# Elevated levels of β–human chorionic gonadotropin and human placental lactogen between 11-13 weeks' gestation and subsequent pregnancy complications in Omani women

*Andrzej Krolikowski, MD, PhD, Fikra Al Busaidi, MD, Adil Al Wahaibi, MSC.*

The association between abnormal levels of maternal serum β-human chorionic gonadotrophin (β-HCG) and human placental lactogen (HPL) measured in early pregnancy and future poor pregnancy outcome is fairly well established.[1,2] However, most publications concerning this subject come from so called "Western Countries" and refer to European female populations. It is not clear whether the same conclusions apply to Arabic women. Little is known on how such prognostic information can be used to avoid future complications of pregnancy and improve their outcome. Inspired by the above questions, we undertook a prospective study, which was designed to assess the efficiency of maternal serum biochemical markers β–HCG and HPL for the detection of different pregnancy and labor complications. The blood samples were taken from pregnant patients who attended the antenatal clinic at Sultan Qaboos University Hospital in Muscat, Sultanate of Oman, from December 2001 to October 2002. These patients were selected randomly. A total of 200 Omani women, none diabetic, with singleton pregnancies between 11 and 13 weeks' gestation were recruited into the study. Gestational age was calculated from the first day of the last menstrual period, unless ultrasonography showed a discrepancy of more than 14 days. Excluded from the study were pregnancies with fetal anomalies, multiple gestations and insulin dependent maternal diabetes. Biochemical analysis of both maternal serum markers was performed in the clinical biochemistry laboratory using an automated immunometric technique supplied by Beckman Coulter for β-HCG and manual radioimmunoassay utilizing a gamma radiation scintillation counter for HPL. Both assays underwent internal, trilevel quality controls. The selected patients were monitored for the following complications: pregnancy induced hypertension (PIH), gestational diabetes, polyhydramnios, antepartum hemorrhage, intrauterine growth retardation (IUGR) (birth weight <10th per centile for gestation), low Apgar score (7 or less) and emergency cesarean section.

Seventy-five patients did not develop any pregnancy complications and delivered vaginally. This was our control group. Eighty-five patients

**Table 1 -** β-human chorionic gonadotrophin levels versus complications of pregnancy.

| Type | n | Subset for alpha =0.05 1 | 2 |
|---|---|---|---|
| APH | 10 | 62293.10 | |
| Polyhydramnios | 14 | 65386.93 | |
| Cesarean section | 14 | 66179.14 | |
| Diabetic | 15 | 70155.33 | |
| Control | 75 | 76859.81 | |
| Low Apgar score | 10 | | 118967.73 |
| PIH | 11 | | 122226.20 |
| IUGR | 11 | | 151006.27 |
| Sig. | | 0.931 | 0.185 |

APH - antipartum hemorrhage, PIH - pregnancy induced hypertension, IUGR - intrauterine growth retardation, Sig - significance
Means for group in homogenous subsets are displayed.
a) Uses harmonic mean sample size = 13.230.
b) The group sizes are unequal. The harmonic mean of the group sizes is used. Type l error levels are not guaranteed.

**Table 2 -** Human placental lactogen levels versus complications of pregnancy.

| Type | n | Subset for alpha =0.5 1 |
|---|---|---|
| PIH | 11 | .950 |
| Low Apgar score | 10 | .991 |
| Polyhydramnios | 14 | .993 |
| APH | 10 | 1.030 |
| IUGR | 11 | 1.136 |
| Diabetic | 15 | 1.260 |
| Cesarean section | 14 | 1.336 |
| Control | 75 | 1.415 |
| Sig. | | .424 |

APH - antipartum hemorrhage, PIH - pregnancy induced hypertension, IUGR - intrauterine growth retardation, Sig - significance
Means for groups in homogenous subsets are displayed.
a) Uses harmonic mean sample size = 13.230.
b) The group sizes are unequal. The harmonic mean of the group sizes is used. Type l error levels are not guaranteed.

developed one of the above mentioned problems during pregnancy or in labor. Forty patients dropped out from the study due to insufficient information on the course of their pregnancies or they developed more than one complication and were excluded from statistical analysis. This includes 2 cases of stillbirth and 3 patients who delivered before term (the numbers were too small to draw any significant conclusions). The maternal serum β-HCG and HPL levels of the patients from both groups were compared. The analysis of variance (ANOVA) test was used to establish significant difference between the 2 groups. To compare the means individually with the control, the student–Newman–Keuls test was used. Details of association between different levels of β-HCG and adverse pregnancy outcomes are presented in **Table 1**. β-human chorionic gonadotrophin levels were significantly higher among women who developed PIH in later stages of pregnancy. The infants of mothers with elevated levels of β–HCG developed IUGR more frequently and were delivered with lower Apgar score in comparison to the babies from the control group. The differences are statistically significant. Women who developed antepartum hemorrhage, polyhydramnios, gestational diabetes and whose labor ended up with emergency cesarean section had lower levels of β-HCG in early pregnancy, although these differences are not proven statistically. There was no significant difference in the levels of HPL between women with evaluated complications of pregnancies and the control group in our study (**Table 2**).

We have found that elevated β-HCG levels in our study were associated with pre-eclampsia. This finding is consistent with the reports of Yaron et al[2] and appears to support the theory that vascular changes within the placenta, which may ultimately lead to pre-eclampsia, begin in early pregnancy.[3] These early placental changes result in hypoperfusion of placental villi and an increase in β-HCG production. Lieppman et al[4] found that an unexplained increased level of β-HCG is associated with risk of preterm delivery and delivery of a low birth weight baby. This may be the result of early placental vascular damage, which increases production of β-HCG by hyperplastic cytotrophoblast cells.

Our study, in which there is a statistically significant correlation between high levels of β-HCG and increased numbers of IUGR and newborns delivered in poor condition, confirms the above suggestion. There are several reports that increased levels of β-HCG are associated with such complications of pregnancy as: antepartum hemorrhage, gestational diabetes, preterm delivery, stillbirth and abnormal volume of amniotic fluid.[2,3]

Unfortunately, we were not able to confirm these findings. On the contrary, in some of the above complications, the levels of β-HCG in our study were lower than the control group, although the differences were not statistically significant, thus we cannot make any definite conclusions. Murai et al[5] reports that there is an elevation of HPL in women with pre-eclampsia. He suggests that maternal obesity and HPL converge to adversely effect free fatty acid concentrations in the maternal circulation, which may play a role in pathophysiology of pre eclampsia.[5] Human placental lactogen was also found to increased in other pregnancy complications namely, polyhydramnios, IUGR and low Apgar score.[1] In our study, we did not notice such correlations. We have to acknowledge that our study had one major limitation, it involved a small number of patients and as a result appropriate corrections for maternal factors and gestational age were not possible. However, the strong statistically significant difference in the levels of β-HCG between 2 compared groups seems to prove that elevation of this maternal marker in the early stage of pregnancy is associated with adverse future pregnancy outcome, increased number of PIH, IUGR and poor condition of the newborns in Omani women. This study also stimulates some further questions regarding practical utilization of the above conclusion. Do we need to assess the serum β-HCG level in every pregnant woman or only in selected, high risk patients? If the serum β-HCG level is elevated, should we put the patient on preventive treatment (low dose aspirin) and how closely should we monitor maternal blood pressure? How often should we perform fetal surveillance? To answer these questions, further research is needed. At the moment we suggest that practical use of this prognostic information should be individual, depending on a particular patient and the resources of the medical care provider. In conclusion, our study demonstrates that elevation of β-HCG levels between 11-13 weeks of pregnancy is associated with adverse pregnancy outcome in Omani women. Levels of HPL did not prove to have any significant value as a predictor of pregnancy complications.

**Acknowledgment.** We acknowledge the Internal Grants Funding System of Sultan Qaboos University by which this project, MED–2001–7, was supported.

*Received 18th March 2003. Accepted for publication in final form 20th October 2003.*

*From the Department of Obstetrics and Gynecology (Krolikowski, Al Busaidi), Department of Biochemistry (Al Wahaibi), Sultan Qaboos University, Sultan Qaboos University Hospital, Muscat, Sultanate of Oman. Address correspondence and reprint requests to Dr. A. Krolikowski, PO Box 35, Al Khod 123, Muscat, Sultanate of Oman. Tel. +968 513355 Ext. 3475/3420. Fax. +968 513419. E-mail: andrze@squ.edu.om*

## *References*

1. Harrigan JT, Langer A, Hung CT, Pelosi MA, Washington E. Predictive value of human placental lactogen determinations in pregnancy. ***Obstet Gynecol*** 1976; 47: 443-445.
2. Yaron Y, Cherry M, Kramer RL, O'Brien JE, Hallak M, Johnson MP et al. Second-trimester maternal serum marker screening: Maternal serum μ-fetoprotein, beta-human chorionic gonadotrophin, estriol, and their various combinations as predictors of pregnancy outcome. ***Am J Obstet Gynecol*** 1999; 181: 968-974.
3. Wenstrom KD, Owen J, Boots LR, Du Bard MB. Elevated second - trimester human chorionic gonadotrophin levels in association with poor pregnancy outcome. ***Am J Obstet Gynecol*** 1994; 171: 1038-1040.
4. Lieppman RE, Williams MA, Cheng EK, Resta R, Zingheim R, Hickok DE et al. An association between elevated levels of human chorionic gonadotrophin in the midtrimester and adverse pregnancy outcome. ***Am J Obstet Gynecol*** 1993; 168: 1852-1856.
5. Murai JT, Muzykanskiy E, Taylor RN. Maternal and fetal modulators of lipid metabolism correlate with the development of pre eclampsia. ***Metabolism*** 1997; 4618: 963-967.


## Hashimoto's thyroiditis in school girls in the United Arab Emirates


***Abdulazim M. Mabrouk,*** *MD, CABP*
***Valsamma N. Eapen,*** *PhD, MRC Psych.*


Autoimmune diseases are common that up to 20% of the population in Western societies is estimated to suffer from one or another autoimmune disease.[1] Hashimoto's thyroiditis is an example of an organ specific autoimmune disease. This chronic inflammatory glandular autoimmune disease develops when the immune system attacks self protein expressed on the surface of the thyroid gland. It is characterized by infiltration of the thyroid gland by lymphocytes causing gradual destruction of the gland. Hashimoto's thyroiditis is the most common cause of thyroiditis, and as in the case with other autoimmune disorders, more common among women. Enlargement of the thyroid gland, local tenderness and thyroid function disorder are the common clinical features of the disease. It accounts for many of the enlarged thyroids formerly designated as adolescent or simple goiter. This study was undertaken to examine the clinical and laboratory profile of girls with Hashimoto's thyroiditis diagnosed in the Pediatric clinic of the School Health Department in Al Ain, United Arab Emirates (UAE).

The study was conducted as part of an established screening program for all the school children attending government schools in Al Ain, UAE. During the academic year 2001-2002, 10,549 girls attending the 36 government secondary schools were screened for thyroid problems. Goiter is a common finding detected by school health doctors during the routine medical examination carried out as part of the screening program. During the study period, 110 girls were identified to have enlargement of the thyroid gland. Most of these cases were diagnosed as having simple or adolescent goiter and referred to the pediatrician in the central clinic for further evaluation. For all these patients, thyroid function tests such as thyroxine ($T_4$) and thyroid stimulating hormone (TSH) were carried out. For those found to have diffuse thyroid enlargement, symptoms and signs of thyroid disease or abnormal thyroid function tests, further investigations including thyroid peroxidase and thyroglobulin antibodies were performed. A diagnosis of Hashimoto's thyroiditis was made when the thyroid antibody test was positive.

Of the 110 female students referred for goiter, 11 (10%) were diagnosed as having Hashimoto's thyroiditis, on the basis of thyroid antibody tests. The age range was 12-19 years. Four were UAE nationals, in addition to 3 Palestinians, 2 Somalians, one Syrian and one Sudanese national. **Table 1** shows the clinical characteristics and thyroid profile of these patients. Thyroid function tests revealed 3 of these girls has euthyroid, 3 with subclinical hypothyroidism, 4 hypothyroid and one with subclinical hyperthyroidism. Thyroid scans showed abnormalities in uptake in 6 patients with the uptake of the radioisotope being heterogeneous, patchy or increased. The uptake was normal in the remaining 5 patients. One patient with subclinical hypothyroidism had history of thyrotoxicosis for which thyroidectomy was performed and in another patient hypothyroidism was associated with polyglandular autoimmune syndrome. The latter patient also had hypoparathyroidism, pernicious anemia and secondary amenorrhea, and gave family history of the same syndrome in a 19-year-old sister and neurofibromatosis type 1 in another sister aged 9-year-old. Yet another patient gave history of treatment with thyroxine for hypothyroidism 5 years ago but had discontinued the treatment. Four patients gave family history of thyroid disease. Another 4 patients had learning difficulties resulting in poor school performance. The height of these patients were below the fifth centile. On mental state examination, 6 patients showed features of depression and these patients were further evaluated using Hamilton depression rating scale. The scores suggested the severity of depression to be mild in 3, moderate in 2 and severe in one. The patient with severe depression started on treatment using a selective serotonin reuptake inhibitor. Our findings suggest that Hashimoto's thyroiditis should be suspected in all young people referred for evaluation of diffuse goiter. Mood changes and in particular depression when present should raise the suspicion of Hashimoto's thyroiditis, as affective symptoms are known to be associated with autoimmune