 (3.1)	8 (11.4)	13 (2.1)	<.001

MET, metabolic equivalent of task; BMI, body mass index; CVD, cardiovascular disease; HDL, high density lipoprotein; SD, standard deviation; IQR, inter-quartile range; LDL, low density lipoprotein.
†Cardio-metabolic multimorbidity was defined as as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke.
*For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table S4 Baseline Characteristics by Status of Cardiometabolic Multimorbidity† among Hypertensive Individuals in Sri Lanka (n=790)

Chracteristics	All (n=790)	Cardiometabolic multimorbidity		P value
		Yes (n=287)	No (n=503)	
Age(y), n(%)				<.001
40~49	98 (12.4)	10 (3.5)	88 (17.5)	.
50~59	186 (23.5)	55 (19.2)	131 (26.0)	.
60~69	310 (39.2)	129 (44.9)	181 (36.0)	.
70 and over	196 (24.8)	93 (32.4)	103 (20.5)	.
Male, n(%)	251 (31.8)	100 (34.8)	151 (30.0)	0.16
Formal education(vs. informal), n(%)	761 (96.3)	278 (96.9)	483 (96.0)	0.55
Married (vs. Others), n(%)	524 (66.3)	170 (59.2)	354 (70.4)	0.001
International wealth Index score, n(%)				0.66
0~43	41 (5.2)	13 (4.5)	28 (5.6)	.
43~60	123 (15.6)	50 (17.4)	73 (14.5)	.
60~73	200 (25.3)	74 (25.8)	126 (25.1)	.
73 and above	425 (53.9)	150 (52.3)	275 (54.8)	.
Current smoker (vs. current non-smoker), n(%)	42 (5.3)	15 (5.2)	27 (5.4)	0.93
Physical activity level (MET-min/week), n(%)				0.045
Inactive	187 (24.1)	79 (28.3)	108 (21.7)	.
Minimally active	201 (25.9)	76 (27.2)	125 (25.2)	.
Highly active	388 (50.0)	124 (44.4)	264 (53.1)	.
BMI(kg/m^2), n(%)				0.20
<18.5	54 (6.9)	15 (5.2)	39 (7.8)	.
18.5~23.0	213 (27.1)	88 (30.8)	125 (25.0)	.
23.0~27.5	299 (38.0)	102 (35.7)	197 (39.4)	.
27.5 and above	220 (28.0)	81 (28.3)	139 (27.8)	.
Waist circumference* (cm), n(%)				0.17
0~Q1	159 (20.1)	48 (16.7)	111 (22.1)	.
Q1~Q2	174 (22.0)	59 (20.6)	115 (22.9)	.
Q2~Q3	201 (25.4)	81 (28.2)	120 (23.9)	.
Q3 and above	256 (32.4)	99 (34.5)	157 (31.2)	.
Family history of CVD, n(%)	215 (27.6)	76 (26.9)	139 (28.0)	0.73
HDL (mg/dL), Mean (SD)	55.3 (9.3)	53.5 (9.6)	56.4 (9.0)	<.001
Triglyceride(mg/dL), Median (IQR)	108.7 (85.1,143.2)	112.4 (89.3,145.9)	105.6 (83.6,143.1)	<.001
Total cholestrol (mg/dL), Mean (SD)	209.2 (49.4)	201.7 (52.2)	213.5 (47.3)	0.001
LDL (mg/dL),Mean (SD)	128.9 (42.1)	122.7 (44.0)	132.5 (40.6)	0.002
Statin use,n(%)	272 (34.4)	131 (45.6)	141 (28.0)	<.001

MET, metabolic equivalent of task; BMI, body mass index; CVD, cardiovascular disease; HDL, high density lipoprotein; SD, standard deviation; IQR, inter-quartile range; LDL, low density lipoprotein.
†Cardio-metabolic multimorbidity was defined as as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke.
*For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table S5. Prevalence of Cardiometabolic Conditions Stratified by Quartiles† of Waist Circumference among Individuals with Hypertension in Bangladesh (n=819)

Cardiometabolic conditions*, n[%(95% CI)]	Total (n=819)	0~Q1 (n=211)	Q1~Q2 (n=250)	Q2~Q3 (n=217)	Q3 and over (n=141)	P trend
Cardiometabolic multimorbidity‡	224 [27.4 (24.3,30.5)]	39 [18.5 (13.5,24.4)]	67 [26.8 (21.4,32.7)]	78 [35.9 (29.6,42.7)]	40 [28.4 (21.1,36.6)]	0.003
One cardiometabolic condition	297 [36.3 (33.0,39.7)]	83 [39.3 (32.7,46.3)]	87 [34.8 (28.9,41.1)]	75 [34.6 (28.3,41.5)]	52 [36.9 (28.9,45.4)]	0.56
Three or more cardiometabolic conditions	56 [6.8 (5.2, 8.8)]	5 [2.4 (0.8, 5.4)]	15 [6.0 (3.4, 9.7)]	22 [10.1 (6.5,14.9)]	14 [9.9 (5.5,16.1)]	<.001
Chronic kidney disease (CKD) §	298 [36.4 (33.1,39.8)]	77 [36.5 (30.0,43.4)]	90 [36.0 (30.0,42.3)]	81 [37.3 (30.9,44.1)]	50 [35.5 (27.6,44.0)]	0.96
Diabetes¶	188 [23.0 (20.1,26.0)]	14 [6.6 (3.7,10.9)]	52 [20.8 (15.9,26.4)]	70 [32.3 (26.1,38.9)]	52 [36.9 (28.9,45.4)]	<.001
Heart disease&	150 [18.3 (15.7,21.1)]	20 [9.5 (5.9,14.3)]	52 [20.8 (15.9,26.4)]	52 [24.0 (18.4,30.2)]	26 [18.4 (12.4,25.8)]	0.007
Stroke&&	173 [21.1 (18.4,24.1)]	55 [26.1 (20.3,32.5)]	44 [17.6 (13.1,22.9)]	53 [24.4 (18.9,30.7)]	21 [14.9 (9.5,21.9)]	0.087

95%CI, 95% confidence interval

† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

* Presence of any one of the following alone: diabetes, heart disease, CKD, and stroke

‡Cardiometabolic multimorbidity was defined as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke;

§CKD was defined as the presence of estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73m^2 or urine albumin and creatinine ratio (UACR)≥30 mg/g;

¶Diabetes was defined as a fasting plasma glucose (FPG) ≥126 mg/dL or self-reported use of anti-diabetic medication;

&Heart disease was acertained based on self-reported physician diagnosis;

&&Stroke was determined if an invidual ever had unconciousness or had both abnormal speech and paralyzed face.

Table S6. Prevalence of Cardiometabolic Conditions Stratified by Quartiles †of Waist Circumference among Individuals with Hypertension in Pakistan (n=677*)

Cardiometabolic conditions**, n[%(95% CI)]	Total (n=677)	0~Q1 (n=173)	Q1~Q2 (n=146)	Q2~Q3 (n=136)	Q3 and over (n=222)	P trend
Cardiometabolic multimorbidity‡	69 [10.2 (8.0,12.7)]	6 [3.5 (1.3, 7.4)]	13 [8.9 (4.8,14.7)]	15 [11.0 (6.3,17.5)]	35 [15.8 (11.2,21.2)]	<.001
One cardiometabolic condition	195 [28.8 (25.4,32.4)]	38 [22.0 (16.0,28.9)]	38 [26.0 (19.1,33.9)]	48 [35.3 (27.3,43.9)]	71 [32.0 (25.9,38.6)]	0.013
Three or more cardiometabolic conditions	10 [1.5 (0.7, 2.7)]	1 [0.6 (0.0, 3.2)]	2 [1.4 (0.2, 4.9)]	2 [1.5 (0.2, 5.2)]	5 [2.3 (0.7, 5.2)]	0.18
Chronic kidney disease(CKD) §	115 [17.0 (14.2,20.0)]	27 [15.6 (10.5,21.9)]	21 [14.4 (9.1,21.1)]	25 [18.4 (12.3,26.9)]	42 [18.9 (14.0,24.7)]	0.27
Diabetes¶	132 [19.5 (16.6,22.7)]	12 [6.9 (3.6,11.8)]	22 [15.1 (9.7,21.9)]	35 [25.7 (18.6,33.9)]	63 [28.4 (22.5,34.8)]	<.001
Heart disease&	49 [7.2 (5.4, 9.5)]	6 [3.5 (1.3, 7.4)]	11 [7.5 (3.8,13.1)]	9 [6.6 (3.1,12.2)]	23 [10.4 (6.7,15.1)]	0.015
Stroke&&	49 [7.2 (5.4, 9.5)]	6 [3.5 (1.3, 7.4)]	13 [8.9 (4.8,14.7)]	11 [8.1 (4.1,14.0)]	19 [8.6 (5.2,13.0)]	0.090

95%CI, 95% confidence interval

† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

* Two subjects had no data on waist circumference

** Presence of any one of the following alone: diabetes, heart disease, CKD, and stroke

‡Cardiometabolic multimorbidity was defined as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke;

§CKD was defined as the presence of estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73m^2 or urine albumin and creatinine ratio (UACR)≥30 mg/g;

¶Diabetes was defined as a fasting plasma glucose (FPG) ≥126 mg/dL or self-reported use of anti-diabetic medication;

&Heart disease was acertained based on self-reported physician diagnosis;

&&Stroke was determined if an invidual ever had unconciousness or had both abnormal speech and paralyzed face.

Table S7. Prevalence of **Cardiometabolic** Conditions Stratified by Quartiles† of Waist Circumference among Individuals with Hypertension in Sri Lanka (n=790)

Cardiometabolic conditions*, n[%(95% CI)]	Total (n=790)	0~Q1 (n=159)	Q1~Q2 (n=174)	Q2~Q3 (n=201)	Q3 and over (n=256)	P trend
Cardiometabolic multimorbidity‡	287 [36.3 (33.0,39.8)]	48 [30.2 (23.2,38.0)]	59 [33.9 (26.9,41.5)]	81 [40.3 (33.5,47.4)]	99 [38.7 (32.7,44.9)]	0.050
One Cardiometabolic condition	315 [39.9 (36.4,43.4)]	77 [48.4 (40.4,56.5)]	74 [42.5 (35.1,50.2)]	73 [36.3 (29.7,43.4)]	91 [35.5 (29.7,41.7)]	0.006
Three or more Cardiometabolic conditions	63 [8.0 (6.2,10.1)]	9 [5.7 (2.6,10.5)]	10 [5.7 (2.8,10.3)]	20 [10.0 (6.2,14.9)]	24 [9.4 (6.1,13.6)]	0.083
Chronic kidney disease(CKD) §	462 [58.5 (55.0,61.9)]	104 [65.4 (57.5,72.8)]	102 [58.6 (50.9,66.0)]	112 [55.7 (48.6,62.7)]	144 [56.3 (49.9,62.4)]	0.072
Diabetes¶	302 [38.2 (34.8,41.7)]	35 [22.0 (15.8,29.3)]	66 [37.9 (30.7,45.6)]	85 [42.3 (35.4,49.4)]	116 [45.3 (39.1,51.6)]	<.001
Heart disease&	118 [14.9 (12.5,17.6)]	19 [11.9 (7.4,18.0)]	21 [12.1 (7.6,17.9)]	44 [21.9 (16.4,28.3)]	34 [13.3 (9.4,18.1)]	0.36
Stroke&&	71 [9.0 (7.1,11.2)]	24 [15.1 (9.9,21.6)]	13 [7.5 (4.0,12.4)]	15 [7.5 (4.2,12.0)]	19 [7.4 (4.5,11.3)]	0.021

95%CI, 95% confidence interval

† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

* Presence of any one of the following alone: diabetes, heart disease, CKD, and stroke

‡Cardiometabolic multimorbidity was defined as the presence of two or more chronic conditions of diabetes, heart disease, CKD, and stroke;

§CKD was defined as the presence of estimated glomerular filtration rate (eGFR) ≤60 ml/min/1.73m^2 or urine albumin and creatinine ratio (UACR)≥30 mg/g;

¶Diabetes was defined as a fasting plasma glucose (FPG) ≥126 mg/dL or self-reported use of anti-diabetic medication;

&Heart disease was acertained based on self-reported physician diagnosis;

&&Stroke was determined if an invidual ever had unconciousness or had both abnormal speech and paralyzed face.

36/bmjopen-2019-030584

Table S8. Prevalence of Various Pairs of Conditions by Quartiles† of Waist Circumference (n=2286*)

Pairs, n[%(95%CI)]	Total (n=2286)	0~Q1 (n=543)	Q1~Q2 (n=570)	Q2~Q3 (n=554)	Q3 and over (n=619)	P trend
DM+CKD	230 [10.1 (8.9,11.4)]	26 [4.8 (3.2, 6.9)]	55 [9.6 (7.4,12.4)]	64 [11.6 (9.0,14.5)]	85 [13.7 (11.1,16.7)]	<.001
CKD+Stroke	67 [2.9 (2.3, 3.7)]	31 [5.7 (3.9, 8.0)]	15 [2.6 (1.5, 4.3)]	12 [2.2 (1.1, 3.8)]	9 [1.5 (0.7, 2.7)]	<.001
CKD+HD	55 [2.4 (1.8, 3.1)]	10 [1.8 (0.9, 3.4)]	14 [2.5 (1.3, 4.1)]	19 [3.4 (2.1, 5.3)]	12 [1.9 (1.0, 3.4)]	0.72
DM+HD	42 [1.8 (1.3, 2.5)]	2 [0.4 (0.0, 1.3)]	16 [2.8 (1.6, 4.5)]	11 [2.0 (1.0, 3.5)]	13 [2.1 (1.1, 3.6)]	0.095
HD+Stroke	30 [1.3 (0.9, 1.9)]	7 [1.3 (0.5, 2.6)]	7 [1.2 (0.5, 2.5)]	11 [2.0 (1.0, 3.5)]	5 [0.8 (0.3, 1.9)]	0.70
DM+Stroke	27 [1.2 (0.8, 1.7)]	2 [0.4 (0.0, 1.3)]	5 [0.9 (0.3, 2.0)]	13 [2.3 (1.3, 4.0)]	7 [1.1 (0.5, 2.3)]	0.078

The count of morbidity pairs was calculated for hypertensive individuals with only 2 other conditions.
95% CI, 95% confidence interval; DM, diabetes; CKD, chronic kidney disease; HD, heart disease
† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm
* Two subjects had no data on waist circumference

Table S9. Prevalence of Various Pairs of Conditions by Quartiles† of Waist Circumference in Bangladesh (n=819)

Pairs, n[%(95%CI)]	Total (n=819)	0~Q1 (n=211)	Q1~Q2 (n=250)	Q2~Q3 (n=217)	Q3 and over (n=141)	P trend
DM+CKD	55 [6.7 (5.1, 8.7)]	5 [2.4 (0.8, 5.4)]	16 [6.4 (3.7,10.2)]	18 [8.3 (5.0,12.8)]	16 [11.3 (6.6,17.8)]	<.001
CKD+Stroke	42 [5.1 (3.7, 6.9)]	18 [8.5 (5.1,13.1)]	12 [4.8 (2.5, 8.2)]	9 [4.1 (1.9, 7.7)]	3 [2.1 (0.4, 6.1)]	0.007
HD+Stroke	22 [2.7 (1.7, 4.0)]	5 [2.4 (0.8, 5.4)]	7 [2.8 (1.1, 5.7)]	8 [3.7 (1.6, 7.1)]	2 [1.4 (0.2, 5.0)]	0.88
CKD+HD	19 [2.3 (1.4, 3.6)]	2 [0.9 (0.1, 3.4)]	8 [3.2 (1.4, 6.2)]	9 [4.1 (1.9, 7.7)]	0	0.94
DM+HD	18 [2.2 (1.3, 3.5)]	2 [0.9 (0.1, 3.4)]	8 [3.2 (1.4, 6.2)]	4 [1.8 (0.5, 4.7)]	4 [2.8 (0.8, 7.1)]	0.40
DM+Stroke	12 [1.5 (0.8, 2.5)]	2 [0.9 (0.1, 3.4)]	1 [0.4 (0.0, 2.2)]	8 [3.7 (1.6, 7.1)]	1 [0.7 (0.0, 3.9)]	0.29

The count of morbidity pairs was calculated for hypertensive individuals with only 2 other conditions.
95% CI, 95% confidence interval; DM, diabetes; CKD, chronic kidney disease; HD, heart disease
† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table S10. Prevalence of Various Pairs of Conditions by Quartiles† of Waist Circumference in Pakistan (n=677*)

Pairs, n[%(95%CI)]	Total (n=677)	0~Q1 (n=173)	Q1~Q2 (n=146)	Q2~Q3 (n=136)	Q3 and over (n=222)	P trend
DM+CKD	29 [4.3 (2.9, 6.1)]	2 [1.2 (0.1, 4.1)]	5 [3.4 (1.1, 7.8)]	7 [5.1 (2.1,10.3)]	15 [6.8 (3.8,10.9)]	0.005
DM+Stroke	12 [1.8 (0.9, 3.1)]	0	3 [2.1 (0.4, 5.9)]	4 [2.9 (0.8, 7.4)]	5 [2.3 (0.7, 5.2)]	0.096
DM+HD	7 [1.0 (0.4, 2.1)]	0	2 [1.4 (0.2, 4.9)]	1 [0.7 (0.0, 4.0)]	4 [1.8 (0.5, 4.5)]	0.12
HD+Stroke	5 [0.7 (0.2, 1.7)]	2 [1.2 (0.1, 4.1)]	0	0	3 [1.4 (0.3, 3.9)]	0.71
CKD+HD	4 [0.6 (0.2, 1.5)]	1 [0.6 (0.0, 3.2)]	1 [0.7 (0.0, 3.8)]		2 [0.9 (0.1, 3.2)]	0.80
CKD+Stroke	2 [0.3 (0.0, 1.1)]	0	0	1 [0.7 (0.0, 4.0)]	1 [0.5 (0.0, 2.5)]	0.28

The count of morbidity pairs was calculated for hypertensive individuals with only 2 other conditions.
95% CI, 95% confidence interval; DM, diabetes; CKD, chronic kidney disease; HD, heart disease
† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm
* Two subjects had no data on waist circumference

Table S11. Prevalence of Various Pairs of Conditions by Quartiles† of Waist Circumference in Sri Lanka (n=790)

Pairs, n[%(95%CI)]	Total (n=790)	0~Q1 (n=159)	Q1~Q2 (n=174)	Q2~Q3 (n=201)	Q3 and over (n=256)	P trend
DM+CKD	146 [18.5 (15.8,21.4)]	19 [11.9 (7.4,18.0)]	34 [19.5 (13.9,26.2)]	39 [19.4 (14.2,25.6)]	54 [21.1 (16.3,26.6)]	0.037
CKD+HD	32 [4.1 (2.8, 5.7)]	7 [4.4 (1.8, 8.9)]	5 [2.9 (0.9, 6.6)]	10 [5.0 (2.4, 9.0)]	10 [3.9 (1.9, 7.1)]	0.93
CKD+Stroke	23 [2.9 (1.9, 4.3)]	13 [8.2 (4.4,13.6)]	3 [1.7 (0.4, 5.0)]	2 [1.0 (0.1, 3.5)]	5 [2.0 (0.6, 4.5)]	0.001
DM+HD	17 [2.2 (1.3, 3.4)]	0	6 [3.4 (1.3, 7.4)]	6 [3.0 (1.1, 6.4)]	5 [2.0 (0.6, 4.5)]	0.37
DM+Stroke	3 [0.4 (0.1, 1.1)]	0	1 [0.6 (0.0, 3.2)]	1 [0.5 (0.0, 2.7)]	1 [0.4 (0.0, 2.2)]	0.64
HD+Stroke	3 [0.4 (0.1, 1.1)]	0	0	3 [1.5 (0.3, 4.3)]	0	0.64

The count of morbidity pairs was calculated for hypertensive individuals with only 2 other conditions.
95% CI, 95% confidence interval; DM, diabetes; CKD, chronic kidney disease; HD, heart disease
† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Table S12. Ratio of Odds Rratios (RORs) and 95% Confidence Interval (CI) between Countries for Variables that Had Significant Interactions† with Country

	ROR (95%CI)(P value)		
Variables	**BD vs PK**	**BD vs SL**	**PK Vs SL**
Age 50~59	0.56 (0.28 , 1.12) (0.099)	0.23 (0.1 , 0.52) (<.001)	0.41 (0.17 , 1.01) (0.052)
Age 60~69	1.22 (0.59 , 2.54) (0.59)	0.22 (0.1 , 0.51) (<.001)	0.18 (0.07 , 0.49) (<.001)
Age 70 and over	1.39 (0.61 , 3.15) (0.43)	0.19 (0.08 , 0.42) (<.001)	0.14 (0.05 , 0.37) (<.001)
Family history of CVD	0.37 (0.19 , 0.72) (0.003)	1.03 (0.63 , 1.67) (0.92)	2.74 (1.28 , 5.88) (0.010)
HDL	1.23 (1.04 , 1.45) (0.015)	1.15 (1.03 , 1.27) (0.010)	0.94 (0.79 , 1.11) (0.44)
Statin use	1.82 (0.39 , 8.43) (0.44)	4.62 (1.63 , 13.07) (0.004)	2.54 (0.78 , 8.24) (0.12)

BD, Bangladesh; PK,Pakistan; SL,Sri Lanka; CVD, cardiovascular disease; HDL, high density lipoprotein

†P values for interaction with country were <0.001 for age,0.012 for history of cardivarscular disease, 0.008 for HDL, and 0.006 for statin use, respectively

Table S13. Multivariate Predictors of Cardiometabolic Multimorbidity among Hypertensive Individuals in Each Country

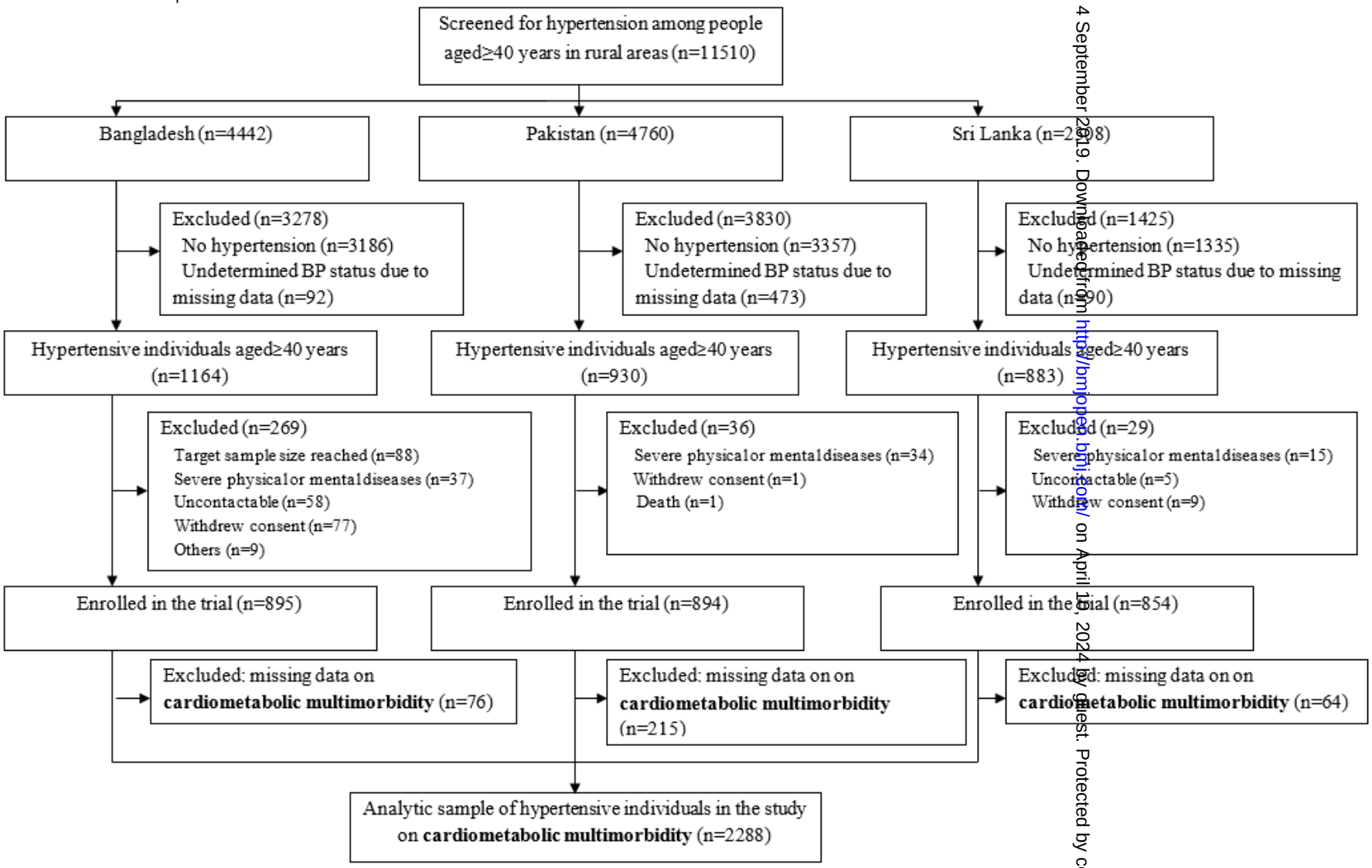
Variable	Bangladesh (n=776) OR (95% CI)	p-value	Pakistan (n=655) OR (95% CI)	p-value	Sri Lanka(n=760) OR (95% CI)	p-value
Age(y)		0.013		0.22		<.001
40~49	1.00		1.00		1.00	
50~59	0.88 (0.56,1.39)	0.58	1.61 (0.89,2.90)	0.11	4.03 (1.91,8.48)	<.001
60~69	1.41 (0.98,2.02)	0.065	1.06 (0.48,2.34)	0.88	6.13 (2.73,13.8)	<.001
70 and over	1.67 (1.11,2.52)	0.015	1.19 (0.51,2.76)	0.69	9.01 (3.56,22.8)	<.001
Gender		0.12		0.27		0.081
Male	1.00		1.00		1.00	
Female	1.47 (0.90,2.39)	0.12	0.72 (0.40,1.30)	0.27	0.66 (0.41,1.05)	0.081
Education		0.22		0.61		0.31
Informal	1.00		1.00		1.00	
Formal	1.22 (0.89,1.67)	0.22	1.20 (0.60,2.40)	0.61	1.51 (0.68,3.36)	0.31
Marrital status		0.97		0.63		0.011
Single or widowed or divorced	1.00		1.00		1.00	
Married	1.01 (0.54,1.88)	0.97	0.75 (0.24,2.35)	0.63	0.73 (0.58,0.93)	0.011
International wealth Index score		0.46		0.17		0.007
0~43	1.00		1.00		1.00	
43~60	1.48 (0.83,2.63)	0.18	2.25 (1.03,4.91)	0.041	1.77 (0.76,4.13)	0.19
60~73	1.58 (0.87,2.88)	0.13	1.84 (0.52,6.46)	0.34	1.75 (1.02,3.03)	0.044
73 and above	1.46 (0.79,2.70)	0.22	1.55 (0.53,4.54)	0.42	1.21 (0.61,2.43)	0.58
BMI(kg/m^2)		0.79		0.88		<.001
<18.5	1.00		1.00		1.00	
18.5~23.0	1.00 (0.55,1.82)	0.99	0.69 (0.20,2.41)	0.56	1.62 (0.91,2.89)	0.099
23.0~27.5	0.86 (0.36,2.06)	0.73	0.68 (0.19,2.40)	0.55	0.85 (0.53,1.38)	0.52
27.5 and above	0.72 (0.34,1.53)	0.39	0.59 (0.16,2.14)	0.42	1.12 (0.54,2.33)	0.75
Smoking		0.51		0.95		0.71
Non current smoker	1.00		1.00		1.00	
Current smoker	1.30 (0.59,2.88)	0.51	0.98 (0.56,1.71)	0.95	1.16 (0.52,2.58)	0.71
Physical activity level(MET-min/week)		<.001		0.96		0.18
Inactive	1.00		1.00		1.00	
Minimally active	1.07 (0.71,1.62)	0.74	0.92 (0.41,2.06)	0.85	0.86 (0.53,1.40)	0.55
Highly active	0.65 (0.48,0.87)	0.004	0.87 (0.34,2.28)	0.78	0.76 (0.53,1.08)	0.13
Waist circumference† (cm)		0.026		0.010		0.002
0~Q1	1.00		1.00		1.00	
Q1~Q2	1.34 (0.83,2.15)	0.23	2.20 (0.84,5.80)	0.11	1.74 (0.98,3.06)	0.057

Variable	Bangladesh (n=776) OR (95% CI)	p-value	Pakistan (n=655) OR (95% CI)	p-value	Sri Lanka(n=760) OR (95% CI)	p-value
Q2~Q3	2.11 (1.26,3.51)	0.004	2.71 (1.07,6.84)	0.035	2.62 (1.23,5.58)	0.013
Q3 and above	1.56 (0.84,2.88)	0.16	3.93 (1.72,9.01)	0.001	2.67 (1.54,4.66)	<.001
Family history of CVD		0.67		0.001		0.82
No	1.00		1.00		1.00	
Yes	0.96 (0.78,1.18)	0.67	2.75 (1.48,5.12)	0.001	0.95 (0.63,1.45)	0.82
Statin use		<.001		0.008		<.001
Nonuser	1.00		1.00		1.00	
User	7.76 (2.76,21.8)	<.001	4.16 (1.45,11.9)	0.008	1.96 (1.42,2.71)	<.001
HDL (mg/dL,per 5 mg/dL increase)	1.04 (0.95,1.13)	0.45	0.87 (0.76,0.99)	0.042	0.89 (0.80,1.00)	0.057
Triglyceride(mg/dL,per 5 mg/dL increase	1.02 (1.01,1.02)	<.001	1.01 (1.00,1.02)	0.017	1.01 (0.99,1.03)	0.26
LDL (mg/dL,per 5 mg/dL increase)	0.99 (0.97,1.01)	0.37	1.00 (0.97,1.03)	0.86	1.01 (0.98,1.04)	0.55

OR, odds ratio; 95% CI, 95% confidence interval; BMI, body mass index; MET, metabolic equivalent of task; CVD, cardiovascular disease; HDL, high density lipoprotein; LDL, low density lipoprotein

† For male ≤82, 82~91, 91~98, ≥98 cm, for female ≤79, 79~88, 88~95, ≥95 cm

Figure S1: Study flow chart of hypertensive individuals included in the study on **cardiometabolic multimorbidity**



STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
3Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5,6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*7,8*
Bias	9	Describe any efforts to address potential sources of bias	7,8
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7,8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8,9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	NA
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	10
Outcome data	15*	Report numbers of outcome events or summary measures	10,11

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11,12
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13,14,15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.