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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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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 Control of Blood Pressure and Risk Attenuation- Bangladesh, Pakistan and Sri Lanka clinical trial.

Main outcome measures CMM was defined as the presence of ≥2 of the conditions: diabetes, chronic kidney disease, heart disease and stroke. Logistic regression was done to evaluate the correlates of CMM.

Results About 25.4% (95% CI 23.6% to 27.2%) of the hypertensive individuals had CMM. Factors positively associated with CMM included residing in Bangladesh (OR 3.42, 95% CI 2.52 to 4.65) or Sri Lankan (3.73, 95% CI 2.48 to 5.61) versus in Pakistan, advancing age (2.33, 95% CI 1.59 to 3.40 for 70 years and over vs 40–49 years), higher waist circumference (2.15, 95% CI 1.42 to 3.25) for Q2–Q3 and 2.14, 95% CI 1.50 to 3.06 for Q3 and above), statin use (2.43, 95% CI 1.84 to 3.22), and higher levels of triglyceride (1.01, 95% CI 1.01 to 1.02 per 5 mg/dL increase). A lower odds of CMM was associated with being physically active (0.75, 95% CI 0.57 to 0.97). A weak inverted J-shaped association between International Wealth Index and CMM was found (p for non-linear=0.058), suggesting higher risk in the middle than higher or lower socioeconomic strata.

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

Strengths and limitations of this study

- This study is the first to evaluate the prevalence and correlates of cardiometabolic multimorbidity (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 (eg, standardised measurements of serum creatinine) and standardised study procedures in all three countries.
- A causal relationship between covariates and 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 generalised 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 and chronic kidney disease (CKD)), is being increasingly recognised 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 with 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 (CVDs) 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 analysed baseline data from the ongoing Control of Blood Pressure and Risk Attenuation- Bangladesh, Pakistan and Sri Lanka (COBRA-BPS) 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 hypothesised 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 and (3) waist circumference will be more strongly associated with CMM than BMI.

METHODS

Population

The present study was performed using the baseline data from COBRA-BPS full-scale study. The study methodology has been described previously.[10] Briefly, COBRA-BPS full-scale study is an ongoing 2-year cluster randomised 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 (≤2.5 km for near and >2.5 for far) from the government primary care clinics such that there were six near and four 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 (BP) to ≥140 mm Hg, or diastolic BP to ≥90 mm Hg based on two readings from 2o 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 mentally comprised leading to the incapability of giving consent.

Online supplementary figure 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 (see online supplementary figure 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 and IWI≥73). Lifestyle factors included smoking status (current smoker vs non-current smoker) and physical activity. Physical activity was evaluated by the short version of the International Physical Activity Questionnaire[12] and was classified as inactive, minimally active and highly active. BMI was calculated as weight (in kilogram)/height (in metres)^2 and was categorised 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 the gender-specific quartiles (for male ≤82, 82–91, 91–98, ≥98 cm, for female ≤79, 79–88, 88–95 and ≥95 cm). Heart disease was ascertained based on self-reported physician diagnosis of angina, heart attack and heart failure. Stroke was determined according to 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 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 ≥126 mg/dL or self-reported use of antidiabetic medication. CKD was defined as the presence of estimated glomerular filtration rate (GFR) ≤60 mL/min/1.73 m^2 or urine albumin and creatinine ratio (UACR) ≥30 mg/g. GFR was estimated using the original CKD- Epidemiology Collaboration 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 traditional cardiovascular risk factors (eg, hypertension and diabetes), and kidney-specific risk factors (eg, dyslipidaemia, anaemia and low-grade inflammation).[16]

The comparison of characteristics between individuals with and without CMM was performed using independent sample t-test for continuous variables and χ^2 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 generalised estimating equation 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. ORs and 95% CIs 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 non-linear associations of CMM with IWI and waist circumference, we further examined their associations with the restricted cubic splines by modelling the two covariates as continuous variables.[17] We used '%RCS_Reg' SAS macro[18] to perform adjusted analysis with five 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 ORs (RORs)[19] and subgroup analysis by country.

All analyses were conducted using SAS V.9.4, and all hypothesis testing was two tailed with p<0.05 set as statistically significant.

Patient and public involvement statement

Patients and public 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).

Online 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 summarised in online supplementary tables S2–4.

CMM conditions

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

CMM and waist circumference

The prevalence of CMM increased across the first three 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 online supplementary tables S5–7. CMM was most prevalent among participants from Sri Lanka (36.3%, 95% CI 33.0% to 39.8%), followed by those from Bangladesh (27.4%, 95% CI 24.3% to 30.5%) and Pakistan (10.2%, 95% CI 8.0% to 12.7%).

The bivariate associations between morbidity pairs and waist circumference are presented in online supplementary table S8. The most frequently observed pair was diabetes and CKD (10.1%, 95% CI 8.9% to 11.4%), and least observed was diabetes and stroke (1.2%, 95% CI 0.8% to 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 (see online supplementary tables S9–11).

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 (%)				<0.001
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)	<0.001
Married (vs others), n (%)	1679 (73.4)	399 (68.7)	1280 (75.0)	0.003
International Wealth Index score, n (%)				<0.001
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 (%)				<0.001
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 (%)				<0.001
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 (%)				<0.001
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)	<0.001
Total cholesterol (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)	<0.001

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

Factors associated with CMM

In multivariate-adjusted analysis, living in Bangladesh or Sri Lanka (vs 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

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 value for trend
Cardiometabolic multimorbidity*	580 (25.4 (23.6 to 27.2))	93 (17.1 (14.1 to 20.6))	139 (24.4 (20.9 to 28.1))	174 (31.4 (27.6 to 35.5))	174 (28.1 (24.6 to 31.8))	<0.001
Single cardiometabolic condition	807 (35.3 (33.3 to 37.3))	198 (36.5 (32.4 to 40.7))	199 (34.9 (31.0 to 39.0))	196 (35.4 (31.4 to 39.5))	214 (34.6 (30.8 to 38.5))	0.56
Three or more cardiometabolic conditions	129 (5.6 (4.7 to 6.7))	15 (2.8 (1.6 to 4.5))	27 (4.7 (3.1 to 6.8))	44 (7.9 (5.8 to 10.5))	43 (6.9 (5.1 to 9.2))	<0.001
Chronic kidney disease (CKD)†	875 (38.3 (36.3 to 40.3))	208 (38.3 (34.2 to 42.5))	213 (37.4 (33.4 to 41.5))	218 (39.4 (35.3 to 43.6))	236 (38.1 (34.3 to 42.1))	0.88
Diabetes‡	622 (27.2 (25.4 to 29.1))	61 (11.2 (8.7 to 14.2))	140 (24.6 (21.1 to 28.3))	190 (34.3 (30.3 to 38.4))	231 (37.3 (33.5 to 41.3))	<0.001
Heart disease§	317 (13.9 (12.5 to 15.4))	45 (8.3 (6.1 to 10.9))	84 (14.7 (11.9 to 17.9))	105 (19.0 (15.8 to 22.5))	83 (13.4 (10.8 to 16.3))	0.005
Stroke¶	293 (12.8 (11.5 to 14.3))	85 (15.7 (12.7 to 19.0))	70 (12.3 (9.7 to 15.3))	79 (14.3 (11.5 to 17.5))	59 (9.5 (7.3 to 12.1))	0.008

*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 ≤60 mL/min/1.73 m^2 or urine albumin and creatinine ratio ≥30 mg/g.
‡Diabetes was defined as a fasting plasma glucose ≥126 mg/dL or self-reported use of antidiabetic 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 paralysed face.
** Cardiometabolic conditions included diabetes, heart disease, CKD and stroke.

Table 3 Multivariate predictors of cardiometabolic multimorbidity among hypertensive individuals in rural Bangladesh, Pakistan and Sri Lanka

	Model 1 (n=2288)		Model 2 (n=2275)		Model 3 (n=2191)	
Variables	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Country		<0.001		<0.001		<0.001
Pakistan	1.00		1.00		1.00	
Bangladesh	3.28 (2.41 to 4.47)	<0.001	3.22 (2.41 to 4.29)	<0.001	3.42 (2.52 to 4.65)	<0.001
Sri Lanka	4.98 (3.76 to 6.58)	<0.001	3.40 (2.50 to 4.63)	<0.001	3.73 (2.48 to 5.61)	<0.001
Age (year)				<0.001		<0.001
40–49			1.00		1.00	
50–59			1.35 (0.99 to 1.86)	0.060	1.29 (0.94 to 1.77)	0.12
60–69			2.08 (1.51 to 2.86)	<0.001	1.82 (1.31 to 2.53)	<0.001
70 and over			2.59 (1.81 to 3.70)	<0.001	2.33 (1.59 to 3.40)	<0.001
Gender				0.32		0.58
Male			1.00		1.00	
Female			0.86 (0.63 to 1.16)	0.32	0.92 (0.67 to 1.25)	0.58
Education				0.046		0.17
Informal			1.00		1.00	
Formal			1.29 (1.00 to 1.64)	0.046	1.20 (0.93 to 1.56)	0.17
Marital status				0.15		0.18
Single or widowed or divorced			1.00		1.00	
Married			0.82 (0.63 to 1.08)	0.15	0.82 (0.62 to 1.10)	0.18
International Wealth Index score				0.025		0.014
0–43			1.00		1.00	
43–60			1.60 (1.11 to 2.31)	0.012	1.63 (1.09 to 2.44)	0.018
60–73			1.64 (1.14 to 2.36)	0.008	1.69 (1.12 to 2.55)	0.013
73 and above			1.38 (0.93 to 2.04)	0.11	1.29 (0.84 to 1.97)	0.25
BMI (kg/m^2)				<0.001		0.24
<18.5			1.00		1.00	
18.5–23.0			1.85 (1.30 to 2.65)	<0.001	1.17 (0.78 to 1.76)	0.45
23.0–27.5			2.13 (1.45 to 3.14)	<0.001	0.90 (0.57 to 1.42)	0.65
27.5 and above			2.44 (1.62 to 3.66)	<0.001	0.89 (0.56 to 1.41)	0.61
Smoking						0.87
Non-current smoker					1.00	
Current smoker					1.04 (0.66 to 1.64)	0.87
Physical activity level (MET-min/week)						0.010
Inactive					1.00	
Minimally active					0.97 (0.71 to 1.30)	0.82
Highly active					0.75 (0.57 to 0.97)	0.029
Waist circumference* (cm)						<0.001
0–Q1					1.00	
Q1–Q2					1.43 (1.03 to 1.99)	0.033
Q2–Q3					2.15 (1.42 to 3.25)	<0.001
Q3 and above					2.14 (1.50 to 3.06)	<0.001
Family history of CVD						0.55
No					1.00	
Yes					1.08 (0.84 to 1.37)	0.55
Statin use						<0.001
Non-user					1.00	

Continued

Table 3 Continued

Variables	Model 1 (n=2288) OR (95% CI)	Model 1 P value	Model 2 (n=2275) OR (95% CI)	Model 2 P value	Model 3 (n=2191) OR (95% CI)	Model 3 P value
User					2.43 (1.84 to 3.22)	<0.001
HDL (mg/dL, per 5 mg/dL increase)					0.96 (0.89 to 1.02)	0.17
Triglyceride(mg/dL, per 5 mg/dL increase					1.01 (1.01 to 1.02)	<0.001
LDL (mg/dL, per 5 mg/dL increase)					1.00 (0.98 to 1.01)	0.57

*For male ≤82, 82–91, 91–98, ≥98 cm, for female ≤79, 79–88, 88–95, ≥95 cm.
BMI, body mass index; CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MET, metabolic equivalent of task.

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) (see online supplementary tables S12 and 13). These associations varied in strength but not direction across the three countries. Multivariable-adjusted restricted cubic spline analyses suggested no evidence of a non-linear association between waist circumference and CMM (p for non-linear trend=0.59 based on model 3) but a weak non-linear association between IWI and CMM (figure 1A, inverted J-shaped, p for non-linear trend=0.058 based on model 3, and figure 1B, p for non-linear 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 three South Asian countries indicated a higher prevalence with one in four individuals having two additional cardiometabolic

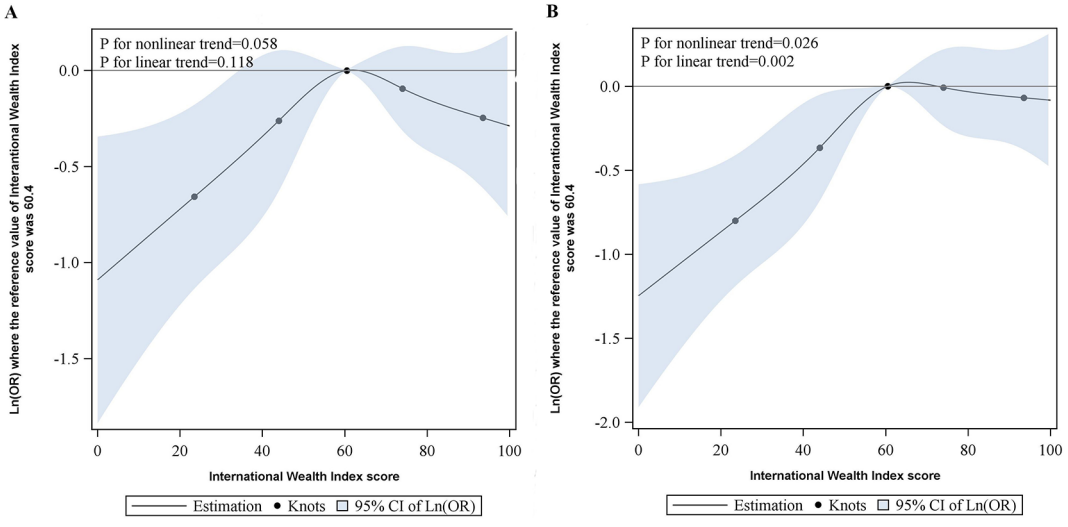

Figure 1 Multiple-adjusted log (ORs) and 95% CIs of cardiometabolic multimorbidity with International Wealth Index Score. A was based on model 3 in table 3, while B was derived based on the model adjusted for only age and gender.

comorbid 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 with 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-income 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 with 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 aetiology 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 programme 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 (eg, standardised measurements of serum creatinine), and standardised 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 comorbidity 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 generalised to all rural-residing hypertensive individuals aged ≥40 years in each country.

In conclusion, our study shows an alarmingly high burden of CMM affecting one in four 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 customised to individual countries. Strategies to manage central obesity may be relevant to the prevention and management of CMM in rural South Asia.

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