Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2018, 7(2): 1-12

The Relationships and Risk Factors Associated with Hypertension, Diabetes, and Proteinuria among Adults from Bheramara Upazila, Bangladesh: Findings from Portable Health Clinic Data, 2013-2016

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ABSTRACT

Objective: *The aim of this study was to investigate the relationships among hypertension, diabetes, and proteinuria and their risk factors in adults who participated in a community-based mobile health check-up service called portable health clinic (PHC) in rural Bangladesh.* ***Methods:*** *Data were collected from 2890 individuals who agreed to participate in the PHC at Bheramara sub-district between 2013 and 2016. Data included basic demographic and health check-up information. Multivariate logistic regression models were used with three outcome variables (proteinuria, diabetes, and hypertension) and four independent and control variables (age, sex, pulse rate, and body mass index).* ***Results:*** *Among participants who had both hypertension and diabetes, 77% had proteinuria. Among those who had diabetes, 55% had proteinuria and 45% had hypertension. Age and sex-adjusted logistic regression models found that diabetes was significantly associated with proteinuria (odds ratio OR=3.0, P=0.005), while the association between hypertension and proteinuria showed borderline significance (P<0.057). Hypertension was significantly associated with diabetes after controlling for age and sex (OR=1.5, P<0.001). Participants aged older than 40 years had higher odds of having diabetes or having hypertension comparing with the odds for participants aged between 15 and 39 years.* ***Conclusions:*** *Prevention of complications in Non-Communicable Diseases (NCD) in Bheramara needs to focus on sub-populations aged older than 40 years and those with hypertension, diabetes, and/or proteinuria. PHC services in rural Bangladesh is important for screening a large number of unaware and undiagnosed diabetic, hypertensive, and proteinuria patients.*

Keywords: Diabetes, Hypertension, Proteinuria, Risk factors, Rural Bangladesh, Portable Health Clinic

INTRODUCTION

Hypertension, diabetes, and proteinuria have enormous public health significance in both developed and developing countries because these conditions are associated with increased risks of developing complications, such as cardiovascular disease (CVD) and chronic kidney disease [1-5]. In Bangladesh, such non-communicable diseases (NCD) account for nearly 60% of all deaths [6,7]. According to a recent report from the World Health Organization (WHO), Bangladesh has a high burden of hypertension among the adult population in rural areas, with an estimated prevalence of 24% [8]. A meta-analysis of diabetic studies conducted in Bangladesh estimated that the prevalence of diabetes among adults had more than doubled, from 4% in 1995-2000 to 9% in 2006-2010 [1] and projected to 13% by 2030 [9]. Under such conditions, both diabetes and hypertension are known to be risk factors for proteinuria [10], which is an early marker of kidney damage and a manifestation of chronic kidney disease [11,12]. In addition, proteinuria is known to be a common complication of both hypertension and diabetes [4,8,10,13]. Despite a need for

the prevention of hypertension, diabetes, and proteinuria in Bangladesh, few studies have examined the co-existence of these diseases and their risk factors, particularly in rural sub-district areas in Bangladesh. Most research on the risk factors for hypertension, diabetes, and proteinuria has been conducted at country and division levels or in areas relatively close to Dhaka city in Bangladesh [1]. Thus, factors associated with these three diseases in other areas of Bangladesh are unclear. The relationships among hypertension, diabetes, and proteinuria and their risk factors have previously been well documented worldwide and also prevalence of diabetes, hypertension and proteinuria in Bangladesh was previously reported [10]. However, few studies have investigated the relationships and the risk factors for these three diseases jointly in a combined approach in Bangladesh. In addition, several previous studies found geographical differences in the relationships and factors associated with proteinuria, diabetes, and hypertension [12,14,15]. It will be meaningful to investigate these in rural sub-district areas in Bangladesh in order to find any potential differences of factors associated with these three diseases comparing with other different areas of Bangladesh or other countries. We have already reported that the prevalence of proteinuria is higher in the western and north-western regions of Bangladesh (17%-28%) than in other regions (6%-9%) [16]. Thus, it is critical to investigate the relationships and factors associated with hypertension, diabetes, and proteinuria in the western rural areas of Bangladesh, including Bheramara sub-districts of the Kushita district. In Bangladesh, a mobile health check-up system called "portable health clinic" (PHC) was introduced in the Bheramara in 2013. PHC is an e-health service delivery system that includes a set of medical sensor devices in a briefcase to allow mobile health check-up and tele-medicine services using Skype in remote rural areas [17-19] (Figure 1). This PHC service, as a role of early detection of NCD, has been implemented by Grameen Communications in Bangladesh since 2010, and it had reached nearly 35,000 people at 32 locations at the beginning of 2017 [20]. In Bheramara, the PHC service has been implemented by healthcare entrepreneurs as a social business for the sustainable provision NCD prevention services. The aim of the present study was to investigate the relationships among hypertension, diabetes, and proteinuria and their risk factors in rural adults who participated in PHC services in Bheramara sub-district between 2013 and 2016.

Figure 1 Portable health clinic box, healthcare entrepreneur, and health check-up result

METHODS

Data Source and Data Collection Procedures

Data were collected from all community residents who agreed to participate in PHC health check-up services between September 2013 and April 2016 in Bheramara sub-district. According to the 2011 Bangladesh census, the Bheramara sub-district has a population of 208,000 in six unions [21]. Bheramara was chosen because of higher prevalence of proteinuria than other regions of Bangladesh [16], scares of previous studies at Western rural areas of Bangladesh and established collaborative research partnerships with local governments and local communities of Bheramara. Participants were individuals of any age who voluntary visited at least one of eight PHC service points that covered all six unions in Bheramara. Prior to the implementation of PHC services, community awareness events were held in Bheramara to inform about availabilities of PHC services at these eight services points. Each of eight service points were located near rural village markets, near the counselor's office, and near elementary schools. These PHC services were scheduled and arranged by project staff from Grameen Communications. Healthcare entrepreneurs were locally recruited and trained as social entrepreneurs by Grameen Communications to provide PHC services in Bangla once every two weeks. Each health check-up service had a nominal fee. For example, a blood pressure test was 10 Taka and a blood glucose test was 30 Taka. Most participants did not undergo all health check-up tests but selected the tests according to their requirements. Participant basic demographic information, such as age, sex, and location, was collected using a standardized registration sheet. During the PHC health check-up, the following

anthropometric and clinical data were measured or tested by the trained healthcare entrepreneurs: 1) height, 2) weight, 3) hip circumference, 4) waist circumference, 5) body temperature, 6) systolic blood pressure, 7) diastolic blood pressure, 8) blood glucose, 9) blood hemoglobin, 10) urinary glucose, 11) urinary protein, 12) urinary urobilinogen, 13) urinary pH, 14) pulse rate, and 15) blood cholesterol. The result of each health check-up test was ranked into one of four different color-coded risk levels as follows: green (healthy), yellow (caution), orange (affected), and red (emergent). Detailed methodologies including privacy and security of collecting patient's personal health data have been described elsewhere [16,17,19].

Dependent and Independent Variables and Measurements

The main outcome variables were hypertension, diabetes, and proteinuria. Hypertension was defined as a systolic blood pressure more than 140 mmHg or a diastolic blood pressure more than 90 mmHg. Based on the definition, the hypertension variable was dichotomously coded as "yes" or "no". Blood pressure was measured using an A&D UA-772PBT. This device can measure not only blood pressure but also pulse rate and arrhythmia. Diabetes was defined as a blood glucose level more than 200 mg/dL at the time of the PHC health check-up. This definition was based on WHO criteria, and diabetes was classified dichotomously as "yes" or "no." A casual blood glucose level was measured, as the time from the participant's last meal was not asked. Diabetes was measured using the Medisafe Fit (Terumo, Tokyo, Japan). A drop of blood was taken from each participant's middle fingertip. Proteinuria was defined as a protein level of more than or equal to 30 mg/dL in urine. It was measured using the dipstick method with Urine Test Stripes Uric 3V, which provides a color scale that indicates five levels of protein as follows: absent (<10 mg/dL), trace (10-20 mg/dL), 1+ (≥30 mg/dL), 2+ (>100 mg/dL), and 3+ (>500 mg/dL). Based on the definition, proteinuria was binary classified as "yes" or "no". The independent variables were overweight or obesity and abnormal pulse rate. The WHO criteria were used to define all variables. Overweight and obesity were defined as body mass index (BMI) values of more than 25 and 30 kg/m^2, respectively. Abnormal pulse rate was defined as a pulse rate of more than 100 beats per minute or less than 50 beats per minute. All of the independent variables were dichotomously coded as "yes" or "no". Age and sex were selected as the main control variables.

Data Analysis

Bivariate analysis was performed to describe the inter-relationships among hypertension, diabetes, and proteinuria. Pearson's chi-square test (bivariate analysis) was performed to describe the unadjusted association between dependent and independent/control categorical variables. Multiple logistic regression analysis was performed to describe the adjusted association of independent variables with the likelihood of hypertension, diabetes, and proteinuria after controlling for age and sex. Each independent variable was included in the logistic regression models separately because the independent variables were highly correlated (multi-collinearity). For example, significant correlations were found between hypertension and overweight/obesity (P<0.001), between abnormal pulse rates and overweight/obesity (P=0.009), and between hypertension and proteinuria (P=0.03) (Supplementary Table 1). Thus, the following four distinct models were used for each dependent variable:

Model 1: Logit Y1 (X) = $\beta 0 + \beta 1$ (age) + $\beta 2$ (sex) + $\beta 3$ (hypertension or diabetes) + ε

Model 2: Logit Y1 (X) = $\beta 0 + \beta 1$ (age) + $\beta 2$ (sex) + $\beta 3$ (abnormal pulse) + ε

Model 3: Logit Y1 (X) = $\beta 0 + \beta 1$ (age) + $\beta 2$ (sex) + $\beta 3$ (overweight or obesity) + ε

Model 4: Logit Y1 (X) = $\beta 0 + \beta 1$ (age) + $\beta 2$ (sex) + $\beta 3$ (hypertension or proteinuria) + ε

All statistical analyses were performed using SPSS version 21 (IBM Corp., Armonk, NY). A P-value <0.05 was considered significant.

RESULTS

Total of 2890 individuals from Bheramara participated in PHC health check-up services during the study period. Among these individuals, those younger than 15 years (19 cases) and those who had missing or inconsistent data (4 cases) were excluded from the analysis. Thus, the total sample size for analysis was 2867 (Figure 2). The most popular health check-up item selected by the participants was blood glucose test for diabetes (n=2539), followed by blood pressure for hypertension (n=2411) and pulse rate (n=2400) (Figure 2). Only 18.8% (n=539) and 15.3% (n=440) of the participants underwent measurement for height/weight and urinary protein, respectively.

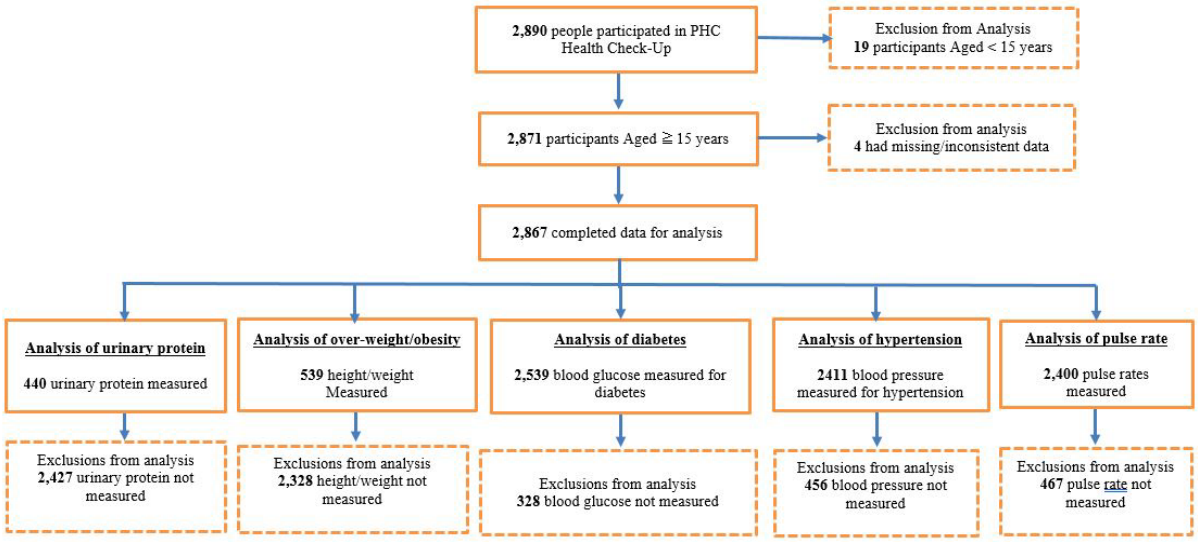

Figure 2 Flow diagram showing participant exclusion and the final sample size of the study

Table 1 shows participant characteristics with regard to age and sex, as well as health status according to the PHC health check-up findings. Most participants (85%) were 30 years of age or older, with a mean age of 44 years, and over 60% were male. An abnormal pulse rate was noted in 12% of the participants. More than one-third of the participants (35%) were overweight or obese, while 11% were underweight. The percentages of participants who had hypertension, diabetes, and proteinuria were 37%, 18%, and 32%, respectively.

Table 1 Socio-demographic characteristics and health status among individuals who participated in the portable health check-up at Bheramara Upazila, Bangladesh between 2013 and 2016

Items	Total	
	N	%
Age (years)	2867	Mean = 44.1
		Range = 15-95
Age groups	2867	-
15-29 years	424	14.8
30-39 years	739	25.8
40-49 years	671	23.4
50-59 years	591	20.6
≥60 years	442	15.4
Sex	2867	-
Male	1758	61.3
Female	1109	38.7
Pulse rate category	2400	-
Normal (50-100 beats/min)	2110	87.9
Abnormal (≤49 or ≥101 beats/min)	290	12.1
BMI category	539	-
Underweight (<18.5 kg/m^2)	60	11.1
Normal (18.5-25 kg/m^2)	292	54.2
Overweight or Obese (≥25 kg/m^2)	187	34.7
Hypertension	2411	-
No	1510	62.6
Yes	901	37.4
Diabetes	2539	-
No	2091	82.4
Yes	448	17.6

Urinary Protein test	440	
Negative (−) <14 mg/dL	200	45.5
Trace (−/+) 15-29 mg/dL	101	23
Positive (+1) 30-99 mg/dL	121	27.5
Positive (+2 or +3) ≥100 gm/dL	18	4.1

Table 2 presents the unadjusted associations of independent variables with hypertension, diabetes, and proteinuria. Both hypertension and diabetes were significantly associated with age group (P<0.001). The percentage of participants with hypertension was significantly higher among those with overweight or obesity (47%) than among those without overweight or obesity (24%) (P<0.001), among those with diabetes (49%) than among those without diabetes (35%) (P<0.001), and among those with proteinuria (35%) than among those without proteinuria (25%) (P=0.026). The percentage of participants with diabetes was significantly higher among those with hypertension (23%) than among those without hypertension (14%) (P<0.001) and among those with proteinuria (13%) than among those without proteinuria (5%) (P<0.004). The percentage of participants with proteinuria was significantly higher among those with diabetes (55%) than among those without diabetes (29%) (P<0.004) and among those with hypertension (38%) than among those without hypertension (27%) (P<0.026).

Table 2 Unadjusted association of independent variables with hypertension, diabetes, and proteinuria

Items	Hypertension (N = 2,411)			Diabetes (N = 2,539)			Proteinuria (N = 440)		
	n/N	%	P for Diff.	n/N	%	P for Diff.	n/N	%	P for Diff.
Sex	N = 2411	-	-	N = 2539	-	-	N = 440	-	-
Male	541/1462	37	0.34	257/1574	16.3	0.015	73/254	28.7	0.081
Female	360/949	37.9		191/965	19.8		66/186	35.5	
Age groups	N = 2411	-	-	N = 2539	-	-	N = 440	-	-
15–39 years	264/993	26.6	<0.001	103/1013	10.2	<0.001	61/190	32.1	0.86
40–49 years	231/568	40.7		116/602	19.3		30/106	28.3	
50–59 years	241/505	47.7		130/531	24.5		24/72	33.3	
≥60 years	165/345	47.8		99/393	25.2		24/72	33.3	
Pulse rate	N = 2388	-	-	N = 2139		-	N = 408	-	-
Normal	756/2099	36	<0.001	322/1892	17	0.12	101/351	28.8	0.033
Abnormal	140/289	48.4		50/247	20.2		24/57	42.1	
Overweight/ obesity	N = 536	-	-	N = 490		-	N = 385	-	-
No	83/350	23.7	<0.001	34/320	10.6	0.48	78/264	29.5	0.5
Yes	87/186	46.8		19/170	11.2		35/121	28.9	
Hypertension	-	-	-	N = 2154	-	-	N = 412	-	-
No	-	-	-	191/1344	14.2	<0.001	81/298	27.2	0.026
Yes	-	-	-	182/810	22.5		43/114	37.7	
Diabetes	N = 2154	-	-	-	-	-	N = 407	-	-
No	628/1781	35.3	<0.001	-	-	-	108/378	28.6	0.004
Yes	182/373	48.8		-	-	-	16/29	55.2	
Proteinuria	N = 412	-	-	N = 407	-	-	-	-	-
No	71/288	24.7	0.026	13/283	4.6	0.004	-	-	-
Yes	43/124	34.7		16/124	12.9		-	-	-

Figure 3 shows that among participants who had both hypertension and diabetes, 77% had proteinuria. Additionally, among those who had both diabetes and proteinuria, 63% had hypertension. Finally, among those who had both hypertension and proteinuria, 26% had diabetes.

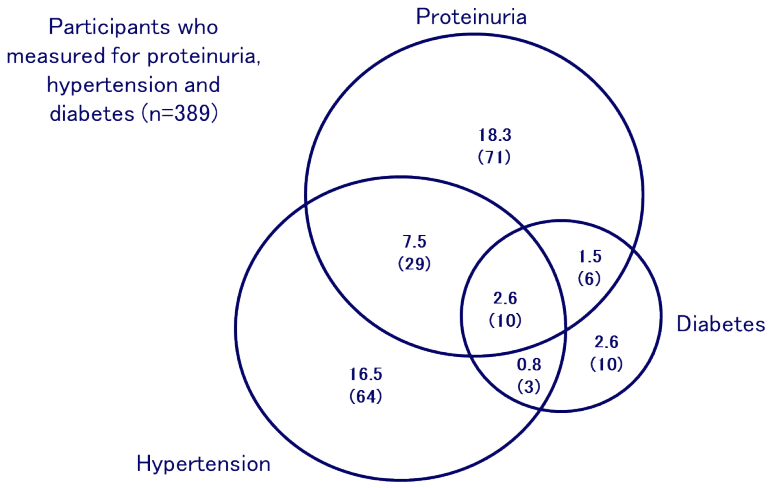

Figure 3 Percentages of participants who had complications of proteinuria, hypertension, and diabetes

Table 3 shows the age- and sex-adjusted and 95% confidence intervals for factors affecting the likelihood of hypertension, diabetes, and proteinuria. The multivariate results from Models 1-3 for hypertension indicated that participants with diabetes, abnormal pulse rate, or overweight/obesity were significantly more likely to have hypertension (OR=1.5, P<0.001; OR=1.7, P<0.001; and OR=3.2, P<0.001, respectively). Model 4 showed that the association between proteinuria and hypertension was borderline significant (OR=1.6, P=0.057). The results of Model 1 for diabetes indicated that diabetes was significantly more likely to occur in participants with hypertension than in those without hypertension (OR=1.5, P<0.001). The results of Model 4 indicated that diabetes was 3 times more likely in participants with proteinuria than in those without proteinuria (P=0.057). With regard to age groups, Models 1-4 showed a statistically significant trend of increases in the ORs for hypertension and diabetes as the age group increased to 40 years or older. The results of Model 1 for proteinuria indicated that proteinuria was significantly more likely to occur in participants with diabetes than in those without diabetes (OR=3.0, P<0.005). The results of Model 2 indicated that the association between proteinuria and hypertension was marginally significant (OR=1.6, P<0.057).

Table 3 Age and sex-adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) for factors associated with hypertension, diabetes, and proteinuria among participants of the portable health clinic

	Hypertension											
	Age and sex-adjusted											
	Model 1 (N = 2,154)			Model 2 (N = 2,388)			Model 3 (N = 536)			Model 4 (N = 412)		
	OR	P	95% CI	OR	P	95% CI	OR	P	95% CI	OR	P	95% CI
Sex												
Male	Reference			Reference			Reference			Reference		
Female	0.99	0.93	0.83–1.19	0.93	0.39	0.78–1.10	1.15	0.49	0.78–1.70	1.65	0.03	1.04–2.60
Age groups												
15–39 years	Reference			Reference			Reference			Reference		
40–49 years	1.84	<0.001	1.46–2.33	1.88	<0.001	1.51–2.35	1.60	0.08	0.95–2.68	2.11	0.016	1.15–3.85
50–59 years	2.34	<0.001	1.84–2.97	2.49	<0.001	1.99–3.13	3.52	<0.001	2.04–6.07	2.60	0.004	1.36–4.95
≥60 years	2.42	<0.001	1.85–3.17	2.49	<0.001	1.93–3.22	4.46	<0.001	2.53–7.89	4.24	<0.001	2.26–7.95
Diabetes												
No	Reference											
Yes	1.52	<0.001	1.21–1.91									
Abnormal pulse rate												
No				Reference								
Yes				1.66	<0.001	1.29–2.14						
Overweight/obesity												
No							Reference					
Yes							3.22	<0.001	2.12–4.87			

Proteinuria												
No										Reference		
Yes										1.59	0.057	0.99–2.57
						Diabetes						
	Model 1 (N = 2,154)			**Model 2 (N = 2,139)**			**Model 3 (N = 490)**			**Model 4 (N = 407)**		
	OR	**P**	**95% CI**	**OR**	**P**	**95% CI**	**OR**	**P**	**95% CI**	**OR**	**P**	**95% CI**
Sex												
Male	Reference			Reference			Reference			Reference		
Female	1.07	0.56	0.85–1.35	1.07	0.55	0.85–1.36	1.26	0.43	0.71–2.26	1.54	0.28	0.70–3.39
Age groups												
15–39 years	Reference			Reference			Reference			Reference		
40–49 years	1.70	0.001	1.24–2.32	1.82	<0.001	1.33–2.49	1.64	0.25	0.71–3.81	1.70	0.35-	0.56–5.13
50–59 years	2.59	<0.001	1.91–3.51	2.88	<0.001	2.13–3.90	2.95	0.009	1.31–6.62	2.92	0.050	1.00–8.52
≥60 years	2.28	<0.001	1.62–3.22	2.53	<0.001	1.80–3.56	2.91	0.012	1.26–6.70	2.72	0.07	090–8.26
Hypertension												
No	Reference											
Yes	1.52	<0.001	1.21–1.91									
Abnormal pulse rate												
No				Reference								
Yes				1.17	0.36	0.83–1.65						
Overweight/obesity												
No							Reference					
Yes							1.06	0.86	0.57–1.97			
Proteinuria												
No										Reference		
Yes										3.00	0.006	1.38-6.50
						Proteinuria						
	Model 1 (N = 407)			**Model 2 (N = 408)**			**Model 3 (N = 385)**			**Model 4 (N = 412)**		
	OR	**P**	**95% CI**	**OR**	**P**	**95% CI**	**OR**	**P**	**95% CI**	**OR**	**P**	**95% CI**
Sex												
Male	Reference			Reference			Reference			Reference		
Female	1.30	0.25	0.84–2.01	1.33	0.21	0.85–2.09	1.70	0.02	1.08–2.68	1.39	0.14	0.90–2.14
Age groups												
15–39 years	Reference			Reference			Reference			Reference		
40–49 years	0.75	0.33	0.43–1.32	0.72	0.26	0.41–1.27	0.63	0.14	0.34–1.16	0.66	0.16	0.37–1.18
50–59 years	1.07	0.84	0.58–1.95	1.01	0.98	0.55–1.84	1.13	0.70	0.61–2.11	0.98	0.94	0.53–1.80
≥60 years	0.88	0.69	0.47–1.65	1.00	0.99	0.55–1.83	1.03	0.92	0.55–1.94	0.93	0.82	0.50–1.73
Diabetes												
No	Reference											
Yes	3.00	0.005	1.38–6.51									
Abnormal pulse rate												
No				Reference								
Yes				1.60	0.12	0.88–2.91						
Overweight/obesity												
No							Reference					
Yes							1.00	0.99	0.60–1.64			
Hypertension												
No										Reference		
Yes										1.59	0.057	0.99–2.57

DISCUSSION

To our knowledge, this is the first study to investigate the relationships and factors associated with hypertension, diabetes, and proteinuria jointly in the western region of rural Bangladesh. In this community-based study, the key finding was that among participants with both hypertension and diabetes, nearly 80% had proteinuria. In addition, among participants with diabetes, more than half had proteinuria and nearly half had hypertension, while among participants with hypertension, 38% had proteinuria and 23% had diabetes. The results also indicated that diabetes was

significantly associated with proteinuria after adjusting for age and sex, while the association between hypertension and proteinuria showed borderline significance. These findings suggest that although proteinuria, diabetes, and hypertension highly co-exist, proteinuria may have a stronger relationship with diabetes than with hypertension in rural areas of western Bangladesh. One possible reason for this is the larger proportion of unaware residents with diabetes than unaware residents with hypertension in rural western Bangladesh. According to recent population-based studies on diabetes and hypertension in Bangladesh [22,23], among individuals with diabetes, about 60% were unaware of their diabetic status, while among individuals with hypertension, about 50% were unaware of their hypertensive status. In addition, only 14.2% of diabetic patients were receiving treatment that controlled their blood sugar level [22] compared with 27% of hypertensive patients [23]. The higher proportion of unaware and uncontrolled diabetic patients may be due to the lack of diagnostic and treatment facilities for diabetes in rural Bangladesh [24]. These findings support our contention that unware diabetes patients who have not received diabetic treatment for a long time are more likely to develop proteinuria than those who aware and controlled diabetic patients. In rural Bangladesh, number of unaware and untreated hypertensive patients is also high, particularly among elderly people from rural Bangladesh [23,25,26], owing to the lack of access to and inadequate equipment and medicines for NCD prevention and treatment service [26,27]. Considering these situations, the simple dipstick urine test together with the blood glucose test and blood pressure measurement used in PHC health check-up services could be an effective approach to screen a large number of undiagnosed diabetic and hypertensive patients at the early disease stage before the development of complications. Such joint screening could detect and identify individuals at high-risk of mortality from all causes and CVD, because proteinuria, diabetes, and hypertension are known risk factors for CVD and all-cause mortality [28]. Further studies are needed to examine the cost effectiveness of PHC services for the prevention of NCD.

The other key findings of our study were that diabetes was significantly associated with hypertension and vice versa after controlling for age and sex, and that participants aged over 40 years showed higher odds of having diabetes or hypertension compared with the odds for participants aged between 15 and 39 years. These findings are consistent with the results of previously published studies in other areas of Bangladesh and in India [2-5,13,26,29,30].

It is noteworthy to mention that overweight/obesity was not associated with diabetes but was associated with hypertension. These findings are inconsistent with the results of a previous meta-analysis and systematic review conducted in developed countries [31,32]. However, in Bangladesh, a number of studies found no significant association between diabetes and overweight/obesity using the international standard BMI cut-off point of ≥25 kg/m^2 [33-35]. Among the previous studies in Bangladesh, 23 kg/m^2 was suggested as the optimal BMI cut-off point for screening diabetes [34,35]. In our sample, when overweight/obesity was defined as BMI ≥23 kg/m^2, the association with diabetes was still not statistically significant (Supplementary Table 2). However, when BMI was equal to or less than 22 kg/m^2, the association with diabetes became statistically significant. These results may indicate that a single universal cut-off point for overweight (≥25 kg/m^2) may not be applicable in the rural adult population of Bangladesh and even those who have BMI between 22 kg/m^2 and 25 kg/m^2 may be a high-risk group for diabetes compared to those who have BMI equal to or less than 22 kg/m^2. Further investigations are needed to define appropriate BMI cut-off values in rural Bangladesh.

The present study had some limitations. First, the study sample from PHC health check-up services is unlikely to be representative of all adults in the Bheramara sub-district. Our participants are likely to be unhealthy individuals who identified and paid for PHC health check-up services. The study results are strictly illustrative of individuals who voluntarily participated in PHC services in Bheramara, and the results provide general insights into the relationships among hypertension, diabetes, and proteinuria and their risk factors. Second, our multivariate regression models did not include potential confounding factors such as family history of diabetes/hypertension, socio-economic, environmental, and behavioral factors including smoking, physical activity, and diet-related information of the participants. Further studies should include wider range of potential risk factors for hypertension, diabetes, and proteinuria. Third, although the dipstick test for proteinuria has been used successfully in a field study [36], the urine dipstick analysis used in this study was only a semi-quantitative estimation of the severity of proteinuria [15]. However, even if errors occur, these errors are likely to be random. Fourth, for the diagnosis of diabetes, only the casual blood glucose level (≥200 mg/dL) was used. According to the WHO [37,38], the recommended diagnostic criteria for diabetes are a fasting plasma glucose level ≥126 mg/dL, a 2-hour plasma glucose level ≥200 mg/dL, and an HbA1c level ≥6.5%. However, it was difficult to implement these criteria in our field study of rural Bangladesh. Fifth, of the 2890 individuals who

participated in PHC health check-ups, only 440 (15%) decided to pay for the urinary protein test compared with 2539 (88%) for the blood glucose test and 2411 (83%) for blood pressure measurement. Because this study was conducted as a pilot project of the social business service delivery model for locally recruited healthcare entrepreneurs in order to provide healthcare services sustainably in a rural community, participation in each health check-up item was completely dependent upon the participant's request or demand. Finally, this is a cross-section survey which does not allow us to investigate the causality between hypertension and proteinuria, indicating that proteinuria can be a cause or consequence of hypertension. However, the dynamics of diabetes in relation to hypertension and proteinuria have already been established worldwide as well as the relationships between hypertension and diabetes and proteinuria and diabetes. Thus, the causal pathways among these three diseases cannot be misled in this study, rather this study focused on the relationships and the risk factors for these three diseases.

CONCLUSION

Despite these limitations, this study provided insight into diabetic complications with proteinuria, as well as factors associated with proteinuria, diabetes, and hypertension. These three diseases were highly co-existed and associated with each other as risk factors. PHC health check-up services in rural Bangladesh was found to be effective to screen a large number of unaware and undiagnosed diabetic, hypertensive, and proteinuria patients at the early disease stage before the development of complications. The study also found other key risk factors for hypertension, such as older age (≥40 years), overweight/obesity, and abnormal pulse rate. Moreover, the study findings shed light on the need to identify an appropriate BMI cut-off point for the risk of developing diabetes or proteinuria in rural Bangladesh. For the prevention of complications in NCD, a combined set of health check-up services using PHC should be promoted, particularly for those older than 40 years of age and those having hypertension, diabetes, or proteinuria in the western part of rural Bangladesh. Future studies on the risk factors of proteinuria, diabetes, and hypertension in Bangladesh should consider other potential factors including socio-economic factors, health-related behavioral factors, and environmental factors in other geographic areas of Bangladesh.

DECLARATIONS

Acknowledgement

This research project described in this paper was supported by Toyota and Grameen Communications, Bangladesh. I would like to thank all who supported and participated in the project. Particular thanks are owed to Ms. Nazneen Sultana who provided valuable comments and assistance.

Conflict of Interest

The authors report no conflicts of interest.

Ethics and Consent

Data collection from each participant was performed in accordance with the Declaration of Helsinki. The study was approved by the ethics committee at the Kyushu University Institutional Review Board (#24-048). Verbal informed consent was obtained from all participants who received detailed explanation about the study purposes by the field research assistants.

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Supplementary Table 1 Unadjusted association of independent variables with hypertension, diabetes, proteinuria, and overweight/obesity

Items	Hypertension (N = 2,411)			Diabetes (N = 2,539)			Proteinuria (N = 440)			Overweight/obesity (N = 539)		
	n/N	%	P for Diff.	n/N	%	P for Diff.	n/N	%	P for Diff.	n/N	%	P for Diff.
Sex	N = 2411		0.34	N = 2539		0.015	N = 440		0.081	N = 539		0.17
Male	541/1462	37.0		257/1574	16.3		73/254	28.7		97/296	32.8	
Female	360/949	37.9		191/965	19.8		66/186	35.5		90/243	37.0	
Age groups	N = 2411		<0.001	N = 2539		<0.001	N = 440		0.73	N = 539		<0.001
15–29 years	74/364	20.3		38/351	10.8		24/64	37.5		16/83	19.3	
30–39 years	190/629	30.2		65/662	9.8		37/126	29.4		47/142	33.1	
40–49 years	231/568	40.7		116/602	19.3		30/106	28.3		72/135	53.3	
50–59 years	241/505	47.7		130/531	24.5		24/72	33.3		36/95	37.9	
≥60 years	165/345	47.8		99/393	25.2		24/72	33.3		16/84	19.0	
Pulse rate	N = 2388		<0.001	N = 2139		0.12	N = 408		0.033	N = 528		0.009
Normal (50–100 beats/min)	756/2099	36.0		322/1892	17.0		101/351	28.8		149/453	32.9	
Abnormal (≤49 or ≥101 beats/min)	140/289	48.4		50/247	20.2		24/57	42.1		36/75	48.0	
Hypertension	-	-	-	N = 2154		<0.001	N = 412		0.026	N = 536		<0.001
No	-	-	-	191/1344	14.2		81/298	27.2		99/366	27.0	
Yes	-	-	-	182/810	22.5		43/114	37.7		87/170	51.2	

Diabetes	N = 2154		<0.001	-	-	-	N = 407		0.004	N = 490		0.48
No	628/1781	35.3		-	-	-	108/378	28.6		151/437	34.6	
Yes	182/373	48.8		-	-	-	16/29	55.2		19/53	35.8	
Proteinuria	N = 412		0.026	N = 407		0.004	-	-	-	N = 385		0.50
No	71/288	24.7		13/283	4.6		-	-	-	86/272	31.6	
Yes	43/124	34.7		16/124	12.9		-	-	-	35/113	31.0	
Overweight/obesity	N = 536		<0.001	N = 490		0.48	N = 385			-	-	-
No	83/350	23.7		34/320	10.6		78/264	29.5	0.50	-	-	-
Yes	87/186	46.8		19/170	11.2		35/121	28.9		-	-	-

Supplementary Table 2 Age and sex-adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) for factors associated with diabetes among participants of the portable health clinic

	Diabetes								
	Age and sex-adjusted								
	Model 1: BMI ≥23.0 kg/m² (N = 490)			Model 2: BMI ≥22.5 kg/m² (N = 490)			Model 3: BMI ≥22.0 kg/m² (N = 490)		
	OR	P	95% CI	OR	P	95% CI	OR	P	95% CI
Sex									
Male	Reference			Reference			Reference		
Female	1.25	0.46	0.70–2.24	1.22	0.50	0.68–2.20	1.16	0.61	0.65–2.10
Age groups									
15–39 years	Reference			Reference			Reference		
40–49 years	1.52	0.32	0.66–3.51	1.56	0.30	0.68–3.58	1.55	0.30	0.67–3.55
50–59 years	2.81	0.013	1.25–6.33	2.86	0.011	1.27–6.44	2.80	0.013	1.24–6.31
≥60 years	3.14	0.008	1.35–7.30	3.19	0.007	1.37–7.42	3.11	0.009	1.34–7.22
Overweight/obesity									
No	Reference			Reference			Reference		
Yes	1.73	0.078	0.94–3.19	1.80	0.065	0.96–3.34	2.28	0.016	1.17–4.47