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Predictive Value of Raised Midtrimester β-HCG in P.I.H.

Pankaj Desai, Sonal Rao

Dept. of Obst. & Gyn., Medical College & S.S.G. Hospital, Vadodara – 390001.

Summary

Newer applications of HCG are now confined to its immunological face rather than its endocrinal face. In this prospective study we have tried to find out whether HCG can predict pre-eclampsia. Maternal serum HCG at mid-trimester was considered raised if the levels were more than 2 MOM. Sixty two patients (68.9%) with values of βHCG > 2 MOM developed P.I.H. It was found that amongst those who developed PIH with high βHCG did it early in pregnancy – pre-eclampsia remote from term. In this study it was found that HCG was most efficient in predicting this type of pre-eclampsia.

Introduction

The concept of high-risk obstetrics is relatively new. It is indeed a constant endeavour of obstetricians to identify the risk involved in any given pregnancy and if possible predict high risk conditions. If prediction becomes possible, prevention will follow naturally. In recent times seemingly diverse obstetric conditions like recurrent missed abortions, pre-eclampsia remote from term, recurrent still births, IUGR, etc. have been found to have a strong immunological basis (Adinolfi 1986, Desai et al 2000). They are no more thought to be diverse and are grouped under one section of obstetrics.

Human chorionic gonadotropin has been acknowledged as a hormone for years. Recent studies have unraveled its immunological face so much that newer applications of HCG are now confined to the immunological face rather than its endocrinal face. Many reasons have been given for suspecting the role of HCG in predicting immunological conditions in obstetrics (Sayeed et al 1984). In this prospective study we have tried to find out whether HCG can predict pre-eclampsia.

Subjects & Methods

This prospective study was carried out in Dept. of Obst. & Gyn. Medical College and S.S.G. Hospital, Baroda. The main objective was to evaluate the utility of HCG in predicting pre-eclampsia. Subjects enrolled for this study were under two portals

1) Those in whom there was a past history of any one or more immunological conditions
   P.I.H. remote from term
   R.S.A. of missed abortions type
   Recurrent still births
   Accidental hemorrhage
   IUGR

2) Those in whom there was a family history of P.I.H. or those subjects treated for long standing infertility or elderly primi-gravidae of age more than 35 years.

Enrolment was done as early as possible in pregnancy and HCG estimation was done from maternal serum preferably at 15 or 16 weeks of pregnancy. In

Table I
Weeks of pregnancy at which HCG tested

Weeks of Pregnancy	No. of Cases	> 2 MOM	< 2 MOM
15	35	15	20
16	93	32	61
17	23	16	07
18	41	17	24
19	02	01	01
20	26	09	17

instances where the subjects registered after 16 weeks but before 20 weeks, maternal serum HCG was solicited at enrolment. Multiples of medians (MOM) were calculated from charts of norms available for that week of pregnancy. Maternal serum HCG at mid-trimester was considered raised if the levels were more than 2 MOM for that week of pregnancy. The value of 2 MOM is likely to change over a period of weeks therefore accurate determination of gestational age was vital. In all cases the gestational age was reconfirmed by ultrasound to increase the accuracy of results on enrolment. However, no enrolment was done after 20 weeks of pregnancy.

These cases were prospectively followed up for development of P.I.H. defined by-

- Hypertension: as diagnosed by any one of the following criteria on at least two occasions at least 6 hours apart:
  - A rise of 30mm Hg or more in systolic BP, a rise of 15mm Hg or more in diastolic BP, a systolic BP of 140 mm Hg or more, a diastolic BP of 90mm Hg or more.
    B.P. was measured with a cuff that had width of about 40% of the arm circumference, and length encircling 80% of upper arm. Patients were sitting with the right arm horizontally placed at heart level. In lateral decubitus position, the B.P. is 10/20 mm Hg. lower than the true values.
- Proteinuria as diagnosed by urinary protein greater than 300 mgms/dl in a 24-hour urine collection, or greater than 0.1 g/l in a random sample.
- Edema when generalized, greater than 1+ pitting edema after 12 hours rest in bed, or weight gain of 1kg or more in 1 week.
- βHCG estimation was done by ELIZA technique. Results so obtained were evaluated by standard tests of statistical evaluation. They were counter checked on SPSS software.

Results

Two hundred & twenty subjects were enrolled for the study and were completely followed up. This study was carried out between 1st February 1995 to 31st January 2000 over a period of five years.

As shown in table I most of the cases were studied at 15, 16, 17 and 18 weeks of pregnancy. However, 18 of the 2220, who enrolled late, could be studied only at 19 and 20th week.

Table II
βHCG > 2 MOM

	No.
Subjects with βHCG > 2 MOM	90
βHCG < 2 MOM	130

There were 90 mothers with serum βHCG levels > 2 MOM and 130 with < 2 MOM. This is crucial in the light of the fact that the enrolment criteria were same for both the groups.

Table III
Development of PIH

	> 2 MOM		< 2 MOM	
	No.	%	No.	%
PIH developed	62	68.9	21	16.15
No. PIH	28	31.1	109	83.85

At dfl, X^2 significant, $P < 0.001$

Sixty two (68.9%) of the 90 subjects with values of βHCG > 2 MOM (68.9%) developed P.I.H. against 21 of the 130 (16.15%) βHCG < 2 MOM. This difference is statistically significant ($p<0.001$).

Table IV
Duration of pregnancy at which PIH developed

	βHCG > 2 MOM		βHCG < 2 MOM	
Weeks	No.	%	No.	%
> 32 weeks	03	4.8	18	85.71
28-32 weeks	51	82.7	03	14.28
< 28 weeks	08	12.9	00	0.0

At df2, X^2 significant, $P < 0.001$

It was very significant that 59 of the 62 who developed PIH had βHCG levels > 2 MOM. On the other hand 18 of the 21 (85.7%) mothers who developed P.I.H.

with βHCG < 2 MOM did it after 32 weeks. This difference was also highly significant ($p<0.001$).

Discussion

This study was undertaken to examine the possibility of using HCG to predict P.I.H. more so P.I.H. remote from term. Colour Doppler is a sensitive technology for early prediction of P.I.H. (Steel et al 1990). But its accessibility in day to day clinical practice is limited. The age-old tests like roll over test have lost their sheen following quite a few important studies showing their inefficiency. It is therefore necessary to find methods of predicting PIH which are relatively easy to access and reasonably accurate in prediction.

βHCG has now established its immunological face. At the same time pre-eclampsia especially preeclampsia remote from term is now accepted as having a strong immunological basis. We therefore examined the possibility of predicting pre-eclampsia by estimation of maternal serum βHCG. Explanation as to why HCG may rise in PIH given by Helonca et al (1996) who said that this rise was probably a secretory response of the trophoblasts to an immunological insult. Mid trimester is the time around which these changes that produce this response in βHCG levels are becoming overt. Therefore this period was decided upon for the study βHCG levels in PIH by (Hsu et al 1994). It was around this time i.e. 15, 16, 17 or 18th week that this estimation was carried out. It was interesting to find that the rise in levels of βHCG predicted pre-eclampsia fairly well. 68.9% subjects who had high βHCG levels at mid-trimester developed PIH (Yadav & Gupta 1997, Lukas et al 1998). However Jauniax et al (1988), Morsink & Korman (1995) have also shown that maternal serum βHCG has a significant influence in predicting pre-eclampsia. Our results are consistent with those of these workers.

Pre-eclampsia remote from term is a distinct entity. It has a strong immunological basis as has been shown in many studies (Purwar et al 1993, Desai and Desai 1994, Desai et al 2000). In this study it was found that HCG was most efficient in predicting pre-eclampsia remote from term. This is quite understandable, as there is a common immunological link between the two.

However, this is not a case for the indiscriminate use of βHCG in predicting pre-eclampsia for all uncomplicated cases including uncomplicated primigravidae nor do we, in any way, recommend its use for the purpose of mass screening. It seems to have a definite role in cases with specified adverse obstetric outcomes in the past with a strong immunological basis. To what extent is this parameter useful in prognosticating the outcome is not studied herein as our methodology was designed with a specific aim of prediction rather than prognostication.

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