Original Article

C-Reactive Protein in Hypertensive Patients

C-Reactive Protein and Coagulation Activation Markers in Hypertensive Patients

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ABSTRACT

Objective: To study C-reactive protein, D-dimer, PT and APTT in hypertensive patients.
Study Design: Descriptive study
Place and Duration of Study: This study was conducted at the Pathology Department of Bacha Khan Medical College Mardan and Medical Department of MMC Teaching Hospital Mardan from June 2017 to September 2018.
Materials and Methods: In this study a total of 100 hypertensive patients and 50 healthy individuals as a control group were included in the study. All patients were subjected to evaluate for CRP, D-dimer PT and APPT.
Results: A total 60% of Hypertensive patients Showed Elevated CRP levels. Mean CRP levels was 2.67±0.256 mg/l significantly elevated as compared to control group .75% of the hypertensive patients also showed elevated D-dimer level. Mean D-dimer levels were 500-1000 ng/ml in 50% of patients and 1000-2000 ng/l in 25% of patients, which were significantly elevated as compared to control group. PT and APTT were also prolonged in 6% and 8% of Hypertensive patients. Mean PT and APTT were 16.525±0.253 seconds and 45.2541±0.526 seconds respectively. P value for CRP and D-dimer were p<.00235 and p<.00316 respectively
Conclusion: The study concluded that hypertension is associated with significantly elevated CRP and D-dimer levels which indicate both inflammatory and Hemostatic abnormality. Prolong PT and APTT also indicate abnormality in coagulation system. Both elevated CRP and D-dimer levels are independent risk factors for cardiovascular and thromboembolic events. This gives useful information to the clinician to strictly watch the Hypertensive patients for immediate control and treatment to improve patient's life style and reduce further complications from the disease.
Key Words: Hypertension, CRP, D-dimer, PT, APPT.

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INTRODUCTION

Hypertension is a common public health problem all over the world.[1] it is common, easily detectable and easily treatable but lead to complication if not treated properly.[2] Hypertension is associated with both inflammation and hemostatic abnormality and is therefore hypertension in elevated range is an established and independent risk factor for cardiovascular disease.[3]

C-reactive protein is a marker of systemic inflammation and is suggested to be associated with increased risk of hypertension[4] but its measurement has been related to cardiovascular risk and is associated with chronic and long lasting inflammation of blood vessels leading to coronary heart disease, peripheral artery disease, and stroke.[5] CRP is plasma protein present in trace amount in a healthy individuals whose concentration increases to 100 folds in infection or inflammation[6] but its elevated level has been reported as a significant contributor to coronary heart disease(8) and described as a powerful predictor of myocardial infarction and stroke.[7]

Hemostatic abnormalities and coagulation disturbances also occur in hypertensive patients and thrombosis often complicate the course of patients with hypertension and lead to organ damage.

Fibrinogen is the major determinant and is involved in thrombosis and hemostasis pathway[8] and its level above 3-5 mg/ cause 12 fold increases in the coronary and cardiovascular risk.[9] Thromboembolic phenomenon is better detected by D-dimer levels. D-dimer is a plasmin mediated proteolytic degradation of fibrin clots formation and its degradation and its level increases in any condition were clot formation and its degradation increases.

So elevated level of D-dimer is a good marker for thrombosis and elevated D-dimer levels has been

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reported in hypertensive patients.[10] Studies had been conducted that increased plasma level of fibrinogen, D-dimer and prothrombin fragments occurs in hypertensive patients suggesting that coagulation system is activated in these patients.[11]

The aim of the study is to evaluate inflammatory and hemostatic Markers i.e CRP level, D-dimer level, PT and APTT in hypertensive patients. As Hypertensive patients are associated with elevated levels of CRP and D-dimer levels. As both are independent predictor of cardiovascular events and thrombotic complications. So its elevated level provide immediate information to the clinicians which can guide and help the clinician to provide urgent management to the patients and can reduce further morbidity and mortality from hypertension and reduce the risk of cardiovascular, events, strokes and further organ damage.

MATERIALS AND METHODS

This study was conducted in the pathology department of Bacha Khan Medical College and Medicine Department of MMC teaching Hospital Mardan from Feb 2017 to September 2018.

A total of 100 Hypertensive patients were included in the study whose BP was 160/110 mm and 50 healthy individuals were taken as control group. Patients with hypertension were both males and females. Patients having, infection septicemia, Diabetes Mellitus, History of DVT, malignancy and with pregnancy were excluded from the study, Chronic inflammatory Disease like SLE, Rheumatoid, arthritis, Osteoarthritis, alcoholics and Drugs like steroid were also excluded from the study.

2.5 ml of blood samples were collected from each Hypertensive patients in a tube containing Gel tube to separate Serum for determination of CRP level, and D-dimer levels while 2.5 ml sample blood were also collected in a tube containing SodiumCitrate to separate plasma for determination of PT and APTT.

CRP levels were determined from serum sample using an automated immunology Assay Machine (CLiA system) The CRP test is based on the reaction between the C-reactive protein and antibody in the reagent, reacting with CRP in the sample and the result is automatically expressed by the Machine

D-dimer is a fragments of plasmin mediated proteolytic degradation of fibrin clots formation and its subsequent degradation, So its measurement identify thrombo-embolic condition in a patient

Minutex D-dimer is a semi quantitative method and involves formation of agglutination to give the result. Procedure includes in undiluted sample and this involve to take 20 µl of plasma and mixed with 20µl of D-dimer reagent and observe for agglutination within 3m minuts or 180 seconds. If agglutination seen its level is above 250 ng/ml if no agglutination seen its level is below 250 ng/ml. If positive for agglutination then go for serial dilution. For serial dilution 100µl of plasma is mixed with 100 µl of saline in a tube. Then take 100 µl from 1st tube and put in another tube containing 100 µl Saline and then take 100 µl from the 2nd tube and put in a 3rd tube containing 100 µl Salline.

All this making a serial dilution of 1:2, 2:4 and 1:8. D-dimer is performed on all these dilution according to procedure above if agglutination seen in all dilution this make D-dimer level at the range of 250-500 ng/ml, 500-1000 ng/ml and 1000-2000 ng/ml and raised level identify thromboembolic events in the body. PT and APTT are also hemostatic markers and indicate both the activity of extrinsic and intrinsic pathway. Normal PT is 10-16 seconds and APTT normal value is 39-41 seconds. Its derange level from the normal value indicate hemostatic abnormality in the coagulation system. These investigations were also performed according to standard manual procedure. All data were subjected to statistical analysis by using Chi-Square test and T-test level of significance was set at P value less than 0.005.

RESULTS

A total of 100 hypertensive patients were included in the study. They were both males and females. All these patients were hypertensive and diagnosed for the last 5-7 years. In all these patients CRP level, D-dimer level and PT and APTT were measured.

In our study 60% of patients with hypertension had elevated CRP levels. Mean CRP level was 2.67±0.256 mg/L which were significantly elevated as compared to control healthy individual $P<0.00235$

Similarly D-dimer levels were also performed in all hypertensive patients which showed that75% of the hypertensive patients had elevated D-dimer levels.50% of hypertensive patients had D-dimer level at the range of 500-1000 ng/ml and 30% of the hypertensive patients had D-dimer level at the range of 1000-2000 ng/ml. In all these hypertensive patients D-dimer level was significantly elevated as compared to control group $P<0.00316$. PT and APTT were also performed on all these hypertensive patients. 6% of hypertensive patients showed prolong PT. Mean PT value was 16.525±0.243 second and 8% of the patients showed prolonged APTT. Mean APTT was 46.254±1.526 seconds significantly higher as compared to control group while rest of patients had normal PT and APTT.

Table No.1:Frequency of CRP, D-dimer PT and APTT in hypertensive patients

S.No	Frequency of Parameter	Percentage
1	CRP Level	60%
2	D-dimer Level	75%
3	PT	6%
4	APTT	8%

Table No.2: Mean value for CRP Level, D-dimer level, PT and APTT in hypertensive patients

S.No		Mean Value Of Parameters In Hypertensive Patients	Mean Value For Control
1	CRP level	2.67±0.256 mg/L	1.1±0.256 mg/ml
2	D-dimer Level	50% 500-1000 ng/ml 25% 1000-2000 ng/l	<250 ng/ml
3	PT	16.525±0.243 seconds	14.253±0.256 seconds
4	APTT	46.254±1.526 seconds	41.562±0.256 seconds

CPP P<0.00235 D-dimer P<0.00316 respectively

DISCUSSION

Hypertension is a Medical condition in which the blood pressure remains elevated and high all the time and is a major public health problem worldwide. It is easily detectable and treatable but cause complication if not treated and controlled in time hypertension if not controlled effect system of the body specially vital organ and is usually associated with cardiovascular disease, coagulation and hemostatic system, Atherosclerosis, Myocardial infarction and cerebral Hemorrhage.[12,13]

In the present study 60% of the patient showed elevated CRP level. Mean CRP levels were 2.67±0.256 mg/l .A lot of studies have been conducted in which CRP level were elevated in hypertensive patients. A similar observation has been given by Dawri et al and reported elevated CRP level in hypertensive patients[14] same observation has also been reported by Sinha et al and reported elevated CRP in hypertensive patients.[15] Various authors have performed studies on CRP in hypertensive patients and reported elevated CRP in hypertension.[16,17] C-reactive protein is produced by liver and in infection its level rises up to 1000 times but its normal value 0.3 mg/l in blood can indicate systemic inflammation. The American Heart Association statement suggest that when CRP level less than 1 mg/l There is low risk up to 1-3 mg/l indicate high risk for cardiovascular disease.[18]

CRP can stimulate the building of adhesion molecules such as VCAM-1 and ICAM and Elastin in endothelial cells and also stimulate monocyte to Mack tissue factor causing blood clots in the extrinsic pathway.[19] Hypertension is an inflammatory disease[20] and patients with hypertension has elevated levels of inflammatory markers. CRP increases expression by endothelium plasminogen activator inhibitors to promote vasoconstriction, platelet activation and thrombosis. CRP also up regulateangiotensin receptors. Thus enhancing angiotensin-II induced rise in blood pressure[21] inflammatory markers also produce arterial stiffness[23] and all these suggest vascular inflammation play role in the pathophysiology of hypertension.

In the present study 75% of the patients with hypertension showed elevated D-dimer levels indicating hemostatic abnormality. Various author studied D-dimer levels in hypertensive patients.Kure et al reported elevated D-dimer level in hypertensive patients.[24] Lammertyn et al also reported elevated D-dimer level in hypertension and give similar correlation to our study.[25] Coban et al also reported elevated D-dimer in hypertensive patients.[26]

Similar PT and APTT were also studied in hypertensive patients only 6 out of 100 hypertensive patients showed elevated PT. Mean PT were 16.625±1.256 seconds as compared to control group and 8 out of 100 patients with hypertensive gave prolonged APTT. Mean APTT value was 46.265±1.256 seconds as compared to control group. Shweta et all also reported in their study that hypertension is associated with elevated PT and APTT.[27] A similar correlation has also been shown in the study performed by Chaitanya et al and reported Prolonged PT and APPT in hypertensive patient.[28] PT and APTT prolongation has also been reported in hypertensive patients in a study conducted by Morgani et al.[29]

CONCLUSION

The study concluded that hypertension is associated with both inflammatory and hemostatic abnormality as evidenced by elevated CRP level, elevated D-dimer level, elevated PT and APTT. Elevated CRP and D-dimer are independent risk factor of cardiovascular disease, stroke and thromboembolic complication. So every physician should strictly watch and manage hypertensive patients. on priority basis. As early management of hypertensive patient improve the life style of patient and reduce Morbidity and Mortality resulting from hypertension .measurement of CRP level, D-dimer level and other coagulation profile give immediate information to the clinician regarding hemostatic function of the patients and future predictive risk for thromboembolic events.

Author's Contribution:

Concept & Design of Study:	Subhan Uddin
Drafting:	Murad Ali
Data Analysis:	Ikram Shah
Revisiting Critically:	Subhan Uddin, Murad Ali
Final Approval of version:	Subhan Uddin

Conflict of Interest: The study has no conflict of interest to declare by any author.

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