

# Excessive Amounts of Salt Consumption and Atheroma Formation Among Patients Awaiting Coronary-Artery-Bypass-Grafting at A Tertiary Care Hospital in Sri Lanka

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## Research article

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# Abstract

## Background:

Ischemic Heart Disease(IHD) characterized by atheroma formation, is a leading contributor for the rising disease burden of chronic non-communicable diseases in Sri Lanka. Even though excessive salt-consumption has been attributed with hypertension, documented literature is scarce on exploring its direct association with atheroma formation with primary data. Coronary-Artery- Bypass-Grafting(CABG) is done as a tertiary preventive measure for IHDs. The aim was to estimate the sodium-intake and to describe the association of salt consumption and atheroma formation among preoperative patients undergoing CABG at Sri Jayewardenepura General Hospital, Sri Lanka.

## Methods

A descriptive cross-sectional study was done on a calculated sample size of 213 participants who were awaiting CABG at SJGH. An interviewer-administered Additional file 1 was used, and dietary intake of sodium was calculated with food-frequency tables and web-based tools. A data extraction form was used and details regarding Coronary arterial segments with atheroma formation were obtained from angiogram reports. After exploring the normality, Spearman-correlation-coefficient and Mann-Whitney-U tests were used to explore associations of atheroma formation. Independent association of sodium-intake and Coronary arterial segments affected with atheroma was explored with multiple-logistic regression.

## Results

The sample was with a male preponderance(male to female ratio=3:1). Comorbidities were observed in a notable proportion: diabetes(47%), dyslipidemia(40%), hypertension(56%). The median(IQR) of BMI and waist circumference were 25.00(23.00-27.00)kg/m<sup>2</sup> and 87.00(82.00-91.00)cm. The median(IQR) sodium-intake was 5875.50(4905.25-7091.25)mg. All participants (n=210) had a sodium intake of more than 2000mg/day. Sodium intake(rs=0.599,p<0.001) and BMI(rs=0.634,p=0.034) were significantly associated with atheroma segments whereas age, gender, diabetes, hypertension, dyslipidemia, waist circumference was not(p>0.05). Sodium intake was found to be an independent predictor of affecting "5 or more segments" when multiple logistic regression was applied(OR= 2.25,CI=1.41 to 3.61).

## Conclusions and Recommendations

The daily intake of sodium by a regular person is more than the dietary recommendations in the study sample. Salt intake reflected by sodium intake seemingly increase the risk of atheroma formation in more coronary segments irrespective of age, sex as well as several known disease conditions and risk factors. More research must be promoted with analytical approaches in proving this hypothesis.

## Background

With the ongoing demographic and epidemiological transitions, the chronic non-communicable (NCDs) disease burden is rising in Sri Lanka, in line with the trends of similar settings (1). Cardiac diseases including ischemic heart diseases (IHDs), is one of the main conditions attributing to chronic NCD burden (2), as one of the leading causes for hospital deaths in Sri Lanka (3). Its spectrum of presentations include; stable angina, unstable angina, myocardial infarction and sudden cardiac death (4), all of which are associated with plaque formation (5). Most patients suffering from ischemic heart disease simultaneously present with other co-morbidities including hypocholesteremia and diabetes, increasing the morbidity profile. The tertiary care unit of Sri Jayewardenepura Teaching Hospital has performed cardiac surgeries since 1992. Hence this setting receives referrals from nationwide and has become an ideal location to study CABG.

Even though there was a decline in salt intake with refrigerators replacing its role as a food preservative, with the rise of processed food consumption, again it is on the rise(6). World Health Organization (WHO) recommends a daily consumption of less than 5 grams of salt for an average adult (7). Salt is composed of 40% sodium and 60% of chloride (6). An intake of 5 grams of salt is equivalent to an intake of 2 grams of sodium, which is regarded as its cut off level for an adult per day(7). The main dietary source of sodium is salt(7). Higher intake of salt leading to that of sodium is associated with increased blood pressure. Even though sodium is available in fruits and vegetables, intake of them in fresh form has generally not shown unfavorable associations with health outcomes like increased blood pressure(8). In fact, it is encouraged to eat more than 400 g of fruits or vegetables per day (excluding "potatoes and other starchy tubers") in order to prevent chronic NCDs(9). This shows the value of focusing on the level of salt intake in limiting the sodium intake.

Sodium concentrations of the body components are closely regulated. For instance, sodium concentration is 2–3 mmol/L higher in interstitial fluid compared to plasma fluid and chloride concentration is 5–10 mmol/L higher in interstitial fluid (10). Sodium is known to cause changes in the blood vessels especially by acting on the endothelium. It enters the apical surface of the endothelium according to the concentration gradient through sodium/glucose and sodium/amino acid symporters. Na<sup>+</sup>/K<sup>+</sup> ATPase pump at the basolateral region which consumes ATP is an active process and can increase the interstitial sodium concentration (11).

There is documented indirect evidence suggesting the potential impact of the salt intake on the cardiovascular risk. After a single meal containing 65 mmol sodium, a set of healthy individuals showed a significant increase in their arterial augmentation index, which may explain the increased risk of cardiovascular disease with increased dietary salt intake (12). Similarly, reduced sodium intake has been linked to improved endothelium function, where a modest reduction of dietary salt to 3 g/day improved endothelial function in normotensive, overweight and obese subjects compared to a diet containing a salt intake of 9 g/day (12). Furthermore, salt sensitive hypertension is related to production of abnormalities in the biomarkers of atherosclerosis. Salt sensitive hypertension was also found to be associated with increased selectins and chemokines while reducing MMP-9 and increasing TIMP-1 leading to endothelial extracellular matrix

degradation (13). Salt has coagulative(denaturalize) action on protein in higher concentration (14). Arterial luminal pressure and wall stress that vessels must stand, make tunica media relatively dry.

Although there are studies providing evidence for salt association with arterial stiffness, endothelium function and atherosclerosis-biomarkers in salt-sensitive hypertension, there is a paucity of evidence on the direct relationship between high salt consumption and atheroma formation. Altogether, documented evidence on these aspects are hardly found in Sri Lanka, which has recently been designated as a upper-middle income country (15). Once explored, these observations can be used in fostering the community interventions for the prevention of cardiovascular diseases.

The overall aim of this study was to estimate the level of sodium intake and to describe the association of salt consumption and atheroma formation among preoperative patients undergoing CABG at SJGH, Sri Lanka.

## Methods

A descriptive cross-sectional study was done at Cardiothoracic unit, Sri Jayewardenepura General Hospital. Data was collected from October 2019 to July 2020. Patients who had been admitted for CABG to STGH during the data collection period comprised of the study population.

Minimum sample size at the data collection stage was estimated with the formula ( $n = Z_{(1-\alpha)}^2 SD^2 / d^2$ ) of Charan and Biswas (2013) (16) using the maximum standard deviation recorded in previous literature for sodium intake among patients who have undergone CABG (17). With the expert opinion, a potential higher value was used for the standard deviation for pre-CABG patients. A lower absolute error was used in getting the highest sample size (17). Thus, the required sample size at the data collection stage was 213 when a non-response rate of 20% was assumed.

Data collection was done with an interviewer administered questionnaire (additional file 1) which included four sections: characteristics of the participant, past medical details, details on food intake including salt consumption and affected Coronary Arterial Segment sheet. Extracting the food intake questions was facilitated with picture aids. Salt consumption was calculated in relation to: home-based salt, salt-added foods and restaurant foods. Home-based salt consumption was calculated with meal frequency in the previous month and on the dispensed amount of salt (average salt in a meal). Salt-added foods and restaurant foods were processed with web-based application and food-tables (18, 19). The distribution of coronary segments affected with atheroma using the participant's Angiogram report is included in the Additional file 2.

Data collection was done by three investigators who are medical officers. Data were analyzed using the Statistical Package for Social Sciences version 20. The sodium intake was expressed in milligrams. When the intake was more than 6000 mg, it was categorized as high intake with the conventional cut-off of 2000 mg. The segments affected were categorized as 'up to 5' and '6 or more'. Associations were explored between the salt consumption and atheroma formation with the Spearman correlation coefficient at a significant level of 5%.

Ethics approval was obtained from the ethics review committee of SJGH (Approval No SJGH/19/ERP/07). Relevant administrative permissions were obtained.

## Results

There were 213 participants in the sample. The median (IQR) age of sample was 59.0 (53.0 to 64.0) years. Other characteristics of the study sample are shown in Table 1. Around three fourth of the sample consisted of males and nearly half of the sample were engaged in unskilled manual work-related job.

Table 1  
Characteristics of the study sample

Characteristics	Frequency	Percentage (%)
Gender (n = 213)		
Male	156	73.2
Female	57	26.8
Marital status (n = 213)		
Ever married	210	98.6
Unmarried	3	1.4
Education level		
Up to GCE O/L	138	64.8
Passed O/L	70	35.2
Occupation category (n = 212)		
Labour	104	49.1
Clerical	82	38.7
Mechanic	19	9.0
Executive	7	3.3

The distribution of categorical and numerical potential predictors are shown in Tables 2 and 3. The presence of diabetes, hypertension and dyslipidemia were observed among 40–60% of the participants. About 12% had been exposed to both smoking and betel chewing.

Table 2  
Distribution of categorical potential risk factors

Factor	Frequency	Percentage (%)
<b>Diabetes (n = 213)</b>		
Yes	101	47.4
No	112	52.6
<b>Dislipidemia (n = 213)</b>		
Yes	84	39.4
No	129	60.6
<b>Hypertension (n = 213)</b>		
Yes	120	56.3
No	93	43.7
<b>Smoking and betel chewing (n = 213)</b>		
Smoking only	35	16.7
Betel chewing only	23	11.0
Smoking and betel chewing	26	12.4
No smoking or betel chewing	126	60.0

Table 3  
Distribution of numerical potential covariates

Covariate	Mean (SD)	Median (IQR)
Sodium intake	6093.42 (1874.17)	5875.50 (4905.25 to 7091.25)
BMI	25.29 (3.48)	25.00 (23.00 to 27.00)
Waist circumference	86.28 (8.51)	87.00 (82.00 to 91.00)

All the participants with available sodium intake values (n = 210) had a higher sodium consumption than the conventional cut off of 2000 mg per day. The mean (SD) and median (IQR) of segmental lesions were 5.09 (1.68) and 5.00 (4.00 to 6.00) respectively. Out of them, among 37.1% (n = 79) had more than 5 segments involved.

Bivariate associations of eight selected factors with the number of segments of the coronary arteries affected are mentioned in Table 4. Only BMI level ( $p = 0.034$ ) and the level of sodium intake ( $p < 0.001$ ) showed statistically significant associations.

Table 4  
Associations of the segments involved

Associated factor	Association
Age	$r_s = 0.112, P = 0.106^a$
Gender	$P = 0.122^b$
Diabetes	$P = 0.105^b$
Hypertension	$P = 0.959^b$
Dyslipidemia	$P = 0.507^b$
BMI	$r_s = 0.634, P = 0.034^{a*}$
Waist circumference	$r_s = 0.094, P = 0.414^a$
Sodium intake	$r_s = 0.599, P < 0.001^{a*}$
<sup>a</sup> Analyzed with Spearman correlation coefficient	
<sup>b</sup> Analyzed with Mann-Whitney U test	
*Statistically significant	

The multi-variate analysis for independent predictors done with multiple logistic regression is depicted in Table 5. The level of sodium intake was found to be an independent predictor with a  $p$  value of 0.001. With each increase of sodium intake by 1 gram, the risk of getting “more than 5 coronary segments affected” is increased by 2.25 times.

Table 5  
Independent predictors of the segments involved

Predictor	Beta coefficient	OR (CI)	Association
Age	0.033	1.03 (0.95 to 1.12)	$P = 0.440$
Gender	1.480	4.39 (0.87 to 22.17)	$P = 0.073$
Diabetes	-0.007	0.99 (0.25 to 3.89)	$P = 0.992$
Hypertension	-0.068	0.94 (0.19 to 4.65)	$P = 0.934$
Dyslipidemia	-0.355	0.70 (0.15 to 3.27)	$P = 0.651$
BMI	-0.197	0.82 (0.66 to 1.03)	$P = 0.087$
Waist circumference	0.071	1.07 (0.98 to 1.18)	$P = 0.137$
Sodium intake	0.813	2.25 (1.41 to 3.61)	$P = 0.001^*$
*Statistically significant			

## Discussion

The present study is the first documented study on associated factors of atheroma formation with special emphasis on the association of it with salt consumption. This study revealed that sodium intake (when calculated based on the salt intake) is associated with atheroma formation with at least a moderate strength in a positive direction (20). Even when adjusted for the confounding effect, the significant association between the salt intake and the atheroma formation remained.

All possible measures were done in ensuring the validity of the findings. The dietary history was obtained with multiple verifications. The sodium intake was calculated based on the dietary history by a reliable source. Since the numerical variables were non-normally distributed, non-parametric statistical techniques were used in bivariate analysis. Even though the statistical power of these tests are lower than that of parametric tests, it would have ensured the validity of the interpretations. When the variables were given in numerical form, efforts were done not to categorize them to prevent any associated data-loss. In addition to the  $p$  values, confidence intervals were presented for the beta coefficients following the multivariate analysis.

The study sample showed a preponderance of males reflecting the higher chronic non-communicable disease (NCDs) burden among them which is assumed to be due to the higher exposure of the risk factors. A notable proportion of the sample were with chronic risk factors like diabetes, dyslipidemia and hypertension showing the inter-connected disease burden between these conditions. The BMI and waist circumference points towards the prevailing risk-

conditions the study sample were with. The daily sodium intake was more than the recommended daily limit even for healthy adults. This finding is compatible with the previous literature showing higher levels of sodium intake globally(21).

In the bivariate analysis, diabetes, hypertension and dyslipidemia were not significantly associated with the number of segments involved. This may be due to the fact that the participants of the study sample were awaiting CABG and hence the diagnosed morbidities must have been attended to. The blood sugar levels, blood pressure values and lipid parameter must have been optimized. The BMI was found to be significantly associated with the number of segments (i.e in the bivariate analysis) with a relatively higher strength of association.

Increase of each one unit of sodium intake was significantly associated with having a 2.25 times likelihood of getting "more than 5 segments affected with atheroma", when adjusted for seven more variables. This is an important eye opener for the local setting, which is experiencing an epidemic of chronic NCDs. Given the evidence on the unfavourable association between the salt intake and increased blood pressure, Sri Lankan policy planners are disseminating the message of limiting the daily intake of salt for a maximum of 5 g per adult per day. Evidence of this study which shed light on a probable direct association between the segments with atheroma formation and the salt intake would strengthen the local scientific evidence for limiting the salt intake. At the same time this would help to convince the public more on limiting the salt intake which would have other associated benefits like in the control of hypertension. Furthermore the findings of the present study highlight the necessity of having specific guideline on a more stringent control of salt intake for people with a higher risk of ischemic heart disease. Thus, once proven with more extensive analytical research, the implications of the present study would help in reducing the disease burden of ischemic heart disease (IHDs), limiting the healthcare cost associated with their management and improving the quality of life of the people with IHDs.

The present study was with several limitations. Firstly, in measuring the sodium intake, only the salt intake was taken into account. However salt is the main source of sodium into the human body and is the main external additive in determining the sodium intake. Furthermore, the intake of any mineral through raw vegetables and fruits are generally regarded as harmless(8). Secondly, the dietary consumptions was based on the details given by the participants. The limitations associated with this method have been previously appreciated in literature(22). However several measures were made to ensure that reliable responses were elicited. Even though the association between salt intake and atheroma formation was adjusted to seven confounders, more known or unknown confounders could be there affecting this association. This should also be considered in interpreting the findings.

## Conclusions And Recommendations

The daily intake of sodium in study sample was more than the dietary recommendations. Level of sodium intake when calculated based on the intake of salt, seemingly increase the risk of atheroma formation in more coronary segments irrespective of age, sex as well as several known disease conditions and risk factors. More research must be promoted with an analytical approach in proving this hypothesis. Meanwhile it is worthwhile to consider more stringent control of sodium intake for those who are at a higher risk of getting ischemic heart disease.

## Abbreviations

IHD - Ischemic Heart Disease

CABG - Coronary-Artery- Bypass-Grafting

NCD - Non-communicable disease

WHO - World Health Organization

ATP - Adenosine Tri-Phosphate

MMP-9 - Matrix metalloproteinase 9

TIMP-1 - Tissue inhibitors of metalloproteinase

SJGH - Sri Jayawardenepura General Hospital

IQR - Interquartile range

SD - Standard Deviation

BMI - Body Mass Index

## Declarations

### Ethics approval and consent to participate:

Ethics approval was obtained from the ethics review committee of SJGH (Approval No SJGH/19/ERP/07). Informed written consent was obtained from all participants

### Consent for publication:

Not applicable

#### Availability of data and materials:

The raw data may be made available upon reasonable request from the corresponding authors

#### Competing interests

The authors declare that they have no competing interests

#### Funding:

The study was self-funded by the investigators and was not funded by an external source.

#### Authors' contributions:

HA was the principal investigator and was involved in conceptualization of the research. All authors were involved in planning the research. HA, AD, KW and PG, AR and PKBM were involved in the literature search. HA, KA, AM, PG, AG and TP contributed in preparation of the questionnaire. KW, TP, WS and SS were involved in data collection. HA, PJ, SS, AM and SL contributed in data analysis and the initial interpretations. RJ, RS, and AK did the overall supervision. HA, SL, PKBM, SPRS and BPUP drafted the first manuscript. All authors contributed in editing the manuscript.

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## Supplementary Files

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