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**DRINKING WATER SODIUM AND ELEVATED BLOOD PRESSURE OF
HEALTHY PREGNANT WOMEN IN SALINITY-AFFECTED COASTAL AREAS**

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Abstract

Coastal areas in South-east Asia are experiencing high sodium concentrations in drinking water sources that are commonly consumed by local populations. Salinity problems caused by episodic cyclones and subsequent seawater-inundations are likely (partly) related to climate change and further exacerbated by changes in upstream river-flow and local land-use activities.

Dietary (food) sodium plays an important role in the global burden of hypertensive disease. It remains unknown however if sodium in drinking water – rather than food – has similar effects on blood pressure and disease risk. In this study we examined the effect of drinking water sodium on blood pressure of pregnant women: increases in blood pressure in this group could severely affect maternal and foetal health.

Data on blood pressure, drinking water source, and personal, lifestyle and environmental confounders was obtained from 701 normotensive pregnant women residing in coastal-Bangladesh. Generalised linear mixed-regression models were used to investigate association of systolic and diastolic blood pressure of these – otherwise healthy – women with their water source.

After adjustment for confounders, drinkers of tube well and pond water (high saline sources) were found to have significantly higher average systolic (+4.85 & +3.62 mmHg) and diastolic (+2.30 & +1.72 mmHg) blood pressures than rainwater-drinkers.

Drinking water salinity problems are expected to exacerbate in the future, putting millions of coastal people – including pregnant women - at increased risk of hypertension and associated diseases. There is an urgent need to further explore the health risks associated to this understudied environmental health problem, and feasibility of possible adaptation-strategies.

Key Words

Salinity; drinking water quality; environmental exposure; blood pressure; pregnant women; climate change; Bangladesh

Introduction

Raised blood pressure is a major risk factor for coronary heart disease and the leading risk factor for stroke. It is responsible for an estimated 7.5 million deaths annually, 12.8% of all deaths worldwide¹ and is the leading risk factor for global disease burden (7.0% of global DALYs)². The increasing prevalence of hypertension reflects both ageing populations³ and underlying risk factors such as unhealthy diet (including high sodium intake), lack of physical activity, obesity, stress and excessive alcohol intake^{4,5}. In particular, there is persuasive and concordant evidence from epidemiological studies, clinical trials and animal studies that sodium intake (mainly through food) plays an important role in the global burden of raised blood pressure⁶⁻¹⁰.

In 2008, maternal health authorities in Dacope, a rural sub-district of Bangladesh (Figure 1), reported an unusual increase in incidence of hypertensive events (such as gestational hypertension and preeclampsia) in pregnant women¹¹. Dacope is a relatively poor sub-district and literacy is estimated to be less than 40%. Most people work in agriculture and cultivate rice. Smoking rates and alcohol intake are extremely low, and physical activity is high – particularly during harvest times¹². Extreme weather events such as storm surges and tides have led to contamination of fresh drinking water sources with sea-water. High sodium levels were found in various drinking water sources (mainly tube wells and ponds), with seasonal fluctuations¹³. Therefore the increased hypertension problems were hypothesised to be linked to consumption of saline drinking water rather than the “well known” risk factors listed above. Salinization of drinking water is believed to be associated with climate change

^{14,15}; however, changes in river flow from an upstream barrage, faulty management of polders, shrimp farming and ground water extraction may all contribute further to this process ¹⁶. A recent study in the area reported a dose response relationship between water sodium concentrations and risk of pre-eclampsia, a complication of pregnancy characterized by hypertension¹⁷.

Apart from pre-eclampsia there are several other adverse outcomes associated with increased blood pressure in pregnancy; therefore we investigated - in the present study - blood pressures of 701 non-hypertensive pregnant women residing in Dacope with respect to their sources of drinking water during pregnancy. We hypothesise, that drinking water sodium concentrations are positively associated with systolic and diastolic blood pressure in these women. If we were to find evidence for an association between drinking water sodium and blood pressure in this cross-sectional study, this would contribute to the arguments in favour of prioritising low-saline drinking water alternatives – particularly for pregnant women – to avoid preventable hypertension related burden of disease in salinity affected coastal areas.

We specifically looked at healthy pregnant women and did not include women with pre-eclampsia in the analysis, as pre-eclampsia could be both a consequence and a cause of increased blood pressure. This makes it difficult to establish whether high blood pressure lead to pre-eclampsia in these women, or that pre-eclampsia was caused by other risk factors and induced high blood pressure over the course of the illness.

Methods

The study area is situated in the sub-district of Dacope, part of the Khulna district in Bangladesh's southwest coastal region (Figure1). Dacope is divided into nine administrative unions, with a total population of approximately 158,000 people. The study population

comprised 1020 non-hypertensive controls from a previously conducted case-control study of pre-eclampsia in Dacope. Women recruited in the wet season (n=310) and women with known complications in their pregnancy (n=9) were excluded, leaving 701 women. The dry season was chosen because it is associated with the highest contrasts in drinking water salinization¹³ and minimizes potential confounding by season (mainly related to temperature and (agriculture related) physical activity). In the case-control study all hypertensive pregnant women in the 20th week of their pregnancy and residing in Dacope were eligible during a period of 18 months (Jan 2009 – Jun 2010). For each hypertensive woman five healthy pregnant controls were selected from the same village, and also recruited in their 20th gestational week. Blood pressure, weight, height and mid-upper arm circumference (MUAC - a proxy for nutritional status¹⁸) were measured by trained data collectors. BP was measured in the left arm (resting, with palm up) using a manual sphygmomanometer. Each of the nine data collectors was responsible for one union in the sub-district. All participants were interviewed using a structured questionnaire to obtain data on age, parity, socio-economic status, seasonal changes of water source, underlying illnesses, physical activity, smoking and environmental exposures such as insecticides, and use of various types of local drugs and medicines. All participants were asked to collect a 24h urine sample: 92% of the participants (n= 645) agreed to participate. They were given a container and given instructions to start the collection the next morning, after the first urine excretion. Urinary sodium was measured by Ion Selective Electrode method (ISE). All data collection methods are described in more detail elsewhere¹⁷.

Average sodium concentrations per water source were based on 407 available water samples. These samples were collected by the same research group in the dry season of 2010 and 2011. All samples were analysed at the University of Dhaka, where sodium was measured by the Atomic Absorption method (AAAnalyst 800, Perkin Elmer, USA)¹⁷. The analysis showed

that tube wells had the highest sodium concentrations with a mean concentration exceeding 700mg/l, followed by pond water with an average concentration of approximately 400 mg/l. Harvested rainwater was (as expected) lowest in sodium content.

Participants' water source was categorised as rainwater, pond water, tube well or a combination of sources. Cooking water sources were categorised in the same way with the addition of river water. Information on type of water source drunk in the two weeks prior to the interview was available for all women and was used as proxy for drinking water sodium (high, medium and low).

Data on average and maximum daily temperatures and accumulated rainfall (if any) on the days of data collection were abstracted from the Bangladesh Meteorological Department.

Statistical Analysis

We used multiple linear regression models to investigate association of water source with systolic and diastolic blood pressure. Where possible, missing data for all variables - apart from weather parameters - were imputed using Multivariate Imputation by Chained Equations (MICE) techniques¹⁹. Moving average techniques were used to impute missing values in daily maximum temperature, as temperature tables showed smooth increases and decreases over time and season. Models were adjusted for potential confounders in three phases: firstly adjustment for age, followed by adjustment for age and well-established risk factors (nutritional status, physical activity, parity), and finally also for local social, behavioural and environmental factors. The models were not adjusted for gestational age, as all women were in their 20th gestational week when recruited and examined. Step-wise methods were used for building the models. Log likelihood, Akaike's Information Criterion and Bayesian Information Criterion were used for model selection. In addition, the union of residence of the participant was included as a random effects parameter in the mixed models.

The random effects were assumed to be normally distributed on the log odds scale. A Likelihood Ratio Test was used to test whether the mixed model fit the data better than the linear regression models. Random effects per union were calculated using the Best Linear Unbiased Predictor (BLUP) method ²⁰. Sensitivity analysis was performed excluding unions with significantly higher or lower blood pressure values than average.

Results

Characteristics of the study population are shown in the Supplement (Table S1).

Approximately a third of the participants drank exclusively tube well water (N=241, 34%); another 33% drank pond water (N=229), and 22% reported drinking a combination of those two (N=153). Rain water accounted for 11% of drinking water sources (78 participating women). None of the respondents used river water as drinking water source, but it was used by 25 women (4%) as cooking water source. Women using pond and tube well water as drinking water source had similar baseline characteristics as rain water users, but were more likely to be anaemic, and were more often users of the local stimulant *gull* (smokeless tobacco). The daily temperatures on days that tube well and pond users were interviewed were on average somewhat cooler than the days that rainwater users were interviewed (-1.4°C and -4.1°C respectively). Figure 2 shows drinking water sodium concentration by water source. Median sodium concentration was 31 mg/l for rainwater, 208 mg/l for pond water, and 704 mg/l for tube well water. The median concentration in water ingested by those reported to drink a combination of sources was difficult to establish, as the consumption of each source would vary greatly per person and over time. The concentrations per source were reflected in 24-h urinary sodium (Supplementary Figure S1).

Figure 3 shows median systolic and diastolic blood pressure by water source. Median blood pressure values were higher with increasing sodium concentration by water source: 100/65 mm Hg, 105/70 mm Hg and 110/70 mm Hg for rain, pond and tube well water users

respectively. Users of different water sources were similar in terms of physical activity (Supplementary Table S1) and diet and therefore differences in these potential confounders are unlikely to explain our findings.

Mixed models (Table 1) showed a better fit to the data than linear regression models, though results were similar. Drinking tube-well, pond water and combined sources were significantly associated with higher systolic pressure (+3.62 mmHg [confidence interval: 1.20, 6.04] and +4.85 mmHg [2.55, 7.25] for pond and tube well users respectively) compared with drinking rain water after adjustment for known and context specific confounders. Results of the mixed linear regression models for diastolic blood also showed higher values for pond and tube well users as compared to rainwater users (+1.72 mmHg [-0.36, 3.80] and +2.30mmHg [0.33, 4.23] for pond and tube well users respectively). (Table 1). The uncertainty in the diastolic blood pressure results is possibly (partly) a reflection more variability in the measurement of diastolic compared with systolic blood pressure. As expected, blood pressure was in all models associated with the known risk factors age, nutritional status, physical activity and parity (Supplementary Table S1). Furthermore, daily temperature was significantly and inversely associated with blood pressure. Sensitivity analysis excluding participants from Loudobe, Koilashgonj or Kamarkhola - where blood pressures were significantly above or below average - did not materially alter the results in any of the models.

While the sodium levels in the examined water samples are exceptionally high, concentrations of other water contaminants such as arsenic or other chemicals were found to be relatively low in the area: arsenic was absent in surface water sources such as ponds, and there were relatively low concentrations in shallow surface water sources ²¹.

Discussion

Our study adds to previously reported evidence that highly saline drinking water is associated with higher blood pressure levels^{13,22-26}. Although some studies failed to show this association (e.g.^{27,28}), sodium concentrations evaluated in this study by far exceeded the sodium levels evaluated in those studies. This is of particular interest as blood pressure is directly related to adverse pregnancy outcomes and may increase the chance of low-for-gestational-age (LGA) births^{29,30}. While in the monsoon season women can often rely on rainwater, they will have to switch to a higher saline source if their pregnancy also covers (part of) the dry season. The increases in blood pressure that can be caused by this change in source could significantly increase the risk of adverse pregnancy outcomes; especially as such increase would push the blood pressure of the women into the (pre)hypertensive range.

Concerning guidelines for drinking water quality the WHO states that: “No health-based guideline value has been derived [...], as the contribution from drinking-water to daily intake is small.”³¹ Mention is made of a taste threshold of 200 mg sodium/l and a recommendation of 20 mg/l; in Dacope most pond and tube-well users are drinking sodium levels well beyond this identified ‘taste threshold’. Based on the findings of the present study and the study by Khan et al¹⁷, drinking water is an important source of ingested sodium in Dacope, and this may be the case also in other coastal areas with drinking water salinity problems around the world. Drinking water sodium should in these situations be considered an important potential source of sodium intake, and a risk factor for hypertension and related disorders. Developing international guidelines for maximum sodium content of drinking water would help to prioritize this potential health hazard and facilitate improved drinking water sources in salinity prone (and often poor) areas such as Dacope.

The drinking water salinity problems in coastal Bangladesh, and similar coastal areas worldwide, reflect high vulnerability to extreme weather events and long term climatic

changes¹⁵. The results of the current study may already (partly) be interpreted in the context of extreme weather events: in May 2009 cyclone Aila hit Bangladesh and inundated part of the sub-district of Dacope³². Although our analysis was restricted to the dry season only (from November 2009 onward), the cyclone and resultant flooding may have increased the salinity levels in ponds and tube wells, which was possibly still evident during the dry season measurement campaign in the present study.

In its 5th assessment report, the Intergovernmental Panel on Climate Change stressed strong evidence for significant sea level rise and an increase in the occurrence of sea level extremes³³. Climate change induced extreme precipitation increases the frequency that river embankments will be overtopped³⁴, and hence the risk that ponds and shallow wells within the embankment boundaries will be flooded by saline river water³⁵. Together with the predicted rise in sea levels, this will lead to contamination of the drinking water sources for the population. It is expected that not only the frequency and intensity of the salinity contamination will increase, but due to the moving tide line, a larger area of the delta will be affected in the future³⁵. Therefore, drinking water salinity problems in areas like Dacope are expected to increase in the near future¹⁵. These trends will have a high impact on drinking water quality of vulnerable coastal areas, such as Dacope.

Strengths of the study include its large size, stringent measurement protocols, and detailed attention to potential confounders. Observer bias is unlikely since water sodium concentrations of sources for each participant were unknown at the time blood pressure data were collected. The study was done in a relatively homogenous group (pregnant women) with high levels of physical activity and low rates of obesity; any differences in these variables and food intake patterns (possible confounders of the water-blood pressure association) should have been balanced after adjustment for socio-economic status. Our study also had some limitations. First, information on water source, rather than actual drinking water sodium

concentration was used. Although, there may be considerable variability in sodium concentrations within the same water source type, tube wells and ponds were always found to be significantly more saline than rainwater ¹¹ and similar differences were observed in urinary sodium excretion within each of the drinking water source groups (Supplementary Figure S1). Dietary sodium was not measured in this study. However an estimated dietary sodium intake of 2.23 grams sodium per day (including seasoning habits) was obtained from an ongoing study, and was relatively homogeneous across socio-economic class and village^a. As this study is conducted in the same area it is unlikely that dietary sodium intake varies substantially across water source: sodium intake through water could therefore be considered as important source of sodium intake in this population. Also potassium concentrations in water (and food) were not measured. Stepwise regression methods were used in the analysis phase: although this is used frequently in epidemiological studies, more recently stepwise methods have been challenged by some research groups arguing that it should not be used for causal analysis ³⁶. As in all epidemiological studies, the study might be subject to some residual confounding that was not adjusted for. However, arsenic concentrations – which play an important role in drinking water quality elsewhere in Bangladesh – are very low in the areas investigated in this study. In a recent study, two ponds in the same area have been monitored extensively during a period of 18 months. No high or unusual concentrations of chemicals, metal and minerals (including arsenic), pathogens or other (unexpected) contaminants other than salt were measured.^b Finally this study was restricted to pregnant women only. Due to natural blood pressure changes in the course of the pregnancy³⁷, the effect of water sodium on blood pressure in the general population may be different. Future work might focus on blood pressures in the general population, to obtain a better

^a Drinking water salinity and dietary sodium. Unpublished raw data

^b Imperial College London: Unpublished raw data

understanding of the public health impact of drinking water salinity in coastal areas such as Dacope.

Hypertensive women were excluded from the existing database for the analyses in study, despite the fact that they are potentially an important group to consider when studying the association between drinking-water sodium and blood pressure. Excluding these women may have introduced a small bias in the study and – most probably – lead to a slight underestimation of the estimated effect size. The exclusion of these women was done however, because the vast majority of women in the higher blood pressure ranges were also pre-eclamptic; including pre-eclamptic women in the analysis could have introduced reverse causality problems (see introduction). Nonetheless, despite removing this important group a positive association between drinking water source and blood pressure was found, even in the group of women with blood pressures in the normotensive range only: the effect size of this association in women with higher blood pressure values would be expected to be larger and more significant.

The design of the study allowed only one measurement during the 20th gestational week: different effects of saline water on blood pressure may be found in earlier or later stages of the pregnancy.

Perspectives

Our study found evidence that drinking water with a high sodium concentration from saline contamination is associated with higher blood pressures in normotensive pregnant women in coastal areas of Bangladesh. These changes could be there at the start of the pregnancy – as sodium concentrations of women may differ even before they conceive, or could be induced during pregnancy when a woman is forced to change drinking water source from a rainwater based source to a high-saline alternative, because of depletion of rainwater storage. The likely rise in salinity will put added pressure on safe drinking water sources for millions of people

living in vulnerable coastal areas around the world. Recognition of the health risks associated with water salinity by national and international bodies, as well as setting guideline values for water sodium concentrations, should encourage governments to monitor drinking water quality in coastal areas, explore adaptation strategies and accelerate safe water provision where sodium concentrations exceed guideline values.

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Competing Financial Interests

The authors declare that they have no competing financial interests that might have influenced the performance or presentation of the work described in this manuscript.

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Novelty and Significance

What is new?

This is the first population study on drinking water sodium and blood pressure of pregnant women. The study evaluates consistently high levels of sodium in drinking water in vulnerable deltas in Bangladesh. It is one of the first studies to drinking water sodium and blood pressure in South-East Asia.

The study results indicate that, after controlling for confounders, drinking water sodium is positively associated with blood pressure of (otherwise healthy) pregnant women. It is likely that similar associations apply for women in the upper tier of the normotensive range: when they have to change to a source higher in sodium, their blood pressure could possibly rise to hypertensive values and put them at increased risk of adverse pregnancy outcomes.

Especially in areas with poor health systems and limited facilities to manage pregnancy complications, prevention of risk factors for adverse pregnancy outcomes is of great importance.

What is relevant?

In Bangladesh alone, currently 25 million people live in salinity vulnerable areas; besides the impact on water quality, salinity could also affect crop productivity, and thus threaten health and livelihoods of coastal inhabitants.

Drinking water salinity problems do not limit themselves to Bangladesh, but occur in coastal areas in neighbouring countries, such as in India, Myanmar, Thailand and China, and in deltaic regions in other parts of the world. Climate change models suggest salinity problems are likely to increase in the near future due to an increase in cyclone frequency and intensity and subsequent floods. This is further exacerbated by other activities that allow seawater to encroach further in-land, such as dam constructions and shrimp farming. These trends suggest

that salinity problems will not only become more severe in the future, it will also affect a larger area.

Several adaptation strategies, such as rainwater harvesting, managed aquifer recharge (MAR), distillation and reverse osmosis techniques are available; however there is little information on suitability, acceptability and sustainability of each of those solutions in the rural coastal context.

Summary

There is an urgent need to further quantify the overall health impact of drinking water salinity problems worldwide and to further explore the possibilities of several adaptation strategies in prevention of hypertensive events in coastal populations – including pregnant women and their unborn children.

Figures legends

- Figure 1: Map of the nine unions in the Dacope sub-district
- Figure 2: Dry season water sodium levels measured in Dacope 2009-2010 (mg/litre) per water source type
- Figure 3: Systolic and Diastolic Blood Pressure values measured in the study population per type of water source (P = Pond User; TW = Tube well users)

Table 1: Mixed linear regression of Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) in normotensive women (dry season)

Water source	Univariate*				Multivariate 1†				
	Difference in SBP	P-value	95% Conf. Int.		Difference in SBP	P-value	95% Conf. Int.		
Systolic BP	Rain	<i>Ref</i>	-	-	-	<i>Ref</i>	-	-	-
	Pond	6.10	<0.001	4.04	8.16	5.59	<0.001	3.55	7.63
	Tube Well	6.42	<0.001	4.27	8.56	5.92	<0.001	3.80	8.04
	Combination	5.21	<0.001	3.21	7.21	4.44	<0.001	2.41	5.47
Diastolic BP	Rain	<i>Ref</i>	-	-	-	<i>Ref</i>	-	-	-
	Pond	4.54	<0.001	2.74	6.36	3.81	<0.001	2.06	5.58
	Tube Well	4.21	<0.001	2.33	6.10	3.59	<0.001	1.77	5.42
	Combination	3.55	<0.001	1.80	5.31	2.56	0.004	0.82	4.31

Table 1 (continued)

Water source	Multivariate 2‡				
	Difference in SBP	P-value	95% Conf. Int.		
Systolic BP	Rain	<i>Ref</i>	-	-	-
	Pond	3.62	0.003	1.20	6.04
	Tube Well	4.85	<0.001	2.55	7.15
	Combination	3.51	0.001	1.39	5.63
Diastolic BP	Rain	<i>Ref</i>	-	-	-
	Pond	1.72	0.105	-0.36	3.80
	Tube Well	2.30	0.022	0.33	4.23
	Combination	1.32	0.156	-0.50	3.14

* Adjusted for age

† Adjusted for age, nutritional status, physical activity and parity

‡ Best fit model after adjustment for age, nutritional status, physical activity, parity, outdoor temperature, rainfall, socio-economic status, education, medication, use of local stimulants, exposure to chemicals, underlying diseases