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# Multifactorial inheritance of imminent preeclampsia: a case-control study

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## Abstract

Pre-eclampsia is a major cause of maternal mortality and morbidity, preterm birth, perinatal death, and intrauterine growth restriction. Incidence of hypertensive disorders in India is found to be 10.08 % as observed through the data collected by the National Eclampsia Registry (NER) (11,266 out of 1,11,725 deliveries) over the past 3 years with 2,554 patients out of this presenting with eclampsia. A Case-control study was conducted to investigate the critical role of familial preeclampsia in Pune India. The women who participated in this study were primigravida with age < 25 years old.

**Keywords:** Pregnancy; Pre-eclampsia; India

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## Introduction

Pre-eclampsia is a major cause of maternal mortality and morbidity, preterm birth, perinatal death, and intrauterine growth restriction. Incidence of hypertensive disorders in India is found to be 10.08 % as observed through the data collected by the National Eclampsia Registry (NER) (11,266 out of 1,11,725 deliveries) over the past 3 years with 2,554 patients out of this presenting with eclampsia [1]. Despite the core of idea has remained for 6000 years till now or 400 BC yet 3 major breakthroughs have occurred in understanding the nature of disease [2]. The first was in 1974 when discovered that preeclampsia is associated with failure pseudo vascular development at the level of placenta associated abnormal thromboxane and placental rennin production and both are responsible for hypertension and failure of coagulation system [3]. However, there is a less famous and well-known breakthrough which may be summarized as the isolation of at least 100 genes associated with preeclampsia [4-5]. The mechanism in which those genes control preeclampsia is still to be clarified. Some of those genes involved in preeclampsia works through placenta growth factor and endothelia growth factor PIGF and VEF [6]. In women with preeclampsia those factors which are essential to the normal placentation are severely reduced. In other word the genes coding for them are under expressed. Other genes work through soluble endoglbin which a soluble isoform of coreceptor for is transforming growth factor beta (TGF- beta). Endoglin binds to TGF-beta in association with the TGF-beta receptor. Because the soluble isoform contains the TGF-beta binding domain, it can bind to circulating TGF-beta and decrease circulating levels. In addition, TGF-beta is a proangiogenic

molecule, so the net effect of high levels of sEng is antiangiogenic. There is strong evidence that soluble endoglbin increase significantly at least 3 months prior to the onset of preeclampsia [7]. In other word the gene expression for soluble endoglobin is over expressed among women liable for preeclampsia. Up to this point it might be remembered that preeclampsia is a disease of insulin resistance which is well known to be multi factorial inheritance mode [8].

**Patients and methods**

The study was done in Gupte Hospital, Pune between. All women enrolled in this study were admitted to labor ward and put into two groups study group and control group according to familial. All the women in the study group N=30 were primigravida and term between 37 and 41 weeks and she is cousin with her husband. In addition, the couple's parents were also cousins. All the women in the control group N=30 were primigravida and term between 37 and 41 weeks and she is stranger to her husband and their parents were not related in any form. For both groups the verbal consent to participate in the study was taken as nothing required for the study except the data of their routine investigation. The study protocol was approved by the Bharati Vidyapeeth University Medical College.

*Study design*

As it has been mentioned above the study and the control groups contained both normal women (risk free women), meaning they are not hypertensive, diabetic, multiple gestation, Rh negative women, mal position of the fetal head, mal presentation and all other conditions which require modification in their labor, all women in both group were assessed and managed as active management of labor. These include artificial rupture of the membrane at 4 cm cervical dilatation, use of oxytocin to augment labor contractions, implementation of partogram, electronic fetal heart monitoring and analgesia during labor by pethidine. Active management of the second and third stage of labor by putting the patient in lithotomy position and encourage the patient to push with uterine contraction until crowning of the fetal head were episiotomy was done. And Brands Andrew's method of placental delivery after giving oxytocic drug ergometrine immediately after delivery of the fetus was done. That is summary of the management in women with no preeclampsia in both study groups; the familial or study group, or control or non-familial group. On the other hand, the women with imminent preeclampsia women in both groups underwent totally different course by putting them in the intensive care unit. Women with imminent preeclampsia are those with diastolic blood pressure 110 mmHg or more irrespective of the systolic value. In addition, proteinuria assessment is 4 grams or more per 24 hours. Insertion of at least two wide bore cannula and Foleys catheter to monitor the urinary output. Nothing by mouth was also ensured. Magnesium Sulfate MgSO4 was used as primary anti convulsive drug while hydralazine intravenous infusion was used in our department. In addition, at the time of insertion of the cannula 5 cc of blood was sent for biochemistry analysis in ordinary test tube and 2 cc for evaluation of blood platelets in different test tube with anticoagulation material. While from the Foley's catheter tube a

sample of 5 cc urine was collected and sent for protein over creatinine ratio as a reflection of the 24 total urinary proteins in urine. The blood biochemistry investigation included serum SGPT, SGOT in iu/L units, Fibrinogen in mg/dl unit to assess the severity of liver and kidney impairment. In addition, the platelets count in thousands per ml however we have omitted the three zero digits in the tables for the sake of simplicity for example 150,000 platelets per ml is expressed as 150 /ml. The protein over creatinine ration was measured by Microgram/milligram units so 160ų/m. Both serum uric acid in the blood and urea were measured in mg/dl. In addition to the initial assessment mentioned above meticulous monitoring chart was established with 15-30 minutes intervals for assessment of the blood pressure and expressed as mmHg and signs of Magnesium sulfate toxicity including respiratory rate, maternal heart rate, reflexes in the knee joint. 10 cc of calcium gluconate was prepared as standby for any possible cardiac arrest from overdose of Magnesium as we don't have in our labs facilities for measuring its serum value. The protocol of giving MgSO4 was initial 4-6-gram loading dose initially followed by 2-3 grams per hour as maintenance dose per hour. While hydralazine 5- 10 mg were put in 200- 300 normal saline and infused slowly until blood pressure drops to 140 over 90 mmHg. In addition to the initial values at admission further assessment of fibrinogen, platelets, SGPT and SGOT and blood urea and serum uric were all assessed after 3 and 6 hours. The purpose of those 2 assessments is to measure the area under curve AUC for every patient with severe or imminent preeclampsia for the sake of statistical comparison at the end of the study. Mean arterial blood pressure was calculated from both systolic and diastolic blood pressure values according to the following formula; So, at the end of the study, a total of 30 women with familial with her husband and between their parents were collected as the study group. Further 30 women with no familial neither with her husband and her parents were collected as control Group. Out of 30 patients in the study group 11 women were in imminent or severe preeclampsia that required immediate control of blood pressure and anticonvulsant therapy. Out of 30 patients in the non-familial group or control group 3 women were in imminent preeclampsia and managed as exactly as above.

**Statistical analysis**

The first statistical analysis was done by power analysis to calculate the required sample size for this thesis. Since 10% of the overall admissions are hypertensive while according to the criteria we have chosen for the study group the expected incidence is arbitrary evaluated as 50%. With the above incidences and at alpha error 5% and beta error 80% the required minimum sample size was 25 patients for each group study and control with ratio of control over study equal 1.

Unpaired student t test was used to compare continuous data with test for variance set to automatic in the software. Calculation of the value comparable to75 centiles or above were calculated for systolic, diastolic, blood pressure, SGOT, SGPT, serum uric acid and blood urea to evaluate the ODD ratio for each all variables between familial versus control groups. This test was used to evaluate the correlation between familial and every variable by coding the figure 0 for value under or equal 75 centiles and 1

for values above 75 centiles for every variable. The ODD ratio, 95% CI or confidence interval and P value were calculated to evaluate the associated of the main study variables mentioned above with familial.

**Results**

As it has been mentioned in the previous chapter total of 30 familial women versus 30 non-familial women were collected all at term with preeclampsia. In table 1 the basic criteria of preeclampsia and age were compared between them and it is noticeable that the primary determinant of preeclampsia severity in the form of systolic, diastolic and mean blood pressure and protein over creatinine ratio were all significantly higher in the familial group. In addition, the liver enzymes, coagulation profiles as well as renal marker were also higher in the study group. Yet this finding does not mean it is correlated to familial. To verify whether familial is related the ODD ratio for all the above factors mentioned in table 1 have been calculated and unexpectedly all were higher in the familial group as shown by the 95% confidence interval and P value. The association of all the determinant of preeclampsia severity is genuine finding yet by no mean it can be universal as the collection of patients in both group in this study was not random rather highly selective. This may explain the unusual association between familial and severity of preeclampsia. As a matter of fact, the above table is more confusing than explaining as it only tells that familial is correlated to the preeclampsia, yet the picture is not only bleak rather vague. To expose more about this correlation serial reading after admit ion to the hospital at admission time, 3 and 6 hours of mean blood pressure. Mean arterial blood pressure was calculated by the nonlinear formula given in the previous section of this study. And here is considered as the dependent variable. On the other hand, still serial readings at 0, 3 and 6 hours were done for 6 independent variables through measuring the area under curve of the 3 readings of the followings; Blood urea and serum uric acid for the function of kidneys; Platelets counts and serum fibrinogen for the coagulation status; more importantly serum SGOT and SGPT still at 0, 3 and 6 hours with calculation of the area under curve for each above variable reading. This profile as area under curve is at least 16 times more sensitive than single reading since areas are measured with square units. All the details are given in table figure 1 with the appended table for explanation and table 3 for the rest of the independent variables. In figure 1 below which may be unique and unusual the mean blood pressure at 0, 3 and 6 hours was measures as serial data for all women in both study group and compared with unpaired t student test.

However, un usually here the geometrical mean rather than the arithmetic mean is expressed with median and the 95% confidence interval. The reason behind this is that converting systolic and diastolic blood pressure by the non-linear equation to Mean Blood Pressure has converted the variance from homogenous to none. Since the software used was set to automatic about the variance difference in t student test here it has approximated them by taking the geometrical mean rather than the arithmetic mean. Finally compared with t test and as seen in the appended table the difference in the mean blood

pressure between the study and control groups for area under curve is highly significant; Pressure was taken as serial reading for 0, 3 and 6 hours after admission to the hospital it will be more reliable than single reading as at the admission time only. On the other hand, the choice of area under curve is mandatory here as the data are unfit for assessment by linear regression or ANOVA test for serial reading. The above two tests are only applicable when the parameter in study either decrease or increase continuously with time. Here since with 6 hours all the women have not been delivered such data taken serially are unfit to be compared by them rather area under curve has been used as the optimum and only choice. In the same context 6 independent variables were assessed also in the same manner by area under curve for their serial data taken at 0, 3 and 6 hours and presented in table 3 after the 2 means were compared by t-test for serum fibrinogen and platelets count, serum uric acid and blood urea and those are not important as they appear early in every case of preeclampsia. On the other hand, serum SGOT and SGPT were measured still serially at 0,3, and 6 hours and presented also as areas under the curve which are raised only in severe preeclampsia are all given as shown by their statistical significance about the difference.

What we hope is that the reader does not confuse the readings in the table with the normal range and units of the parameter given in the table. For example, blood urea in general is 20- 40 mg/ dl! While the first figure in the table is 230.818 squared units! Meaning this figure is the area under 3 blood urea estimation at admission or 0 and 3 and 6 hours later and measured here all with unit 2 or squared area and the same for 2 study groups and those areas when compared with t-test the P value is 0.02. As it has been mentioned before mean blood pressure may be considered as a dependent variable while the other 6 variables, renal hematological and renal profiles are independent. Yet having 6 variables is impractical in building a model and for that reason, we implemented best subset regression to extract the most 2 independent variables correlated with mean blood pressure via examining the coefficient of Mallow.

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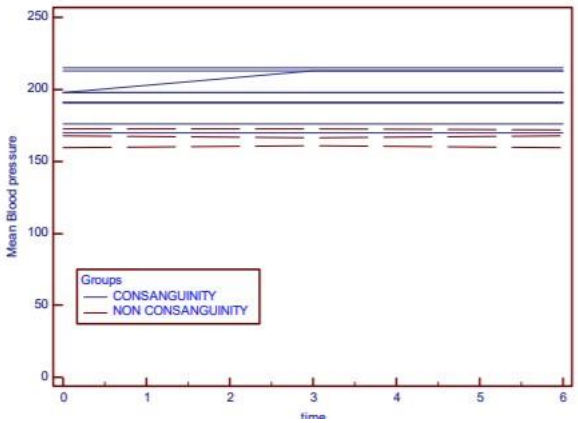
**Table 1.**

The main variables were taken at admission for study and control groups with their statistical comparisons

| Characteristics | Control Group (N=30) | Study Group (N=30) | P value |
|---|---|---|---|
| Age | 24.56±3.62 | 23.13±3.74 | P = 0.1377 |
| Systolic BP | 131±28.98 | 155.86+50.52 | P = 0.0228 |
| Diastolic BP | 75.30±22.14 | 94.10±35.53 | P = 0.0177 |
| Mean arterial BP | 93.95±23.9787 | 114.68±39.82 | P = 0.0176 |
| Mean urine Protein / Creatinine ratio | 0.75±1.42 | 1.91±2.06 | P = 0.0138 |
| Women with imminent preeclampsia | 3(10%) | 11(36.6%) | P = 0.0155 |
| Serum Fibrinogen | 250.8±45.8 | 187.6±16.59 | P = 0.0012 |
| Serum platelets(*1000) | 252.6±45.6 | 182.33±91 | P = 0.0004 |
| Serum SGOT | 26.8±12.37 | 41.5±21.11 | P = 0.0017 |
| Serum SGPT | 26.8±14.22 | 40.53±20.99 | P=0.0030 |
| B Urea | 22.66±2.77 | 29.1±10.92 | P=0.0028 |
| Serum Uric acid | 2.16±2.0 | 4.40±0.24 | P = 0.0002 |

**Figure 1.**

Area under curve for mean blood pressure at 0, 3, and 6 hours has been measured for women in both study group CI; Confidence Interval



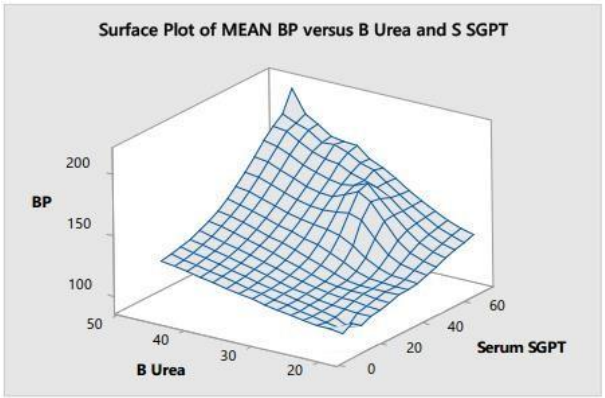




**Figure 2.**

The style of mean blood pressure versus blood urea and serum SPGT levels are presented as mesh plot

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**Table 2.**

Mean of area under curve is presented as mean and standard deviation of serum fibrinogen, platelets count, serum uric acid and blood urea, serum SGPT and SGOT with their statistical differences taken Profile of blood urea and AUC in consanguinity versus non women. CI; Confidence Interval

| B urea | n | Mean | 95% CI | SD | Median | Two-tailed probability |
|---|---|---|---|---|---|---|
| Consanguinity | 11 | 230.818 | 213.371 to 274.265 | 45.321 | 270 | P = 0.0280 |
| Non consanguinity | 3 | 176 | 144.973 to 207.02 | 12.49 | 180 | |
| Uric acid | n | Mean | 95% CI | SD | Median | Two-tailed probability |
| Non consanguinity | 3 | 29.6 | 27.323 to 31.877 | 0.917 | 29.4 | P = 0.0007 |
| Consanguinity | 11 | 44.727 | 40.962 to 48.493 | 5.605 | 42 | |
| Platelets count | n | Mean | 95% CI | SD | Median | Two-tailed probability |
| Consanguinity | 11 | 400.227 | 349.327 to 451.128 | 75.767 | 396 | P < 0.0001 |
| Non consanguinity | 3 | 766.5 | 667.142 to 865.858 | 39.997 | 780 | |
| Serum fibrinogen | n | Mean | 95% CI | SD | Median | Two-tailed probability |
| Non consanguinity | 3 | 730 | 574.866 to 885.134 | 62.45 | 750 | P < 0.0001 |
| Consanguinity | 11 | 423.818 | 389.841 to 457.796 | 50.576 | 426 | |
| SGPT | n | Mean | 95% CI | SD | Median | Two-tailed probability |
| Consanguinity | 11 | 403.227 | 392.329 to 414.126 | 16.222 | 403.5 | P = 0.0462 |
| Non consanguinity | 3 | 380 | 342.490 to 417.510 | 15.1 | 378 | |
| SGOT | n | Mean | 95% CI | SD | Median | Two-tailed probability |
| Consanguinity | 11 | 408.955 | 402.176 to 415.734 | 10.091 | 408 | P = 0.0073 |
| Non consanguinity | 3 | 383 | 332.961 to 303.039 | 20.130 | 391.5 | |

Use ODD ratio and logistic regression to explore correlation between consanguinity and its correlation to various variables among two study groups.

| Complications | ODD Ratio | 95% CI | P value |
|---|---|---|---|
| Systolic > 75 centile | 5.2105 | 1.2784 to 21.2373 | *P = 0.0213* |
| Non-Consanguinity | | Reference group | |
| Diastolic > 76 centile | 3.7632 | 1.037 to 13.64 | *P = 0.0308* |
| Non-Consanguinity | | Reference group | |
| Urinary protein /creatinine >75 centile | 3.7632 | 1.03 to 3.64 | *P = 0.04* |
| None-Consanguinity | | Reference group | |
| SGOT > 75 Centile | 2.76 | 2.01 to 3.64 | *P = 0.033* |
| Non- Consanguinity | | Reference group | |
| SGPT > 75 Centile | 4.7 | `1.65 to 3.45 | *P = 0.01* |
| Non-Consanguinity | | Reference group | |
| Platelets count < 75 Centile | 8.1053 | 1.6115 to 4.7675 | *P = 0.0111* |
| Non-Consanguinity | | Reference group | |
| Serum Fibrinogen < 75 centile | 8.1 | 1.60 to 4.76 | *P = 0.0111* |
| Non-Consanguinity | | Reference group | |
| blood urea > 75 percentile | 5.2105 | 1.2784 to 21.2373 | *P = 0.0213* |
| Non- Consanguinity | | Reference group | |
| Serum Uric Acid > 75 centile | 5.21 | 1.2784 to 21.2373 | *P=0.0003* |
| Non-Consanguinity | | Reference group | |

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In this type of formula construction, the independent variable which has the lowest Cp or coefficient of Mallow is the factor which has the highest correlation with dependent variable, mean blood pressure. This should be stressed as the concept of variance is quite different from the concept of distribution and no correlation exist between them and as shown in the table 4 above that the combination of blood urea and serum SGPT has the best correlation with mean blood pressure as they have the lowest coefficient of Mallow. In the 3dimensional surface plots shown in figure shows visually this fact beyond suspicion. It obvious that both blood urea and serum SGPT are related strongly in proportional way to mean blood pressure which encouraged as building a screening table which may help the practicing physician in predicting the severity of (severe) preeclampsia or imminent which has no chance of any oral therapy or further prolongation of pregnancy. The details are given bellow. In this table the various serum levels intervals of blood urea are given in the left most column while the corresponding rows contains the 1, 2.5, 5, 10, 90, 95, 97.5 and 99 centiles of SGPT serum levels. It should be remarked that this table is not for predicting or evaluating mild preeclampsia rather for imminent preeclampsia which has no more treatment apart from termination of pregnancy. Yet termination of pregnancy requires at least 12 hours of highly delicate decline of blood pressure as well as well establishing $MgSO_4$ Therapy in the form of loading and maintenance dose. Serum levels less than 10 centiles are shaded with green. Serum levels with yellow shading are between 10 and 90 centiles. Serum levels above than 90 centiles are shaded with red. It might be preferable that patients with reading in the red zones or high yellow zones to expedite their delivery before developing more serious complications like acute tubular necrosis, pituitary hemorrhage and further details are given in the discussion

## Discussion

Well to start with preeclampsia is a disease of abnormal placentation which is accompanied by increased production of placental rennin which causes hypertension and prostaglandin F2α which causes low grade disseminated intravascular coagulation syndrome or DIC from the early second trimester till delivery even before the onset of preeclampsia occur [10, 11, 12]. Up to this moment all the finding in this study can be explained namely hypertension, proteinuria, reduced serum platelets and fibrinogen, increased blood urea and serum uric acid and increased serum liver enzymes. However, it doesn't explain the differences in familial group and this can be achieved by the second breakthrough in preeclampsia understanding through the flagged article published in American Journal of Obstetrics and Gynecology in 2011 under the preeclampsia and insulin resistance [13]. In fact, this article represents the second most important breakthrough in preeclampsia understanding. Since all the insulin resistance diseases are transmitted as multi factorial then according to the strict criteria of patient collection followed in this study multi factorial inheritance should have explained the differences between the study and control group seen in this study. As a matter of fact, more 100 genes have been isolated which have been proved to play a key role in preeclampsia genesis. May

be the fact that those genes were all evaluated thoroughly represent the third breakthrough in preeclampsia

understanding but didn't gain popularity since such studies are confined to the advanced western countries only. As it has been mentioned in the introduction both placental growth factor and endothelial growth factor PIGF and VEGF were both increased in abnormal pregnancy complicated by preeclampsia. It goes without saying that placental growth is simply a complex and intricate new vessel formation in such a way that in almost in 40 weeks in human being the highly complex and intricate architecture of the fetal blood and maternal blood interaction at the level of tertiary villous is so delicate to ensure fetal supply with oxygen and other nutrients while disposing toxic contents like urea and uric acid and $CO_2$ out of the fetal circulation. It has been found that both mediators (PIGF, VEGF) were significantly increased among women with preeclampsia since very early in pregnancy. The gene which codes for both factors is over expressed among women with preeclampsia showing intrauterine intra uterine growth restriction and abnormal

Doppler velocity in the umbilical artery in the cells of synctio-trophoblast [14]. In addition to this the expression of this gene is related to insulin resistance by unknown mechanism. Insulin resistance is associated with over expression of this poly morph gene [14]. This gene may explain the differences in the severity of preeclampsia among the two-study group as its transmission is by multi-factorial inheritance and it is very likely that women in the study group has inherited from her both parents [15]. Though immunological factors are not usually related to genetics but rather to the exposure to a certain antigen, it has been found that the secondary wave of trophoblastic invasion mentioned above is somehow related to genetic factors. Practically all women with preeclampsia have failure of the secondary wave of trophoblastic invasion of the spiral arterioles to render them responsive to the circulating vasoconstrictors in the maternal blood. This process has been linked to upregulation metalloproteinase 9 and HLA antigen G [16].

Those 2 factors are needed for successful invasion of the trophoblast to be completely normal. It has been found that the gene responsible for production of those2 factors is grossly under expressed with resulting of poor placentation seen among women with preeclampsia at the level of trophoblast invasion. The mechanism is not clear nor is their correlation to insulin resistance understood. Yet it is very likely that it played a role in our study groups as the inheritance of this gene is still multi factorial. As it has been mentioned above preeclampsia is strongly associated with leakage of protein from the glomeruli and this is the result of gross damage to the endothelial cells. There is strong evidence that endothelial damage and dysfunction is not restricted to the glomeruli rather it is widely generalized especially in the placenta. During normal pregnancy, huge new vessel formation rules the place and the role of proangiogenic and antiangiogenic factors are of great importance and their balance is very

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important in normal pregnancy. Soluble endoglobin which is a form of circulating receptor for transforming growth factors plays a very important role in new blood vessel formation by binding to a cell surface receptor inducing new vessel formation. Since the last receptor is angiogenic soluble globulin is considered as anti angiogeneic factor [17].

There is evidence that in preeclamptic women serum levels of soluble globulin precede the onset of clinical preeclampsia at least 3 months. The reason behind the serum increase of soluble globulin is unknown thought it is associated with insulin resistance. Giving S globulin to rats causes cause hypertension and proteinuria while giving to pregnant rats causes HELLP like syndrome. The increased production of S globulin has correlation with insulin or in other word genetic factors [14]. In fact, the reasons behind soluble endoglobin gene over expression in preeclampsia are unknown. The use of area under curve is another topic which deserves some discussion as AUC is very effective as the unit of measurement is expressed as square unit to detect the slightest differences between 2 sets of data. In addition to analysis of all variables in this study by area under curve they were further analyzed by the best subset regression to calculate the best predictor of blood pressure in severe or imminent preeclampsia which was still taken serially at 0, 3, 6 hours after admission. Surprisingly the best predictors were blood urea and serum SGPT.

Though it may be strange initially and refused by logics. Yet here we are dealing with imminent preeclampsia in other word those women in which blood changes and liver involvement have already started as they reached the stage of imminent preeclampsia. So, the best predictor of mean arterial blood pressure here is not as expected in mild and early onset preeclampsia. The degree of association is measured by Coefficient of Mallow. The 2 best variables chosen were blood urea and SGPT. And from those two variables the correlation with mean arterial blood pressure is evaluated in the form of 3-dimensional mesh surface plot and a table has been predicted from equations which have been skipped from the reader for the sake of avoiding confusion. Yet the table is easy as in the left column the various ranges of blood urea are given while the upper row the serum SGPT for the 1, 2.5, 5, 10, 90, 95, 79.5, and 99 centiles are given. And for further benefit and avoiding any confusion areas less than 10 centiles are shaded with green, areas between 10 and 90 centiles with yellow and areas above 90 centiles with red color. It is expected that women with low blood urea and corresponding serum levels of SGPT are still just have entered the stage of imminent preeclampsia and she has somewhat further 110-12 hours before reaching the critical stage. During this period, it is safe to prepare the patient for induction of labor and control of blood pressure with hydralazine and institution of Magnesium sulfate anticonvulsant therapy which may take in loading and maintenance dose up to 10 hours. Possibly it is safe to wait for this period. Patients in whom readings for blood urea near 90 centiles or above with serum SGPT is more than 90 centiles about serum value possibly have only few hours before developing more sister complications like intracranial

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bleeding, adrenal hemorrhage, liver failure and other highly dangerous complications so it is wise to expedite the delivery as soon as possible.

That is the rationale behind building this table. Of course, the use of this table without prior testing by at least 3 trials is mentioned here only to be condemned.

**In conclusion**, For the time being this study showed data for evaluation purposes and should it show some clinical benefit then further confirmations by trials are encouraged as this area of medical practice remains one of the most challenging fields facing the Obstetrician in charge.

**References**

1. Dekker GA, Sibai BM. Etiology and pathogenesis of preclampsia: current concepts. Am J Obstet Gynecol 1998; 179(5):1359-1375.
2. Brown MA. The physiology of preeclampsia. Clin Exp Pharmacol Physiol 1995;22:781-791.
3. Chandiramani M, Shennan A. Hypertensive disorders of pregnancy: a UK-based perspective. Curr Opin Obstet Gynecol 2008;20:96-101.
4. Bellamy L, Casas JP, Hingorani AD, et al. Preclampsia and risk of cardiovascular disease and cancer in later life; systematic review and metaanalysis. BMJ 2007; 335:974.
5. Farag K, Hassan I, Ledger WL. Prediction of pre-eclampsia: can it be achieved? Obstet Gynecol Sur. 2004; 59:464-482.
6. Skjaerven R, Vatten LJ, Wilcox AJ. Recurrence of pre-eclampsia across generations: exploring fetal and maternal genetic components in a population based cohort. BMJ 2005;331:877.
7. Haig D. Genetic conflicts in human pregnancy. Q Rev Biol. 1993;68:495-532.
8. GOPEC disentangling fetal and maternal susceptibility for pre-eclampsia: a British multicenter candidate-gene study. Am J Hum Genet. 2005;77:127-131 9. Mutze S, Rudnik-Schoneborn S, Zerres K. Genes and the preeclampsia syndrome. J Perinat Med 2008;36:38-58.
9. Colhoun H, McKeigue P, Davey G. Problems of reporting genetic associations with comlex outcomes. Lancet 2003; 361:865-872.
10. Wacholder S, Chanock S, Garcia-Closas M. Assessing the probability that a positive report is false: an approach for molecular epidemiology studies. J Natl Cancer Inst 2004;96:434-442.
11. Isermann B, Sood R, Pawlinski R. The thrombomodulin-protein C system is essential for the maintenance of pregnancy. Nat Med 2003;9:331-337.
12. Brenner B. Thrombophilia and pregnancy loss. Thromb Res 2002; 108:197-202.
13. Lin J, August P. Genetic thrombophilias and preeclampsia: a meta-analysis. Obstet Gynecol 2005;105:182-192.
14. Dalmaz CA, Santos KG, Botton MR. Relationship between polymorphisms in thrombophilic genes and preeclampsia in a Brazilian population. Blood Cells Mol Dis 2006;37:107-110.
15. Fabbro D, D'Elia AV, Spizzo R. Association between plasminogen activator inhibitor 1 gene polymorphisms and preeclampsia. GynecolObstet In- vest 2003;56:17–22.
16. Gerhardt A, Goecke TW. Beckmann MW. The G20210A prothrombin-gene mutation and the plasminogen activator inhibitor (PAI-1) 5G/5G genotype are associated with early onset of severe preeclampsia. J Thromb Haemost 2005 ;3:686-691.
17. Shah NC, Pringle S, Struthers A. Aldosterone blockade over and above ACE-inhibitors in patients with coronary artery disease but without heart failure. J Renin Angiotensin Aldosterone Syst 2006 ;7:20-30.
18. Medica I, Kastrin A, Peterlin B. Genetic polymorphisms in vasoactive genes and preeclampsia: a meta-analysis. Eur J Obstet Gynecol Reprod Biol 2007;131:1 15-126.

19. noue I, Rohrwasser A, Helin CA mutation of angiotensinogen in a patient with preeclampsia leads to altered kinetics of the renin-angiotensin system. J Biol Chem 1995;270:11430-11436.
20. Brennecke SP, Gude NM, Di Iulio JL. Reduction of placental nitric oxide synthase activity in pre-eclampsia. Clin Sci (Lond) 1997;93:51-55.
21. Banyasz I, Bokodi G, Vannay A. Genetic polymorphisms of vascular endothelial growth factor and angiopoietin 2 in retinopathy of prematurity. Curr Eye Res 2006;31:685690.
22. Papazoglou D, Galazios G, Koukourakis MI. Vascular endothelial growth factor gene polymorphisms and preeclampsia. Mol Hum Reprod 2004;1 0:321-324.
23. Foidart J, Hustin J, Dubois M. The human placenta becomes haemochorial at the 13th week of pregnancy. Int J Dev Biol 1992;36:451-453.
24. Helewa ME, Burrows RF, Smith J, (Eds), et al: Report of the Canadian Hypertension Society Consensus conference: Definition, evaluation and classification of hypertensive disorders in pregnancy. Can Med Assoc J 1997;157:715-725.
25. Jauniaux E, Watson A, Hempstock J. Onset of maternal arterial blood flow and placental oxidative stress. A possible factor in human early pregnancy failure. Am J Pathol 2000;157:21112122.
26. Perkins AV. Endogenous anti-oxidants in pregnancy and preeclampsia. Aust N Z J Obstet Gynaecol 2006;46:77-83.
27. Wickens D, Wilkins MH, Lunec J. Free radical oxidation (peroxidation)products in plasma in normal and abnormal pregnancy. Ann Clin Biochem 1981;1 8:158–162.
28. Canto P, Canto-Cetina T, JuarezVelazquez R. Methylenetetrahydrofolate reductase C677T and glutathione Stransferase P1 A313G are associated with a reduced risk of preeclampsia in MayaMestizo women. Hypertens Res 2008;3 1:1015–1019.
29. Gebhardt GS, Peters WH, Hillermann R. Maternal and fetal single nucleotide polymorphisms in the epoxide hydrolase and gluthatione S-transferase P1 genes are not associated with pre-eclampsia in the Coloured population of the Western Cape, South Africa. J Obstet Gynaecol 200 4;24:866-872.
30. Laasanen J, Romppanen EL, Hiltunen M. Two exonic single nucleotide polymorphisms in the microsomal epoxide hydrolase gene are jointly associated with preeclampsia. Eur J Hum Genet 2002;10:569-573.
31. Kramer MS, Platt RW, Wen SW, et al. A new and improved population-based Canadian reference for birth weight for gestational age. Pediatrics. 2001, 108: E35-10.1542/peds 108.2.e35.
32. Ohta K, Kobashi G, Hata A. Association between a variant of the glutathione Stransferase P1 gene (GSTP1) and hypertension in pregnancy in Japanese: interaction with parity, age, and genetic factors. Semin Thromb Hemost 2003;2 9:653-659.
33. Descamps OS, Bruniaux M, Guilmot PF. Lipoprotein metabolism of pregnant women is associated with both their genetic polymorphisms and those of their newborn children. J Lipid Res 2005;4 6:2405-2414.
34. Kim YJ, Williamson RA, Chen K. Lipoprotein lipase gene mutations and the genetic susceptibility of preeclampsia. Hypertension 2001;3 8:992-996.
35. Atkinson KR, Blumenstein M, Black MA. An altered pattern of circulating apolipoprotein E3 isoforms is implicated in preeclampsia J Lipid Res 2009;50:7180.

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