Asian Pacific Journal of Tropical Biomedicine

journal homepage:www.apjtb.com

Document heading doi:10.12980/APJTB.4.2014D153

Correlation between anthropometric measurement, lipid profile, dietary vitamins, serum antioxidants, lipoprotein (a) and lipid peroxides in known cases of 345 elderly hypertensive South Asian aged 56-64 y-A hospital based study

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PEER REVIEW

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Comments

Over all the paper is very informative and gives very scientific information, which makes us to rethink on various aspects causing the higher blood pressure in subjects. This paper is written well with correlation of so many risk factors which could be additional causes of the extent of blood pressure changes apart from the ones published elsewhere. Further research could be initiated on extensive analysis of individual risk factors in a large number of subjects so that the relative risk could be stratified.
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ABSTRACT

Objective: To address the association of dietary vitamins, anthropometric profile, lipid profile, antioxidant enzymes and lipid peroxidation in hypertensive participant compared with normotensive healthy controls.

Methods: Dietary intake of vitamins was assessed by 131 food frequency questionnaire items in both hypertensive participants and normotensive age-sex matched healthy controls. The associated changes in serum antioxidants and lipid peroxidation were also assessed along with lipid profile and anthropometric measurements in both groups of subjects under study.

Results: Dietary vitamins intake was higher in hypertensive participants excepting for vitamin B2 and ascorbic acid compared to normotensive controls. Anthropometric variables in the hypertensive showed significant differences in weight, body mass index, waist circumference, hip circumference, waist-hip ratio and mid-arm circumference. The total cholesterol, low-density lipoprotein cholesterol, triglyceride were significantly higher (P<0.001) in hypertensive except high-density lipoprotein cholesterol which was significantly higher (P<0.001) in normotensive. The serum endogenous antioxidants and enzyme antioxidants were significantly decreased in hypertensive except serum albumin levels compared to normotensive along with concomitant increase in serum lipoprotein (a) malondialdehyde and conjugated diene levels.

Conclusions: Based on the observations, our study concludes that hypertension is caused due to interplay of several confounding factors namely anthropometry, lipid profile, depletion of endogenous antioxidants and rise in oxidative stress.

KEYWORDS

Anthropometry, Lipid profile, Dietary vitamins, Antioxidants, Lipid peroxides, Lipoprotein (a), Hypertension, South Asian

1. Introduction

Hypertension is one the major public health problem worldwide[1]. Those individuals who are hypertensive are also at an increased risk for stroke, heart disease, and renal failure. Etiological factor related to essential hypertension has a genetic component but, lifestyle factors such as diet, sedentary habits, lack of exercise, smoking also have an impact in causation of hypertension[2]. In experimental studies, both human and animal models, Insulin resistance and glucose intolerance are most commonly observed phenomenon in relation to hypertension[3]. Increased reactive aldehyde, methylglyoxal is an aftermath of aberration in glucose metabolism[4]. Methylglyoxal binds

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Foundation Project: Supported by a grant from Confederation of Epidemiological Associations registered under Government of Kerala (Grant No. 30-955/2012 CEA).

Article history:
Received 12 Jan 2014
Received in revised form 20 Jan, 2nd revised form 23 Jan, 3rd revised form 31 Jan 2014
Accepted 22 Feb 2014
Available online 28 Apr 2014

to both sulfhydryl and amino groups of proteins forming conjugates/advanced glycation end products. This disrupts protein structure and function furthermore can affect vascular calcium channels, enzymes, and tissue proteins leading to increased oxidative stress[2]. These alterations also impair endothelial functions with uninterrupted increase in intracellular free calcium, peripheral vascular resistance, and hypertension[5]. Even though it sounds simple, but the relationship between hypertension, oxidative stress and antioxidants is very complex and inadequately understood. Oxidative stress may play a role in the patho-physiology of hypertension as proved by experimental evidence but the same mechanism does not conform in humans. However it is suggested by research findings that *in vivo* oxidation of low-density lipoproteins, primarily by oxygen-free radicals, may increase atherogenesis[6]. Hypertension associated long-term infusion of angiotensin II is linked to the stimulation of oxidant production, leading to reduced bioactivity of NO and the activation of NAD(P)H oxidase[7].

The relationship of hypertension with antioxidants and oxidative stress is therefore of much interest. Various scientific studies[8] have reported on the associations between antioxidants and cardiovascular disease, myocardial infarction and mortality, but fewer studies have focused on the relationship between antioxidant measures and hypertension. Even though, study suggested no concrete links and evidence of an association between blood pressure and intakes of either carotene or vitamin E, still mixed reports have come up where links between blood pressure and dietary antioxidants have been re-established.

Several studies have linked dietary supplementation with antioxidants rich vegetables and fruits including ascorbic acid, vitamin B1, B2 and B3 along with vitamin A and the quinone enzyme Q10 in decreasing blood pressure in animal models and humans with essential hypertension[9]. These antioxidants can act as potent antihypertensive agents by reducing aldehyde conjugate/advanced glycation end product formation and oxidative stress, by improving insulin resistance and endothelial function, or by normalizing calcium channels and peripheral vascular resistance[10].

Study conducted among Australians has shown that the levels of antioxidants are lower and levels of uric acid and malondialdehyde are higher in hypertensive participants compared to normotensive participants[11]. So, dietary supplementation with antioxidants proves to be a beneficial, inexpensive, first-line alternate treatment modality for hypertension. It is reported that increased oxidative stress may be both a cause as well as a consequence of hypertension[12]. Based on *in vivo* experimental evidence it is shown that oxidized low-density lipoproteins (LDL) formed by oxygen-free radicals may increase hypertension-related atherogenesis, and antioxidants may be beneficial in this regard[9]. Previous findings concerning associations between serum measures of antioxidants and hypertension have however been inconsistent.

In the current study it is hypothesized that some significant association between serum levels of antioxidants and markers of oxidative stress with hypertension could be established.

2. Materials and methods

Three hundred and forty five hypertensive participants and 345 age-sex matched normotensive healthy controls were taken for this study. The study was conducted for a period of three years from May 2007 to April 2010. The design of this study was pre-approved by the Institutional Ethical Committee Board of the institution and informed consent was obtained from the hypertensive participants and controls.

2.1. Cases

Eligible cases with patients aged 56-64 year (201 men and 144 women) who were diagnosed of hypertension were recruited for the study.

2.2. Controls

For each case subject, 2 control subjects matched by age (within 5 years), sex, and hospital were obtained from outpatient clinics or inpatient wards. The study identified 345 eligible control subjects. Controls were selected by using predominantly any of these two methods depending on the hospital. In the first method, we accompanied a particular physician during an outpatient clinic, according to a weekly schedule of clinics and wards. At the end of each consultation, the physician or the physician's assistant invited the patient to speak with us about his or her lifestyle and diet. Patients matching the required age and sex profile were eligible according to study criteria and were then informed of the study and asked to participate. In these situations, participation was 100%. In the second method, we independently identified control patients from clinics and wards. We attempted to approach all individuals present in a particular outpatient clinic or in a specified ward. In large clinics, patients were screened for eligibility and invited to participate according to their queue number (highest number first). This method was used to prevent bias in the selection of controls. Overall participation was high (97%). Basic demographic information was collected from all persons who were approached. If an individual fit the required age and sex profile and was eligible, we briefly explained the study and asked whether the patient was willing to participate. Thus the study included 345 age-sex matched healthy volunteers (201 men and 144 women).

2.3. Data collection

Interviews were conducted in hospital wards or clinics by us and lasted 30 min. Informed consent was obtained from all study subjects. The interviews included various life style factors such as education, socio-economic status, income and type of job. Details of major cardiovascular risk factors such as smoking, alcohol intake, diabetes, obesity and hypertension were obtained. We also collected data on socioeconomic status, smoking history, diabetes, and hypercholesterolemia, family history of cardiovascular disease (including ischaemic heart disease, angina,

myocardial infarction, hypertension, diabetes, stroke, sudden death, and bypass surgery), dietary intake, types of fat or oils used in cooking, nutritional supplement use, and physical activity.

2.4. Dietary intake by 24-hour dietary record

The patients and controls were given the food items which they were supposed to mark including the quantity consumed[13]. This was carried for three times in the same subjects to avoid biasness and to get more accuracy in intake. The dietary intake was tabulated and the amount of vitamins was calculated from the food consumed.

2.5. Anthropometric measurements

Anthropometric measures (height, weight, and hip and waist circumferences) were obtained and body mass index (weight in kg divided by height in meters squared) and waist-hip ratio were calculated. Their height, weight, waist-hip ratio and blood pressure were recorded. Height was measured in centimeters and weight in kilograms using calibrated spring balance. Supine waist girth was measured at the level of umbilicus with a person breathing silently. Standing hip girth was measured at inter-trochanteric level. Waist and hip measures were assessed by using a standardized tape measure, with waist measures taken at the midpoint between the costal margin and ileac crest, and hip measures were taken at the widest circumference.

2.6. Blood pressure

The blood pressure was measured using standard mercury manometer. At least two readings at 5 min intervals as per World Health Organization guidelines were recorded[14]. If high blood pressure (≥140/90 mmHg) was noted a third reading was taken after 30 min. The lowest of the three readings was taken as blood pressure.

2.7. Collection of samples

Blood (10 mL) was collected after overnight fasting in different containers.

From EDTA vial, 5.0 mL of blood was taken. Red cells were washed 3-4 times with ice-cold normal saline and used for estimation of glutathione peroxidase, superoxide dismutase and catalase.

From plain vial, remaining blood was allowed to clot and serum was separated by centrifugation for 5 min at 5000 r/min and was used for determination of lipid profile, malondialdehye and conjugated dienes, and other assays as described.

2.8. Lipid and serum profile measurements

2.8.1. Lipid profile

Total cholesterol, triglycerides, and high density lipoprotein cholesterol (HDL-C) were estimated by enzymatic methods using the kits obtained from Randox Laboratories Limited, Crumlin, UK. Plasma LDL-cholesterol (LDL-C)was determined from the values of total cholesterol and HDL-cholesterol using the following formulae:

$$\text{LDL-C} = \frac{\text{T C-TG-HDL-C (mg/dL)}}{5}$$

All chemicals of analytical grade were obtained from Sigma Chemicals, India.

2.8.2. Serum albumin

Serum albumin was measured by bromocresol green dye binding method[15].

2.8.3. Serum uric acid

Serum uric acid was estimated by the method of Brown based on the development of a blue color due to tungsten blue as phosphotungstic acid is reduced by uric acid in alkaline medium[16].

2.8.4. Serum total bilirubin

Serum total bilirubin was estimated by Jendrassik and Grof method[17].

2.8.5. Glutathione peroxidase

The glutathione peroxidase activity was determined by the procedure of Paglia and Valentine[18].

2.8.6. Superoxide dismutase

Superoxide dismuatse enzyme activity was measured by superoxide dismuatse assay kit using rate of inhibition of 2-(4-indophenyl)-(4-nitrophenol)-5-phenyltetrazolium chloride reduction method modified by Sun *et al*[19].

2.8.7. Catalase

Catalase activity was measured spectrophotometrically as described by Beutler[20,21].

2.8.8. Malondialdehyde

Malondialdehyde levels were estimated by thiobarbituric acid reaction[22].

2.8.9. Conjugated dienes

Conjugated dienes levels were measured by Recknagel and Glende method[23] with little modification.

All chemicals of analytical grade were obtained from Sigma Chemicals, India.

2.8.10. Lipoprotein (a)

The lipoprotein (a) levels were determined by latex-enhanced turbidimetric method.

2.8.11. Ascorbic acid

Estimation of vitamin C was carried out by Roe and Kuether method[24].

2.9. Statistical analysis

Data was entered in Microsoft Excel for Windows 2007. The mean±SD was obtained using Excel software. The two-sample-*t*-test value was obtained between the various hypertensive participants and the controls. The distribution of '*t*'-probability was calculated depending on '*n*' and significance of the test was obtained. *P* value less than 0.05 was considered as significant.

3. Results

Dietary vitamins intake was higher in hypertensive participants excepting for vitamin B2 and vitamin C which was higher in normotensive controls as shown in Table 1. Anthropometric variables in hypertensive participants showed significant differences in weight, BMI, waist circumference, hip circumference, waist-hip ratio and mid-

Table 1
Mean dietary intake of vitamins in control and hypertensive participants (mean±SD).

Vitamins	Normotensive (*n*=345)	Hypertensive (*n*=345)	*P* value (95% *CI*)
Vitamin A (μg)	2208.7±158.3	2324.3±189.2	<0.01 (2290.86-2357.73)
Vitamin B1 (mg)	1.9±0.6	2.4±0.6	<0.05 (2.29-2.50)
Vitamin B2 (mg)	1.9±0.4	1.7±0.5	<0.01 (1.61-1.78)
Vitamin B3 (mg)	18.7± 2.7	22.8±5.2	<0.01 (21.91-22.08)
Vitamin C (mg)	445.7±82.8	387.6±123.8	<0.001 (365.72-409.47)

Table 2
Anthropometric data of normotensive and hypertensive participants (mean±SD).

Anthropometric variables	Normotensive (*n*=345)	Hypertensive (*n*=345)	*P* value (95% *CI*)
Age (years)	59.93±3.2	61.07±3.14	0.0018 (60.51- 61.62)
Range (years)	(56-64)	(56-64)	
Height (m)	1.63±0.05	1.63±0.07	0.088 (1.61-1.64)
Weight (kg)	66.83±4.02	71.97±5.41	<0.01 (71.01-72.92)
BMI (kg/m^2)	24.34±1.34	26.15±1.44	<0.01 (25.89-26.40)
Waist circumference (cm)	92.63±2.98	102.95±5.88	<0.01 (99.91-101.98)
Hip circumference (cm)	99.27±5.76	105.81±5.09	<0.01 (104.91-106.70)
Waist-hip ratio	0.93±0.03	0.95±0.03	<0.01 (0.94-0.95)
Mid arm circumference (cm)	27.67±1.62	30.62±1.98	<0.01 (30.02-31.21)
Biceps skin fold thickness (mm)	7.15±1.89	7.48±1.37	<0.001 (7.06-7.89)
Triceps skin fold thickness (mm)	10.93±1.36	12.92±1.66	<0.001 (12.41-13.42)
Systolic blood pressure (mmHg)	119.71±5.67	143.57±11.31	<0.001 (140.14-146.99)
Diastolic blood pressure (mmHg)	76.78±4.62	91.87±8.77	<0.001 (89.21-94.52)

Table 3
Lipid profile in normotensive and hypertensive participants (mean±SD).

Variables	Normotensive (*n*=345)	Hypertensive (*n*=345)	*P* value (95% *CI*)
Total cholesterol (mg/dL)	156.67±17.69	196.36±17.68	<0.001 (193.23-199.48)
HDL-C (mg/dL)	54.35±5.59	39.38±5.73	<0.001 (38.36-40.39)
Triglycerides (mg/dL)	109.84±13.62	149.37±18.23	<0.001 (146.14-152.59)
LDL-C (mg/dL)	97.58±13.72	130.73±16.32	<0.001 (127.84-133.61)

Table 4
Antioxidant status in normotensive and hypertensive participants (mean±SD).

Serum parameters	Normotensive (*n*=345)	Hypertensive (*n*=345)	*P* value (95% *CI*)
Serum albumin (g/dL)	4.6±0.5	4.8±0.4	<0.001 (4.72-4.87)
Serum uric acid (mg/dL)	5.6±1.7	4.9±0.7	<0.001 (4.77-5.02)
Serum ascorbic acid (mg/dL)	4.8±1.3	3.2±0.6	<0.001 (3.09-3.30)
Serum total bilirubin (mg/dL)	0.7±0.3	0.6±0.3	<0.01 (0.54-0.65)
Serum superoxide dismutase (U/gHb)	1769.5±28.4	756.5±197.6	<0.0001 (721.57-791.42)
Serum glutathione peroxidase (U/gHb)	62.4±4.7	39.4±7.2	<0.0001 (38.12-40.67)
Serum catalase (k/gHb)	248.3±22.6	213.4±38.2	<0.001 (206.64-220.15)

Table 5
Lipoprotein (a) and lipid peroxidation levels in normotensive and hypertensive participants (mean±SD).

	Normotensive(*n*=345)	Hypertensive (*n*=345)	*P* value (95% *CI*)
Serum Lipoprotein (a)(mg/dL)	2.6±1.3	12.8±3.1	<0.0001 (12.25-13.34)
Serum malondialdehyde (nmol/L)	4.8±0.8	17.3±2.3	<0.0001(16.89-17.70)
Serum conjugated dienes (μmol/L)	23.3±3.2	53.7±4.7	<0.0001(52.86-54.53)

arm circumference whereas highly significant differences were observed in biceps and triceps skin fold thickness, systolic and diastolic blood pressure as shown in Table 2. The total cholesterol, LDL-C, triglyceride were significantly higher (P<0.001) in hypertensive participants except HDL-C which was significantly higher (P<0.001) in normotensive healthy controls as shown in Table 3. The serum endogenous antioxidants were significantly decreased in hypertensive participants except serum albumin levels compared to normotensive healthy controls. Also the enzyme antioxidants were also significantly lowered in hypertensive as shown in Table 4. The mean serum lipoprotein (a), malondialdehyde and conjugated diene levels in hypertensive participants were significantly higher (P<0.0001) compared with controls as shown in Table 5.

4. Discussion

Hypertension remains the major risk factor for cardiovascular diseases which is the leading cause of morbidity and mortality in all developed and developing countries in the world including India[25]. Even though antioxidants and vitamins have antihypertensive effects by reducing oxidative stress and improving endothelial functions but still no clear results have been validated from researches. It is mentioned that dietary supplementation with antioxidants may prove to be beneficial and inexpensive and can be the best treatment modality for hypertension, but due to insignificant thumb print, still we are on the search of links between these two components and establish their association. In this hospital based study, the relationship between hypertension, antioxidants and oxidative stress in hypertensive participants in mid-adult life was examined. The study was designed to identify and evaluate potential link between the serum antioxidants, their dietary antioxidants intake (mainly from vitamins) with respect to hypertension. The subjects selected for the study comprised of 345 normotensive healthy controls, 56-64 year and 345 hypertensive participants, 56-64 year.

4.1. Dietary antioxidants intake

Of the dietary vitamins intake measured, the hypertensive participants had significantly higher consumption of vitamins A, B1 and B2 compared to normotensive healthy age-sex matched controls. The current study observed higher antioxidant vitamins consumption in hypertensive participants compared to normotensive healthy controls, excepting for vitamin C which was higher in controls. The matter of debate arises why the antioxidant status was comparatively lower in hypertensive participants compared to controls even though they had higher exogenous intake of antioxidants vitamins through the food stuffs. The basis could be partially explained with the nullifying effect of these vitamins by various inter-plays of oxidants and pro-oxidants which could have been higher in hypertensive participants, making it failed to provide adequate protection from oxidants[26]. Earlier studies have emphasized to increase the antioxidants in diet and clinical trials have shown effective results. Though a beneficial role for vitamins in hypertension has long been explored but the data are still inconsistent[27], and it is not affirmative with several findings.

Extensive studies have been conducted on intake of vitamin C and it has been suggested by several epidemiological studies that vitamin C status inversely associated with blood pressure[28].

Previous studies have reported that vitamin C level was lower in hypertensive patient, compared to the general population[29]. The observations from the current study conform with the previous studies.

Several mechanisms have been proposed in connection with reduction of blood pressure of an individual by increasing the vitamin C intakes through diet and also if their levels are higher in serum. The beneficial effects of vitamin C are well understood. It serves as a potent blood pressure stabilizer in normalizing the blood pressure, due to its antioxidant properties. As an antioxidant, it has enormous roles to play and it sustains a special function in maintenance of blood pressure by its interference with production of free oxygen radicals and peroxides and also stimulate the synthesis of prostaglandins such as prostacyclin, which is vasodilator in nature[30]. Apart from that, it also induces the release of norepinephrine from adrenal glands, which reduces the plasma level of sodium. Vitamin C is more than an antioxidant and its effects on neurotransmitters may contribute to its anti-hypertensive activity[31].

Vitamin C not only enhances the nitric oxide synthase activity but also augments guanylate cyclase sensitivity to nitric oxide[32]. Last but not the least it may reduce insulin resistance which in turn causes endothelium-dependent, nitric oxide-mediated vasodilation[33]. Apart from direct links in lowering hypertension, it also attenuates hypertension related conditions such as endothelial damage or arterial stiffness[34].

4.2. Anthropometric variables

When the anthropometric variables were analyzed it was observed that there were highly significant differences in both biceps and triceps skin fold thickness in hypertensive participants when compared with normotensive controls. Earlier study conducted among elderly Malaysian also observed significantly higher anthropometric profile especially waist and hip circumference, waist to hip ratio and body mass index in hypertensive subjects as observed in the current study[34]. Another study conducted in Turkey on hypertensive subjects stressed on the clinical usefulness of

waist to hip ratio as a useful tool in screening obese patients with elevated blood pressure[35]. Yet another cross-sectional study among Brazilian men also observed similar findings as the current study[36]. They also reported significantly higher anthropometric profile in hypertensive subjects compared to normotensive controls but highlighted waist circumference as the only independent anthropometric measurement related to hypertension. Another study conducted on Turkish hypertensive adults also observed similar findings as the current study where they reported overweight, obese and waist circumference among hypertensive adults as important factors affecting both systolic and diastolic blood pressure in Turkish hypertensive adults[37].

So from the observations made by most of the study in various countries, it is implicative of the fact that anthropometric profiles in hypertensive subjects are bound to be higher than normotensive subjects. It can be concluded from the aforementioned observations that obesity, waist circumference and waist to hip ratio are important observations in hypertensive subjects.

4.3. Observations of lipid profile

The mean total cholesterol level of hypertensive participants [(196.36±17.68) mg/dL] was significantly (P<0.001) higher when compared with controls [(156.67±17.69) mg/dL]. The mean high density lipoprotein-cholesterol level in the hypertensive [(39.38±5.73) mg/dL] was significantly lower (P<0.001) compared with normotensive controls [(54.35 ±5.59) mg/dL]. Triglyceride values observed in hypertensive participants was [(149.37±18.23) mg/dL] significantly higher than controls [(109.84±13.62) mg/dL]. The mean LDL-C levels in hypertensive participants was [(130.73±16.32) mg/dL] significantly higher than controls [(97.58±13.72) mg/dL].

Earlier studies carried out on forty hypertensive patients also observed a significantly higher levels of total cholesterol, triglyceride and LDL-C compared to normotensive controls[38].

Yet another study carried out in Spain in hypertensive patients with dyslipidemia treated with lipid lowering therapy also observed a significantly higher levels of triglycerides and lower levels of HDL-C in hypertensive patients compared to normotensive controls. It was reported from the study that despite of treatment with lipid lowering drugs, the lipid profile in hypertensive patients remained on the higher levels when compared with controls and this could be area of concern as it could be a potent cardiovascular risk[39]. Even the study carried out among hypertensive Nigerians reported significantly elevated levels of total cholesterol, triglyceride and LDL-C but the levels of HDL-C were comparable with normotensive[40].

Also studies conducted earlier among hypertensive subjects in Malaysia, Brazil and Turkey reported similar findings which concurred with the current study[34-37]. So it can be presumed that all hypertensive subjects have higher lipid profiles compared to normotensive.

4.4. Antioxidant status

The serum endogenous antioxidants namely albumin, uric acid, ascorbic acid, bilirubin showed varied results in hypertensive participants. The study observed higher serum albumin in hypertensive participant with a concomitant decrease in serum uric acid, ascorbic acid and bilirubin. The enzyme antioxidants namely superoxide dismutase, catalase and glutathione peroxidase were significantly lowered in hypertensive participants when compared with normotensive controls.

A population based cross-sectional study conducted in Norway observed a positive correlation with serum albumin concentration with hypertension and the current study also observed similar findings[41]. Though albumin is an antioxidant and is cardio protective in nature due to its free radical scavenging properties, it positively correlated with hypertension. Another study conducted at New Delhi on mild hypertension subjects observed the serum albumin levels drastically decreased in the hypertensive patients compared to healthy normotensive controls[42], and their findings does not concur with the current study.

The current study observed significantly lower levels of uric acid in hypertensive participants when compared with normotensive controls. The findings of this study does not conform with the previous study report where they observed higher level of uric acid in hypertensive subjects and claimed it to be a potent risk factor in the patients, and further stressed on the use of allopurinol in lowering the incidence of hypertension[43].

With respect to vitamin C, the current study observed significantly lowered levels in hypertensive participants and it is very much agreeable with the findings of the previously studies[44,45].

The bilirubin levels in hypertensive participants were slightly lower than the normotensive controls. It is well known that bilirubin, though end product of heme degradation, has antioxidant potential which is mediated by the inhibition of nicotinamide adenine dinucleotide phosphate-oxidase oxidase (NADPH)[46,47], a key source of oxidants in phagocytic and non-phagocytic cells, and of protein kinase C activity[47,48]. Several studies have been published showing the relation between serum bilirubin and oxidative stress-mediated diseases, including angiotensin II-mediated hypertension[49]. The lowered levels of bilirubin in hypertensive participants conform with the observations of previous studies[50] where they suggested bilirubin as a prognostic marker in pulmonary arterial hypertensive patients and demonstrated that hyperbilirubinemia is associated with advanced right heart failure and markedly reduces the chances of survival in patients.

The current study observed that the antioxidant enzymes namely superoxide dismutase, glutathione peroxidase

and catalase were found to be significantly lowered in hypertensive participants when compared with normotensive controls. The findings of the current study conform to the previous studies conducted on the similar line[51-56]. A study based on elderly hypertensive patients who were on their usual anti-hypertensive drugs and to link their association with glutathione antioxidant defense system observed increased activities of glutathione peroxidase and reductase along with higher concentration of glutathione in treated hypertensive patients compared to healthy normotensive subjects. They concluded from their study that during medication alterations in activities are likely to be related to the effect of treatment of NO bioavailability[53]. In fact, antihypertensive drugs are proven to have antioxidants properties and they have ability to lower oxidative stress[53,57,58]. From the study it is also observed that the drastic elevation of glutathione levels is due to decreased oxidative stress caused by antihypertensive drugs or else it could be due to adaptive mechanisms to oxidative stress. Of many one of the mechanisms that ties antioxidant and antihypertensive properties can be decreased level of superoxide radical $O_2^{\bullet-}$ when hypertensive patients are on anti-hypertensive drugs. This effect can be mediated by increased level of glutathione which is known to prevent platelet-derived growth factor-mediated production of reactive oxygen species by NADH/NADPH oxidase, which is considered to be the main source of vascular reactive oxygen species and $O_2^{\bullet-}$ in particular[59-61]. Moreover, glutathione in reaction with peroxynitrite ONOO- forms S-nitrosothiols, which have the ability to inhibit NADPH oxidase[53,62-64]. Furthermore, S-nitrosothiols subsequently release NO over prolonged time, thus extend the half-life of NO many-fold and in consequence relax vascular tissue[53,65-67].

4.5. Lipoprotein (a) and lipid peroxidation

The mean serum lipoprotein (a), malondialdehyde and conjugated diene levels in hypertensive participants were higher when compared with controls.

Studies conducted earlier also observed similar findings as observed in the current study[26,68].

Based on the observations, our study concludes that hypertension is caused due to interplay of several confounding factors namely anthropometry, lipid profile, depletion of endogenous antioxidants and rise in oxidative stress.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

The author extends his sincere thanks to all the participants of the current study. The author also thanks to the medical students and interns of the study center and all the supporting staffs involved in data collection and entry. This study was supported by a grant from Confederation of Epidemiological Associations registered under Government of Kerala (Grant No. 30-955/2012 CEA).

Comments

Background

Hypertension is one of the major public health problem worldwide. It is one of the major risk factor for cardiovascular disease. It is a cumulative effect of antioxidant and oxidant imbalance which could be additive risk in causing hypertensive. Apart from these, there could be various other parameters which can affect the blood pressure in an individual including the lipid profile, anthropometry, obesity, lipoprotein (a), *etc*. The current study was based on assessment of risk variables in hypertensive patients compared to normotensive. The author analyzed the vitamin intake from various dietary sources, along with anthropometric variables and risk factors which could be additive risk in hypertension. This study is done on analysis of various risk factors and their association with hypertensive and normotensive subjects.

Research frontiers

The current study was done to analyze the various risk factors which could be associated with hypertension and it is first of its kind done working with various parameters and analyzing the additive risk associate with hypertension. No such study was done earlier.

Related reports

No such reports have been published or reported earlier.

Innovations & breakthroughs

The markers like lipoprotein (a), conjugated diene, and malondialdehyde are significantly higher in hypertensive along with concomitant decrease in the levels of antioxidants level in serum which could be associated with raised blood pressure. Also body mass index and obesity could be risk factors in these subjects with higher blood pressure.

Applications

Timely measurement of antioxidants and risk variable parameters could assess the extent of progression of additional risks in hypertensive subjects.

Peer review

Over all the paper is very informative and gives very scientific information, which makes us to rethink on various aspects causing the higher blood pressure in subjects. This paper is written well with correlation of so many risk factors which could be additional causes of the extent of blood pressure changes apart from the ones published elsewhere. Further research could be initiated on extensive analysis of

individual risk factors in a large number of subjects so that the relative risk could be stratified.

References

[1] Kizhakekuttu TJ, Widlansky ME. Natural antioxidants and hypertension: promise and challenges. *Cardiovasc Ther* 2010; **28**(4): e20-e32.

[2] Tripathi JS, Byadgi PS, Narasimha MK. The role of psychological factors in aetiopathogenesis and management of obesity related disease. *J Appl Pharm Sci* 2011; **1**(5): 32-34.

[3] Shanik MH, Xu Y, Skrha J, Dankner R, Zick Y, Roth J. Insulin resistance and hyperinsulinemia. Is hyperinsulinemia the cart or the horse? *Diabetes Care* 2008; **31**(Suppl 2): S262-S268.

[4] Hipkiss AR. Accumulation of altered proteins and ageing: causes and effects. *Exp Gerontol* 2006; **41**(5): 464-473.

[5] Girouard H, Ladecola C. Neurovascular coupling in the normal brain and in hypertension, stroke and Alzheimer disease. *J Appl Physiol* 2006; **100**(1): 328-335.

[6] Witztum JL, Steinberg D. The oxidative modification hypothesis of atherosclerosis: does it hold for humans? *Trends Cardiovasc Med* 2001; **11**(3-4): 93-102.

[7] Förstermann U. Nitric oxide and oxidative stress in vascular disease. *Pflugers Arch* 2010; **459**: 923-939.

[8] Riccioni G, Bucciarelli T, Mancini B, Corradi F, Di Ilio C, Matte PA, et al. Antioxidant vitamin supplementation in cardiovascular diseases. *Ann Clin Lab Sci* 2007; **37**(1): 89-95.

[9] Beg M, Sharma V, Akhtar N, Gupta A, Mohd J. Role of antioxidants in hypertension. *J Indian Acad Clin Med* 2011; **12**(2): 122-127.

[10] Ceriello A. Possible role of oxidative stress in the pathogenesis of hypertension. *Diabetes Care* 2008; **31**(Suppl 2): S181-S184.

[11] Parslow RA, Sachdev P, Salonikas C, Lux O, Jorm AF, Naidoo D. Association between plasma antioxidants and hypertension in a community-based sample of 415 Australians aged 60-64. *J Hum Hypertens* 2005; **19**: 219-226.

[12] Grossman E. Does increased oxidative stress cause hypertension? *Diabetes Care* 2008; **31**(Suppl 2): S185-S189.

[13] International Epidemiological Association. Relative validity and reproducibility of a diet history questionnaire in Spain. III. Biochemical markers. EPIC Group of Spain. European Prospective Investigation into Cancer and Nutrition. *Int J Epidemiol* 1997; **26**: S110-S117.

[14] Rose GA, Blackburn H, Gillum RF, Prineas RJ. *Cardiovascular survey methods. WHO Monograph Series No. 56.* 2nd ed. Geneva: World Health Organisation; 1982.

[15] Perry BW, Doumas BT. Effect of heparin on albumin determination by use of bromocresol green and bromocresol purple. *Clin Chem* 1979; **25**: 1520-1522.

[16] Brown H. The determination of uric acid in human blood. *J Biol Chem* 1945; **158**: 601-608.

[17] McPhaul L, Kershaw M, Tilque D, Eckfeldt JH. A 2,4-dichlorophenyl diazonium-based method for total bilirubin without interference from indican in uremic sera. *Clin Chem* 1985; **31**(7): 1229-1231.

[18] Paglia DE, Valentine WN. Studies on the quantitative and qualitative characterization of erythrocyte glutathione peroxidase. *J Lab Clin Med* 1967; **70**: 158-169.

[19] Sun Y, Oberly LW, Li Y. A simple method for clinical assay of superoxide dismutase. *Clin Chem* 1988; **34**: 497-500.

[20] Beutler E. *Red cell metabolism: a manual of biochemical methods.* 3rd ed. New York: Grune and Stratton; 1984, p. 105.

[21] Beutler E, Duron O, Kelly B. Improved method for the determination of blood glutathione. *J Lab Clin Med* 1963; **61**: 882-888.

[22] Bernheim S, Bernheim MLC, Wilbur KM. The reaction between thiobarbituric acid and the oxidant product of certain lipids. *J Biol Chem* 1948; **174**: 257-264.

[23] Recknagel RO, Glende EA Jr. Spectrophotometric detection of lipid conjugated dienes. *Methods Enzymol* 1984; **105**: 331-337.

[24] Roe JH, Kuether CA. The determination of ascorbic acid in whole blood and urine through the 2,4-dinitrophenylhydrazine derivative of dehydroascorbic acid. *J Biol Chem* 1943; **147**: 399-407.

[25] American Heart Association. *Heart disease and stroke statistics-2003 update.* Texas, USA: American Heart Association; 2003.

[26] Kumar A, Ramiah S. Cardiovascular risk factors in normolipidemic acute myocardial infarct patients on admission -do dietary fruits and vegetables offer any benefits? *Online J Health Allied Sci* 2010; **9**(3): 3.

[27] Honarbakhsh S, Schachter M. Vitamins and cardiovascular disease. *Br J Nutr* 2009; **101**(8): 1113-1131.

[28] Eger S, Rimbach G. Which sources of flavonoids: complex diets or dietary supplements? *Adv Nutr* 2011; **2**: 8-14.

[29] Nwanjo HU, Oze G, Okator MC, Nwosu D, Nwankpa P. Oxidative stress and non-enzymic antioxidant status in hypertensive patients in Nigeria. *Afr J Biotechnol* 2007; **6**(14): 1681-1684.

[30] Schildknecht S, Daiber A, Ghisla S, Cohen RA, Bachschmid MM. Acetaminophen inhibits prostanoid synthesis by scavenging the PGHS-activator peroxynitrite. *FASEB J* 2008; **22**: 215-224.

[31] Virdis A, Ghiadoni L, Qasem AA, Lorenzini G, Duranti E, Cartoni G, et al. Effect of aliskiren treatment on endothelium-dependent vasodilation and aortic stiffness in essential hypertensive patients. *Eur Heart J* 2012; **33**(12):1530-1538.

[32] Hirashima O, Kawano H, Motoyama T, Hirai N, Ohgushi M, Kugiyama K, et al. Improvement of endothelial function and insulin sensitivity with vitamin C in patients with coronary spastic angina: possible role of reactive oxygen species. *J Am Coll Cardiol* 2000; **35**: 1860-1866.

[33] Solzbach U, Hornig B, Jeserich M, Just H. Vitamin C improves endothelial dysfunction of epicardial coronary arteries in hypertensive patients. *Circulation* 1997; **96**: 1513-1519.

[34] Latiffah AL, Hanachi P. To investigate the relation of hypertension and anthropometric measurement among elderly in Malaysia. *J Appl Sci* 2008; **8**: 3963-3968.

[35] Yalcin BM, Sahin EM, Yalcin E. Which anthropometric measurements is most closely related to elevated blood pressure? *Fam Pract* 2005; **22**: 541-547.

[36] Cassani RS, Nobre F, Pazin-Filho A, Schmidt A. Relationship

between blood pressure and anthropometry in a cohort of Brazilian men: a cross-sectional study. *Am J Hypertens* 2009; **22**(9): 980-984.

[37] Hilal Y, Acar TN, Koksal E, Gezmen KM, Akbulut G, Bilici S, et al. The association of anthropometric measurements and lipid profiles in Turkish hypertensive adults. *Afr Health Sci* 2011; **11**(3): 407-413.

[38] Sarkar D, Latif SA, Uddin MM, Aich J, Sutradhar SR, Ferdousi S, et al. Studies on serum lipid profile in hypertensive patient. *Mymensingh Med J* 2007; **16**(1): 70-76.

[39] Hermida Ameijeiras A, Lopez Paz JE, Pena Seijo M, Calvo Gonzalez G, Romero Miguez ML, Martinez Durán V, et al. Lipid profile in hypertensive patients treated with lipid lowering therapy. *J Hypertens* 2010; **28**: e378-e379.

[40] Idemudia J, Ugwuja E. Plasma lipid profiles in hypertensive Nigerians. *Int J Cardiovasc Res* 2009; doi: 10.5580/117f.

[41] Høstmark AT, Tomten SE, Berg JE. Serum albumin and blood pressure: a population-based cross-sectional study. *J Hypertens* 2005; **23**(4): 725-730.

[42] Yadav A, Singh R. Amylase as an early serum marker for kidney damage in mild hypertension-a pilot study. *Int J Pharma Bio Sci* 2010; **1**(4): B236-B238.

[43] Feig DI, Soletsky B, Johnson RJ. Effect of allopurinol on blood pressure of adolescents with newly diagnosed essential hypertension a randomized trial. *JAMA* 2008; **300**(8): 924-932.

[44] Aghasadeghi K, Zibaee Nezhad MJ, Eftekhari MH. Modulation of blood pressure in hypertensive patients by vitamin C. *Int Cardiovasc Res J* 2009; **3**(1): 16-20.

[45] Bruno RM, Daghini E, Ghiadoni L, Sudano I, Rugani I, Varanini M, et al. Effect of acute administration of vitamin C on muscle sympathetic activity, cardiac sympathovagal balance, and baroreflex sensitivity in hypertensive patients. *Am J Clin Nutr* 2012; **96**(2): 302-308.

[46] Ryter SW, Choi AM. Heme oxygenase-1/carbon monoxide from metabolism to molecular therapy. *Am J Respir Cell Mol Biol* 2009; **41**(3): 251-260.

[47] Datla SR, Dusting GJ, Mori TA, Taylor CJ, Croft KD. Induction of heme oxygenase-1 *in vivo* suppresses nadph oxidase-derived oxidative stress. *Hypertension* 2007; **50**: 636-642.

[48] Paravicini TM, Touyz RM. NADPH oxidases, reactive oxygen species, and hypertension clinical implications and therapeutic possibilities. *Diabetes Care* 2008; **31**(Suppl 2): S170-S180.

[49] Regino WO, Velasco H, Sandoval H. The protective role of bilirubin in human beings. *Rev Col Gastroenterol* 2009; **24**(3): 293-301.

[50] Chin HJ, Song YR, Kim HS, Park M, Yoon HJ, Na KY, et al. The bilirubin level is negatively correlated with the incidence of hypertension Korean population. *J Korean Med Sci* 2009; **24** (Suppl): S50-S56.

[51] Rodrigo R, Prat H, Passalacqua W, Araya J, Guichard C, Bächler JP. Relationship between oxidative stress and essential hypertension. *Hypertens Res* 2007; **30**(12): 1159-1167.

[52] Lob HE, Vinh A, Li L, Blinder Y, Offermanns S, Harrison DG. Role of vascular extracellular superoxide dismutase in hypertension. *Hypertension* 2011; **58**(2): 232-239.

[53] Rybka J, Kupczyk D, Kedziora-Kornatowska K, Motyl J, Czuczejko J, Szewczyk-Golec K, et al. Glutathione-related antioxidant defense system in elderly patients treated for hypertension. *Cardiovasc Toxicol* 2011; **11**(1): 1-9.

[54] Chrissobolis S, Didion SP, Kinzenbaw DA, Schrader LI, Dayal S, Lentz SR, et al. Glutathione peroxidase-1 plays a major role in protecting against angiotensin ii-induced vascular dysfunction. *Hypertension* 2008; **51**: 872-877.

[55] Ardanaz N, Yang XP, Cifuentes ME, Haurani MJ, Jackson KW, Liao TD, et al. Lack of glutathione peroxidase 1 accelerates cardiac-specific hypertrophy and dysfunction in angiotensin ii hypertension. *Hypertension* 2010; **55**: 116-123.

[56] Saraswathi R, Sankar D, Ali A, Uehara Y, Abe S, Sambandam G, et al. A pilot assessment of oxidative stress byproducts and antioxidant activities among Indian patients with various stages of hypertension. *Clin Exp Hypertens* 2011; **33**(7): 437-443.

[57] Abbas RF, Sulaiman AA, Maroufz BH, Hussain SA. Concentration-effect relationship for the radical scavenging activity of telmisartan in nitrite-induced hemoglobin oxidation: *in-vitro* study. *Pharmacie Globale: International Journal of Comprehensive Pharmac* 2011; **8**(9): 1-5.

[58] Cohen RA, Tong XY. Vascular oxidative stress: the common link in hypertensive and diabetic vascular disease. *J Cardiovasc Pharmacol* 2010; **55**(4): 308-316.

[59] Moreira da Silva F, Marques A, Chaveiro A. Reactive oxygen species: a double-edged sword in reproduction. *Open Vet Sci J* 2010; **4**: 127-133.

[60] Mohara M, Greabu M, Muscurel C, Duţă C, Totan A. The sources and the targets of oxidative stress in the etiology of diabetic complications. *Romanian J Biophys* 2007; **17**(2): 63-84.

[61] Cristóvão AC, Choi DH, Baltazar G, Beal MF, Kim YS. The Role of NADPH oxidase 1-derived reactive oxygen species in paraquat-mediated dopaminergic cell death. *Antioxid Redox Signal* 2009; **11**(9): 2105-2118.

[62] Lubos E, Handy DE, Loscalzo J. Role of oxidative stress and nitric oxide in atherothrombosis. *Front Biosci* 2008; **13**: 5323-5344.

[63] Kang J, Pervaiz S. Mitochondria: redox metabolism and dysfunction. *Biochem Res Int* 2012; doi: 10.1155/2012/896751.

[64] Yu J, Weïwer M, Linhardt RJ, Dordick JS. The role of the methoxyphenol apocynin, a vascular NADPH oxidase inhibitor, as a chemopreventative agent in the potential treatment of cardiovascular diseases. *Curr Vasc Pharmacol* 2008; **6**: 204-217.

[65] Nossaman BD, Kadowitz PJ. Potential benefits of peroxynitrite. *Open Pharmacol J* 2008; **2**: 31-53.

[66] Jin RC, Loscalzo J. Vascualr nitric oxide: formation and function. *J Blood Med* 2010; **1**: 147-162.

[67] Li L, Hsu A, Moore PK. Actions and interactions of nitric oxide, carbon monoxide and hydrogen sulphide in the cardiovascular system and in inflammation-a tale of three gases! *Pharmacol Ther* 2009; **123**: 386-400.

[68] Dominguez LJ, Galioto A, Pineo A, Ferlisi A, Ciaccio M, Putignano E, et al. Age, homocysteine, and oxidative stress: relation to hypertension and type 2 diabetes mellitus. *J Am Coll Nutr* 2010; **29**(1): 1-6.