hPL: Physiologic and Pathophysiologic Observations

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Serum human placental lactogen (hPL) levels were studied in 806 women in late pregnancy. The hPL levels were positively correlated with birth weight but were unrelated to maternal age, parity, socioeconomic status, or the sex of the newborn. The hPL levels peaked at 37 weeks' gestation and then declined moderately. An individual's hPL levels in late pregnancy are quite constant week to week. Patients with severe chronic hypertension have low hPL values; those carrying twins have high values.

Despite an extensive literature on serum human placental lactogen (hPL) [also called human chorionic somatomammotropin (hCS)], several basic clinical questions concerning this placental protein hormone remain unresolved.[1] We have recently completed a relatively large study of serial hPL determinations in late pregnancy. The usefulness of hPL as a predictor of perinatal outcome is the subject of a separate report.[2] This paper presents data relevant to the following questions: 1) What is the relationship between hPL levels in late pregnancy and the birth weight of the newborn? 2) What is the pattern of hPL values by week in late pregnancy? 3) How consistent are an individual's weekly hPL values in late pregnancy? and 4) What are the hPL values in certain abnormal conditions of pregnancy?

Materials and Methods

Volunteers from our high-risk clinic and routine antepartum clinics were enrolled in the study from September 1976 through June 1977. The only entry requirements were the presence of a living fetus and the absence of labor. At each antepartum visit from 34 weeks' gestation until delivery, a serum sample was obtained which was analyzed in duplicate for hPL by radioimmunoassay using a standard commercial kit (New England Nuclear). Hospitalized patients had weekly samples taken. The separated serum samples were frozen until analysis. The intraassay coefficient of variation was 3.9%; the interassay coefficient of variation was 13.9%.

The hPL results were not reported. Therefore, obstetric management was not influenced by the serum hPL levels.

Following delivery, data sheets were completed using information provided by the hospital records of the mothers and newborns. Demographic data, identified risk factors, maternal course during pregnancy, fetal surveillance test results, neonatal outcome data, and hPL values were recorded and subsequently transferred to magnetic tape for computer analysis.

Eight hundred six patients with at least 1 hPL determination delivered at University Hospitals. They and their 818 offspring (12 sets of twins) form the study population.

Two hundred forty-two babies were delivered to women whose pregnancies were defined as being at risk prior to labor, because 1 or more of the following had occurred: antepartum admission to the hospital, antepartum fetal heart rate (FHR) testing, urinary estrogen determination, amniocentesis for fetal maturity testing, and/or a Δ optical density (OD) determination at 450 nm. Factors accounting for the at-risk status are listed in Table 1. Risk patients were placed in group 1 if they spontaneously went into labor and were placed in group 2 if delivery was effected because of concern for the mother and/or fetus.

Five hundred seventy-six babies were delivered to women not considered to be at risk prior to labor. They were not admitted to the hospital prior to labor,

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Table 1. Antepartum Factors Accounting for At-Risk Status

Factor	Group 1	Group 2	Total
Postmaturity (known and suspected)	39	20	59
Premature rupture of the membranes	22	31	53
Chronic hypertension	12	19	31
Preeclampsia	6	18	24
Third-trimester bleeding	15	5	20
Diabetes mellitus	1	11	12
Suspected IUGR	10	2	12
Twins	10	0	10
Isoimmunization	4	4	8
Previous cesarean section	10	1	11
Renal disease	3	3	6
Premature labor	4	1	5
Bad obstetric history	2	3	5
Autoimmune disease	3	0	3
Cardiac disease	2	1	3
Other	24	5	29
	167	124	291*

* 242 births—certain patients had multiple risk factors; 576 births occurred in patients who were not at risk antepartum.
IUGR = Intrauterine growth retardation.

nor did they have antepartum FHR testing, urinary estrogen assays, or third-trimester amniocenteses performed. Some of these patients may have been high risk because of maternal age, socioeconomic status, or other factors, but the specific clinical and laboratory measures generally undertaken on our service in pregnancies we consider to be at risk were absent.

If there was a discrepancy between the clinical estimate of gestational age and that suggested by physical examination of the newborn, the latter was chosen as indicating gestational age. Appropriateness of birth weight for gestational age was determined from the Colorado growth chart.[3] Severe hypertension was defined as a usual rather than a peak blood pressure of ≥140/90 mmHg.

In diabetic pregnancies the average total daily insulin requirement in the third trimester was compared with the nonpregnant insulin dosage for each patient. Two patients with an insulin increase of > 100% were compared with 7 patients with an increase of < 100%.

The 806 women studied had a total of 1986 serum samples analyzed for hPL. The number of samples per patient ranged from 1 to 8 (Table 2). Seventy-one percent of the patients had their final sample obtained within 7 days of delivery and 81% within 10 days of delivery.

Statistical methods used were as follows: hPL–birth weight relationships: correlation coefficients and multiple regression analyses[4]; birth weight–gestational age–hPL relationships: Bonferroni t test[5]; hPL weekly pattern: Duncan's multiple range test[6]; individual patient hPL consistency: intraclass correlation coefficients[4]; comparison of mean hPL levels in various conditions: Student's t test.[4]

Results and Discussion

Relationship Between hPL and Birth Weight

Although hPL levels are generally considered to be significantly correlated in a positive manner with placental weight, the literature is divided on the question of the relationship between hPL levels in late pregnancy and birth weight.[1] Certain reports have described a positive relationship[7,8]; others have not.[9-11]

The mean hPL level for each of the 794 women who was delivered of a single fetus was determined, and these were correlated with the birth weights of the newborns. Mean hPL levels in late pregnancy were significantly correlated with birth weight, $r = 0.173$ ($P < 0.001$). Other factors positively correlated with birth weight were: gestational age, $r = 0.360$ ($P < 0.001$), male sex of the newborn, $r = 0.159$ ($P < 0.001$), and multiparity, $r = 0.070$ ($P < 0.05$). Birth weight was unrelated to the patient's socioeconomic status. Of the factors studied, gestational age was demonstrated by multiple regression analyses to be the most highly correlated with birth weight. The mean hPL correlation was stronger than that of the parity of the mother or of the sex of the newborn. Mean hPL levels were unrelated to maternal age, socioeconomic status, parity, or sex of the newborn. Figure 1 demonstrates significant mean hPL differences ($P < 0.01$) among patients who were delivered of small-, appropriate-, or large-for-gestational-age babies.

Since serum hPL levels are related to placental weight, and since newborn and placental weights are positively correlated, it is not surprising that our data

Table 2. The Number of Serum Samples per Patient Analyzed for hPL

No. of samples	No. of patients	(%)
1	318	(39)
2	179	(22)
3	112	(14)
4	84	(10)
5	61	(8)
6	36	(4)
7	11	(1)
8	5	(1)
	806	(100)

hPL = Human placental lactogen.

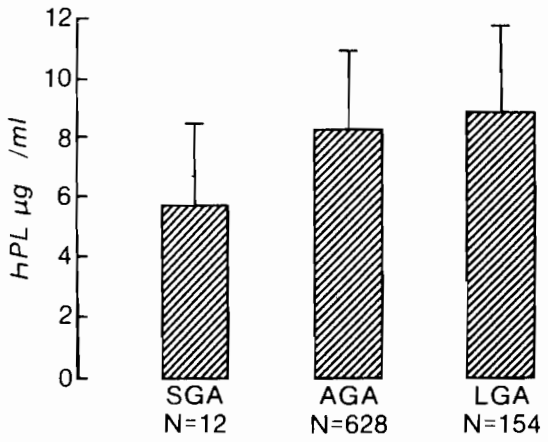

Figure 1. Mean hPL levels as related to birth weight–gestational age categories. SGA = Small for gestational age; AGA = appropriate for gestational age; LGA = large for gestational age. Lines above bars represent 1 standard deviation.

demonstrate a relationship between mean hPL levels in late pregnancy and birth weight. As can be seen in Figure 1, however, considerable overlap in hPL levels exists among the different birth weight–gestational age categories. This helps explain the limited value of low hPL levels in identifying small-for-gestational-age fetuses in a general obstetric population.[2]

Weekly hPL Pattern in Late Pregnancy

Several patterns of serum hPL levels in late pregnancy have been described.[8,10,12–18] Peak values have been reported at 35,[8] 37–38,[15] 39,[13] and 40 weeks' gestation.[16] Certain authors describe a decline in late pregnancy,[13,15,16] while others describe a plateau after 34[12] or 36 weeks' gestation.[18]

Our data, based on 1983 determinations, are presented in Figure 2 (3 determinations for week 43 have been excluded). Peak mean hPL levels (8.8 µg/ml) occurred at 37 weeks' gestation. This level is significantly higher than that at 34 weeks' gestation (7.8 µg/ml; $P < 0.05$). After 37 weeks' gestation there was a moderate decline in mean hPL levels to 7.1 µg/ml at 42 weeks' gestation. The 42-week value is significantly lower than all of the others ($P < 0.05$). As has previously been reported,[19] the distribution of hPL values in late pregnancy is skewed with a greater spread of values above than below the mean.

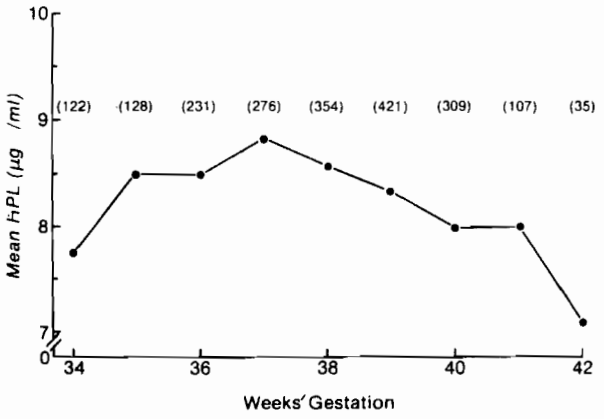

Figure 2. Mean hPL levels by weeks' gestation. The number of samples tested for each week are in parentheses.

Individual Consistency of hPL Values

Although an individual's hPL levels in late pregnancy may vary within a day by ± 15%,[19] there is little information regarding the consistency of an individual patient's hPL values week to week in late pregnancy. To estimate this consistency in our study population, intraclass correlation or reliability coefficients were computed separately for those patients tested 2, 3, 4, or more times in late pregnancy. Due to computational limitations, the coefficients summarized in Table 3 were computed separately for the number of samples tested in late pregnancy.

The reliability coefficient quantifies the consistency of hPL determinations from week to week within a subject. If the hPL readings show little variation relative to the variation among patients, the reliability coefficient will be significantly larger than 0, although by definition it will never be greater than 1. The levels of significance (Table 3) indicate that the reliability of hPL readings is greater than 0, regardless of the number of times a patient is tested in late pregnancy. This suggests that multiple weekly samples from an individual in late pregnancy may provide little more information than that provided by 1 or 2 samples.

hPL Levels in Various Conditions

Serum hPL levels reflect placental mass. Therefore one might predict that certain conditions would be associated with high or low hPL levels. The 12 women with twins in our study population had a mean hPL level of 12.7 µg/ml, which was significantly higher ($P < 0.01$)

Table 3. Reliability Coefficients Related to the Number of Samples per Patient

No. of samples	No. of patients	Reliability coefficient	Significance
2	179	0.71	$P < 0.001$
3	112	0.64	$P < 0.001$
4	84	0.66	$P < 0.001$
5	61	0.74	$P < 0.001$
6	36	0.64	$P < 0.001$
7	11	0.51	$P < 0.001$
8	5	0.33	$P < 0.01$

than the mean level of patients with singleton pregnancies (8.3 μg/ml). Patients with severe hypertension in our study population ($N = 9$) had a mean hPL level of 5.9 μg/ml, which was significantly lower ($P < 0.01$) than that of the remainder of the study population (8.3 μg/ml). No other statistically significant differences in mean hPLs for the conditions listed in Table 1 were found. This may reflect in part small numbers in some of the categories and also the heterogeneity of the patients in each category, with some having mild or no disease (eg, Rh-sensitized patients carrying Rh-negative fetuses, and patients with suspected intrauterine growth retardation delivering appropriate-for-gestational-age babies).

Because hPL affects carbohydrate and lipid metabolism and is thought to be in part responsible for the diabetogenic effects of pregnancy, the relationship of hPL levels to the insulin requirements of pregnant diabetics has received previous attention. Although Soler et al[20] could not relate the increased insulin requirement during pregnancy to hPL levels, Ursell and coworkers[21] found significantly higher hPL levels in patients whose insulin requirements rose > 100% during pregnancy.

The few patients in this study who required insulin prior to pregnancy ($N = 9$) did not demonstrate a relationship between the incremental insulin required and hPL levels.

Conclusions

The hPL levels in late pregnancy are positively correlated with birth weight. The hPL levels peak at about 37 weeks' gestation and then decline. This decline continues until at least 42 weeks' gestation. In late pregnancy, individuals generally show little variation in hPL levels from week to week. The hPL levels reflect placental mass. They are high in twin pregnancy and low in patients with severe chronic hypertension.

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