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EVALUATION OF MATRIX METALLOPROTEINASE-9 [MMP] ACTIVITY IN HYPERTENSION

Biochemistry

Nelapati Swetha Vinela* Ph.D scholar, Department of Biochemistry, Mamata Medical College, Khammam. *Corresponding Author

M. Vijaya Bhaskar Professor and Guide, Department of Biochemistry, Mamata Medical College, Khammam, Telangana, India.

T. Praveen Assistant Professor, Department of Anatomy, Saraswati Medical College, Unnao, U.P, India.

ABSTRACT

Hypertension (HTN) can be defined as sustained elevation of systemic arterial pressure above 140/90mm of Hg. It is the level of pressure at which institution of therapy reduces related morbidity and mortality. According to JNC 8 hypertension is classified into primary or essential hypertension and secondary hypertension. Over 90% of patients with high blood pressure have essential Hypertension. Prehypertension is not considered a disease, but identifies those who are likely to progress to stage 1 or stage 2 HTN in the future. Samples were collected from newly diagnosed 200 cases of prehypertension and 200 cases of essential hypertension. 201 cases of Normotensive subjects were recruited from General Medicine Dept. or admitted (IP) under General Medicine Unit of Mamata General Hospital, Khammam. Matrix metalloproteinases are proteolytic enzymes that degrade the extracellular matrix (ECM), the basement membrane, and play a role in tissue repair and vascular remodeling. At this point, 23 MMPs have been identified in humans. Increased serum MMP 9 mean values were seen in essential hypertension group **(0.162±0.031)** when compared with prehypertension **(0.183±0.036)** and control group **(0.250±0.070)**. The difference between the groups was significant statistically with p-value <0.05.and also found MMp-9 levels were increased as the severity of disease the increased.

KEYWORDS

Normotension, Prehypertension, Essential hypertension,MMP-9.

INTRODUCTION:

Over one billion individuals are affected by hypertension worldwide and estimated to reach upto 1.56 billion by the year 2025.According to JNC 8 hypertension is classified into primary or essential hypertension and secondary hypertension. Over 90% of patients with high blood pressure have essential Hypertension.Prehypertension is not considered a disease, but identifies those who are likely to progress to stage 1 or stage 2 HTN in the future.(James PA.,etal.2014)

Matrix metalloproteinases are proteolytic enzymes that degrade the extracellular matrix (ECM), the basement membrane, and play a role in tissue repair and vascular remodeling. At this point, 23 MMPs have been identified in humans, but substrate specificity for MMPs is not completely characterized. Gelatinase B or 92 kDa type IV collagenase, also known as matrix metalloproteinase-9 (MMP-9) plays an important role in the pathogenesis of hypertension.20 (Hideaki Nagase.,et al.2006)

MMP-9 was first identified as a neutral protease isolated from human neutrophils MMP-9 degrades type VI collagen, proteoglycan and lamina. MMP-9 is produced by various tumor cells and inflammatory cells such as, neutrophil, eosinophil, monocyte, lymphocyte, and alveolar macrophage.Vessel remodeling is associated with structural rearrangement of existing wall material around smaller vessel and extra cellular matrix components(Corbel M.,et al.2000). Vessel hypertrophy involves abnormal smooth muscle cell proliferation, hypertrophy, and excessive accumulation of extracellular matrix (ECM), which may be localized to a region or throughout the vessel wall (Bayramoglu A.,et al.2009 and Chakrabarti S.,et al.2003). Increased MMP-9 levels have been consistently implicated in vascular remodeling associated with hypertension in patients. Elevation of plasma MMP-9 has been associated with increased arterial stiffness and elevated blood pressure in essential hypertension.Alternations of ECM components and/or ECM architecture and/or cell- ECM attachments are observed in hypertension(Ahmed S.H.,et al 2006 and Berg G.,et al.2011).

The MMP proteolytic system and the natural tissue endogenous inhibitors (TIMPs) regulates ECM metabolism. When MMP and/or TIMP activity is altered they may modify hypertension-related accumulation of ECM proteins. MMP modulation of ECM may also occur, by integrin-mediated signaling, in cytoskeletal rearrangement of the vessel wall (Weber KT.,et al.1989).

Pressure overload induced by increased arterial pressure and altered remodelling in the blood vessels causes additional compensatory remodelling in both vascular and cardiac tissues(Katholi RE.,et al.2011). Excessive extracellular matrix deposition and generation of inflammatory cells contributes to the progression of vascular remodelling process, arteries with high pressure show increased MMP-9 activity compared with vessels under normal pressure(Li H.,et al.2000).

MATERIALS AND METHODS

Samples were collected from newly diagnosed 200 cases of prehypertension and 200 cases of essential hypertension. 201 cases of Normotensive subjects were recruited from General Medicine Dept. or admitted (IP) under General Medicine Unit of Mamata General Hospital, Khammam. Study was conducted after taking approval from the institution ethical committee. consent taken from the patients before the the sample and data collection.MMP 9 levels were quantitatively measured by ELISA assay.

Inclusion Criteria

Study group patients of essential hypertension according to JNC7 criteria (≥140/90 mmHg) were included based on average of two BP readings on two different occasions.Subjects with prehypertension were recruited based on average of two BP readings within 120/80mmHg to 139/89mmHg on two different occasions (JNC7 criteria), And normotensives (BP <120/80mm Hg.) were included based on average of two BP readings measured with help of mercury sphygmomanometer after 5 mints of rest in the sitting position on two different occasions. Subjects between 20yrs to 50yrs of age were included.

Statistical analysis:

The date was statistically analyzed. The student t- test was used to compare the mean value of MMP-9 among case and control subjects.

RESULT:

The study sample was 601 sbjects, distributed in to 200 samples of prehypertension, 200 samples of essential hypertension and 201 samples of control for comparing the MMP-9 levels to determine its increasing or decreasing trends, the mean value for each group was determined. The MMP 9 levels were found significantly different among three groups.

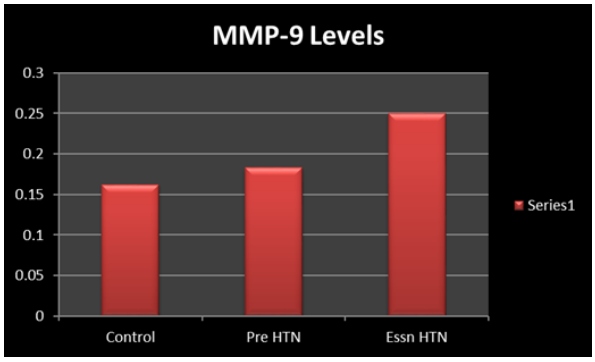
Increased serum MMP 9 mean values were seen in essential hypertension group **(0.162±0.031)** when compared with prehypertension **(0.183±0.036)** and control group **(0.250±0.070)**. The

difference between the groups was significant statistically with p-value <0.05.and also found MMp-9 levels were increased as the severity of disease the increased.

Table.1: Comparison of mean MMP-9 levels among control and case groups.

Group		MMP9 (ng/ml)	P value
Control	Mean±SD	0.162±0.031	<0.0001
Pre HTN	Mean±SD	0.183±0.036	<0.0001
HTN	Mean±SD	0.250±0.070	<0.0001

Diagram: Comparison of mean MMP-9 levels among control and case groups.



DISCUSSION:

Ayşegül bayramoglu.,et al (2006) and Derosa et al (2006) in their studies reported that MMP 9 enzyme levels were significantly higher(p<.0001) in hypertensive patients compared to controls.

Onal et al. (2009); Derosa et al. (2006) also reported that MMP 9 enzyme levels were significantly higher(p<.0001) in hypertensive patients compared to controls and the role of MMP-9 enzyme system is important in pathogenesis of hypertension concluding that these parameters may help as clinical marker.

Jose Fernando Vilela-Martin et.al (2015) in their study found there was difference of MMP-9 among the groups (p=0.04). The statistical difference occurred between PH and HT (125.6 x 95.4 ng/ml; p=0.03), but no difference between NT and PH (120.5 x 125.6 ng/ml; p=0.68), and between NT and HT (120.5 x 95.4 ng/ml; p=0.9).

CONCLUSION

MMP-9 is important for vascular remodeling; MMP-9 directly degrades extracellular matrix (ECM) proteins and activates cytokines and chemokines to regulate tissue remodeling. Abnormal MMP levels can stimulate vascular inflammation, a potential contributor in the pathogenesis and progression of hypertension.Circulating MMP-9 levels may be promising markers of those matrix metabolism alterations. Knowledge on MMPs could lead to more effective treatmentstrategies or approach to CVDs or other types of diseases. Future research and large population studies should be done to study role of MMP 9 in hypertension to remove small study bias.

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