

# Prevalence of Dyslipidemia in Patients with Malignant Hypertension.

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## ABSTRACT

**Background:** This study was designed to examining the prevalence of dyslipidaemia in patients with malignant hypertension. **Methods:** We have attempted to compare patients presenting with MHT to normotensive controls and patients with untreated essential hypertension. **Results:** Anticipated differences in blood pressure, serum creatinine concentration was greater in the MHT group than in either of the other two groups. Total LDL-cholesterol concentrations similar in all three groups (table 2). The most notable finding, however, was of markedly lower HDL-cholesterol concentrations in the MHT group ( $p < 0.01$ ). The total: HDL-cholesterol ratio was therefore significantly higher in the MHT group than either of the other two groups. Serum triglycerides were greater in the MHT group than in the NC group ( $p = 0.03$ ). These analyses show that whilst the differences in HDL-cholesterol concentration between the MHT group and the other two groups remained, there were no differences in serum triglycerides or measures. Results for total and LDL-cholesterol concentration remained unchanged. **Conclusion:** MHT may be associated with an abnormal lipid profile especially total cholesterol, triglycerides and LDL-cholesterol concentration characterized by low-HDL-cholesterol concentrations. Higher levels of these lipids may be contributed due to physical inactivity, stress, increased age, alcohol consumption and high consumption of dietary fat etc.

**Keywords:** Malignant Hypertension, Lipid Profile & Dyslipidaemia.

## INTRODUCTION

Hypertension is a major health problem worldwide. The term ‘Malignant hypertension (MHT)’ was first described by Volhard and Fahr, is a rapidly progressive and fatal syndrome, if left untreated.<sup>[1]</sup> MHT is a rare condition characterized by the presence of marked hypertension in association with bilateral retinal haemorrhages, and/or exudates, with or without papilloedema.<sup>[2]</sup> Thus including grade III and IV retinopathy of Keith Wagener Barker classification.<sup>[2-4]</sup> While effective blood pressure control has significantly improved prognosis, these patients still have a substantially higher morbidity and mortality when compared to non-malignant hypertensive controls matched for age and level of blood pressure. This excess mortality and morbidity is largely due to atherosclerotic complications and renal failure.<sup>[5]</sup> It is now accepted that elevated low-density lipoprotein (LDL) cholesterol is an independent, modifiable risk factor for atherosclerotic cardiovascular disease.<sup>[6,7]</sup> However,

a number of authors have described an ‘atherogenic lipid profile’ consisting of HDL-cholesterol and increased serum triglyceride concentrations. In this phenotype, the concentration of LDL-cholesterol may be normal or only slightly raised. However, LDL is not a single entity but consists of a heterogeneous group of particles of differing sizes and there is a preponderance of smaller particles. These smaller particles are more atherogenic: they have reduced affinity for LDL receptors and are less readily removed from the circulation by the liver,<sup>[9]</sup> are better able to penetrate the arterial intima and are more easily oxidized by free radicals, resulting in rapid uptake by macrophage scavenger receptors and enhanced foam cell formation. Indeed, a preponderance of small LDL particles has been shown to be associated with both coronary and carotid artery disease.<sup>[10,11]</sup> Interest in the ‘atherogenic lipid profile’ has been raised by the presence of prospective observational studies showing increased risk of vascular events in individuals with raised triglycerides, low HDL-cholesterol.<sup>[12,13]</sup> Additionally, there is some evidence that fibrates, which improve this dyslipidaemia through their action on lipoprotein lipase activity, may reduce the brisk of vascular events in patients exhibiting this phenotype.<sup>[14]</sup> The

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present study was aimed at examining the prevalence of dyslipidaemia in patients with malignant hypertension.

## MATERIALS AND METHODS

This present study was conducted in Department of Biochemistry, AIIMS, Bhubaneswar, India during the period from August 2014 to January 2015. The patients were taken from the Department of Medicine, AIIMS, Bhubaneswar. Total of 393 hypertensives seen over a period of 6 months at the AIIMS, Bhubaneswar, 12 patients were found to have malignant hypertension. Consecutive patients admitted to department of medicine, AIIMS, Bhubaneswar with a diagnosis of malignant hypertension were recruited into the study and compared with patients with non-malignant, essential hypertension and normotensive controls. A detailed clinical examination was performed in all patients. MHT was defined as the presence of severe hypertension in association with bilateral retinal linear or flame-shaped haemorrhages and/or cottonwool exudates, with or without papilloedema on funduscopy.<sup>[6]</sup> This definition fulfils the existing clinical criteria for MHT, which includes both Grade III and IV of the Keith, Wagener & Barker classification.<sup>[3,6]</sup> Consecutive patients with untreated, essential, non-malignant hypertension were recruited from new referrals to a hypertension outpatient clinic at a AIIMS, teaching hospital. Hypertension was defined as systolic blood pressure >160mmHg and/or diastolic blood pressure >90mmHg, measured by the patients primary care physician and confirmed at the hypertension clinic on at least two separate occasions. Patients in this group had either no hypertensive retinal changes, or grade I or II hypertensive retinopathy. Those receiving antihypertensive medication were excluded. Normotensive controls free from overt vascular disease were recruited from two local primary care centres. Those with a history of hypertension, those receiving antihypertensive drugs and those with blood pressure >160/90 mmHg were excluded. Blood pressure was measured in the sitting position using a standard mercury sphygmomanometer according to the

recommendations of the British Hypertension Society.<sup>[16]</sup> Diastolic blood pressure was recorded at the disappearance of sounds. The mean of two measurements taken 5 min apart was recorded. Venous blood was taken and allowed to clot. Samples from patients with MHT were taken within 24 hrs of admission to hospital. The generated data were subjected to appropriate statistical analysis, and unpaired 't' test was applied to determine the differences in measurable quantities at the 5% level of significance.

## RESULTS & DISCUSSION

This present study, we have attempted to compare patients presenting with MHT to normotensive controls and patients with untreated essential hypertension. Twelve patients with MHT were compared with 273 patients with untreated essential NMHT, 75 normotensive controls shown in [Table 1]. Although the age and sex distribution in the NMHT and NC groups, were similar, there were significantly more men in the MHT group. Antihypertensive treatment was used by only four individuals in the MHT group: metoprolol, nifedipine, valsartan and moxonidine (2 patients). By design, no patient in the NC or NMHT groups was receiving antihypertensive drugs. In addition to the anticipated differences in blood pressure, serum creatinine concentration was greater in the MHT group than in either of the other two groups. Total LDL-cholesterol concentrations similar in all three groups in [Table 2].

The most notable finding, however, was of markedly lower HDL-cholesterol concentrations in the MHT group ( $p<0.01$ ). The total: HDL-cholesterol ratio was therefore significantly higher in the MHT group than either of the other two groups. Serum triglycerides were greater in the MHT group than in the NC group ( $p=0.03$ ). These analyses show that whilst the differences in HDL-cholesterol concentration between the MHT group and the other two groups remained, there were no differences in serum triglycerides or measures. Results for total and LDL-cholesterol concentration remained unchanged.

**Table 1: characteristics of controls, non-malignant hypertensive and malignant hypertensive.**

| Variables                       | Normotensive (mean±SD) | Non-malignant hypertensive (mean ±SD) | Malignant hypertensive (mean ±SD) |
|---------------------------------|------------------------|---------------------------------------|-----------------------------------|
| Age in years                    | 54.3±13.50             | 53.6±12.64                            | 52.7±11.60                        |
| Male/Female                     | 40/35                  | 141/132                               | 10/2                              |
| Systolic Blood pressure (mmHg)  | 132.5±3.0              | 174.5±5.35                            | 238.7±6.08                        |
| Diastolic Blood pressure (mmHg) | 78.3±3.32              | 101.5±3.27                            | 142.3±4.16                        |
| Pulse pressure (mmHg)           | 56.2±4.99              | 73.7±4.91                             | 98.4±4.90                         |
| Plasma Glucose mg/dl            | 91.8±5.59              | 82.8±5.59                             | 109.9±6.39                        |
| Serum Creatinine mg/dl          | 5.5±0.06               | 4.9±0.04                              | 7.6±0.06                          |

**Table 2: lipid profile in controls, non-malignant hypertensive and malignant hypertensive.**

| Parameters                   | Normotensive (n=75) | Non-malignant hypertensive (n=273) | Malignant hypertensive (n=12) | P- value |
|------------------------------|---------------------|------------------------------------|-------------------------------|----------|
| Total cholesterol mg/dl      | 145.26±20.69        | 214.96±36.72                       | 213.94±18.6                   | 0.72     |
| Triglycerides mg/dl          | 90.70±35.04         | 131.00±55.42                       | 132.15±56.39                  | 0.03     |
| HDL-cholesterol mg/dl        | 26.66±6.63          | 26.12±5.81                         | 16.21±4.23                    | <0.01    |
| LDL-cholesterol mg/dl        | 96.46±21.2          | 154.64±53.25                       | 168.3±57.1                    | 0.024    |
| Total: HDL cholesterol ratio | 4.44±04.21          | 6.22±07.1                          | 12.19±1.7                     | <0.01    |

This present study, we have attempted to compare patients presenting with MHT to normotensive controls and patients with untreated essential hypertension. Patients with diabetes mellitus or overt vascular disease that subclinical atherosclerosis was not present in any of the study participants. However, the use of pre-defined criteria for the definition of vascular disease applied to all three study groups minimizes the likelihood of confounding by vascular disease. Other confounders include drug therapy and an acute phase response. The effects of drug treatment have largely been avoided, although a small proportion (2/12) of the MHT group had received antihypertensive medication prior to admission. An acute phase response may be responsible for reductions in both LDL- and HDL-cholesterol concentrations and an increase in serum triglycerides, for example after acute myocardial infarction.<sup>[17]</sup> This takes sometimes to develop (about 18hrs in the case of acute myocardial infarction) and may persist for several weeks. It is difficult to estimate the extent to which the results in the MHT group may have been affected by an acute phase response, as it is not possible to be certain of the time at which the illness developed. However, all samples were taken within 18hrs of hospital admission. It is also reassuring to note that LDL-cholesterol concentrations were similar in all the three groups. Despite MHT being reported to be an increasingly rare disease, we have not noted a decline in our clinical practice and have previously reported on the AIIMS, BBSR MHT register, which probably represents one of the largest series in the literature.<sup>[6]</sup> The cohort in the present analysis was prospectively recruited over approximately 6months and apart from being one of the first investigations into dyslipidaemia in MHT per se, probably represents one of the largest prospective cohorts of MHT investigation in this way. Dyslipidaemia in MHT is relevant as in spite of improved overall survival in patients with MHT, due to the advent of new antihypertensive drugs, there remains a significant excess mortality and morbidity in these patients,<sup>[5]</sup> much of which is due to atherosclerotic vascular diseases such as stroke and myocardial infarction.<sup>[6]</sup> However, we recognize that in the present paper, our findings are based on only 12 cases of MHT and that they will need confirmation in further studies.

This study presents our experience with malignant hypertension in 12 patients in a tertiary care hospital in the south east part of India. In developed countries with the advent of effective antihypertensive drugs,

malignant hypertension has become uncommon.<sup>[20]</sup>

The present data reveal that of the 393 hypertensives registered in a clinic treating hypertensive patients during this 6 month period, 3.05% had malignant hypertension. The patient group is selective and does not reflect the incidence of malignant hypertension in the general population of hypertensives. The commonest cause of malignant hypertension was essential hypertension, accounting for 69.46% of patients. The predominance of essential hypertension in this study indicates that early detection and control of essential hypertension has yet not become effective in India. An autopsy study of malignant hypertension in the Bantu population in Johannesburg,<sup>[18]</sup> showed a similarly high prevalence of essential hypertension, while studies from developed countries reveal secondary causes to be dominant.<sup>[19,20]</sup>

## CONCLUSION

These findings suggest that MHT may be associated with an abnormal lipid profile especially total cholesterol, triglycerides and LDL-cholesterol concentration characterized by low-HDL-cholesterol concentrations. Higher levels of these lipids may be contributed due to physical inactivity, stress, increased age, alcohol consumption and high consumption of dietary fat etc. Thus, analysis and follow-up of these patients with malignant hypertension confirms that essential hypertension continues to remain the most common cause of malignant hypertension in India.

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