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THE ROLE OF HSCRP AS A MARKER IN PREDICTING HYPERTENSION IN MIDDLE AGED ADULTS

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ABSTRACT

Introduction: Hypertension in a very prevalent disease of current times and is a risk factor of coronary artery disease and stroke. CRP is elevated in serum in response to variety of inflammatory stimuli. hsCRP is highly sensitive than CRP and can be detected even in low levels expressed in early stages of inflammation.

Materials and Methods: The study comprised of total of 100 participants who were grouped as Group I comprising of 50 normotensive patients (<140mmHg & <90mmHg) and Group II (>140mmHg & >90mmHg) hypertensive patients. Patients in the age range of 40-60yrs were selected for the study. Patients with hypertensive complications, alcohol, oral contraception, post menopausal women, lactating mothers, prolonged systemic infections, injuries, prolonged medication were excluded from the study. Resting supine blood pressure was recoded using sphygmomanometer; palpatory and auscultatory method was used to record systolic and diastolic blood pressure. Venous blood samples were collected and serum was used to assess the serum hsCRP using ELISA kit. Mean±SD was used to represent continuous data and p value of <0.05 was implied as statistically significant.

The participants of the study were predominantly females (63) and in the age group of 18-60 years. The values of FBS, PPBS, HbA1c and Vit D were compared among Group I and Group II and were statistically significant. 36 patients of Group II had Vit D deficiency, 9 patients had insufficient Vit D and only 5 patients had sufficient Vit D. Vit D showed an inverse relationship with HbA1c more strongly than other parameters.

Results: Among 100 participants **t**here were a total of 45 males and 55 females in the present study in the age range of 40-60yrs. Majority of the participants in Group I were 50-55yrs and in Group II 55-60yrs (**p<0.001**). The mean and standard deviation of BMI in Group I and II was 23.26±1.88 and 29.4±2.47 respectively (**p<0.001**). The mean and standard deviation of pulse rate in Group I and II was 83± 6.59 and 81.84 ± 8.44 respectively (p=0.445). The systolic

and diastolic blood pressure in Group I and Group II were 114.7±5.64 & 75.7±8.34; 158.23±17.84 & 95.68±9.87 (**p<0.001**). Correlation of serum hsCRP level and blood pressure showed a positive R value of 0.2131 with systolic BP (**p<0.05**) and 0.4132 with diastolic BP (**p<0.001**). The serum hsCRP levels noted in Group I were 34 low risk, 10 intermediate risk and 6 high risk and in Group II were 2 low risk,17 intermediate risk and 31 high risk participants. The serum hsCRP level in Group I was 0.76±0.15 and in Group II 1.63±1.18 (**p<0.001**).

Conclusion: hsCRP is readily available with long half-life hence can be used as a cost effective technique which can detect small quantities of CRP. Elevated levels of hsCRP can detect hypertensive changes in early stages hence can be considered as a marker of hypertensive patients with risk. Thus early detection of hypertension can prevent cardiovascular risk.

Key words: Diastolic blood pressure, hsCRP, hypertension, Systolic blood pressure

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Introduction

Hypertension is one of the most commonly encountered diseases in the out-patient setting. It is an inflammatory vascular disease associated with major risk factor like stroke, cardiovascular disease, vascular and renal disease.[1] Hypertension is caused by Angiotensin II which triggers an inflammatory response increasing vascular permeability which causes migration and adhesion of inflammatory markers, increases levels of VEGF causing proliferation of vasculature and increases level of endothelin leading to stiffening of vasculature.[2] The prevalence of hypertension in India is estimated as 2-15% in urban areas and 2-8% in rural regions.[3]

C Reactive Protein (CRP) belongs to pentraxin family of protein synthesised by liver in acute phase. CRP level in serum increases in acute inflammatory conditions, trauma and acute infections. High sensitive CRP (hsCRP) is more sensitive than standard CRP and hence detects even small increase in CRP expressed in early stages of inflammation and thus can detect diseases earlier and prevent complications. Thus, hsCRP assay helps in assessing low grade systemic inflammation in the absence of an overt systemic inflammation.[4]

Thus the aim of the study was to assess the serum levels of hsCRP in middle aged patients to predict hypertension.

Materials and methods

The current study was the prospective cross-sectional study which was performed at a private clinical setup for over a period of one year from Jan 2023- Feb 2024. The present study was conducted according to local and global ethical norms. The present study comprised of 100 participants who were divided into two groups Group I and Group II. Group I comprised of 50 normotensive patients and Group II comprised of 50 untreated patients with new onset hypertension not under medication. The study participants above the age group of 40-60 years with new onset diabetes without medication were included in the present study. Participants with systolic pressure of < 140mmHg and diastolic pressure of < 90mmHg were

included in Group I and participants with systolic pressure of > 140mmHg and diastolic pressure of >90mmHg were included in Group II. Patients with hypertensive complications, alcoholic, pregnant or lactating women, women on oral contraceptives, post-menopausal women on hormonal therapy, patients suffering from prolonged systemic infection, injuries, prolonged medication, diabetes mellitus were excluded from the present study. The age group of patients of the present study was in the range of 40-60 years to avoid age related complications.

Resting supine blood pressure was recorded using a mercury sphygmomanometer from the participants. Palpatory method (reappearance of radial pulse) was used to know the approximate systolic blood pressure. Auscultatory method provided the systolic blood pressure (phase I of Korotkoff sounds) and diastolic blood pressure (phase IV/ V of Korotkoff sounds). Three recordings with 2 minute interval were obtained and the average was considered for analysis.

Blood samples were collected under strict aseptic precautions and the serum was collected for analysing hsCRP using ELISA kit. CRP levels were obtained by using high sensitivity CRP (hsCRP) assay kits.

The dependable variables of the study were age, gender, BMI, Pulse rate, systolic blood pressure and diastolic blood pressure and independent variable was serum hsCRP levels. Statistical Package for Social Sciences (SPSS 20) was used to analyse the data. The dependable and independent variables among Group I and Group II were compared and represented as Mean±SD and p value of <0.05 was inferred as statistically significant.

Results

The present study was a prospective cross sectional study conducted on 100 participants who were randomly selected and divided into 2 groups. Group I comprised of 50 normotensive patients andGroup II comprised on 50 hypertensive patients with new onset hypertension not under medication. The participants of the study were 40-60yrs age and the mean and standard deviation of age in Group I was 58.95±11 and in Group II was 68.4±10 with a p value of <0.001. The study participants comprised of total 45 males and 55 females. (Table 1) In Group I there were 23 males and 27 females whereas in Group II there were 22 males and 28 females. (Chart 1)

	Group I (n=50)	Group II (n=50)	P value
Age	58.95±11	68.4±10	<**0.001**
Gender	Males 23	Males 22	----
	Females 27	Females 28	

Table 1 showing distribution of age gender in the study participants

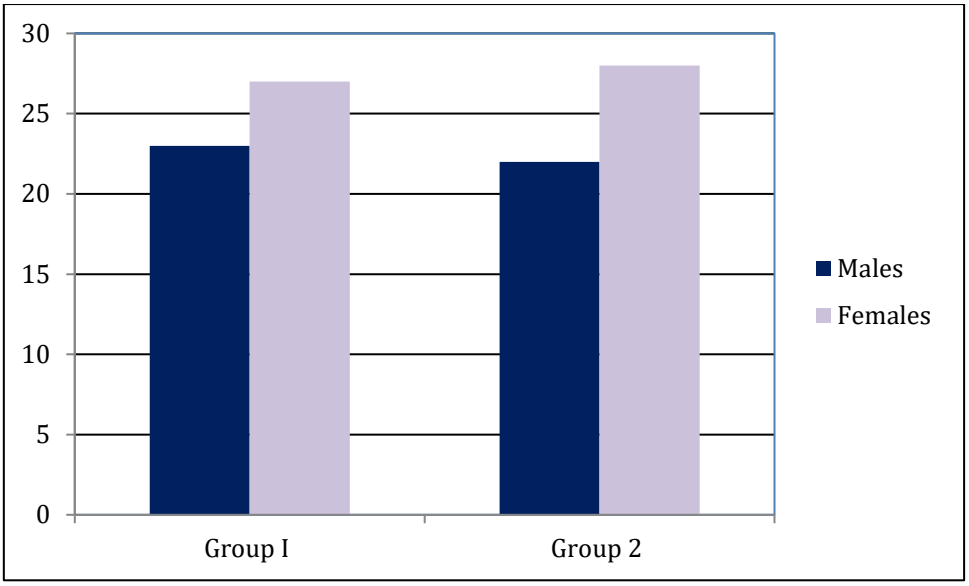

Chart 1: Bar graph showing distribution of males and females in Group I and Group II

BMI in Group I showed mean and standard deviation of 23.26±1.88; in Group II it was 29.4±2.47 and the p value was <0.001. The pulse rate recorded in Group I participants was 83± 6.59 and 81.84 ± 8.44 in Group II participants and the p value noted was 0.445. (Table 2)

Physiological parameters of the study			
	Group I (n=50)	Group II (n=50)	P value
BMI	23.26±1.88	29.4±2.47	**<0.001**
Pulse rate/min	83± 6.59	81.84 ± 8.44	0.445

Table 2 showing physiological parameters of participants in the present study

The systolic blood pressure measured in Group I participants was 114.7±5.64 and in Group II was 158.23±17.84 whereas, the diastolic blood pressure in Group I was 75.7±8.34 and in Group II 95.68±9.87 and the p value noted was <0.001. (Table 3)

Baseline values of the clinical parameters			
	Group I (n=50)	Group II (n=50)	P value
BP Systolic	114.7±5.64	158.23±17.84	**<0.001**
BP Diastolic	75.7±8.34	95.68±9.87	**<0.001**

Table 3 showing the baseline values of systolic and diastolic blood pressure noted in Group I and Group II

The correlation of hsCRP and systolic pressure showed R value of 0.2131 and for diastolic blood pressure it was 0.4132 and the p value noted was <0.05 and <0.001 respectively.

The serum hsCRP level assessed among the participants was categorised as low risk (<1mg/l), intermediate risk (1-3mg/L) and High risk (>3mg/L). In Group I, 34 participants belonged to low risk, 10 intermediate risk and 06 high risk. In Group II there were 02 low risk, 17 intermediate risk and 31 high risk participants. (Table 4) (Chart 2)

Serum hsCRP level	Group I (n=50)	Group II (n=50)
Low risk (<1mg/L)	34	02
Intermediate risk (1-3mg/L)	10	17
High risk (>3mg/L)	06	31

Table 4 showing serum levels of hsCRP among normotensive and hypertensive participants of the study

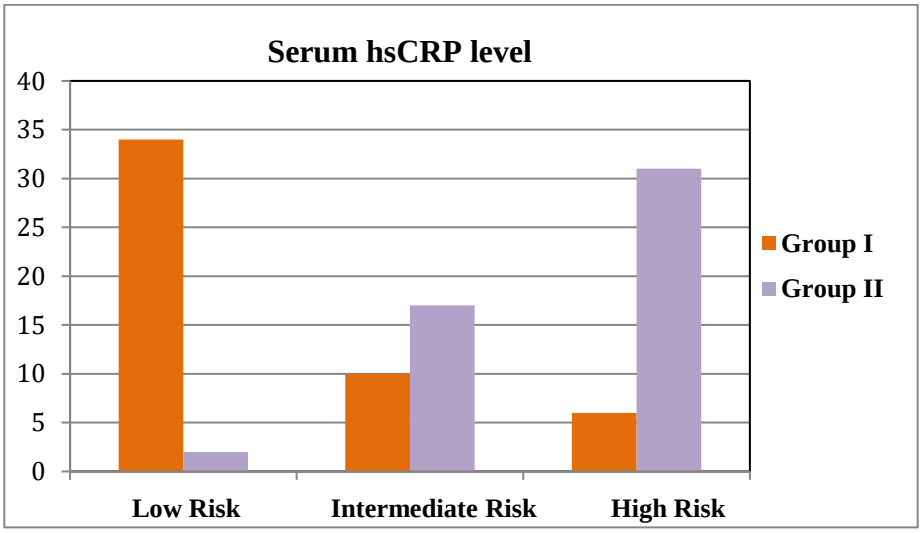

Chart 2: Bar graph showing distribution of hsCRP in Group I and Group II

In the present study the serum hsCRP level noted in Group I was 0.76±0.15 and in Group II it was 1.63±1.18 and the p value noted was <0.001. (Table 5)

Serum hsCRP levels			
	Group I (n=50)	Group II (n=50)	P value
Serum hsCRP (mg/L)	0.76±0.15	1.63±1.18	**<0.001**

Table 5 showing serum hsCRP levels in participants of Group I and Group II

The linear correlation between hsCRP and blood pressure was measured using Pearson coefficient correlation. It was noted that both systolic and diastolic pressure showed as positive correlation with serum hsCRP with R value of 0.2131 (**p<0.05**) and 0.4132 (**p<0.001**) respectively. (Table 6)

Correlation of hsCRP and blood pressure		
	Correlation coefficient (R value)	P value
Systolic BP	0.2131	**<0.05**
Diastolic BP	0.4132	**<0.001**

Table 6 showing positive correlation of hsCRP and blood pressure

Discussion

Hypertension is a commonly occurring disease and is diagnosed by measuring systolic and diastolic blood pressure; as per the current hypertension guidelines systolic pressure of ≥130mmHg and diastolic pressure of ≥80mmHg is hypertension.[5] Hypertension is a major risk factor for cardiovascular disease, atherosclerosis, coronary artery disease, stroke and kidney failure. Thus, reduction of these risk factors reduces the complication therefore resulting in improved cardiovascular mortality and morbidity.[6]

CRP is a pentameric protein synthesised by the liver and its level rises in response to inflammation. It was 1st discovered by Tillet and Frances in 1930 and is so named because it reacts with C polysaccharide of Streptococcus pneumoniae. It is an acute phase reactant whose levels are increased in acute and chronic stimuli, infections, burns, major trauma, surgery and inflammatory conditions where CRP levels may increase 100 folds or more.[7] It has a relatively long half-life of 18 to 20 hr owing to its stable structure. It does not exhibit diurnal variations in relation to food intake. Measurement of CRP aids as a proxy for general wellness and was initially used to monitor variety of inflammatory conditions but now it is used as an indicator of certain disease like cardiovascular disease and atherosclerosis in otherwise asymptomatic patients.

hsCRP is more sensitive than standard CRP tests as it determines slight changes in CRP levels typically between 1-3mg/L. Elevated levels of hsCRP is noted frequently prior to myocardial infarction, stroke, peripheral arterial disease and sudden cardiac death in otherwise healthy patients.[8] Highest concentrations of CRP are found in serum hence can be easily detected. In the past decade, high-sensitivity assays with rapid turnaround times for measurement have become available. High sensitive assays like immunonephlometry technique, immunolatex and ELISA can detect hsCRP effectively and help quantify low grades of systemic inflammation, in the absence of overt systemic inflammatory or immunologic disorders.[9]

American Health Association AHA and centre for Disease Control CDC has classified serum hsCRP levels for risk groups of CVD globally as [10]

- Low risk group: <1mg/L
- Intermediate risk: 1-3mg/L
- High risk: >3mg/L

Thus in the present study we opted to assess and compare the levels of serum hsCRP in normotensive and hypertensive patients using ELISA kit.

The majority of the study population belonged to the age range of 50-55 years in Group I whereas in Group II the range was 55-60yr and was noted to be statistically significant. It is generally found that hsCRP gradually increases as age increases. The findings of Tang 2018 and Solim 2023 suggested that age is a significant factor influencing hsCRP levels.[11,12]

Tang 2018 found that hsCRP level in Chinese is higher in males than in females and it is sensitive indicator of healthy ageing. Kaptoge 2010 found that hsCRP levels were higher in males than in females.[11,13] However findings of Sharmila 2020 found that female hypertensive patients showed elevated levels of hsCRP compared to males but was not significant.[14] Women on oral contraceptives and post-menopausal women on hormone replacement therapy show elevated levels of hsCRP and thus were excluded in our study.

In the current study we noted that serum hsCRP level increased with increase in BMI in both males and females. This finding of the study was consistent with findings of Mahajan 2009 and Shalia K 2012.[15] Sedentary life style and high BMI are associated with increase in hsCRP levels.[16] BMI and abdominal adiposity can be surrogates for elevated hsCRP levels as visceral adipose tissue acts as a source of IL-6 which inturn induces production of hsCRP.[17]

Pulse rate was assessed and compared among normotensive and hypertensive in our present study but was not significant. The findings of the present study contradict the findings of Jerome 2002 and George Davey 2005. Elevated pulse rate increases inflammatory levels and is associated with increase production of hydrogen peroxide which in turn can stimulate inflammatory signalling pathways. George Davey 2005 also found that for every increase in pulse pressure of 1.19mmHg there is doubling of CRP.[18,19]

Systolic blood pressure in our study was significantly elevated in hypertensive than compared to normotensive and is similar to findings of George 2005. Lakoski 2005 found that systolic BP was associated with CRP but not diastolic pressure and considered systolic pressure as an individual variable.[20] Vasanthi 2022 found that systolic and diastolic pressure were significantly elevated in hypertensive than in normotensive but did not show correlation with hsCRP levels.[3] Lakoski findings shows that the mean systolic BP is 2mmHg higher in those who have hsCRP level >3mg/L.[20] Findings of Le He 2022 found that both systolic and diastolic pressures correlated with CRP.[21] Shao-Yuan 2013 showed that CRP predicts systolic blood pressure but not diastolic pressure in Taiwanese population.[22]

In 2001, Bautista was the 1st to propose CRP levels as independent risk factor for hypertension but this finding was questioned due to the small sample size of their study and the fact that there was high prevalence of hypertension. Higher baseline concentrations of CRP indicate higher risk of cardiovascular incident, with hsCRP levels over 3 mg/L representing the highest risk.[20] But Sesso 2003 suggested that CRP was an independent risk factor in hypertensive patient even after adjusting other risk factors. He also suggested that patients with higher hsCRP were more likely to develop hypertension. [23] Bellelli G 2001 also proposed CRP as an independent predictor of hypertension.[24]

In the present study we found that the level of hsCRP was significantly elevated in hypertensive than in normotensive. The finding of our studies is similar to the findings of Vasanthii 2022 who found that hsCRP was increased in patients who were on antihypertensive drugs.[3] Hui Hui Liu 2019 showed that combination of elevated hsCRP and hypertension greatly increases the cardiovascular risk in patients.[25] But contrast to our findings, Bautista 2003 and Sharmila 2020 in their study showed no statistical correlation of hsCRP levels with hypertension. [14] Li Pan 2019 findings did not support hsCRP as a risk factor of prehypertension or hypertension among Yi people.[26]

Inflammatory marker especially hsCRP have been correlated with systolic and diastolic pressure. Early detection of hsCRP levels aids in instigating hypertensive drugs where hsCRP is elevated even without overt hypertension and can reduce or prevent vascular complication. Mendel 1996 showed in the study that a weak positive correlation between hsCRP with systolic pressure whereas no correlation with diastolic BP. [27] Contrast to this finding Fernandez-Real 2001 found no correlation between hsCRP with systolic and diastolic BP. [28] Satwika Sinha 2014 found that association between diastolic blood pressure and hsCRP in pre hypertensive patient group but not in controls and hypertensives.[29]

Rhode 1999 showed a significantly positive correlation of hsCRP with both systolic and diastolic BP. [30]

Ki Chul Sung 2003 and workers found hsCRP to be an independent risk factor for development of hypertension in Korean population.[31]

The limitation of the study larger sample size and randomized clinical trial would yield even better statistical results. We did not include other risk factors of hypertension like smoking life style family history, lipid profile etc. The study did not investigate the association of CRP levels with FBS, diabetes, and clustering risk factors.

Conclusion

CRP is a good candidate because it has a long serum half-life of 19 hours and its level is unaffected by eating and sleeping. Thus, hsCRP can be used as a marker for development of hypertension in early stages and thus a marker for predicting cardiovascular risk. As the quality of life improves, fewer people get disease; this is the most cost-effective way to reduce medical costs. hsCRP has emerged as an important, powerful and characteristic predictor of future cardiovascular disease and metabolic abnormalities in ostensibly healthy men and women. As CRP is positively associated with blood pressure and hypertension and thus pharmaceutical agents which lower CRP levels may be beneficial.

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