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Original Research Article

Assessment of serum uric acid and plasma ascorbic acid in Pregnancy induced hypertension

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Abstract: Oxidative stress plays a crucial role in the pathogenesis of various diseases including pregnancy induced hypertension (PIH). Previous studies have suggested that uric acid not only acts as an antioxidant but also act as an important factor in precipitation of disease process by inducing inflammation. However, there is no satisfactory explanation for its role in PIH. The objective of present study was to determine the level of serum urate and plasma ascorbate in PIH patients and to determine their role in disease process. Serum uric acid and plasma ascorbic acid levels were estimated by using standard methods in 40 patients of PIH and in 40 age matched healthy volunteers, served as control. The values were expressed as Mean ± SD and data from patients and controls were compared using students't' test. Serum urate levels were significantly high ($p<0.05$) and plasma ascorbate levels were significantly low in patients as compared to control. These finding suggest that elevated serum urate level is associated with enhanced protective mechanism against oxidative stress and decreased ascorbate level is due to its free radical scavenging and urate radical repairing action in PIH. Therefore, ascorbate supplementation in drug/diet regime in these patients can prove to be protective. In addition, serum uric acid and ascorbic acid are efficient marker of oxidative stress status in PIH patients.
Keywords: Pre-eclampsia, oxidative stress, uric acid, ascorbic acid, endothelial dysfunction

INTRODUCTION:-

Normally pregnancy is characterized by a heavy demand of metabolic energy, leading to an increased requirement for oxygen and an elevation in maternal basal metabolic rate (BMR) due to enhanced work with respect to maternal circulation, respiration, renal function and increased tissue mass. To meet this increased energy requirement during pregnancy, the human placenta is highly vascularized and sufficiently exposed to high maternal oxygen partial pressure. The consequent accelerated intake and utilization of oxygen and the increased activity of the mitochondrial electron transport chain leads to the generation of high levels of reactive oxygen species (ROS) and an accompanying elevated level of oxidative stress [1].

ROS mediated oxidative stress plays a significant role in the etio-pathogenesis of certain diseases including pre-eclampsia [2]. To combat with oxidant mediated injury, the most important biological antioxidants would appear to be vitamin C, uric Acid, vitamin E, glutathione peroxidase, catalase and superoxide dismutase etc. Vitamin C, an exogenous water soluble antioxidant functions as primary defense against free radicals in plasma and disappeared more quickly. It has a significant role in protecting plasma lipids against peroxidation (i.e. anti atherosclerotic effect) and positive correlation with HDL-cholestrerol [3]. Moreover, ascorbate concentration in blood has been found to be protective in normal pregnancy as well as growth of the foetus [4].

Uric Acid, an end product of purine metabolism and is thought to act as an endogenous antioxidant in vivo. It is an endogenous, preventive and chain breaking antioxidant which contributes about 65% of free radical scavenging action stabilizes ascorbate, protects DNA and erythrocytes from oxidative damage [5]. Bainbridge and Roberts reported that uric acid is able to promote inflammation, oxidative

stress and endothelial dysfunction, and thus, considered it as pathogenic factor in preeclampsia [6]. Indeed, it is even not clear at this stage whether uric acid has damaging or protective effect in pre-eclampsia. Therefore, the objectives of present study were to estimate serum uric acid and plasma ascorbic acid levels in pre-eclampsia and to determine the relationship of these two parameters with disease complexity which may confer us more rational approach to the treatments of such complicated conditions.

MATERIALS & METHODS:-

In the present study, 40 normotensive women & 40 subjects of PIH were taken in study group i.e. Group I and Group II respectively. A general information or pre-experimental questionnaire regarding demographic information, family history and limited physical examination including blood pressure measurement was completed from all the subjects after taking their informed consent and approval of protocol by ethics committee of college. *Inclusion criteria:* The pregnant women having blood pressure greater than 140/90 mm Hg diagnosed after 20 weeks of gestation with evidence of proteinuria (~200mg/l) and fulfilled National Institute for Health and Clinical Excellence (NICE) guidelines 107, were grouped as PIH subjects (Group II). *Exclusion criteria*: Patients with diabetes mellitus, family history of hypertension, smoking habit, renal insufficiency, hepatic disease, obese (BMI > 30), taking lipid lowering drugs or diuretics were excluded.

Fasting blood samples were collected in EDTA vials from the anticubital vein of the study group subjects and processed immediately. Serum uric acid was estimated by Caraway's method and plasma ascorbate by Mc Cormick and Greene method spectrophotometrically [7, 8]. Values were expressed as Mean ± SD. The significance of mean difference between groups was compared by using Student's t-test and distribution of probability (P).

RESULT:

In the present study, serum uric acid levels were significantly high in patients with PIH patients as compared to healthy normotensive pregnant women served as controls (Table 1, $p<0.001$) whereas plasma ascorbic acid levels were significantly low in patients as compared to controls ($p<0.05$), as represented in Table 1 and Figure 1. A statistically significant negative correlation was observed between rise in serum urate level and fall in plasma ascorbate level in PIH patients. ($r = - 0.76$).

Table 1: Demographic profile along with serum uric acid and plasma ascorbic acid level in control and patient group (Mean ± SD)

S.No.	Parameter	Control group	Patient group	Level of Significance	% Increase	% Decrease
1.	No. of samples	40	40	-	-	-
2	Age (years)	29.5 ± 3.0	31.4 ± 2.7	-	-	-
3	Systolic blood pressure (mmHg)	121 ± 4.5	146 ± 5.8	p<0.05	20.66	
4	Diastolic blood pressure (mmHg)	80 ± 3.0	94 ± 4.0	p<0.05	17.5	
5	Uric acid (Mg %)	4.22 ±0.58	6.87 ±1.75	p<0.001	62.7%	-
6	Ascorbic acid (mg %)	0.81 ± 0.14	0.45 ± 0.08	p<0.05	-	44.4%

Where, p<0.1: Non-significant, p<0.05: Significant; p<0.001: Highly Significant;

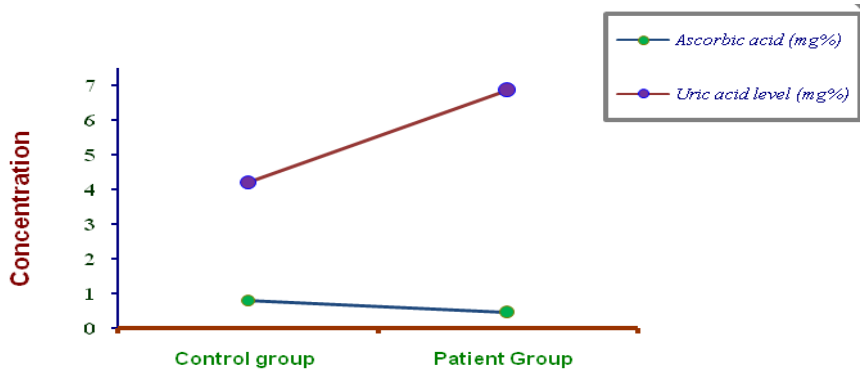

Fig-1: Serum Uric acid and plasma ascorbic acid levels in study group subjects

DISCUSSION:

Pregnancy induced hypertension is a dangerous complication of pregnancy that affects 5–10% of pregnancies and is characterized by hypertension [9, 10]. Despite intense research efforts to unveil the etiology of pre-eclampsia, it remains enigmatic. However, a growing body of evidence supports the understanding that the disease begins in the utero-placental unit, is amplified by oxidative stress, and ends in the maternal endothelium. It has been reported that large amount of free radicals eg. Superoxide radical ($O_2^{\cdot}$), hydrogen peroxide and highly reactive hydroxyl radical ($OH^{\cdot}$) are released by preeclamptic placenta which not only interacts with nitric oxide (NO) to form peroxynitrite but also causes structural and functional damage to cellular DNA, proteins and cell membranes [11].

To combat with oxidant mediated injury, there are various sorts of antioxidants present in the body. Amongst these, uric acid and ascorbic acid are important biological antioxidant present in extra cellular fraction. Ames et al. pointed out the fact that urate provides antioxidant defense against radicals causing cancer and aging in humans which in turn direct the researchers towards the antioxidant role of uric acid in preeclampsia. In the present study, serum urate concentration was found to be significantly high ($p<0.001$) in the patients as compared to healthy controls. Our findings were in agreement with the previous findings of Manny *et al.;* [12]. According to them, elevation of uric acid may be a protective response of the body in order to oppose the harmful effects of free radical activity and oxidative stress. In addition, elevated serum uric acid concentrations predict the development of hypertension as well as reflect impaired endothelial integrity, in which endothelial dependent vascular relaxation produced by nitric oxide (NO) is reduced [13].

Another most important antioxidant in human extracellular fluid is ascorbic acid which disappears rapidly under condition of oxidative stress [14]. In the present study, plasma ascorbate concentration was found to be significantly low in pre-eclamptic patients ($p<0.01$) as compared to control and negative correlated ($r = – 0.76$) with that of serum urate levels. Our findings were quite similar to the findings of Zhang *et al.;* [4]. The main reason behind the depletion of ascorbate level in pre-eclamptic patients is due to its reaction with free radical in order to scavenge them. Maple and Mason documented the fact that the ascorbic acid not only scavenges reactive oxygen species but also repairs the urate radical generated by attack of free radicals on uric acid. As a consequence, uric acid level increases with simultaneous decrease in ascorbate level, under condition of oxidative stress [15]. These studies ensure us that another reason of decreased ascorbate level in preeclampsia, as observed in the present study, is due to urate radical repairing action of ascorbate as well.

CONCLUSION:

Thus, we conclude that both uric acid and ascorbic acid are important biological antioxidant in pre-eclampsia patients, and alteration in their level is not only the risk factor for the development of PIH but also a useful tool in the assessment of oxidative stress status in PIH patients. High level of uric acid provide antioxidant defense against free radicals and low level of ascorbate is due to its urate radical repairing & free radical scavenging action in PIH patients. Furthermore, it is suggested that regular monitoring of blood pressure and serum uric acid along with antioxidant supplementation may not only predict PIH development but also prevent the development of PIH.

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