

Study of relationship between CRP, bilirubin and selected anthropometric parameters with hypertension

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Abstract

Background: There are many recent studies showing that hypertension, and cardio-vascular disease is linked to inflammation. The higher CRP levels are significantly correlated with hypertension. CRP estimation is used as a surrogate marker in evaluation and predicting the prognosis of all hypertensive patients. Many of the epidemiologic studies had shown the association of CRP levels with future cardiovascular events and hypertension. Bilirubin has been shown to be an effective antioxidant both in vitro and in vivo. The excess body fat and distribution is an important contributor to the association between obesity and high BP. **Aims and objectives:** The objective was to study the relationship between CRP, Bilirubin and selected anthropometric parameters among both hypertensive and non hypertensive subjects. **Methods:** We have conducted a hospital based descriptive observational study using purposive non random sampling method on 150 subjects; 87 hypertensive and 77 were non hypertensive. Age, systolic BP, diastolic BP, weight, height, waist circumference, hip circumference, SAD, total Bilirubin, T cholesterol, HDL-C, Triglycerides, LDL-C were primary continuous variables. BMI, WHR, WHtR were taken as secondary variables. **Results:** CRP, Waist circumference, WHtR and SAD have a positive correlation with both systolic and diastolic BP. Odds ratio was 12.18 for CRP. Total Bilirubin levels have a negative correlation with systolic and diastolic BP. Odds ratio was 7.81. Diastolic BP had positive correlation with Weight, Hip circumference and BMI. **Conclusion:** We had demonstrated elevated CRP, low Bilirubin levels, abnormal SAD and Waist circumference were associated with blood pressure levels. These parameters are useful and cost-effective tool for predicting and evaluating Hypertension.

Key words: SAD, Bilirubin, Anthropometry, Hypertension

Introduction

Hypertension is a global challenge. Risk factors for hypertension have only been partially understood. Some studies have shown that hypertension is associated with a low grade inflammatory pathology and this process is also involved in endothelial dysfunction and atherosclerosis [1, 2]. The loss of vasodilator and anti-atherogenic properties is probably because of an inflammatory marker CRP which is thought to decrease nitric oxide production in the endothelial cells and thus promoting vasoconstriction, platelet adhesion and thrombosis [3]. Thus many studies suggest a strong

relationship between CRP and cardiovascular disease [4]. Further CRP is an early marker of systemic inflammation and it can also be easily detected by blood examination. Hence CRP estimation should be recommended in evaluation and in predicting the prognosis of all hypertensive patients.

Several studies have also reported bilirubin to be an effective antioxidant which scavenges peroxy radicals and also as a substance which suppresses oxidation of LDL cholesterol, thus suggesting its protective role in hypertension and cardiovascular disease and so protecting one from mortality risk secondary to coronary heart disease [5].

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In certain studies, hemoxygenase -1 has been shown to decrease the BP levels and sometimes the development of hypertension itself. The reason could be that hemoxygenase 1 causes increased bilirubin levels in the body which thus exerts its antihypertensive property [6,7].

Obesity is a well known risk factor for most of the non communicable diseases and especially cardiovascular disease and hypertension [8]. Anthropometry is one of the most commonly used non invasive technique to measure obesity [9]. Other than the commonly used indicators of obesity like BMI and WHR, sagittal abdominal diameter which measure visceral fat [10,11] and another indicator waist circumference is finding an important role as a marker of obesity [9]. The studies on western and urban Indian population had shown correlation between hypertension and different anthropometric parameters [12,13,14,15]. The aim of this study was to find any association between hypertension and different anthropometric and certain other biomarkers in rural South Indian population.

Material and Methods

Study design and study population: The present hospital based study conducted on 150 subjects, among which 87 were hypertensives and 77 were non hypertensives visiting medicine OPD at KVG Medical College Hospital, Sullia, Karnataka. It was a descriptive observational study done from 1 October 2014 to 30 April 2015 using purposive non random sampling method. All subjects were included in the study.

Inclusion Criteria: The study was conducted among individuals with 40 years of age and above who were not on any medications except anti hypertensives who are willing to be part of our study.

Ethics Statement: The protocol was approved by the Institutional Ethical Committee. Informed consent was obtained from all the study participants.

Exclusion Criteria: Subjects with spinal deformity, abdominal tumor, lump, significant ascites, pregnant females, pathological diseases like cancer, insufficient renal and hepatic diseases and chronic inflammatory pathologies and in whom anthropometric measurements were not feasible [16]. Individuals with high liver test values (which are indicative liver injury or disease). Subjects with Alanine transaminase (ALT) >40 IU/L were excluded to avoid a confounding effect by Gilberts

syndrome and other hepatobiliary disease. CRP levels can also increase in conditions like acute renal failure, bacterial infections, smoking, meningitis and trauma and patients with these issues will also be excluded from the study [3]. CRP levels above 10mg/dL indicates chronic inflammation.

Steps in conducting the data collection: Detailed history was taken. A thorough clinical examination of all patients was done in each subject. Blood pressure was measured thrice with five-minute interval on the left arm with a mercury sphygmomanometer. The average of three readings was considered for analysis. Elderly with systolic BP of >140 mmHg and/or diastolic BP of >90 mmHg and/or those on medications for hypertension were considered as hypertensives [17].

Complete laboratory work up was also done:-

1. Serum CRP levels
2. Lipid profile: Serum total cholesterol, HDL, LDL and triglycerides
3. Serum Bilirubin , total and direct
4. Fasting and postprandial plasma glucose
5. Renal function tests
6. Standard 12 lead ECG.
7. X-Ray chest PA view

Early morning blood samples were obtained from all patients after clear instruction that they have to fast for 12 hours over night. The level of C-reactive protein was determined by latex-enhanced nephelometry method having sensitivity 0.5—320 mg/L and could not detect CRP levels of <0.5mg/L (AGAPEE- MISPA-1 Autoanalyser. Total Bilirubin was determined by modified dimethyl sulfoxide DMSO method which is having the sensitivity 0.01—20 mg/dL. (AGAPPE-MISPA Nano Autoanalyser). Lipid profile by AGAPE-MISPA Nano Autoanalyser. (TC-cholesterol oxidase method, TG-glycerol 3-phosphate oxidase method, HDL-C by direct qualitative determination, LDL-C by calculation).

Anthropometric measurements like weight and height of the subjects were measured using appropriate standard equipment and procedures. Weight was measured with minimum clothing using a digital weighing scale (nearest to 100 mg). Measurement of height was done using a stadiometer, with the subject made to stand with feet together after removing the footwear. BMI was calculated as weight (Kg) divided by height in meters square. Subjects were classified as overweight and obese based on the WHO recommended

cut off values [18]. Waist circumference >90 cm and >80 cm were considered as obese for men and women respectively, to calculate abdominal or central obesity [19]. Waist circumference (WC) was measured according to WHO criteria in standing position after normal expiration, midway between the lower rib margin and the iliac crest .

The waist-hip ratio is the index of regional distribution of body fat. It is the ratio between the waist circumference values and the hip circumference (HC). The anatomical place used for assessment of HC was the height of the greater trochanter as recommended by the WHO. Waist hip ratio of 0.80 and more in female and 0.90 and more in males were considered as having abdominal obesity [20].

Results

The present study was done among 150 subjects of whom 87 were hypertensives and 77 were non hypertensives.

Table-1: Background Characteristics of Study Population.

| Sl. No | Variable Name | Mean | Standard Deviation | Median | Minimum | Maximum |
|--------|-----------------------|-------|--------------------|--------|---------|---------|
| 1 | Age in years | 58 | 10.4 | 57.5 | 40 | 85 |
| 2 | Systolic BP in mmHg | 133.5 | 23.8 | 130 | 90 | 220 |
| 3 | Diastolic BP in mmHg | 83.6 | 12.8 | 80 | 60 | 140 |
| 4 | Weight in kg | 59.1 | 13.7 | 56.5 | 35 | 116 |
| 5 | Height in cmt | 162.2 | 9.1 | 163 | 133 | 186 |
| 6 | Waist cir. in cmt. | 82.7 | 13.1 | 81 | 54 | 124 |
| 7 | Hip circum in cmt | 89.5 | 10.7 | 88 | 62 | 137 |
| 8 | SAD in cmt. | 18.65 | 2.29 | 18 | 15 | 25 |
| 9 | CRP in mg/dl | 2.15 | 1.4 | 2 | 0.5 | 6.0 |
| 10 | Tot cholest. in mg/dl | 182.9 | 42.3 | 179.5 | 110 | 323 |
| 11 | HDL mg/dl | 43.4 | 10.6 | 41 | 23 | 87 |
| 12 | LDL mg/dl | 121.3 | 41.5 | 112.5 | 30 | 258 |
| 13 | TG mg/dl | 184.5 | 68.1 | 188.5 | 35 | 597 |
| 14 | T. Bilirubin | 0.92 | 0.36 | 0.80 | 0.3 | 2.5 |
| 15 | D. Bilirubin | 0.21 | 0.15 | 0.20 | 0.1 | 1.0 |
| 16 | BMI | 22.5 | 4.8 | 21.7 | 13.7 | 47 |
| 17 | Waist Height ratio | 0.52 | 0.08 | 0.5 | 0.32 | 0.78 |
| 18 | Waist Hip ratio | 0.92 | 0.08 | 0.91 | 0.69 | 1.31 |

Table 1 shows the background characteristics of the study population. Measures of central tendency for each variable are given in it.

Table-2- Correlation of various parameters of blood pressure and their odds of having hypertension.

| SL. NO | Variable Name | With Systolic BP | | With Diastolic BP | | R ² Value | df | Odds Ratio |
|--------|--------------------|--------------------------|--------------|--------------------------|--------------|----------------------|----|------------|
| | | Corrrelation Coefficient | Significance | Corrrelation Coefficient | Significance | | | |
| 1 | CRP | 0.341 | <0.01 | 0.41 | <0.01 | 49.8 | 1 | 12.18 |
| 2 | Total Bilirubin | -0.29 | <0.01 | -0.210 | <0.01 | 26.2 | 1 | 7.81 |
| 3 | Weight | 0.12 | >0.01 | 0.196 | <0.01 | | | |
| 4 | Waist circum | 0.21 | <0.01 | 0.214 | <0.01 | | | |
| 5 | BMI | 0.12 | >0.01 | 0.21 | <0.01 | 7.441 | 1 | 2.11 |
| 6 | Waist Hip ratio | 0.147 | >0.01 | 0.09 | >0.01 | 3.116 | 1 | 1.77 |
| 7 | HDL | -0.085 | >0.01 | -0.107 | >0.01 | 2.59 | 1 | 0.598 |
| 8 | LDL | 0.01 | >0.01 | -0.007 | >0.01 | 0.009 | 1 | 1.03 |
| 9 | Waist Height ratio | 0.22 | <0.01 | 0.219 | <0.01 | | | |
| 10 | Hip Circumference | 0.177 | >0.01 | 0.213 | <0.01 | | | |
| 11 | SAD | 0.264 | <0.01 | 0.309 | <0.01 | | | |

Table 2 shows the correlation of various parameters with blood pressure and their odds of having hypertension. It was seen that systolic BP was correlated with CRP, total Bilirubin, WC, WHt R and SAD whereas Diastolic BP was correlated with CRP, total Bilirubin, weight, BMI, WC, WHt R, HC and SAD.

Table-3: Comparing means of systolic and Diastolic BP with different variable categories used in the study.

| | | Systolic BP | | | Diastolic BP | | |
|------------------|-------------|-------------|-------|---------|--------------|-------|---------|
| | | Mean | SD | P Value | Mean | SD | P Value |
| Waist circumf | LOW(>85cm) | 130.5 | 24.7 | >0.01 | 81.84 | 12.75 | >0.01 |
| | HIGH(>85cm) | 138.1 | 21.5 | | 86.31 | 12.36 | |
| Total cholestrol | NORM(<250) | 133.36 | 23.8 | >0.01 | 83.69 | 12.7 | >0.01 |
| | HIGH(>250) | 135 | 24.2 | | 82.63 | 13.69 | |
| Waist hip ratio | NORM(<0.88) | 131 | 25.3 | >0.01 | 82 | 13.3 | >0.01 |
| | HIGH(>0.88) | 134.4 | 23.16 | | 84.2 | 12.5 | |
| HDL | NORM(>40) | 134.3 | 26.5 | >0.01 | 84.24 | 11.8 | >0.01 |
| | LOW(<40) | 132.9 | 21.8 | | 83.13 | 14.22 | |
| LDL | NORM | 137.04 | 25.77 | >0.01 | 85.27 | 14.22 | >0.01 |
| | HIGH | 131.89 | 22.7 | | 82.8 | 12.01 | |
| Bilirubin | NORMAL | 138.9 | 22.2 | <0.01 | 86.1 | 12.6 | <0.01 |
| | HIGH | 123.8 | 23.0 | | 78.7 | 11.8 | |

From table 3 we can conclude that there was no statistically significant difference between different variable categories and Systolic BP as well as Diastolic BP except for the variable Bilirubin. High Bilirubin level are found in those with low BP or vice versa.

Table- 4: Comparing the means of systolic and Diastolic BP with BMI, and CRP categories.

| | With Systolic BP | | | | With Diastolic BP | | | |
|-----|------------------|-------------|------|-------|-------------------|-------------|------|-------|
| | | Mean square | F | SIGN | | Mean square | F | SIGN |
| BMI | Between group | 1068.3 | 1.92 | >0.01 | Between group | 658 | 4.28 | <0.01 |
| | Within group | 556 | | | Within group | 153 | | |
| CRP | Between group | 6643 | 13.5 | <0.01 | Between group | 2288 | 16.7 | <0.01 |
| | Within group | 489 | | | Within group | 136 | | |

From table 4 we can conclude that there was a statistically significant difference in systolic BP between the 3 CRP groups but not with four BMI groups. There was a statistically significant difference in diastolic BP between the 3 CRP groups as well as the four BMI groups.

Table-5: Prediction of different variables based on other independent variables collected in the study.

| Variable Prediction | Independent Variables | Regression Coefficient | df | F | SIGN |
|---------------------|--|------------------------|----|-------|-------|
| Systolic BP | 104+4(CRP)+(-13.7) (total bilirubin)+ 1.79(SAD) | 0.44 | 4 | 9.552 | <0.01 |
| Diastolic BP | 62.08+ 3.46(CRP) +0.17(waist circum) | 0.46 | 5 | 8.557 | <0.01 |

Table 5 shows that systolic and diastolic BP could be predicted with the various independent variables used in the study.

Discussion

Anthropometric and certain other parameters were correlated with systolic and diastolic blood pressures of the study subjects. In our study, it was found that CRP was significantly associated with both systolic and diastolic blood pressure which was also found to be statistically significant with p value < 0.05. This finding is consistent with study done by Sung KC et al [22]. The odds ratio was also found to be very high which signifies a strong association between blood pressure and CRP levels. The diabetic patients were excluded in our study since it might confound the result, as diabetics are prone to infections which may in turn rise CRP levels [22]. In yet another study done by, Schillaci G , it is shown that elevated CRP was associated with increased Systolic Blood pressure only and not with Diastolic blood pressure [23]. Statins and other antihypertensive medications especially angiotensin II receptor blockers are thought to reduce CRP levels [24, 25, and 26]. But because of feasibility reasons we have not excluded these in our study.

Our study revealed a negative correlation between serum Bilirubin and both systolic and diastolic blood pressures. A study done by Katurzyna Bergmann et al, showed similar findings except that they had found correlation with other parameters also, like waist hip ratio, apo B, apo A, non HDL-C [27]. Since the objective of this study was only to compare some selected parameters with blood pressure, such correlations were not attempted in our study.

When anthropometric parameters are considered in our study, we have measured weight, waist circumference, BMI, waist hip ratio, waist height ratio, hip circumference and sagittal abdominal diameter. It was found that waist circumference, waist height ratio and sagittal abdominal diameters had a statistically significant correlation with systolic and diastolic blood pressure but with a small correlation coefficient. Similar positive correlation of SAD and waist circumference was found in studies done by Souza C [28] and Oliveira

J [29]. In the present study, a regression analysis was done which found SAD to be an independent risk factor which predicted SBP and waist circumference which predicted DBP. Riserus et al found that SAD showed the strongest correlation to the majority of the individual risk factors among men, whereas in women SAD was equal to that of Waist circumference [21].

Conclusions and Recommendation

Our study setting was a rural tertiary care hospital situated in Karnataka. We still could demonstrate that elevated CRP, low Bilirubin levels, abnormal SAD and Waist circumference were associated with higher blood pressure levels. Our data suggests these parameters are useful and cost-effective tool for predicting and evaluating Hypertension. Further research with bigger sample and a better sampling technique needs to be done more so in an urban setting so that the findings could be generalized. Future researchers can take that interesting topic and do research on it.

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Permission from IRB: Yes

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