

## Evaluation of Maternal Outcome in Pre-Eclamptic Toxemia (PET) at Altitude >5000 feet With Pet at Altitude <5000 feet

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### ABSTRACT

**Background:** Hypertensive disorders of pregnancy are responsible for significant maternal and perinatal morbidity and are the second leading cause of maternal mortality. Etiology of PET remain unclear despite extensive research because the disorder is heterogeneous, the pathogenesis can differ in woman with various risk factors.

**Aim:** To compare maternal outcome in PET at altitude  $\geq 5000$  feet with PET at altitude  $< 5000$  feet.

**Methodology:** This descriptive case series study was conducted in D.H.Q Hospital Bagh for two years from September 2008 to 2010. Patient with PIH with positive protein urea were included in this study. Total 200 cases were taken 100 from area  $> 5000$  feet and 100 from  $< 5000$  feet. Incidence of PET, eclampsia, intrauterine growth retardation and pre-maturity were recorded.

**Results:** Patients came from high altitude had adverse maternal outcome when compared with low altitude group. The frequency of severe pre-eclampsia was significantly ( $< 0.05$ ) higher in high altitude group. In high altitude group 62% cases and in low altitude group only 29% cases presented with severe PET. In high altitude group out of these 62 cases, 15 (24%) patients developed eclampsia in contrast to 3 (10%) patients from low altitude group, abruptio placenta was seen more frequent in high altitude group 16(26%) vs. 4(13%) in low altitude group. The frequency of ARF, 13(21%) vs. 4(13%) cases and coagulopathy 6(9.6%) vs 1(3%) cases was noted significantly ( $< 0.05$ ) more common in patients coming from high altitude. Only 2(3%) cases of HELLP syndrome were seen in high altitude group. The proportion of raised liver enzymes was seen significantly ( $< 0.05$ ) greater in high altitude group. There were 4 maternal deaths in high altitude group, 2 due to eclamptic seizure and 1 case due to coagulopathy and one case due to HELLP syndrome.

**Conclusion:** There is strong association between adverse maternal outcome and high altitude of  $> 5000$  feet in term of pregnancy complications in patients of PET.

**Keywords:** PET, High altitude, Maternal Complications, Eclampsia, Placental Abruption.

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### INTRODUCTION

Hypertensive disorders of pregnancy are responsible for significant maternal and perinatal morbidity and are the second leading cause of maternal mortality.<sup>1</sup> Pre-eclampsia is defined as the diastolic B.P  $> 90$ mmHg or systolic B.P  $> 140$ mmHg at least two reading 4-6 hrs apart in previously normotensive patient after 20 week gestation with presence of 300mg /litter or more protein in 24 hr urinary specimen. PET characterized as mild or severe. Severe hypertension (diastolic B.P $> 110$ mmHg), coagulopathy, thrombocytopenia, liver function disorder, ARF and IUGR are the feature of severe diseases<sup>2</sup>.

It is a disease of 2<sup>nd</sup> half of pregnancy occurring mainly after 20 weeks of gestation. The prevalence of hypertension in pregnancy is between 5-11% and

effect women of mainly under 20 year of age. inadequate invasion of trophoblast which results in placental ischemia as a result of insufficiently dilated uterine spiral arteries is thought to be an initial cause in pathogenesis of pre-eclampsia<sup>3</sup>.

Incidence of pre-eclampsia ranges from 3-7% for nulliparous and 1-3% for multiparous. Pre-eclampsia is the major cause of maternal mortality and morbidity<sup>4</sup>. Etiology of PET remain unclear despite extensive research because the disorder is heterogeneous, the pathogenesis can differ in woman with various risk factors. Risk factor for PET include nulliparity family history of pre-eclampsia multiple pregnancy, maternal age, renal disease and. autoimmune disease<sup>5</sup>.

The prognosis is much more severe when pre-eclampsia develop very early in the pregnancy. HELLP syndrome and eclampsia is most dangerous complication of PET and may develop before and after delivery. At high altitude, hypoxia effect on maternal and fetal outcome. One of greatest physiological challenge during pregnancy is to maintain an adequate supply of oxygenated blood to

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the uteroplacental circulation for fetal development. This challenge is magnified under condition of limited oxygen supply. High altitude impairs fetal growth, increase incidence of pre-eclampsia and as a result significantly increases the risk of maternal morbidity and mortality<sup>6</sup>.

Placental hypoxia is involved in development of PET and pregnant women at high altitude are considered to be at risk of reduced uteroplacental blood flow, oxidative stress and increase maternal vascular reactivity. High altitude shifts the individual risk for the development of preeclampsia because of impact on multiple physiological systems, no one of which can be specifically pointed to as causal<sup>7</sup>.

Increase frequency of PET in high altitude resident has been attributed to greater placental hypoxia, small uterine artery diameter and low uterine artery blood flow. At high altitude adverse outcome were significantly more.<sup>9</sup> Globally, pre-eclampsia and eclampsia account for 10-15% of maternal deaths.<sup>10,11</sup> Maternal mortality is extremely high in Pakistan especially in remote areas where health care facilities and antenatal care facilities are limited. This study has been planned to find out maternal complication in patients of severe PET and to assess any difference in patients coming from high altitude of >5000 feet and low altitude of <5000 feet.

## MATERIAL AND METHODS

One hundred patients from area of altitude >5000 feet and 100 from <5000 feet. Approval of the study was taken from hospital ethical committee before start of the study. Incidence of PET, eclampsia, intrauterine growth retardation and pre-maturity were recorded. All these cases were followed till delivery. Women were categorized to have severe pre-eclampsia if their systolic blood pressure was equal or greater than 160 mm Hg or diastolic blood pressure greater than 110mmHg on 2 occasions at least 6 hours apart on bed rest together with the presence of significant proteinuria. Women who had active seizures beside the previously described presentation were classified as eclamptic cases. Information regarding demographic characteristics like age, gestational age, area, blood pressure, protein urea and maternal complications were recorded on a pre-designed proforma. Descriptive statistics were used to present the data in the form of frequency and percentages for qualitative data. Chi-square test was applied to find the association of maternal complications in both groups of high and low altitude area. P-value <0.05 was considered significant.

## RESULTS

Maternal characteristic has been summarized in table 1. Majority of cases in both groups had age in interval of 18-35 yrs (70% vs 64% in high and low altitude respectively). Most of the cases in both groups presented at gestational age between 28-37 weeks (85% vs. 88%) in high and low altitude groups respectively. In our study 66% patients in high altitude group and 63% in low altitude group were multiparous, while 34% vs. 37% were nulliparous in high and low altitude groups respectively.

Patients came from high altitude had adverse maternal outcome when compared with other group. The frequency of severe pre-eclampsia was significantly associated with high altitude. It was significantly (<0.05) higher in high altitude group as compared to patients came from <5000 feet altitude group. Out of 100 patients 62% cases develop severe pre-eclampsia while in second group only 29% cases had severe PET. Complications associated with severe PET are given in table 2.

In high altitude group out of these 62 cases, 15 (24%) patients developed eclampsia in contrast to 3 (10%) patients from low altitude group which is significantly (<0.05) higher rate. Significantly (<0.05) more cases of abruption-placenta were seen in high altitude group 16 (26%) vs. 4 (13%) in low altitude group. The frequency of ARF, 13 (21%) vs. 4 (13%) cases and coagulopathy 6 (9.6%) vs 1 (3%) cases was noted significantly (<0.05) more common in patients coming from high altitude in comparison with patients from low altitude group. Only 2 (3%) cases of HELLP syndrome were seen in high altitude group but there was no case of HELLP in low altitude group. The proportion of raised liver enzymes was seen significantly (<0.05) high in <5000 feet low altitude group in contrast to >5000 feet high altitude group. In low altitude group 8 (27%) cases of severe PET developed hepatic complication of raised liver enzymes in contrast to high altitude group in which 10 (16%) cases had raised liver enzymes. There were 4 maternal deaths in high altitude group due to eclamptic seizure 1 case of coagulopathy and one case of HELLP syndrome. In high altitude group 38% cases had mild pre-eclampsia and no serious maternal complication occurred in these patients having good maternal outcome. 71% cases at low altitude had mild diseases with no serious maternal or fetal outcome. All cases of mild preeclampsia at both high and low altitude were managing conservatively and deliver between 36 to 38 week gestations

Table 1: Maternal characteristic of the patient in both groups

Characteristics	Pts from altitude >5000 feet (n=100)	Pts from altitude <5000 feet (n=100)	P Value
<b>Maternal age</b>			
<18	08	04	>0.05*
18-35	70	64	
>35	22	32	
<b>Gestational age WKS</b>			
<28	07	02	>0.05*
28-37	85	88	
>38	08	10	
<b>Parity</b>			
Nulliparous	34	37	>0.05*
Multiparous	66	63	

\*The p-value is significant at 5% level of significance

Table 2: Comparison of maternal complication with severe pre eclampsia in patients living at altitude &gt;5000 feet with patients living at altitude less than 5000 feet.

Complication	Patients from altitude >5000 feet with Severe PET (n=62)	Patients from altitude <5000 feet with Severe PET (n=29)	P value
Eclampsia	15 (24%)	03 (10%)	<0.05*
Placental Abruption	16 (25%)	04 (13%)	<0.05*
ARF	13 (21%)	04 (13%)	<0.05*
Coagulopathy	06 (9.6%)	01 (3%)	<0.05*
HELLP Syndrome	02 (3%)	00	>0.05**
Hepatic complication (raised liver enzymes)	10 (16%)	8 (27%)	<0.05*
No complication	00	9 (31%)	<0.05*

\*The p-value is significant at 5% level of significance

\*\*The p-value is not significant at 5% level of significance

## DISCUSSION

In developing countries like ours antenatal care (ANC) even if only conducted once, remains an important factor in assessing the health status of women during pregnancy. There is a critical linkage between maternal outcome and maternity care services. Access to antenatal care, early detection of the disorder, careful monitoring and appropriate management are crucial elements in the prevention of pre-eclampsia related deaths<sup>12</sup>.

In developed countries research findings emphasize the importance of quantitative and qualitative adequacy of ANC. In UK after the inception of the National Health Service, which allowed free comprehensive antenatal care for all, a significant reduction in the incidence of eclampsia was noted in the United Kingdom, probably as a result of the early detection of pre-eclampsia and its management<sup>13</sup>.

In this study we found that frequency of severe PET at high altitude was more as compare to low altitude. As 62% patients at high altitude presented with severe pre-eclampsia in contrast to 29% patients in low altitude group, so incidence of PET was more at high altitude. The important barriers for poor ANC utilization among the women from high altitude were

either related to physical inaccessibility to the health facility or related to poverty & low educational level, as a result, significantly increases the risk of perinatal and maternal morbidity and mortality among women from high altitude area.

In this present study 25% patients presented with abruption at high altitude while 13% cases had abruption at low altitude group. Murphy and Stirrat showed 15% abruption placenta. In another study it was reported that in PET at high altitude, pro-inflammatory cytokine and TNF alpha were more that adversely influence diseases severity<sup>14</sup>. The present study showed that 2% cases at high altitude had HELLP syndrome both of these cases in teen age group with early onset pre-eclampsia less than 28 week gestation. There was no case of HELLP syndrome in people at low altitude. Other studies reported a comparatively high proportion of 21% case of HELLP syndrome which is elevated than present study.<sup>14</sup> ARF develop in 14% cases at high altitude while in 2% cases in low altitude group. 9.6% cases at high altitude develop coagulopathy while in low altitude group coagulopathy was not observed<sup>15</sup>.

According to the results of our study the frequency of ARF, (21% vs. 13%) cases and coagulopathy (9.6% vs 3%) cases were noted significantly (<0.05) more common in patients coming

from high altitude in comparison with patients from low altitude group. The results of our study are showing more frequent complications of ARF and coagulopathy than results from previous reported studies which might be high lighting more poor social, educational and health care status of patient of our study. Some other studies also reported that ARF was the most common maternal complication. In addition to hypoxia at high altitude may be the other common cause of worse outcome, since patients had less health facilities. They had no regular antenatal visit with poor control of B.P and no history of intake of calcium, vitamin D and low dose aspirin, all of which could have preventive role.<sup>16</sup> Maternal mortality in present study was 4 cases of maternal death in whole study sample. Maternal mortality is extremely high in Pakistan where 1 in 89 women dies of maternal cause with preeclampsia and eclampsia as one of major cause.<sup>17</sup> Following are the factors which can contribute to maternal morbidity and mortality: late referral to hospital, delay in hospital management, lack of transport, un-booked status of patients, high parity, prolongs state of unconsciousness and multiple seizures prior to admission<sup>18</sup>.

It is obvious from the literature shows that severe pre-eclampsia and eclampsia is more frequent among older women, those with multiple pregnancy, lower gestational age, primigravidae, and nulliparae.<sup>19,20</sup> In my study it occurs in multiparous women in 66% and 63% case in high altitude and low altitude group respectively. Mark A Brown also noted that 2/5<sup>th</sup> of the women were parous.<sup>21</sup> Previous researches in the literature show that all maternal and neonatal complications were more frequent at high altitude<sup>22</sup>. The result of our study also support this that pregnant women living in high altitude of >5000 feet had a high tendency of maternal complications during pregnancy in comparison to pregnant women in low altitude area.

In our study we note that usually the patients from high altitude presented at advance stage of disease that is when already IUGR has been developed or after mother has got irreversible condition and it required premature delivery to save the mother. In addition to altitude, hereditary factors as well as common environmental or behavior exposure may predispose to increase pre-eclampsia risk and its need to stress on these factors

## CONCLUSION

There is strong association between adverse maternal outcome and high altitude of >5000 feet in term of pregnancy complications in patients of PET.

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