

Relationship between serum heat-stable alkaline phosphatase level and pregnancy*

Cao Guo-Xian¹, Xiao Wei-Hong¹, Yu Hui-Xin¹, Li Wei-Yi¹,
Huang Xu-Quan¹ and Ding Mei-Juan²

(¹ State Key Laboratory of Nuclear Medicine, Jiangsu Institute of Nuclear Medicine, Wuxi 214063;

² Jinhua Hygienic School, Jinhua 321000, Zhejiang Province)

Abstract Serum heat-stable alkaline phosphatase (HSAP) level in 649 cases of normal pregnancy and 164 cases of high-risk pregnancy is measured by radioimmunoassay (RIA). The results indicate that the HSAP level in normal pregnancy increased proportionally with gestation weeks ($r=0.9843$). In 33 cases of pregnancy induced hypertension and 21 cases of intrauterine fetal growth retardation, the HSAP level is significantly low. In 7 cases of neonatal asphyxia and 26 cases of fetal distress, the HSAP level in the mother's serum is also low. In 53 cases of intrahepatic cholestasis of pregnancy, the HSAP level is similar to those of normal pregnancy. This study illustrates that HSAP RIA can play an important role in the evaluation of placental function and fetal prognosis for cases of high-risk pregnancy.

Keywords Alkaline phosphatase, Radioimmunoassay, Pregnancy, Placenta

1 Introduction

There are varieties of enzymes in the human placenta, and their activities are closely interrelated with metabolism of the placenta. Heat-stable alkaline phosphatase (HSAP) is one of the special enzymes which are formed in the placenta and secreted into blood.^[1] In the case of normal pregnancy, the HSAP level in serum proportionally increases with gestation weeks, which is in accord with the growth of the placenta. In the case of high-risk pregnancy, on the other hand, the HSAP level in serum is obviously different from that of normal.^[2,3] Therefore, measuring pregnant women's serum HSAP level can play an important role in the evaluation of placental function and fetal prognosis for cases of high-risk pregnancy. The routine methods to measure HSAP level generally are to examine enzyme activity, such as King-armstrong's method. But, the results of these methods may be easily disturbed by other materials in serum, pH, temperature and other factors of the assay system.

We have reported the method of HSAP radioimmunoassay (RIA) for measuring HSAP level in pregnant women's serum^[2], and the results demonstrate that the method is of high sensitivity, specificity and stability. Therefore, we

use the method to determine the serum HSAP levels of normal and high-risk pregnancy in order to establish the relationship between HSAP level and normal or high-risk pregnancy.

2 Materials and methods

2.1 Patients

We studied 649 cases of normal and 164 cases of high-risk pregnancy which were treated at Suzhou Medical College's Hospital, Suzhou Hospital for Women and Children, and Wuxi Hospital for Women and Children. All of the 164 cases of high-risk pregnancy had received diagnosis, including 33 cases of pregnancy induced hypertension, 21 cases of intrauterine fetal growth retardation, 26 cases of fetal distress, 7 cases of neonatal asphyxia, 53 cases of intrahepatic cholestasis of pregnancy, 9 cases of prolonged pregnancy, 3 cases of threatened premature labor, 3 cases of premature rupture of membranes, 1 cases of hydramnios, 1 case of oligoamnios, 4 cases of hepatopathy, 2 cases of congenital heart disease and 1 case of anaemia.

Serum samples were collected from normal and high-risk pregnancy.

2.2 Methods

The assay was carried out according to our method.^[2] The diluent buffer was 0.02 mol/L

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phosphate-buffered saline, pH 7.5, containing 9g/L sodium chloride and 2g/L bovine serum albumin. The reagents were added to and incubated in 10×75mm disposable glass test tubes. These test tubes included standard tubes (STA), unknown serum sample tubes (US), nonspecific binding tubes (NSB) and HSAP-free tubes (HF), respectively. The final volume of the initial incubation mixture was 0.4ml and contained the following in the order given. (a) Diluent buffer: 100μl (STD and US), 300μl (NSB) and 200μl (HF). (b) 100μl HSAP standards (3.9, 15.6, 62.5, 250 and 1000μg/L HSAP, respectively) for STD or 100μl patient's serum samples for US. (c) 100μl anti-HSAP in a 1:100000 dilution (STD, US and HF). (d) 100μl ^{125}I -HSAP to provide approximately 10000 counts per min in diluent buffer

(STD, US, NSB and HF).

After incubation for 24h at 4°C, 500μl rabbit serum and 100μl anti-rabbit serum were added to each tube, and incubated continuously for an additional 30 min at 37°C. These tubes were then centrifuged at 2500 g for 20 min at 4°C, and the radioactivity in the precipitate was counted.

3 Results

3.1 HSAP level of normal pregnancy

Table 1 shows that with the advance of gestation weeks, HSAP level increased proportionally. The relationship between HSAP level and gestation weeks can be expressed by the following equation

$$\ln y = 0.1905x - 0.5035$$

Its correlation coefficient is 0.9843.

Table 1 HSAP level of normal pregnancy (μg/L)

Weeks	cases	$\bar{x} \pm s$	Weeks	cases	$y(\text{mean} \pm \text{SD})$
<8	8	1.88±0.75	25~	33	151.11±142.45
9~	18	3.60±2.79	27~	25	159.31±82.58
11~	15	5.55±2.99	29~	35	252.34±172.34
13~	32	6.83±3.84	31~	43	515.64±221.66
15~	21	13.23±9.98	33~	70	531.25±255.93
17~	23	15.73±16.20	35~	65	586.54±296.43
19~	30	24.60±22.63	37~	61	656.29±188.04
21~	34	44.36±28.75	39~	67	808.28±175.62
23~	28	79.71±55.37	41~42	41	811.04±167.10

Table 2 HSAP level of high-risk pregnancy (μg/L, mean ±SD)

Weeks	cases	normal	cases	PIH	cases	IFGR	cases	ICP	cases	FD	cases	NA
31~32	43	515.64 ±221.66	5	323.00 ±119.12	4	282.50 ±87.30	4	230.00 ±98.99	1	230	--	--
33~34	70	531.25 ±255.93	4	335.62 ±102.38	3	252.33 ±86.67	5	361.80 ±178.51	1	213	--	--
35~36	65	586.54 ±296.43	5	406.14 ±93.03	4	259.50 ±92.87	12	591.67 ±138.4	7	355.86 ±133.50	3	493.3 ±11.5
37~38	61	656.29 ±188.04	10	467.57 ±154.41	5	316.60 ±62.30	24	560.00 ±179.93	9	269.67 ±86.06	4	447.50 ±139.40
39~40	67	808.28 ±175.62	9	518.63 ±178.36	5	367.60 ±191.12	8	651.25 ±244.36	8	482.0 ±285.84	--	--

3.2 HSAP level of high-risk pregnancy

HSAP level of high-risk pregnancy is listed in Table 2. HSAP level of pregnancy induced hypertension (PIH) is significantly lower than that of the same gestation weeks of normal pregnancy ($P < 0.05$ or $P < 0.01$). HSAP level of intrauterine fetal growth retardation (IFGR) is also obviously lower than that of the same gestation weeks of normal pregnancy ($P < 0.05$ or

$P < 0.01$). In cases of neonatal asphyxia (NA) and fetal distress (FD), HSAP levels in the mother's serum are lower than that of normal ($P < 0.05$). In cases of intrahepatic cholestasis of pregnancy (ICP), the HSAP level is similar to that of normal pregnancy. The data of the following diseases, due to less cases, are statistically no sense and unlisted, and we only make a short description. The HSAP level of pro-

longed pregnancy (above 43 weeks) compared with that of normal pregnancy (39~42 weeks) has no significant difference ($P < 0.05$). The HSAP levels of premature of membranes, hydramnios, oligoamnios, threatened premature labor and hepatopathy are obviously lower than that of normal. There is no difference of HSAP level between congenital heart disease or anaemia and normal.

4 Discussion

There are several isoenzymes of alkaline phosphatase (AP), and HSAP is the most important one, which is abundant in the placenta and secretes into mother's blood. HSAP level in blood increases proportionally with gestation weeks according to our test. It demonstrates that HSAP level is closely interrelated with function and metabolism of the placenta, and can reveal whether pregnancy is normal or not.

HSAP level of pregnancy induced hypertension is significantly lower than that of normal. PIH, causing arteriolar spasm of the whole body, organ's anoxia and dysfunction, results in placental infarction, trophocyte swelling and placental blood supply decrease. As a result, synthesis, secrete and transfusion into mother's circulation of HSAP are decreased. HSAP level, therefore, can be used to evaluate PIH and prognosticate mother and fetal.

Placental function is closely related to fetal's development. During all of the gestation, increase in blood stream flowing into uterus and placenta is proportionally to that of fetal's weight and gestation weeks.^[4] But in state of illness, such as blood stream flowing into uterus and placenta does not increase enough or even decrease, villus will be injured due to ischemia and anoxia, and dysfunction appears. Finally, placental function is decreased, and it results in intrauterine fetal growth retardation. For the 21 cases of IFGR, HSAP level is obviously lower than that of normal, which shows that placental function decreased. It is coincident with Ronin's opinion.^[5]

For the cases of fetal distress and neonatal asphyxia, HSAP level is lower than that of normal, which demonstrates our method being useful in fetal's prognosis. But sometimes HSAP

level is not clearly different from that of normal, which may be caused by umbilical cord. If the mother's HSAP level could be serially assayed, it would be advantageously to find out whether fetal distress or not. When HSAP levels are constantly at low value, it often means fetal distress.

There is a little difference in HSAP level between intrahepatic cholestasis of pregnancy and normal. When suffered from intrahepatic cholestasis, the liver presents an ischemia of tissue around janitrix, an increase of pressure in hepatic vena sinus, and then hepatic cells are pressed. It results in intrahepatic cholestasis and jaundice.^[6] AP level is obviously increasing with the development of intrahepatic cholestasis. However, it originates from the liver but from the increase in HSAP isoenzyme. HSAP level, therefore, has not significant change. If HSAP level and AP level are measured at the same time, the great unsuitability can be found between HSAP level and AP level. Nevertheless, it can reveal the advance of intrahepatic cholestasis or placental dysfunction.

Since Cayle found the increase of AP level in normal pregnancy,^[7] a variety of methods have been studied. The results were not so encouraging because the measurement of enzymes is very complex and easily disturbed by many factors. Our HSAP RIA method has been applied to clinical diagnosis, and the results illustrate that the HSAP RIA is of accuracy and replication, and can be used to evaluate placental function and diagnose fetal for the cases of high-risk pregnancy.

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