

## Study of Plasma Metanephrine Level As Biochemical Parameter in Pregnant Women with Preeclampsia

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### Abstract:

Pregnancy- including hypertension(PIH), also known as preeclampsia, is one of the major causes of maternal and fetal death. This study was carried out on 30 pregnant women with preeclampsia and 30 healthy pregnant women as control ranging in age mean  $\pm$ SD (28.84 $\pm$ 3.55) years , BMI (26.80 $\pm$ 9.78) Kg/m<sup>2</sup> and gestation age(30.82 $\pm$ 0.75)week.

The aim of this research was studied the plasma Metanephrine level and other biochemical parameters such as Hemoglobin(Hb), serum Protein, S. Albumin, Globulin, Albumin/Globulin ratio (Alb/Glu. ratio), S.Glutamate Pyruvate aminotransferase (GPT), S.Glutamate Oxaloacetate aminotransferase(GOT). The obtained results have been compared with 30 healthy pregnant women as control group. The result showed that there was significant increase in mean value of Hb in group A(pregnant women with preeclampsia) when compared to group B(healthy pregnant women). The present study showed no significant changes was observed in the level of S. Protein, globulin, Alb./Glu. ratio, GPT and GOT as compared to control group. While Albumin showed a significant decrease in group A(pregnant women with preeclampsia) when compared with group B(healthy pregnant women) and significant increase in the levels of metanephrine, metanephrine/protein ratio, metanephrine/Alb ratio in group A (pregnant women with preeclampsia) to group B(healthy pregnant women).The present study conclude that the increase in the levels of metanephrine, metanephrine/protein ratio, metanephrine/Alb ratio in pregnant women with preeclampsia may be used as a marker to evaluate the development of disease. The current study recommend to take more case and measurement metanephrine in plasma and urine.

**Key word: Preeclampsia, Hemoglobin, Metanephrine, S. Protein, GPT, GOT, Albumin, Globulin .**

### Introduction:

Hypertensive diseases in pregnancy are of the main reasons of maternal, fetal and neonatal morbidity and mortality. Since preeclampsia is a multisystem disorder with different clinical characteristics, prevention, diagnosis and therapy of this disease require a close interdisciplinary cooperation[1,2].Preeclampsia is a multisystem disease unique to human pregnancy characterized by

hypertension and organ system involvement[3]. The disease is responsible for considerable morbidity and mortality, complicating 5-8% of pregnancies. Death are due to intracranial hemorrhage and cerebral infraction[4], acute pulmonary oedema, respiratory failure and hepatic failure or rupture. Sever maternal complications include antepartum hemorrhage due to placental abruption,

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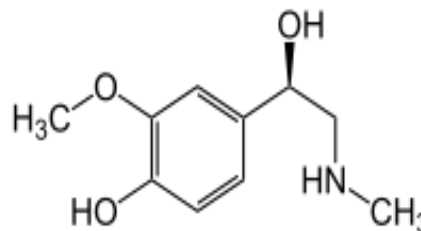
eclampsia, cerebrovascular accidents, organ failure and disseminated intravascular coagulation. Preeclampsia is the leading cause of fetal growth restriction, intrauterine fetal demise and preeclampsia birth[5]. Women who experience preeclampsia are at increased risk of hypertension, cerebrovascular disease and ischaemic heart disease, in later life[6]. Anaesthetists are frequently involved in the multi-disciplinary management of critically ill women with preeclampsia, and clinical practice should be based on current scientific evidence[7].

Abnormal liver function test occur in 20% to 30% of pregnancies complicated by preeclampsia[8] and are associated with poor maternal and fetal outcomes. However, there is no consensus as to which levels are abnormal. GOT and GPT levels do not change during uncomplicated pregnancy and the same as the non-pregnant values[9].

Acute clinical symptoms that danger fetus life in preeclampsia correlate with distinct activity of GOT and GPT[10].

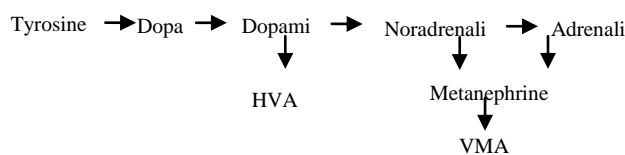
The plasma free metanephrine test measures the amount of metanephrine and normetanephrine in the blood. These substance are metabolites of epinephrine(adrenaline)and norepinephrine. Epinephrine and norepinephrine are catecholamine hormones that help regulate the flow and pressure of blood throughout the body and play Catecholamines are produced in the medulla- the interior protein of the adrenal glands and secreted into the blood. Once these hormones have completed their actions, they are metabolized to inactive compound. Norepinephrine breaks down into normetanephrine and vanillymandelic acid (VMA) and epinephrine becomes metanephrine see figure(1), and VMA. Both of the

catechol amines and their metabolites are normally found in small fluctuating quantities in the blood and urine[11].



**Fig.(1): metanephrine or 4-(1-hydroxy-2-methylamino-ethyl)-2-methoxy-phenol**

Metanephrine is produced in the pathway[12]:



This study aimed to evaluate metanephrine as a marker in pregnant women with preeclampsia also study the of other biochemical parameters such as hemoglobin, total protein, serum albumin, serum globulin, enzymes GOT and GPT in pregnant women who develop preeclampsia .

### Material and Method:

The present study comprises of 30 who were pregnant women with preeclampsia admitted to the pregnancy care centers located in many areas of the city of Baghdad, and 30 healthy pregnant women as control ranging in age mean  $\pm$  SD (28.84 $\pm$ 3.55) years. The subjects with obesity, diabetes mellitus under medication and untreated diabetes, Severely anaemic (<7.0gm% of Hb) and those Suffering from any other systemic disorder were excluded from the study. Analysis of variance followed by taking 5ml of blood have been collected into two tubes, one containing EDTA for measurement of blood hemoglobin (Hb), WBC count. The plasma was

separated by centrifugation at 3000 rpm for 15 minutes, then transferred immediately to a clean dry plain tube and anticoagulant tube for measuring metanephrine. The blood in the second part was allowed to clot for at least 10-15 min. at room temperature, centrifuged for (10) min. at (4000xg). Serum was removed for the measurement of biochemical parameters. Serum protein and albumin level were measured by spectrophotometric methods supplied by Bio. labo., France. The GOT and GPT levels in human serum by spectrophotometric methods supplied by Randox kit. Serum globulin concentration was determined mathematically from the subtraction the value of albumin concentration from that of total protein. The concentration of albumin divided by the concentration of globulin was expressed as albumin to globulin ratio. The plasma metanephrine were

measured by Enzyme Linked Immunosorbent Assay (ELISA)

All statistical analyses in studies were performed using SPSS version 17.0 for Windows (Statistical Package for Social Science, Inc., Chicago, IL, USA). Descriptive analysis was used to show the mean and standard deviation of variables. The significance of difference between mean values was estimated by Student T-Test. The probability  $P < 0.05$  = significant,  $P > 0.05$  = non-significant. Correlation analysis was used to test the linear relationship between parameters.

### Result and Discussion

The results were observed as follows of 30 pregnant women with preeclampsia, 30 normal pregnant woman were serve as Control group . Demographic distribution of groups of women according to definite characteristics were shown in table 1 .

**Table 1: The mean and standard deviation of Age, weight and Gestation age in group A [pregnant women with preeclampsia], group B [healthy pregnant women].**

Characteristic	Group A[n=30]	Group B[n=30]	P Value
Age[year] Mean $\pm$ SD Range	31.88 $\pm$ 3.86 27.00-39.00	28.84 $\pm$ 3.55 26.00-37.00	>0.05
Weight[Kg] Mean $\pm$ SD Range	78.07 $\pm$ 10.43 62.50-90.00	76.80 $\pm$ 9.78 68.00-83.00	>0.05
Gestation age [Week] Mean $\pm$ SD Range	30.51 $\pm$ 0.92 25.5-32.50	30.82 $\pm$ 0.75 25.20-33.00	>0.05
Systolic blood pressure[ mm Hg]	179.12 $\pm$ 5.33	118.33 $\pm$ 6.33	<0.001
Diastolic blood pressure[ mm Hg]	107.10 $\pm$ 5.87	81.00 $\pm$ 6.20	<0.001

\*Significant at 0.05 level of significance.

There was A significant increase [ $p < 0.05$ ] in mean value of Hb in group A [pregnant women with preeclampsia] when compared to group B [healthy pregnant women] as shown in table 2. In women who have hypertensive disorders of pregnancy, particularly those with preeclampsia, blood volume does not increase, which results in a relatively higher hemoglobin concentration. In the study

by Pritchard et al [13,14], the average hematocrit for women with preeclampsia was 0.405, compared with a mean of 0.374 for women with a normal pregnancy. This difference in hematocrit is equivalent to a 20 g/L difference in hemoglobin and shows the extent of the sever failure of plasma expansion due to preeclampsia. Several other studies showed that higher hemoglobin concentration

during pregnancy result from hypovolemia or hemo concentration, which is usually the result of preeclampsia or pregnancy- induced hypertension[15,16].

The mean levels of sera protein ,globulin, Alb/Glu ratio ,GPT and GOT showed no significant change in group A[pregnant women with preeclampsia] comparing to group B [healthy pregnant women] , while albumin showed a significant decrease in group A when compared with group B(  $P<0.01$ ) as shown in table 2. During pregnancy, albumin decreases and changes over time[17]. This is explained by an increase in

plasma and interstitial volume, and possibly by an increase in albumin metabolism. Moreover, albumin is lower in women with preeclampsia than in healthy pregnant women [18].Increased capillary permeability secondary to endothelial damage seems to be partly responsible for this finding[19].

There were A highly significant increase in mean levels of Metanephrine, Metanephrine/protein ratio and Metanephrine/albumin ratio in group A[pregnant women with preeclampsia]comparing to group B [healthy pregnant women]  $P<0.001$ ) as shown in table 1 and figure 1

**Table 2: The mean and standard deviation of Hb ,protein , albumin,globulin,Alb/Glu.ratio,GOT,GPT,Metanephrine,Metanephrine/protein ratio and Metanephrine/albumin ratio in group A[pregnant women with preeclampsia],group B [healthy pregnant women].**

Characteristic	Group A[n=30]	Group B[n=30]	P Value
Hb(g/dl)	11.57 ± 0.78	10.13 ± 0.83	<0.05
T.S. Protein[g/dl]	6.03 ± 0.73	6.22 ± 0.43	>0.05
S.Albumin [g/dl]	3.81±0.69	4.20±0.27	<0.01
S. Globulin [g/dl]	2.22±0.65	2.02±0.47	>0.05
Alb./Glu. ratio	1.94 ±0.90	2.20±0.57	>0.05
S.GOT [IU/L]	16.40 ± 2.51	14.53± 2.86	>0.05
S.GPT[IU/L]	14.50 ± 2.30	14.33 ± 2.39	>0.05
P. Metanephrine[Pg/dl]	91.24 ± 18.89	40.06 ± 7.46	<0.001
Metanephrine/protein ratio	14.71 ± 3.04	6.79 ± 1.81	<0.001
Metanephrine/Albumin	21.82 ± 4.77	10.93 ± 3.29	<0.001

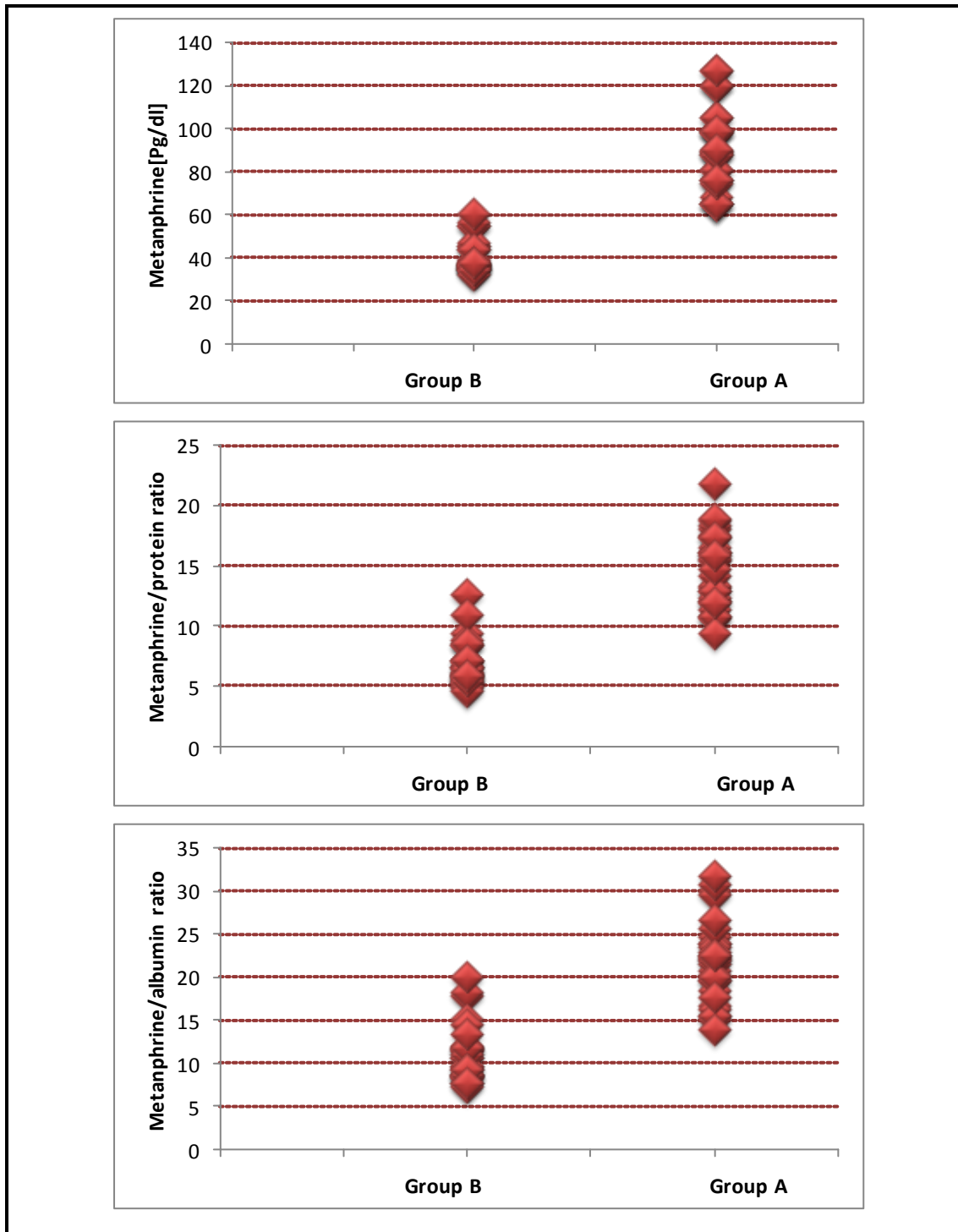
\*Significant at 0.05 level of significance.

Norepinephrine is converted to epinephrine by phenyl ethanolamine N-methyltransferase (PNMT); cortisol serves as a cofactor for phenyl ethanolamine N-methyltransferase, and this is why epinephrine-secreting pheochromocytomas are almost exclusively localized to the adrenal medulla. Metabolism of catecholamines occurs through two enzymatic pathways. Catechol-O-methyltransferase (COMT) converts epinephrine to metanephrine and norepinephrine to normetanphrine by meta-O-methylation[20].

Metanephrine and normetanphrine are oxidized by monoamine oxidase (MAO) to vanillymandelic acid by oxidative deamination. Monoamine oxidase also may oxidize epinephrine and norepinephrine to dihydroxymandelic acid, which is then converted by catechol-O-methyltransferase to vanillymandelic acid. Dopamine is also metabolized by monoamine oxidase and catechol-O-methyltransferase, with the final metabolite homovanillic acid[20].Plasma metanephrine and normetanphrine levels are low, and the

increase in the concentrations may be due to the relatively long half-life of these compounds, ongoing secretion by the cells and, to a lesser degree, peripheral conversion of secreted catecholamine into metanephrine .In

these cases, repeat plasma and urinary metanephrine testing, additional measurement of plasma or urinary catecholamine, or imaging procedures might be indicated.



**Fig.1: Mean distribution of Metanephrine, Metanephrine/protein ratio and Metanephrine/albumin ratio in group A [pregnant women with preeclampsia], group B [healthy pregnant women].**

The present study conclude that the increase in the levels of metanephrine, metanephrine/protein ratio, metanephrine/Alu ratio in pregnant women with preeclampsia may be used as a marker to evaluate the development of disease..

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## دراسة مستوى بلازما ميتنافرين كدالة كيموحيوية عند النساء الحوامل المصابات بارتفاع ضغط الدم

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### الخلاصة:

ان ارتفاع ضغط الدم المصاحب للحمل الذي يعرف بأسم preeclampsia يعد أحد الأسباب الرئيسية لوفاة الأم والطفل الحديث الولادة. شملت هذه الدراسة 30 حالة مرضية (النساء المصابات بارتفاع ضغط الدم المصاحب للحمل) و30 حالة طبيعية (نساء غير مصابات بارتفاع ضغط الدم المصاحب للحمل) تراوحت معدل أعمارهن (28.84±33.5) سنة ومعدل كتلة الجسم (76.80 ± 9.78) كغم/م<sup>2</sup>، فضلاً عن معدل مدة الحمل (30.82±0.75) اسبوع. يهدف البحث الحالي الى دراسة مستوى الميتانفرين اضافة للتغيرات الحاصلة بمستويات كل من الهيموغلوبين، البروتين الكلي، اليومين مصل الدم، كلوبيولين مصل الدم، الألبومين، أنزيم الاسبارتيت أمينو ترانسفيريز، أنزيم الألبومين، أنزيم الميتانفرين/الألبومين. أشارت النتائج الى وجود اظهرت الدراسة زيادة معنوية ملحوظة في مستوى الهيموغلوبين عند المجموعة A (النساء المصابات بارتفاع ضغط الدم المصاحب للحمل) مقارنة بالمجموعة B (نساء غير مصابات بارتفاع ضغط الدم المصاحب للحمل)، في حين لا يوجد تغير معنوي ملحوظ في مستويات كلا من البروتين الكلي، الكلوبولين، نسبة الألبومين/الكلوبيولين، أنزيم الاسبارتيت أمينو ترانسفيريز، أنزيم الألبومين، أنزيم ترانسفيريز مقارنة بالمجموعة الضابطة. في حين وجد نقصان ملحوظ في مستوى الألبومين في المجموعة A (النساء المصابات بارتفاع ضغط الدم المصاحب) مقارنة بالمجموعة B (نساء غير مصابات بارتفاع ضغط الدم المصاحب للحمل) وكذلك زيادة ملحوظة في مستويات كل من الميتانفرين، ونسبة الميتانفرين/البروتين الكلي ونسبة الميتانفرين/الألبومين في المجموعة A (النساء المصابات بارتفاع ضغط الدم المصاحب للحمل) نسبة الى المجموعة B (نساء غير مصابات بارتفاع ضغط الدم المصاحب للحمل). تستنتج الدراسة الحالية الى امكانية استخدام الزيادة في مستويات، ميتانفرين، نسبة ميتانفرين/البروتين، نسبة نسبة ميتانفرين/الألبومين، لدى النساء الحوامل والمصاب بارتفاع ضغط الدم كعلامة لتقييم وضع المرض. توصي الدراسة الحالية بأخذ المزيد من النساء الحوامل المصابات بارتفاع ضغط الدم اضافة الى قياس مستوى الميتانفرين في الادرار.