International Journal of Medicine Research
ISSN: 2455-7404; Impact Factor: RJIF 5.42
Received: 01-01-2020; Accepted: 03-02-2020; Published: 05-03-2020
www.medicinesjournal.com
Volume 5; Issue 1; January 2020; Page No. 109-113

Human chorionic ganadotropllin level as predictor of preeclampsia in Al-Zahra teaching hospital

Dr. Entessar Abd Al-Rassol[1], Dr. Saba Fouad Abd Al-Razak[2]
[1, 2] Al- Karkh Healthe Directorate, Baghdad, Iraq

Abstract
Background: Preeclampsia is a form of hypertension disorder of pregnancy is characterized by development of concurrent hypertension and proteinuria sometimes progressing into a multiorgan cluster of varying clinical feature. Many biochemical markers of preeclampsia have been recognized in maternal serum one of them is serum Beta human chorionic gonadotrophin.
Aim of the study: To evaluate the level of HCG in the detection of severity of preeclampsia
Study & design: Prospective cross section study of maternal human HCG level in patient with preeclampsia comparison with the control group in AL- Zahra teaching hospital
Material& Method: The patient included in this study will be divided into two group, 50 control group who are normotensive and 50 preeclamptic patient which further divided into mild and sever A complete clinical history was taken from each woman including maternal age, parity, gestational age, and other questions related to this condition and blood sample was taken for biochemical and hematological investigation. the blood samples were centrifuged for 15 minutes, sera collected &stored in deep freeze until the assay was performed in the same laboratory by ELISA (enzyme linked immune sorbent assay) and sent for liver function test, renal function test, complete blood picture and HCG
Results: There is no significant difference were observed in age and parity of preeclamptic group in comparison with the control group there is significant in relationship in the systolic, diastolic blood
pressure and body mass index between preeclampsia group &the control group (and the SGOT, SGPT, blood urea serum creatinine, serum uric acid significantly increase in preeclampsia group in comparison with the control group(pevalue <0.001) but there is no significant difference in the level of ALP &TSB between 2 groups and there is significant increment in the hCG level between preeclampsia and control group and there is further significant increment in the hCG level between sever preeclampsia and mild preeclampsia
Conclusion: Serum HCG level may be involved in the pathophysiology of preeclampsia and it can be used as a marker to detect the severity of preeclampsia.

Keywords: preeclampsia, pathophysiology, serum

Introduction

Hypertension is defined as a change of blood pressure recorded on at least two occasions 6 hourly apart with or without proteinuria before or after 20 week gestational age. diastolic blood pressure 90mmHg and systolic blood pressure 140 mmHg [1] Hypertension disorder in pregnancy can be diagnosis by 1-Either arise in diastolic blood pressure of more than or equal to 15mmHg or systolic blood pressure more than 30 mmHg or.
2-Diastolic blood pressure of equal or more than 90mmHg on two occasions four hours apart or 110mmHg on one occasion and proteinuria [2]

Criteria for the diagnosis of proteinuria

Protienuria is present when the urinary protein concentration is greater than 300mg during 24hours period. The 24 hours urine collection is the definitive test for the diagnosis of proteinuria; however,if it is not available, the concentration of at least 30mg /dl (at least l+on dipstick testing) in at least two random urine samples collected at least 6 hours apart may be used.

[3] Pre-eclampsia is an idiopathic disorder of pregnancy characterized by proteinuric hypertension Recent estimates indicate that over 63000 women die worldwide each year because of preeclampsia and its complication ;with 98% of these occurring in developing countries [4]. In the UK preeclampsia is the second largest cause of both direct maternal and perinatal loss, responsible for the death of six to nine women annually and over 175 babies more than10% of women will develop preeclampsia in the first pregnancy and although the over whelming majority of these will hare successful pregnancy out comes, the condition can give rise to severe multisystem complication including cerebral hemorrhage, hepatic and renal dysfunction and respiratory compromise, The development of strategies to prevent and treat the disorder has been challenging due to an incomplete understanding of the underlying pathogenesis [5]
classification The general classification of hypertensive disorder recommended by the working group repot on High blood pressure in pregnancy 2000 and adopted by the American college of obstetricians —Gynecologists [ACOG] IN 2002

Box 1-1

General classification of Hypertensive disorders of pregnancy:

+ Preeclampsia or eclampsia [hypertension and proteinuria unique to pregnancy

+ Chronic hypertension

+ Chronic hypertension with superimposed preeclampsia

• Gestation or transient hypertension without protienureia

Based on National institutes of health working Group Report of High blood Pressure in pregnancy 2000. (6)

Classification of Hypertensive disorder during pregnancy

Gestational hypertension It is an elevated blood pressures about 140/90 mmHg taken while the patient is seated after 20 WKs gestation age in previously norrnotensive non-protienuric woman and resolves within 6WKs after birth. It affects 6-7% of pregnancies with increased risk of developing pre eclampsia 15-26%.

Chronic hypertension is defined as hypertension present before conception, before 20WKs gestation or persisting more than 6wks postpartum and it complicate 3-5% of pregnancies. Superimposed pre eclampsia on chronic hypertension is defined as onset of new signs and symptoms of preeclampsia after 20wks gestation in woman with chronic hypertension [new onset proteinuriam

Preeclampsia Is a multi-system disorder characterized by hypertension, proteinuria and non-dependent edema, it can present in a wide variety of way and not always in the classical fashion, it is a leading cause of mortality, morbidity and common cause of prematurity and hospital admission and it remains a relatively common cause of death in pregnancy in the developed world [8] It is subdivided into

1. **Mild pre eclampsia:** Defined as third trimester blood pressure greater than 140/90 mmHg accompanied by proteinuria greater than 300mg/24 hr, or 2p1us on dipstick and non-dependent edema [face and hand].
2. **Sever preeclampsia:** Defined as increase blood pressure greater than 160/110 mmHg accompanied by proteinuria greater than 5gm /24 hr(or3+to 4) protein on dipstick on two occasion or mild preeclampsia that developed certain associated symptom like altered consciousness, Headache, Visual changes, Epigastric pain, Right upper quadrant pain, Oliguria [400m1 in 24hours, pulmonaryedema, thrombocytopenia (platelets 100,000/ mm3 and eclampsia [9, 10]

Incidence of preeclampsia

Preeclampsia complicated 3-5% of first pregnancies and 1% of subsequent pregnancy with around 5-10% of cases being sever [11] The increase in incidence of pregnancy induce hypertension however over the age of 35 years probably reflect undiagnosed chronic hypertension with superimposed pregnancy induced hypertension [2]

Pathophysiology

Preeclampsia is mainly a systemic endothelial disorder as causing activation of platelets and diffuse ischemic disorder whose most obvious clinical manifestations involve the kidney (hence the proteinuria, edema and hyperuricemia), the liver (hence the hemolysis, elevated liver enzymes and low platelets, or HELLP syndrome)and the brain (hence eclamptic convulsions). Hypertension is explained by increased vascular reactivity this is due to endothelial dysfunction with imbalance between prostacyclin and thromboxane A2 The aggressive substances for endothelium are thought to be placental in origin and the cause of their release is explained by placental ischemia related to a defect of trophoblastic invasion of spiral arteries, the etiology of this later defect is unknown but involve immunogenic mechanism with genetic predisposition. In nulliparous the selection of high —risk population is still a subject of research. The two most promising criteria are abnormal Doppler velocimetry of uterine arteries at around 20Thweek of amenorrhea and abnormally high plasma levels of beta HCG at 17 the week of amenorrhea [13]. The term pregnancy induced hypertension has not been discarded, because development of hypertension especially in nulliparous cannot be differentiated from transient hypertension except retrospectively." Most current hypotheses regarding the pathophysiologic mechanism of pregnancy induced hypertension point to early placental abnormalities. Consequently, management is directed towards detection of the disorder at an early stage and to effect, or at least ameliorate progression in an attempt to achieve fetal maturity while preventing maternal complications [15].

Risk factor

1. 1-Maternal risks First pregnancy, new partner, age younger than 18 years, or older than 35, history of previous preeclampsia, Family history of pre eclampsia in first degree relative, black race, secondary causes of hypertension such as; hypercortisolism, hyperaldosteronism, pheochromocytoma, or renal artery stenosis, Preexisting diabetes (typel, typell), obesity, thrombophilia, systemic lupus erythromatosus and Renal disease.
2. Fetal /placental: - Multiple gestation, non-immune fetal hydrops, and hydatiformmole

HCG

HCG is glycoprotein with lipid structure that expressed in trophoblast and various malignant tumor, physiological concentration of HCG significantly increased in vitro capillary formation and migration of endothelial cell in a dose dependent manner and has a novel function in uterine adaptation to early pregnancy [16]. HCG is a double chain glycoprotein consisting of an alpha subunit chain of amino acid and beta subunit chain of amino acid. HCG is closely related to other gonadotrophins luteinizing hormone (LH) and follicle stimulating hormone FSH [17], As well as in embryos as early as the 6-8 cell stage and is secreted by syncytotrophoblast of the placenta in to both the fetal and maternal circulation [18]. In a 28 day cycle with ovulation occurring at day 14, HCG can be detected in urine or serum in minute quantities around day 23 or 5 days before the expected menstruation. Its function includes facilitation of implantation as well as maintenance and development of the corpus luteum [17]. HCG stimulates both adrenal and placental steroidogenesis by providing the fetal test with increasing level of testosterone that induce virilization and sexual differentiation in males [19]. HCG plasma level rise rapidly, doubling approximately every 2-3 day and peak around 100,000 mIU/mI and in the later part of the first trimester of pregnancy. At 3-4weeks gestation the mean doubling time of HCG is 2(+/-) 1.5 days at 9-10 weeks. The average peak HCG level is approximately 110,000 mIU/M1 and occur at10 weeks of gestation [20] HCG secretion is related to the mass

of HCG has secreting trophoblastic tissues. In vivo, the release of HCG has been correlated with the widths of trophoblast tissue from 4-20 weeks and with placental weight from 20-38 week coincide with the proliferation of immature trophoblastic villi and the extent of the syncytial layer. As expected the declining HCG levels are associated with a relative reduction in the mass of the synytiotrophoblat and cytotrophoblastic tissue and gradual increase in dimeric HCG correspond with a similar increase in placenta weight and villas volume [19]. The level continue to fall from 16 to 22 week at a slower rate to become approximately 10% of first trimester value however, during the third trimester mean HCG level rise in gradual, significant manner is started from 22 weeks until term [18] Therefore, HCG level mirror the placental morphologic transformation from an organ of invasion to an organ of transfer in fact level of the beta subunit of HCG is mirror to those of dimeric HCG. The alfa-subunit is undetectable until around 6 weeks gestation, this rises is in sigmoid fashion to reach peak level at 36week [19]. Respecting to the regulation of production and secretion HCG secretion appears to be related to

1-Placenta GnRH release plasma. In vitro HCG is released in pulses at a frequency and amplitude that correlates with the release of placenta GnRH

2- HCG production is stimulated by glucocorticoid and In vitro cyclic AMP (c AMP) analogues and the decidua-derived active in augment HCG secretion [20]. Because the possible role of HCG in pathophysiology of preeclampsia is not well understood and change in its level can reflect the placental reaction to the preeclampsia, we are promoted to determine correlation of serum concentration of B HCG and preeclampsia [6].

Material and Method

This study was done in Al-Zahra teaching Hospital between April 2012 to September 2012. at this time 100 pregnant women at term pregnancy between 3740 weeks admitted to the hospital were included in the study after written consent from each women with explaining the purpose of our study, 50 of them had normal pregnancy and regarded as a control group and 50 of them had hypertension disorder of pregnancy and regarded a study group. The study group was further subdivided in to 31 patient who have mild preeclampsia (the blood pressure 140 / 90) and 19 of them have severe preeclampsia (when patient had blood pressure more than 160 / At time of admission a complete clinical history was taken from each women including maternal age, parity, gestational age, and other questions related to this condition and then ask about any symptom of severe preeclampsia headache, epigastric pain and blurred visiono Clinical examination was done to the patient including checking BP, measured in sitting position with suitable arm cuff with patient at rest using mercury sphygmomanometer, BMI of patients calculated by weight in kg divided by height in fundal height and urine for albumino Blood sample was taken for biochemical and hematological investigation blood samples were centrifuged for 15 minutes, sera collected and stored in deep freeze until the assay was performed in the same laboratory by ELISA (enzyme linked immune sorbent assay) [22] and sent for liver function test,renal function test, complete blood picture hCG. The following condition were excluded: multiple pregnancy, chronic hypertension, diabetes mellitus chronic renal disease and other systemic disease in the selected lady.

Statistical analysis

Statistical analysis was done by using SPSS (statistical package for social sciences) version 1 T We use independent sample T-test to measure the difference between two measurement data and use analysis of variance (ANOVA) to measure the difference between more than two measurements data. We set P value <0.05 as significant.

Results

Table 1: comparison between preeclampsia and control in different Variables.

Characteristic	Normal(50)	Mild pe (31)	Sever pe (19)	P Value
	Mean± sd	Mean±SD	Mean±SD	
Age	25.02±5.516	26.45±60521	28.58±60727	0.069
Para	1.10±1.515	1.21±1.436	1.13±1.383	0.282
Systolic blood pressure	115.50±6.095	144.03±5.231	165.53±6.432	<0.001
Ediastolic blood pressure	70.30±5.556	94.35±4.608	107.63±8.558	<0.001
Body mass index	27.100±2.1783	28.681±2.1384	30.33±3.9719	<0.001

- No significant difference were observe in age and parity of preeclampsic group in comparison with the control group
- There is significant in relationship in the systolic diastolic blood pressure and body mass index between preeclampsia group & the control group (p-value<0.001)

Table 2: comparison between cases and controls in different lab.

Characteristic	Normal (50)	MILD (31)	Sever Pe (19)	P Value
	Mean±SD	Mean±SD	Mean±SD	
SGOT	26.62 ±6.250	32.77±8.582	33.84±9.564	<0.001
SGPT	17.04±4.389	19.32±3.970	21.16±6.768	0.003
ALP	201014±490955	202052±34.662	211.22±34.640	0.593
Blood UREA	24.42±4.440	28.58±8.445	23.32±8.327	<0.001
Serum Creatinine	0.7620±0.21466	0.9613±0.20925	1.0700±0.18616	<0.001
Sreum Urid	4.1170±0.93617	408455±1027006	5.5879±1.08043	<0.001
TSB	0.6560±0.20389	0.5468±0.22499	0.6189±0.23709	0.063

In this table the sgot, sept, blood urea serum creatinne. Serum uric acid signi Fcantly increase in preeclampsia group in comparison with the control group (p-value <0.001) but there is no significant difference in the level of ALP&TSB between 2 group.

Table 3: demonstrate the difference in the HCG level between preeclampsia and controls.

Characteristic	Normal (50)	Mild PE (31)	Sever PE (19)	P Value
	Mean±SD	Mean ± SD	Mean±SD	
HCG	24424.56±5980.0692	7668032±51226.275	116796.26±59210.189	<0.001

Table 4: comparison between mild and sever PE regarding HCG.

Characteristic	Mild PE(31)	Sever PE(19)	P Value
	Mean±SD	Mean±SD	
HCG	7668032±51226.275	116796.26±59210.189	0.001

There is significant increment in the HCG level between preeclampsia & control group as show in the table number.3 and there further significant increment in the HCG level between sever preeclampsia and mild preeclampsia.

Discussion

Preeclampsia remains a leading cause of maternal and prenatal morbidity and mortality. It is a pregnancy specific disease characterized by development of concurrent hypertension and proteinuria, sometimes progressing into a multiorgan cluster of varying clinical features. Because our hospital is a referral center, the rates of sever preeclampsia were higher than generally expected for overall pregnant population. In table number 1. There is a significant increase in body mass index between preeclampsia group & the control group (p-value<0.001). This result has an agreement with Voigt *et al* (2008) [24] who found that 37.9% patients in the BMI >30 category had preeclampsia and 1.2% in the BMI <25 category had preeclampsia [23] In our study the SGOT, SGPT, blood urea, serum creatinin and serum uric acid significantly increases in preeclampsia group in comparison with the control group (p-value <0.001) this agree with Tayar *et al*. who found deterioration in renal function test represented? By increase B. urea. S. creatinine and uric acid that all due to ischemic changes in organ, arterial constriction, endothelial swelling and intravasation fibrin deposition all that explain the deterioration of renal function which increase with severity of preeclampsia [24, 25]. Also, there is significant increment in the HCG level between preeclampsia & the control group as shown in the table number.3 and there further significant increment in the HCG level between sever Preeclampsia and mild preeclampsia. This comparable with the Zahra Basirat study [26, 27] who match 40 term that a higher s. HCG level can be a helpful marker in the detected of severity of preeclampsia [28, 29].

Conclusion

The result of study showed that the level of s.hcg in both form of preeclampsia (sever &mild) is higher compared to normal cases, also this elevation was higher in sever than in mild form, so a high s. HCG level can be a helpful marker in the detected of severity of preeclampsia [30].

Recommendation

Our study elevated HCG level in preecamptic patient so we suggest:

1. The measurement beta HCG in booking visit to help in early diagnosis of patient at risk of patient at risk of preeclampsia to assist proper monitoring and management.
2. Serum HCG level can a helpful marker in the diagnosis and management of this disease to identify a subgroup of preeclampsia patient who need intensive observation.

References

1. Interational Students Edition Obstetrics by Ten Teachers 19thedition Edited by Philip N Baker and Louise Kenny, 2011-10-p122.
2. William B, Poulter NR, Brown MJ, Davis M, Meinne GT, Potter TF, *et al*. Guideline for management of the fourth working party of the British hypertension society, 2004 BHJ. JHUM Hypertensions, 2004; 18:139-85.
3. Duley L; preeclampsia and the hypertensive disorder of pregnancy.Br. Med Bull, 2003, 6.
4. Word Health organization Trend in Maternal Mortality, 1990. to 2008 General; WHO, 2010 a valuable at
5. http./.who. int/publi cation/2010/9789241500265 -erg-p df
6. Dew Hursts Text Book of obstetrics and Gynaecology Edited by Ekeith Edmonds Eighth Edition Wiley 11-101
7. Hacker. Editio Gambon. Hobel international Edition HACKER and MOORES Essentials of OBSTETRICS and Gynecology. 2011(fifth edition). CH.14, P 174.
8. Duleyl; preeclampsia and hypertensive disorder of pregnancy.British Med Bull, 2003; 67:161-76. (Medline)
9. Simon J. Pregnancy complication oxford Of obstetrics and gynecology, 2nd.Edi,2010;43.105
10. Bron MA, Wang MX, Buddle M Liet. 91 Albumin execretory rat in normal and hypertensive pregnancy. Clinc. sci-(loud), 1994; 86:25-255,
11. Bron MA, Buddl ML. Hypertensive in pregnancy; Maternal and Fetal outcomes according to laboratory and clinical features. Med. J Aust, 1996; 165:360-365.
12. Robson SC. Hypertensive disorder of pregnancy Dewhurts text book of obstetrics and gynecology of postgraduates, 6th. Edition, 1999, 166-77
13. Hallak Mr. Hypertensive disorders of pregnancy High risk pregnancy management option, second Edition, 1999, 639-699.
14. Onderoglu LS. Elevated 2ndtrimester human chorionic gonadotropin level associated with adverse pregnancy outcome. In JntIGynecolo. obstet. 1997; 56(3)245-9.
15. Gary F. Cunningham; Hypertensive disorder in pregnancy. In Williams obstetrics,20thAppleton and lang, 1997, p;694
16. Fathima Paruk. Treatment of severe preeclampsia/eclampsia syndrome. In progress in

obstetrics and gynecology, Vol.14, churchil Livingston publication, 2000, p; 103.
17. Alexander BT, Ulnas MT, Bennett WA, Khalil RA. Pathophysiology of preeclampsia.Linking placental ischemia /hypoxia with micro vascular dysfunction microcirculation, 2002; 9:147-160.
18. Braunstein GD, Groden JM, Vai Tukait. is and ROSSGR Secretory rate of human chrionicgonadotrphin by Gynecology, 2005; 115:447-50.
19. Verhelst J, Abs RM, Aiter D, *et al*. Cabergolin in the treatment of hyperprolactinemia J Cin Endocrinol Metab, 1999; 84:2518.
20. Scheithauer BW, Sano T Kovacskt, *et al*. the pituitary gland in pregnanc; aclinical pathologic and immune histochemical, mayochin prOc, 2000; 65:461.
21. Kotarba DD, Garner PR, Perkin S. Changes in serum free thyroxin, free tri iodothyronine.thyroid stimulating hormone reference intervals in normal term pregnancy J Obstet G ynecol, 1995; 15:5.
22. Interational Students Edition Obstetrics by Ten Teachers 19thedition Edited by Philip N Baker and Louise Kenny, 2011-5-p55.
23. Odell WD, *et al* Pulsatile secretion of chorionic gonadotrophin (HCG); indication and techniques for the clinical laboratory Ann.Clin Biochem, 1990, 27:183-194.
24. Voigt M, Strobe S, Zygmut M, Krafezyk B, Schneider KT, Briese V, *et al*. Obesiy and pregnancy —arisk profile Z Gebutshilfe Neonatal. 2008; 212(6):201-5.
25. Tayor RN, Musci TJ, Kuhn RM, Roberts JM. Partial characterization of a normal growth factor from the blood of women with preeclampsia. Am J, 2011, 1285-91
26. Basirat MD, Shahnazbarat MD, Mahmood Hajiahmadi Saudi, Med, J. 2006; 27(7)1001.
27. Casart YC, Camejo MI, Proverbio F, Febres F, Febres F. Bioactivity of serum HCG in Preeclampsia. Obstet Gynecol, 2001; 98:463-46527.
28. Ramzi Gokdeniz, Erdal Arigulou. Elevated serum BHCG level in sever preeclampsia. Turk J Med. Sci, 2000; 30:43- 45.
29. Hsu CD, Chan DW, Iriye B, Johnson TR, Hong SF, Repke JT, *et al*. Elevated serum chorionic gonadotrophin as evidence of secretary response in sever preeclampsia AM J Obestet Gynecol, 1994; 170:1135-1138.
30. Gurbuz A, Mengulluoglu M, Gedikbasi A, Ozturkmen M, Kabaca, *et al* Can serum HCG values be used in differential diagnosis of pregnancy complicated by hypertension, 2004; 23:1-12.
31. Feng Q, Cui S, Yang W. Clinical significance of HCG and human placental lactogen in serum of normal pregnancies and patient with pregnancy induced hypertion. Zhoghua Fu Chan Ke Za Zhi, 2000; 35:648-650.