

The level of thermostable alkaline phosphatase in maternal serum as a test of foeto-placental function

by

A. RONDINELLI, L. SCIVOLI and A. BEGGIO

The placental enzyme most studied in the human is without any doubt the alkaline phosphatase which is thermostable at 65°C. The placental origin of this enzyme has been demonstrated by several authors (¹⁻³⁵); and the possible diagnostic applications of its determination during pregnancy have been repeatedly debated (^{16, 17, 36-48}).

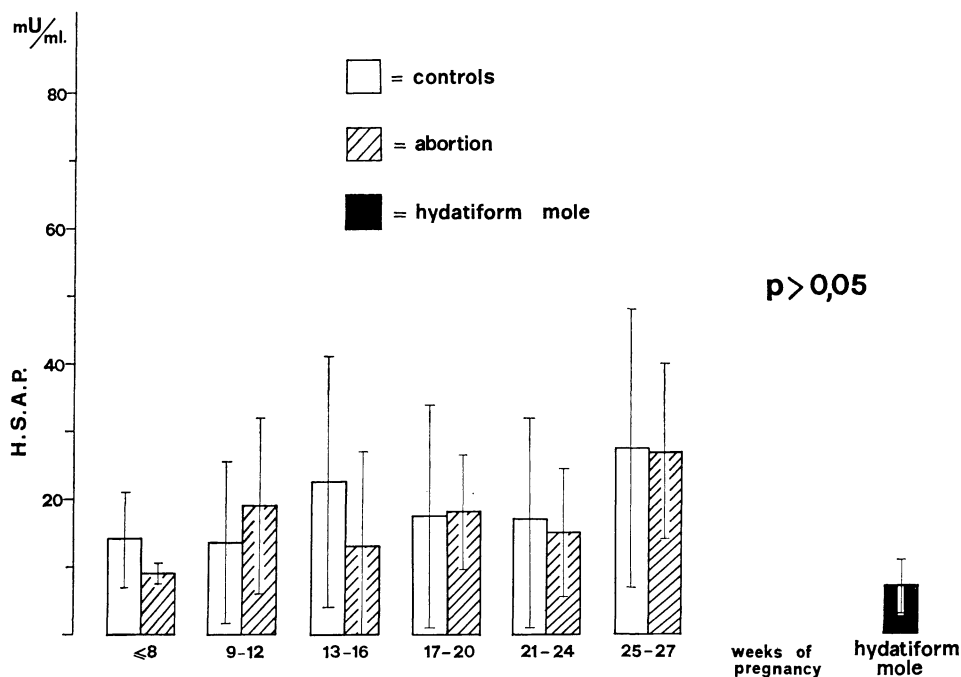
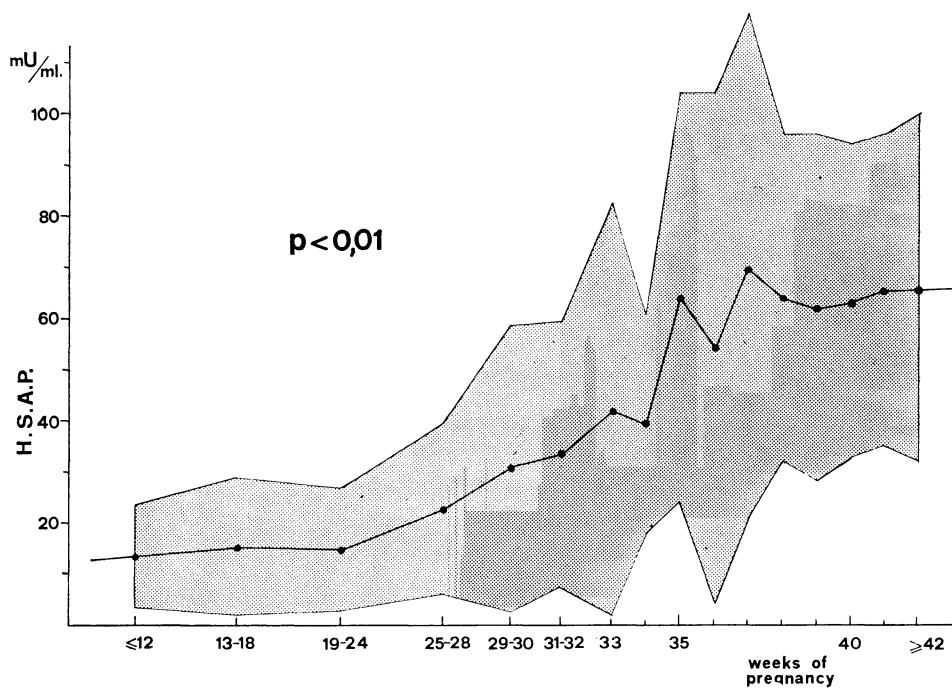
Contradictory findings have been reported by different authours ond sometimes even by the same group of authors in successive pubblications, regarding the diagnostic and prognostic value of the determination of this enzyme in maternal serum as a measure of foeto-placental function. In this paper our findings are reported together with a comparison between determination of thermostable alkaline phosphatase and other foeto-placental function tests.

MATERIALS AND METHODS

Our study is based on the results of the determination of thermostable alkaline phosphatase in 786 specimens of serum from 625 pregnant women at different stages of pregnancy. The determination of the enzyme was carried out after heating in a thermostat at 65°C for 30 min., using the method of Bessey and Lowry. The cases studied were sub-divided in different groups on the basis of gestation time, different maternal diseases complicating the pregnancy, characteristics of foetal growth, fate of the foetus or infant, weight of the placenta, maternal urinary oestriol levels and foetal biparietal diameter by the use of ultrasonic waves. These two latter estimations were carried out on the day when blood was taken from the mother for determination of the enzyme. The results were subjected to statistical analysis.

RESULTS

The variations in the level of thermostable alkaline phosphatase found in maternal serum during the course of pregnancy are reported in Figure 1. The curve appears to be biphasic; rather flat and low in the first 24 weeks of gestation and then rising progressively in the following weeks with a distinctly significant increase in the period between the 34th and 35th week. During the first 24 weeks of pregnancy no significant differences were found between miscarriages and controls, while in two cases of vesicular mole, included in the case study, extremely reduced levels of the enzyme were found (Figure 2). Average levels significantly above



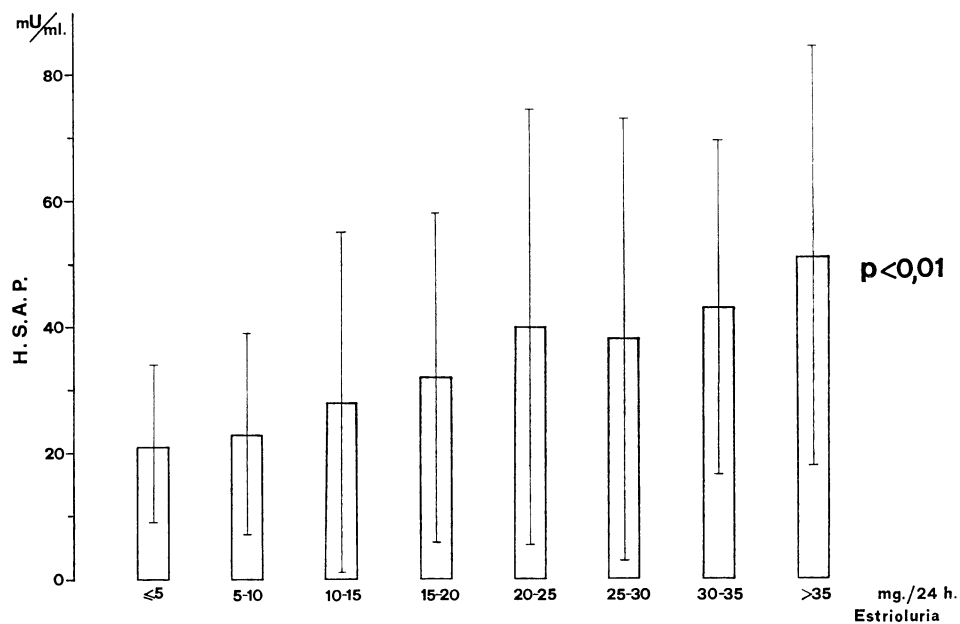


FIG. 3 - correlation between H.S.A.P. levels and estriol excretion.

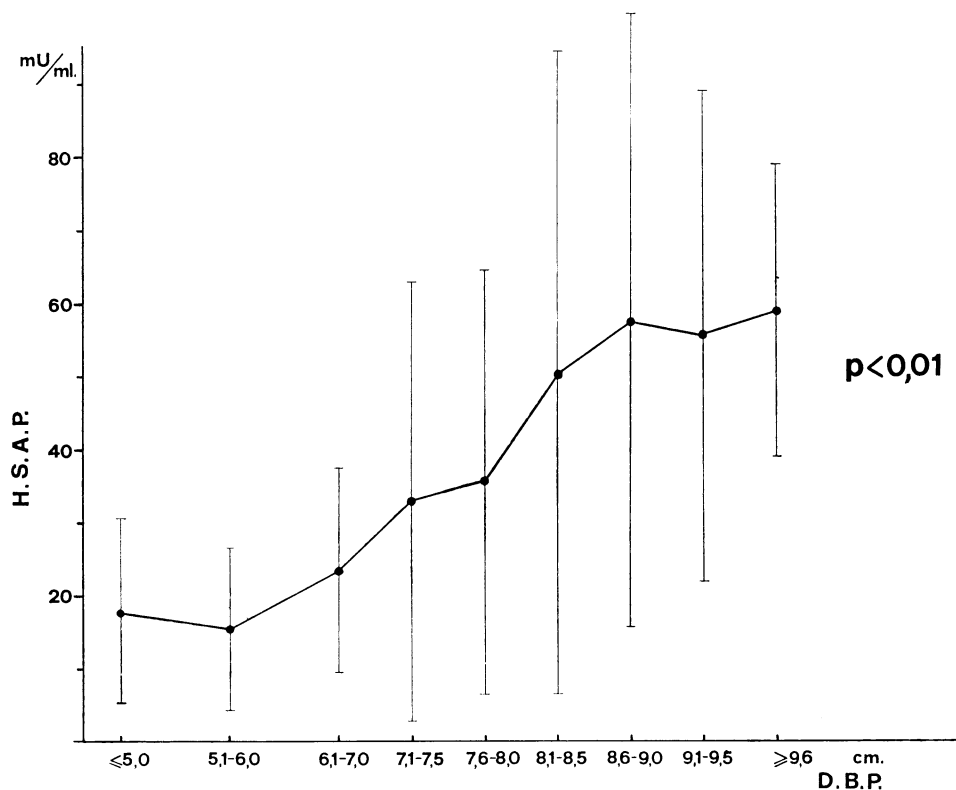


FIG. 4 - correlation between H.S.A.P. levels and measures of fetal biparietal diameter evaluated by ultrasounds.

normal were found in pregnant patients suffering from hypertensive toxæmia of the 3rd trimester and from liver complications of pregnancy, while average values lower than normal, but not statistically significant, were found in cases of severe anaemia of pregnancy with a history of stillbirth and threat of premature delivery. Abnormal values were found in 6 out of 17 cases (35.3%) of retarded intrauterine foetal growth, in 15 out of 39 cases (38.5%) of foetal overgrowth, in 70% of intrauterine deaths and only in 27.3% of early neonatal deaths. The distribution of values outside the normal range occurs indiscriminately below and above normal, and in 4 cases out of 7 of pregnancies involving twins the enzymatic levels were clearly above normal, in the 5th case being at the upper limits of the variability range. The maternal serum enzyme level appears to be independent of the placental weight and is only noticeably reduced, but not significantly, in cases of obvious placental hypoplasia (placental weight less than 300 g).

In Figure 3 average values and relative standard deviations of the serum thermostable alkaline phosphatase level are given in comparison with the level of maternal urinary excretion of oestriol. A good and statistically significant correlation exists between the two parameters.

COMMENT

Our studies have confirmed that during the course of pregnancy levels of thermostable alkaline phosphatase in the maternal serum progressively increase. This increase starts at the 24th week of pregnancy and is more obvious from the 34th week onwards. This result, however, must be assessed in the context of the finding that, parallel to the progressive increase in average enzyme level, there is a simultaneous obvious increase in the range of variability, a fact which reduces the possibility of diagnostic application of this dose determination. The findings that in the first 24 weeks of pregnancy the enzymatic level persistently remains low, that there are no significant differences between abortions and controls, that in cases of vesicular mole the enzymatic level is particularly reduced, confirm the hypothesis that thermostable alkaline phosphatase is produced principally by the mature syncytial trophoblast. The marked enzymatic increase in the last 6 weeks of gestation, when the nutritional requirements of the foetus are definitely greater, can be explained by the fact that since this enzyme is directly involved in the processes of glycogen and phospholipid hydrolysis, the transfer of important nutritional factors across the placenta to the foetus is facilitated, thus providing for the increased metabolic requirements of the foetus in this last phase of pregnancy. Among the other results of this study, it seems to us worth noting the excellent correlations found between the enzymatic values and maternal urinary oestriol excretion and between the enzymatic values and foetal biparietal diameter (measured using ultrasonics). This fact justifies continuation of the determination of thermostable alkaline phosphatase, which is useful in the study of foeto-placental function, in addition to other diagnostic methods but not instead of them.

SUMMARY

The values obtained for alkaline phosphatase thermostable at 65°C in 786 samples of serum from 625 pregnant patients at various gestation times have been examined. The average level of the enzyme remains rather low in the first 24 weeks of pregnancy and later increases progressively, particularly from the 34th

week. Significantly higher values were found in hypertensive toxæmia and in pathological liver complications of pregnancy. A good correlation was shown between enzyme values and the level of oestriol in the maternal urine and the foetal biparietal diameter (measured using ultrasonic). The results have been subjected to statistical analysis.

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