Published by Oxford University Press on behalf of the International Epidemiological Association
International Journal of Epidemiology 2012;41:462–471
doi:10.1093/ije/dyr191

NON-COMMUNICABLE DISEASES

Betel quid chewing in rural Bangladesh: prevalence, predictors and relationship to blood pressure

Julia E Heck,[1]* Erin L Marcotte,[1] Maria Argos,[2] Faruque Parvez,[3] Alauddin Ahmed,[4] Tariqul Islam,[4] Golam Sarwar,[4] Rabiul Hasan,[4] Habibul Ahsan[2,3] and Yu Chen[5]

[1]Department of Epidemiology, University of California, Los Angeles, CA, USA, [2]Department of Health Studies, University of Chicago, Chicago, IL, USA, [3]Mailman School of Public Health, Columbia University, New York, NY, USA, [4]Columbia University and University of Chicago Research Office in Bangladesh, Mohakhali, Dhaka, Bangladesh and [5]Department of Environmental Medicine, New York University School of Medicine, New York, NY, USA

*Corresponding author. Julia Heck, Department of Epidemiology, UCLA School of Public Health, Box 951772, 650 Charles E. Young Drive, Los Angeles, CA 90095-1772, USA. E-mail: jeheck@ucla.edu

Accepted 31 October 2011

Background Betel quid is chewed by 600 million people worldwide and it has been linked to obesity and cardiovascular disease. The purpose of our study was to examine the prevalence and predictors of betel quid chewing in a rural area of Bangladesh, and determine its effects on body mass index (BMI) and blood pressure.

Methods In this population-based prospective study, we analysed data on 19 934 Bangladeshi adults. Linear and multivariate logistic regression was used to determine the socio-demographic predictors of betel quid chewing and the effect of betel quid on change in BMI and on systolic and diastolic blood pressure, pulse pressure, arterial pressure, overweight or obesity, and hypertension.

Results At baseline, betel quid was chewed by 33.2% of the cohort (35.5% of men, 31.6% of women). In a subsample in which we collected methods of use, 17.5% chewed it without tobacco and 82.5% chewed it with tobacco. In multivariate analysis, betel quid chewing was associated with female sex, older age, tobacco smoking and lower socio-economic status, as measured by fewer years of formal education and not owning land. Betel quid was chewed more times per day among women and older persons. At follow-up, persons who chewed betel quid without tobacco had higher systolic blood pressure, diastolic blood pressure and arterial pressure in comparison with never users. After controlling for other explanatory variables, chewing betel quid without tobacco was associated with general hypertension [odds ratio (OR) 1.48, 95% confidence interval (CI) 1.04–2.10] and systolic hypertension (OR 1.55, 95% CI 1.01–2.37). We did not observe associations of betel quid chewing with BMI or overweight.

Conclusions Betel quid chewing is likely contributing to high blood pressure in Bangladesh, particularly among women.

Keywords Areca, obesity, hypertension, smokeless tobacco, pulse pressure, arterial pressure

Introduction

An estimated 600 million people worldwide, 10% of the world's population, chew betel quid. A mild stimulant, betel quid contains dried or cured areca nut, slaked lime, catechu and flavouring ingredients, wrapped in betel leaf, with tobacco sometimes added. It is an established cause of oral cavity and oesophageal cancers, and when mixed with smokeless tobacco, of pharyngeal cancer.[1]

There is evidence for the effect of betel quid on the cardiovascular system. After chewing commences, betel quid causes the immediate effects of vasoconstriction, an elevated pulse rate (among all users) and blood pressure increases (in new users only).[2] Betel quid contains four arecal alkaloids (primarily arecoline, but also arecaidine, guvacine and guvacoline), with arecoline causing short-term hypoglycaemia. The arecal alkaloids also produce nitrosamine derivatives, which have potential diabetogenic and carcinogenic effects.[3] Betel quid is also a source of exposure to trace levels of some heavy metals, some of which, such as arsenic or manganese, may increase risk of hypertension.[4–6] Betel quid activates the sympathetic nervous system, inducing the secretion of adrenal medullary cathecholamines.[2] It appears to be related to elevated homocysteine, a risk factor for heart disease.[3,7] Betel quid chewing can also induce periodontal disease, a known risk factor for cardiovascular disease (CVD).[8]

CVDs are the leading cause of death worldwide. The mortality rates in Bangladesh for ischaemic heart disease and cerebrovascular disease are high and increasing more rapidly than those seen in the West and in other Asian countries.[9] High cardiovascular mortality is a recent phenomenon in Bangladesh, due in part to increasing life expectancy and steep drops in communicable disease deaths in the past several decades. Karar and colleagues have estimated a >3000% increase in CVD and cerebrovascular disease deaths in Bangladesh from 1986 to 2006.[10] There is also evidence that Bangladeshi migrants to the West have high rates of CVD, as well as poor glycaemic, lipid and blood pressure control.[11–13] Possible reasons for the high rates of CVD in Bangladesh are the increasing prevalence of lifestyle risk factors such as smoking and smokeless tobacco use, obesity, high intakes of fats and processed foods, and betel quid chewing, as well as a lack of awareness of prevention and treatment for heart disease.[14–17]

Few population-based estimates exist on the prevalence and determinants of betel chewing in Bangladesh. A 2006 nationwide survey found 17.5% of men chewed betel quid with tobacco;[18] estimates were not available on use among women. Convenience samples of Bangladeshi migrants in the West have yielded high rates (30–95%) of betel quid chewing.[19–21] Despite this, only a small number of epidemiologic studies have investigated the relation between betel quid chewing and cardiovascular health, finding possible links to obesity, the metabolic syndrome, type 2 diabetes mellitus and overall higher cardiovascular mortality.[2,22–31] The purpose of this investigation was to report the use of betel quid in a large cohort of Bangladeshi men and women and to assess the associations of betel quid with socio-demographic factors, body mass index (BMI) and blood pressure.

Methods

The Health Effects of Arsenic Longitudinal Study (HEALS) was established in Araihazar, Bangladesh, to evaluate cancer and other health effects of exposure to drinking water arsenic. Details of the study have been described previously.[32] During 2000–01, the study recruited 11 746 individuals ('original cohort'). During 2006–08, the cohort was expanded ('expansion cohort'), using the same recruitment procedures, to include an additional 8287 individuals living in the study area. Inclusion criteria, which were chosen to ensure greater stability of residence, were being married and having lived in the same *bari* (cluster of homes) for the previous 5 years. All subjects were aged 18–75 years at the initial interview. The overall response rate was 97.5%. Follow-up data are collected every 2 years.

After obtaining verbal informed consent, data were collected by standardized in-person interview by trained interviewers. At baseline, participants were asked about their present and past use of betel quid, the number of times per day betel was chewed, the duration of betel use and in the expansion cohort only, and whether betel was chewed with jorda (tobacco leaves). They were queried as to their use of cigarettes or bidis (hand-rolled cigarettes), as well as questions on demographics, religion and socio-economic measures (television and land ownership, occupation, years of education). Diets were assessed using a food frequency questionnaire.[33] Clinical evaluations were done by local trained physicians. As their use has diminished in the study area, the use of *guul* (creamy snuff) and *hukka* (pipe smoking) was collected in the original cohort only. The present study used baseline data from both the original and expansion cohorts, totalling 20 033 individuals. Of this group, we excluded six participants who did not answer the question on betel quid chewing, 12 persons with unlikely blood pressure measurements (systolic recorded as lower than diastolic) and 88 expansion cohort participants who did not complete the food frequency questionnaire, yielding a final sample size of 19 934.

Cross-sectional studies in the literature have suggested a transient effect on blood pressure from smoking cigarettes, while the effect from smokeless tobacco is less evident.[34,35] In order to discern the independent effect of betel quid separate from tobacco, the analysis of health outcomes at follow-up was limited to the expansion cohort, because only

those participants were asked whether they chewed betel quid with or without tobacco. At follow-up, 357 expansion cohort participants were unavailable for interview. Of these, 53 died, 139 migrated out of the study area, 116 were temporarily travelling, 3 were sick or hospitalized and 46 were not available for other reasons. An additional 31 people refused the follow-up clinical interview. Thus, follow-up analyses were based upon 7792 persons from the expansion cohort with data collected by May 2010.

At each follow-up, participants were examined by local trained physicians. Clinical evaluations recorded information on, among other factors, height, weight, blood pressure, hypertensive medication use (expansion cohort only), and problems with gums. We did not collect information on abdominal obesity; however, it is expected to be low in our population.[36,37] In the expansion cohort, the ALPK2 Aneroid Sphygmomanometer was used at all time points for blood pressure measurement. Measurements were taken with participants in a seated position after 5 min of rest, with the cuff around the upper left arm, in accordance with recommended guidelines. To reduce false positive measurements of high blood pressure due to the transient stress response to medical professionals ('white coat hypertension'), two additional measurements were taken after 2–3 min of rest for respondents found to have systolic blood pressure of $\geqslant$140 mmHg or diastolic blood pressure of $\geqslant$90 mmHg at the first measurement, and the measurement with the lowest blood pressure was recorded.

A reliability study of blood pressure measurements was conducted in 61 subjects. Three measurements were taken regardless of blood pressure levels at the first measurement. We computed intraclass correlation coefficients for systolic and diastolic blood pressure separately. The reliability of blood pressure measurement was good, with all intraclass correlation coefficients between 0.92 and 0.94. The absolute differences among measurements were 0.9–2.0 and 0.7–2.8 mmHg for systolic and diastolic blood pressure, respectively.

The HEALS study was approved by the Ethical Committee of the Bangladesh Medical Research Council and the Institutional Review Boards at Columbia University and the University of Chicago.

Statistical analyses

We first conducted descriptive analyses to compare current, past or never betel use by socio-demographic and health variables. *P*-values were computed using chi-squared tests or analysis of variance. Multivariate logistic regression was used to ascertain the relation between socio-demographics and ever betel quid chewing compared to never users. We described the frequency of betel use and examined associations between cigarette and betel use.

We calculated BMI as [weight in kilograms/(height in metres)^2] and defined overweight as BMI 25 to $<$30 and obesity as BMI $\geqslant$ 30; because of the small proportion of obese participants, we combined these groups in regression analyses. Using follow-up measurements, we examined the relationship between betel quid and blood pressure and BMI using multivariate linear and logistic regression analyses. We defined systolic hypertension as $\geqslant$140 mmHg, diastolic hypertension as $\geqslant$90 mmHg, and general hypertension as systolic and/or diastolic hypertension. We examined pulse pressure, defined as the difference between systolic and diastolic blood pressure and arterial pressure, calculated as [1/3 (SBP + 2$\times$ DBP)]. These measures have been used in other studies of vascular health.[38] Analyses controlled for baseline age, sex, BMI, educational attainment, occupation, religion, marital status, land ownership, change in weight over the follow-up period, the use of hypertensive medications at follow-up, pack-years of cigarette/bidi smoking, baseline blood pressure, diabetes at baseline, and daily consumption of meats (grams per day/kilogram body weight), vegetables (grams per day/kilogram body weight) and fruits (grams per day/kilogram body weight). We did not adjust for *hukka* or *guul* use because data on these substances were not available for the expansion cohort. We further conducted stratified analysis by sex.

Results

Overall, 33.2% of the study population chewed betel quid at the time of baseline interview and an additional 1.7% had chewed it in the past. There was a slightly higher prevalence in men than women (Table 1). Among persons asked whether they chewed betel quid with tobacco, 82.5% chewed it with tobacco whereas 17.5% chewed it without tobacco. When queried as to the length of use, betel quid users reported having chewed it for an average of 10.7 years (SD 9.8; median 7 years).

In multivariate logistic regression analyses, ever betel quid chewing was more common in women, older adults, those with no formal education, those employed in business, tobacco smokers and persons who did not own land. We conducted a sensitivity analysis of the predictors of betel quid use comparing participants who chewed betel quid with tobacco to persons who chewed it without tobacco (data not shown). Compared with the group who chewed betel quid without tobacco, we observed slightly stronger associations with cigarette/bidi smoking, older age and not owning land among persons who chewed it with tobacco.

On average, betel quid was chewed 5.2 (SD 3.9; median 4) times per day. Daily chewing frequency was higher among persons who chewed it with tobacco (mean 5.6, SD 3.9) than persons who

Table 1 Prevalence of betel quid chewing[a] and multivariate logistic regression of relationship between ever betel quid use and socio-demographic factors ($n = 19\,934$)

	Percent who used betel quid			
	Current users ($n = 6615$)	Former users ($n = 343$)	P-value[b]	**Adjusted OR for ever betel quid use (95% CI)[c]**
Sex			<0.0001	
Male	35.5	2.9		Referent
Female	31.6	0.9		2.76 (2.25–3.38)
Age (years)			<0.0001	
18–29	7.6	0.3		Referent
30–39	27.4	1.3		4.44 (3.96–4.98)
40–49	52.1	2.0		12.00 (10.65–13.51)
>50	63.0	4.8		21.68 (18.86–24.93)
Marital status			<0.0001	
Married	32.6	1.7		Referent
Divorced/separated/widowed	57.6	2.7		1.03 (0.83–1.29)
Education			<0.0001	
No formal	42.5	1.9		2.00 (1.81–2.20)
1–5 years	30.8	1.7		1.65 (1.49–1.82)
⩾6 years	20.4	1.5		Referent
Occupation			<0.0001	
Farmer	43.7	3.3		Referent
Business	44.3	3.7		1.49 (1.27–1.74)
Daily labourer	22.2	2.2		1.01 (0.81–1.26)
Factory	40.1	2.9		0.78 (0.66–0.93)
Homemaker[d]	50.7	5.9		1.05 (0.83–1.31)
Others	31.4	0.9		1.13 (0.95–1.34)
Unemployed	32.8	1.8		1.06 (0.80–1.40)
Religion			0.0003	
Muslim	33.0	1.7		Referent
Hindu/other[e]	37.5	2.8		1.08 (0.93–1.27)
Land ownership			0.06	
Yes	32.4	1.7		Referent
No	33.9	1.8		1.15 (1.07–1.24)
Television ownership			0.1	
Yes	32.7	1.6		Referent
No	33.5	1.8		0.95 (0.89–1.03)
Smoking pack-years			<0.0001	
None	26.5	0.9		Referent
⩽5	45.9	2.4		3.31 (2.88–3.80)
>5–10	42.2	3.5		2.63 (2.26–3.06)
>10–15	49.9	2.2		2.90 (2.45–3.43)
>15–20	47.7	3.3		2.30 (1.89–2.79)
⩾20	50.5	6.1		2.45 (2.09–2.86)

[a]Betel quid users include persons who chew betel with or without tobacco.
[b]P-values computed by chi-square.
[c]All odds ratios control for all other variables in the table.
[d]Of women (93.1%) identified their occupation as homemaker.
[e]Other religions were reported by six participants (<0.05%).
OR, odds ratio; 95% CI, 95% confidence interval.

Table 2 The frequency of betel quid chewing per day at baseline, by selected characteristics[a]

	Frequency per day of betel quid chewing						
	⩽1	2	3	4–5	6–7	⩾8	*P*-value
All participants	4.4	10.7	25.2	27.4	12.6	19.7	
Type of betel quid[b]							<0.0001
Chewed without tobacco	6.5	17.0	38.6	25.4	5.1	7.4	
Chewed with tobacco	2.6	5.8	20.4	28.0	17.0	26.2	
Sex							<0.0001
Male	7.1	16.2	24.1	24.0	9.8	18.9	
Female	2.3	6.4	26.2	30.1	14.7	20.3	
Age (years)							<0.0001
18–29	8.2	16.9	29.3	26.5	8.2	10.8	
30–39	6.4	13.0	26.2	28.3	11.3	14.9	
40–49	3.6	9.3	25.3	27.8	12.0	22.2	
>50	2.7	9.0	23.6	26.3	15.7	22.7	
Smoking, ever							<0.0001
Current	8.3	19.5	28.2	24.3	8.1	11.6	
Past	1.8	4.6	17.6	28.9	16.4	30.8	
Never	2.7	6.9	25.5	28.9	14.2	21.7	
Smoking (pack-years)							<0.0001
None	2.7	6.9	25.5	29.0	14.2	21.7	
1–5	6.9	13.6	25.7	27.9	11.2	14.7	
6–10	5.8	16.1	25.3	27.4	10.0	15.5	
11–15	7.9	16.4	27.1	22.8	7.7	18.0	
16–20	6.4	16.4	26.7	27.9	9.4	13.3	
⩾20	5.2	14.9	22.4	21.7	12.9	22.9	
Land ownership							0.4
Yes	4.7	11.0	25.4	26.4	12.4	20.1	
No	4.1	10.3	25.1	28.4	12.8	19.3	
Religion							0.9
Muslim	4.4	10.7	25.4	27.5	12.6	19.5	
Hindu/Other[c]	4.6	11.0	23.9	25.9	12.4	22.2	

[a]Among current betel quid chewers only *(N* = 6615), including persons who chew betel quid with or without tobacco. *P*-values computed by chi-square.
[b]Among expansion cohort participants only.
[c]Other religions were reported by 6 participants (<0.05%).

chewed betel quid without tobacco (mean 3.8, SD 2.3), a pattern seen regardless of sex, age or smoking status. In general, betel quid was chewed more times per day among women in comparison with men and among persons aged ⩾40 years in comparison with those <40 years (Table 2). Frequency of betel quid consumption was highest among never smokers and persons who had quit smoking tobacco. We did not observe differences in frequency of betel quid chewing by land ownership or religion.

Table 3 describes baseline health characteristics according to betel quid use. Former betel quid users had higher blood pressure measurements than persons in other groups. Persons who chewed betel quid without tobacco had higher blood pressure values than persons who chewed betel quid with tobacco. Weight and BMI were highest among never betel quid users. Systolic, diastolic and general hypertension were most frequent among former betel quid users and people who chewed betel quid without tobacco.

At follow-up, the prevalence of general hypertension was 9.3% (9.7% among males, 9.0% among females). Of those with hypertension, 36.2% had been previously diagnosed. Hypertensive medications were

Table 3 Baseline health characteristics by betel quid use[a]

Health measure at baseline	Mean (SD) or betel quid use (%)				
	Current user, betel chewed without tobacco ($n=430$)	Current user, betel chewed with tobacco ($n=2009$)	Former betel user ($n=65$)	Never betel user ($n=5683$)	*P*-value
Age (years)	44.7 (8.5)	44.8 (8.8)	47.6 (9.2)	33.0 (9.5)	<0.0001
Height (cm)	153.4 (8.6)	153.6 (8.1)	154.9 (7.9)	154.4 (7.9)	<0.0001
Weight (kg)	46.6 (9.5)	46.0 (9.0)	46.9 (9.4)	47.7 (8.6)	<0.0001
BMI (kg/m^2)	19.7 (3.3)	19.4 (3.2)	19.5 (3.3)	20.0 (3.2)	<0.0001
Systolic blood pressure (mmHg)	124.4 (20.3)	120.3 (17.9)	129.5 (21.3)	118.5 (14.3)	<0.0001
Diastolic blood pressure (mmHg)	78.6 (11.3)	76.4 (10.3)	79.5 (11.4)	75.8 (9.9)	<0.0001
Pulse pressure (mmHg)	45.7 (13.1)	43.9 (11.9)	49.9 (13.2)	42.7 (9.3)	<0.0001
Arterial pressure (mmHg)	93.9 (13.6)	91.0 (12.1)	96.2 (14.1)	90.0 (10.7)	<0.0001
Overweight or obese (BMI $\geqslant$ 25)	6.1	6.0	7.7	7.7	0.05
Systolic hypertension ($\geqslant$140 mmHg)	16.7	11.8	29.2	7.2	<0.0001
Diastolic hypertension ($\geqslant$90 mmHg)	14.2	9.5	16.9	8.5	0.0001
General hypertension (systolic $\geqslant$140 mmHg and/or diastolic $\geqslant$90 mmHg)	20.5	14.9	29.2	11.0	<0.0001
High pulse pressure ($\geqslant$55 mmHg)	17.0	13.8	30.8	8.9	<0.0001

[a]Among expansion cohort participants who completed the initial clinical evaluation ($N=8187$). *P*-values computed by chi-square and ANOVA.

Table 4 Multivariate regression analysis of health measures at follow-up[a]

Health measure	Current user, betel chewed without tobacco ($n=409$)		Current user, betel chewed with tobacco ($n=1931$)		Former betel user ($n=63$)	
	β (SE)	*P*-value	β (SE)	*P*-value	β (SE)	*P*-value
BMI (kg/m^2)	0.001 (0.08)	0.9	−0.06 (0.04)	0.2	0.02 (0.18)	0.9
Systolic blood pressure (mmHg)[b]	1.39 (0.62)	0.03	0.24 (0.36)	0.5	0.17 (1.48)	0.9
Diastolic blood pressure (mmHg)[b]	1.15 (0.45)	0.01	−0.16 (0.26)	0.6	−0.22 (1.08)	0.8
Pulse pressure (mmHg)[b]	0.35 (0.47)	0.5	0.26 (0.27)	0.3	0.9 (1.11)	0.4
Arterial pressure (mmHg)[b]	1.23 (0.47)	0.009	0.03 (0.27)	0.9	−0.06 (1.11)	0.9
Health measure	OR (95% CI)		OR (95% CI)		OR (95% CI)	
Overweight or obese (BMI $\geqslant$ 25)	0.60 (0.32–1.11)		0.88 (0.61–1.28)		1.27 (0.29–5.50)	
Systolic hypertension ($\geqslant$140 mmHg)[b]	1.55 (1.01–2.37)		1.20 (0.89–1.62)		0.94 (0.36–2.51)	
Diastolic hypertension ($\geqslant$90 mmHg)[b]	1.32 (0.89–1.96)		0.98 (0.75–1.30)		1.01 (0.39–2.65)	
General hypertension (systolic $\geqslant$ 140 mmHg and/or diastolic $\geqslant$ 90 mmHg)[b]	1.48 (1.04–2.10)		1.05 (0.82–1.35)		1.02 (0.44–2.35)	
High pulse pressure ($\geqslant$55 mmHg)[b]	1.43 (0.91–2.24)		1.16 (0.85–1.59)		1.82 (0.79–4.16)	

[a]Among expansion cohort participants who completed the follow-up interview and evaluation ($N=7785$). The top portion of Table 4 treats the outcome variable as a continuous measure, and therefore the results shown are from a multivariate linear regression. In the bottom portion of the table, we dichotomized the variables based on the cutoffs shown and present the resultant logistic regression analyses. Regressions controlled for sex, baseline age, pack-years of tobacco smoking, BMI at baseline, the use of hypertensive medications at follow-up, education, land ownership, religion, marital status, and daily intake of meats, vegetables and fruits. Referent group is never betel users.

[b]Regressions also control for baseline blood pressure, change in weight over the time period and diabetes at baseline.

OR, odds ratio; 95% CI, 95% confidence interval; SE, standard error.

Table 5 Multivariate regression analysis of health measures among users of betel without tobacco, comparing male and female participants[a]

Health measure	Women ($n=251$)		Men ($n=158$)	
	β (SE)	*P*-alue	β (SE)	*P*-value
BMI (kg/m^2)	−0.03 (0.11)	0.8	0.04 (0.09)	0.6
Systolic blood pressure (mmHg)[b]	1.91 (0.82)	0.02	0.52 (0.96)	0.6
Diastolic blood pressure (mmHg)[b]	1.78 (0.59)	0.003	−0.03 (0.72)	0.9
Pulse pressure (mmHg)[b]	0.17 (0.61)	0.8	0.59 (0.74)	0.4
Arterial pressure (mmHg)[b]	1.82 (0.61)	0.003	0.17 (0.73)	0.8
Health measure	OR (95% CI)		OR (95% CI)	
Overweight or obese (BMI ⩾ 25)	0.63 (0.30–1.34)		0.50 (0.15–1.67)	
Systolic hypertension (⩾140 mmHg)[b]	1.81 (1.08–3.04)		1.34 (0.60–2.99)	
Diastolic hypertension (⩾90 mmHg)[b]	1.57 (0.97–2.56)		1.02 (0.48–2.14)	
General hypertension (systolic ⩾140 mmHg and/or diastolic ⩾90 mmHg)[b]	1.67 (1.08–2.59)		1.36 (0.73–2.53)	
High pulse pressure (⩾55 mmHg)[b]	1.41 (0.80–2.51)		1.49 0.69–3.21)	

[a]Among expansion cohort participants who completed the follow-up interview and evaluation ($N=7785$). The top portion of the table treats the outcome variable as a continuous measure, and therefore the results shown are from a multivariate linear regression. In the bottom portion of the table, we dichotomized the variables based on the cutoffs shown and present the resultant logistic regression analyses. Regressions controlled for baseline age, pack-years of tobacco smoking, BMI at baseline, the use of hypertensive medications at follow-up, education, land ownership, religion, marital status, and daily intake of meats, vegetables and fruits. Referent group is never betel users.
[b]Regressions also control for baseline blood pressure, change in weight over the time period and diabetes at baseline.

taken by 4.5% of expansion cohort participants. The prevalence of overweight was 7.7% and obesity 0.9%.

At follow-up, the use of betel without tobacco was associated with higher systolic and diastolic blood pressure, and higher arterial pressure (Table 4). General hypertension and systolic hypertension were also associated with the use of betel quid without tobacco. Former betel quid users and persons who chewed betel quid with tobacco did not differ from never users in any of the health measures at follow-up. We observed no associations between betel quid and overweight or BMI. We did not observe a trend for higher systolic blood pressure among persons who chewed betel more frequently ($P=0.9$) or who had chewed it for a longer duration ($P=0.7$). Only seven participants (<0.05%) reported problems with their gums at follow-up.

We conducted further analyses to compare male with female participants. We observed stronger associations among women than men of an effect of betel quid without tobacco on blood pressure (Table 5).

Discussion

In this large population-based prospective study of rural Bangladeshis, we observed a considerable burden of betel quid use, with just over one-third of participants reporting ever use in their lifetime. The prevalence was only slightly higher among men than women, in contrast to tobacco, which is used by many more Bangladeshi men than women (64.0 vs 14.4% of HEALS participants and 53.6 vs 23.8% nationally, with women much more likely to chew tobacco than smoke it).[14,39] Although a study in Taiwan found more frequent use of betel quid among heavy smokers, in our population the frequency of chewing was highest among never smokers and past smokers, among both men and women.[40] The chewing frequency was slightly lower than that seen in a South Indian study.[41] As has been reported in other Asian countries, we observed a strong increasing gradient of betel quid use with older age, perhaps signalling a generational shift towards lower betel quid use.[42] We observed much higher use of betel quid among those with a lower socio-economic status, indicated by a lower level of educational attainment, no land ownership and unemployment.

In comparison with a 2006 study, which observed that 17.5% of men chewed betel quid with tobacco, we found that 22.5% of men chewed betel quid with tobacco.[18] Use of chewing tobacco is 1.5–3 times higher in rural areas of Bangladesh in comparison with urban areas,[14] and it is possible that our results may reflect slightly higher betel quid chewing in rural areas.

The prevalence of general hypertension that we observed, 12.7% at baseline and 9.3% at follow-up, was similar to that seen in other Bangladeshi studies.[43,44] Hypertension rates in Bangladesh are

lower than what is seen in other Asian countries.[43] While urbanization and adoption of the 'Western lifestyle' are increasing rates of hypertension in many Asian countries, our population of rural Bangladeshis ate a diet traditional to the region (high in rice, fish, fruits and vegetables) and very few were overweight or obese.[45,46] While we did not collect information on physical activity, the low level of industrialization in the Araihazar area has kept study participants employed in more traditional jobs, many of which involve physical labour, such as labourer or farmer.[45]

Despite the considerable global burden of betel quid chewing, only a small number of studies have examined its effects on cardiovascular health.[22–25,47] We observed elevated systolic blood pressure, diastolic blood pressure, arterial pressure and hypertension among persons who chewed betel quid without tobacco. Although among men, β-values for betel quid chewing were generally positive and point estimates were generally above unity, the effect was stronger among women. Similar to other studies, there was no clear pattern of increased risk with longer duration or greater frequency of use.[48] We observed no increased risk of high blood pressure among persons who chewed betel quid with tobacco. This is consonant with other research that has not observed a clear relationship between smokeless tobacco use and hypertension.[34] Hypertension was also more common among former betel quid users.

Given the widespread use of betel quid in Asia, a deleterious effect on cardiovascular health is of concern. While average adult blood pressure measurements are lower in Bangladesh in comparison with other Asian nations, awareness of hypertension is poor.[16,49] Only 36% of our participants with general hypertension had been previously diagnosed, and <5% of all subjects were taking antihypertensive medication. The differences in mean blood pressure and hypertension prevalence among betel quid chewers are of concern because even small changes in blood pressure impact mortality. In a pooled analysis of 1 million adults from 61 prospective studies, a 2-mmHg lower usual systolic blood pressure would decrease stroke mortality by 10%.[50] Increased pulse pressure and arterial pressure has also been associated with greater stroke mortality.[50,51]

Although betel quid has previously been linked to greater risk of obesity,[25–27] we did not observe such an effect on BMI from betel quid use, with point estimates below unity. In the HEALS population there is a positive relationship between BMI and socio-economic measures (including land and television ownership, occupation and years of education), with less educated and less wealthy individuals, who also have higher rates of chewing betel quid, having a greater likelihood of having a BMI < 18.5.[52] Although we have controlled for socio-economic factors in our analysis, there is the possibility of residual confounding. In addition, betel quid is believed to modulate metabolic signals that control appetite, suppressing hunger and thus potentially increasing the risk of malnutrition.[48] Bangladesh has high rates of malnutrition and low prevalence of overweight, particularly in rural areas.[53] In the HEALS population, the mean BMI at follow-up was 20.3 and only 8.6% were overweight or obese, while 37.7% had a BMI < 18.5.

This study has several limitations, the first of which is that it was not designed with a focus on betel quid, and thus we are lacking additional information on the quantity of betel quid chewed, possible changes in chewing frequency over time and other factors that may be of interest. We also did not collect additional health information such as cholesterol or physical activity levels, which may shed additional light on betel quid's effects. We also did not have information on family history of hypertension; however, the low awareness of hypertension, both in our population and in Bangladesh in general, suggests that there is a strong chance that family members with hypertension would be unaware of their condition. In addition, the large sample size of our study must be taken into account when interpreting results. While our study is large and population based, our sample consists of rural, married adults and estimates of prevalence may not be generalized to urban areas. We do not expect the exclusion of unmarried persons to strongly affect generalizability, as marriage is nearly universal in Bangladesh.[54]

In conclusion, betel quid chewing may be contributing to the burden of vascular diseases in Bangladesh. Its use was common in our rural Bangladeshi population, particularly among older adults. A potential increase in blood pressure is of concern given the widespread use of betel quid in Asia and in migrant communities in the West. Bangladesh is facing an increasing burden of CVD and interventions in that country should be designed to address this growing health problem.

Acknowledgments

This work was supported by the US National Institutes of Health (P42ES10349, P30ES09089, R01CA107431, R01ES017541, P30ES000260, R01CA102484 and R21ES018960, R21ES019986 to J.E.H.). The authors would like to thank Dr Julie Will for her comments on the manuscript. J.E.H. conceptualized the study, led the analyses and wrote the manuscript. E.L.M. contributed to conducting statistical analyses and writing revisions of the manuscript. M.A. contributed to the interpretation of data and reviewed drafts of the manuscript. F.P., A.A., G.S., T.I. and R.H. contributed to study design and data management. H.A. and Y.C. designed the study and wrote the study protocol. All authors contributed to and approved the final manuscript.

Conflict of interest: None declared.

KEY MESSAGES

- There is a considerable burden of betel quid chewing in Bangladesh.
- Betel quid chewing was associated with older age and lower socioeconomic status.
- Chewing betel quid without tobacco was related to increases in systolic and diastolic blood pressure and to general and systolic hypertension.

References

[1] IARC Monographs Program. A review of human carcinogens–Part E. *Lancet Oncol* 2009;**10:**1033–34.

[2] Boucher BJ, Mannan N. Metabolic effects of the consumption of Areca catechu. *Addict Biol* 2002;**7:**103–10.

[3] IARC Working Group on the Evaluation of Carcinogenic Risks to Humans., World Health Organization., International Agency for Research on Cancer. *Betel-quid and areca-nut chewing and some areca-nut-derived nitrosamines*. Lyon, France: IARC Press, 2004.

[4] Al-Rmalli SW, Jenkins RO, Haris PI. Betel quid chewing elevates human exposure to arsenic, cadmium and lead. *J Hazard Mater* 2011;**190:**69–74.

[5] Al-Rmalli SW, Jenkins RO, Haris PI. Betel quid chewing as a source of manganese exposure: total daily intake of manganese in a Bangladeshi population. *BMC Public Health* 2011;**11:**85.

[6] Lee BK, Kim Y. Relationship between blood manganese and blood pressure in the Korean general population according to KNHANES 2008. *Environ Res* 2011;**111:** 797–803.

[7] Knekt P, Alfthan G, Aromaa A *et al*. Homocysteine and major coronary events: a prospective population study amongst women. *J Intern Med* 2001;**249:**461–65.

[8] Parmar G, Sangwan P, Vashi P, Kulkarni P, Kumar S. Effect of chewing a mixture of areca nut and tobacco on periodontal tissues and oral hygiene status. *J Oral Sci* 2008;**50:**57–62.

[9] WHO Statistical Information System. *Causes of death: mortality and health status*. Geneva: World Health Organization, 2002.

[10] Ahsan Karar Z, Alam N, Kim Streatfield P. Epidemiological transition in rural Bangladesh, 1986–2006. *Glob Health Action* 2009;**2:** doi:10.3402/gha.v2i0.1904.

[11] Wild SH, Fischbacher C, Brock A, Griffiths C, Bhopal R. Mortality from all causes and circulatory disease by country of birth in England and Wales 2001–2003. *J Public Health* 2007;**29:**191–98.

[12] Chowdhury TA, Lasker SS, Mahfuz R. Ethnic differences in control of cardiovascular risk factors in patients with type 2 diabetes attending an Inner London diabetes clinic. *Postgrad Med J* 2006;**82:**211–15.

[13] Bourke J, Sylvester R, Sharma P. Ethnic variations in the management of patients with acute stroke. *Postgrad Med J* 2006;**82:**13–15.

[14] Flora MS, Mascie-Taylor CG, Rahman M. Gender and locality differences in tobacco prevalence among adult Bangladeshis. *Tob Control* 2009;**18:**445–50.

[15] Rahman M. Arsenic and hypertension in Bangladesh. *Bull World Health Organ* 2002;**80:**173.

[16] Hypertension Study Group. Prevalence, awareness, treatment and control of hypertension among the elderly in Bangladesh and India a multicentre study. *Bull World Health Organ* 2001;**79:**490–500.

[17] States JC, Srivastava S, Chen Y, Barchowsky A. Arsenic and cardiovascular disease. *Toxicol Sci* 2009;**107:**312–23.

[18] Khan MM, Aklimunnessa K, Kabir MA, Kabir M, Mori M. Tobacco consumption and its association with illicit drug use among men in Bangladesh. *Addiction* 2006;**101:**1178–86.

[19] Ahmed S, Rahman A, Hull S. Use of betel quid and cigarettes among Bangladeshi patients in an inner-city practice: prevalence and knowledge of health effects. *Br J Gen Pract* 1997;**47:**431–34.

[20] Nunez-de la Mora A, Jesmin F, Bentley GR. Betel nut use among first and second generation Bangladeshi women in London, UK. *J Immigr Minor Health* 2007;**9:** 299–306.

[21] Bedi R. Betel-quid and tobacco chewing among the United Kingdom's Bangladeshi community. *Br J Cancer Suppl* 1996;**29:**S73–77.

[22] Yen AM, Chen LS, Chiu YH, Boucher BJ, Chen TH. A prospective community-population-registry based cohort study of the association between betel-quid chewing and cardiovascular disease in men in Taiwan (KCIS no. 19). *Am J Clin Nutr* 2008;**87:**70–78.

[23] Lan TY, Chang WC, Tsai YJ, Chuang YL, Lin HS, Tai TY. Areca nut chewing and mortality in an elderly cohort study. *Am J Epidemiol* 2007;**165:**677–83.

[24] Lin WY, Chiu TY, Lee LT, Lin CC, Huang CY, Huang KC. Betel nut chewing is associated with increased risk of cardiovascular disease and all-cause mortality in Taiwanese men. *Am J Clin Nutr* 2008;**87:**1204–11.

[25] Lin WY, Pi-Sunyer FX, Liu CS *et al*. Betel nut chewing is strongly associated with general and central obesity in Chinese male middle-aged adults. *Obesity* 2009;**17:** 1247–54.

[26] Mannan N, Boucher BJ, Evans SJ. Increased waist size and weight in relation to consumption of Areca catechu (betel-nut); a risk factor for increased glycaemia in Asians in east London. *Br J Nutr* 2000;**83:**267–75.

[27] Chang WC, Hsiao CF, Chang HY *et al*. Betel nut chewing and other risk factors associated with obesity among Taiwanese male adults. *Int J Obes* 2006; **30:**359–63.

[28] Guh JY, Chen HC, Tsai JF, Chuang LY. Betel-quid use is associated with heart disease in women. *Am J Clin Nutr* 2007;**85:**1229–35.

[29] Yen AM, Chiu YH, Chen LS *et al*. A population-based study of the association between betel-quid chewing and the metabolic syndrome in men. *Am J Clin Nutr* 2006;**83:**1153–60.

[30] Tseng CH. Betel nut chewing is associated with hypertension in Taiwanese type 2 diabetic patients. *Hypertens Res* 2008;**31:**417–23.

[31] Zhang LN, Yang YM, Xu ZR, Gui QF, Hu QQ. Chewing substances with or without tobacco and risk of cardiovascular disease in Asia: a meta-analysis. *J Zhejiang Univ Sci B* 2010;**11:**681–89.
[32] Ahsan H, Chen Y, Parvez F *et al*. Health Effects of Arsenic Longitudinal Study (HEALS): description of a multidisciplinary epidemiologic investigation. *J Expo Sci Environ Epidemiol* 2006;**16:**191–205.
[33] Chen Y, Ahsan H, Parvez F, Howe GR. Validity of a food-frequency questionnaire for a large prospective cohort study in Bangladesh. *Brit J Nutr* 2004;**92:**1–10.
[34] Asplund K. Smokeless tobacco and cardiovascular disease. *Prog Cardiovasc Dis* 2003;**45:**383–94.
[35] Poulter NR. Independent effects of smoking on risk of hypertension: small, if present. *J Hypertens* 2002;**20:** 171–72.
[36] Zaman MM, Choudhury SR, Ahmed J, Numan SM, Islam MS, Yoshiike N. Non-biochemical risk factors for cardiovascular disease in general clinic-based rural population of Bangladesh. *J Epidemiol* 2004;**14:**63–68.
[37] Rahman MM, Rahim MA, Nahar Q. Prevalence and risk factors of type 2 diabetes in an urbanizing rural community of Bangladesh. *Bangladesh Med Res Counc Bull* 2007;**33:**48–54.
[38] Pastor-Barriuso R, Banegas JR, Damian J, Appel LJ, Guallar E. Systolic blood pressure, diastolic blood pressure, and pulse pressure: an evaluation of their joint effect on mortality. *Ann Intern Med* 2003;**139:**731–39.
[39] MacKay J, Eriksen M. *The Tobacco Atlas*. Geneva: World Health Organization, 2002.
[40] Wen CP, Tsai SP, Cheng TY *et al*. Uncovering the relation between betel quid chewing and cigarette smoking in Taiwan. *Tob Control* 2005;**14(Suppl 1):**i16–22.
[41] Bhat SJ, Blank MD, Balster RL, Nichter M. Areca nut dependence among chewers in a South Indian community who do not also use tobacco. *Addiction* 2010;**105:** 1303–10.
[42] Gupta PC, Ray CS. Epidemiology of betel quid usage. *Ann Acad Med Singapore* 2004;**33:**31–36.
[43] Martiniuk AL, Lee CM, Lawes CM *et al*. Hypertension: its prevalence and population-attributable fraction for mortality from cardiovascular disease in the Asia-Pacific region. *J Hypertens* 2007;**25:**73–79.
[44] Zaman MM, Rouf MA. Prevalence of hypertension in a Bangladeshi adult population. *J Hum Hypertens* 1999;**13:** 547–49.
[45] Heck JE, Nieves JW, Chen Y *et al*. Protein and amino acid intakes in a rural area of Bangladesh. *Food Nutr Bull* 2010; **31:**206–13.
[46] Heck JE, Chen Y, Grann VR, Slavkovich V, Parvez F, Ahsan H. Arsenic exposure and anemia in Bangladesh: a population-based study. *J Occup Environ Med* 2008;**50:** 80–87.
[47] Chu NS. Cardiovascular responses to betel chewing. *J Formos Med Assoc* 1993;**92:**835–37.
[48] Javed F, Bello Correra FO, Chotai M, Tappuni AR, Almas K. Systemic conditions associated with areca nut usage: a literature review. *Scand J Public Health* 2010;**38:** 838–44.
[49] WHO South-East Asia Region. *Risk factors for noncommunicable disease: results in the South-East Asia region*. New Delhi, India: WHO, 2008.
[50] Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002; **360:**1903–13.
[51] Weitzman D, Goldbourt U. The significance of various blood pressure indices for long-term stroke, coronary heart disease, and all-cause mortality in men: the Israeli Ischemic Heart Disease study. *Stroke* 2006;**37:** 358–63.
[52] Heck JE, Nieves JW, Chen Y *et al*. Dietary intake of methionine, cysteine, and protein and urinary arsenic excretion in Bangladesh. *Environ Health Perspect* 2009; **117:**99–104.
[53] Jahan K, Hossain M. Institute of Nutrition and Food Science. *Nature and Extent of Malnutrition in Bangladesh: Bangladesh National Nutrition Survey, 1995–96*. Dhaka: Institute of Nutrition and Food Science, University of Dhaka, 1998.
[54] Islam MM, Mahmud M. Marriage patterns and some issues related to adolescent marriage in Bangladesh. *Asia Pac Popul J* 1996;**11:**27–42.