

SERUM HISTAMINASE IN NORMAL AND HIGH RISK PREGNANCY

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Presence of a suitable uterine and biochemical environment and adequate placental function are essential factors for the implantation of fertilised ovum and normal growth and development of foetus. Better foetal salvage in cases of high-risk pregnancy depends on early recognition of impaired placental function and foetal growth retardation so that a safe delivery can be effected before irreversible damage to the fetus. Study of enzymes to assess the placental function is of recent interest.

Histaminase is an enzyme which is known to increase tremendously during pregnancy due to its synthesis in placenta. Hence the present study was conducted to find out the diagnostic and prognostic significance of serum histaminase in normal and high risk pregnancies.

Material and Method

Present study was conducted on 325 subjects the detailed distribution of which is show in Table I. Cases with allergic

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disorders, eosinophilia and with heart disease were excluded because histaminase has been reported to rise in these conditions.

TABLE I
Distribution of Cases

Sl. No.	Type of Cases	No. of Cases
I	Non-pregnant cases	45
II	Normal pregnant cases	150
	(a) Ist trimester	50
	(b) IInd. trimester	50
	(c) IIIrd trimester	50
III	High-risk pregnancies	
	(a) Threatened abortions	50
	(b) Toxaemia of pregnancy	50
	(c) Rh. incompatibility	10
	(d) Postmaturity	10
	(e) Missed abortion	10
	Total	325

All the cases were submitted to systemic vaginal and speculum examination. Cases of toxaemia of pregnancy were divided into severe when B.P. was above 160/110 with significant proteinuria and oedema, mild to moderate when B.P. was below 160/110 m.m. and proteins were present in urine in traces only with or without oedema. Re-estimations were made at 7-10 days interval in some cases of threatened abortions and toxaemia of

pregnancy. Estimation of serum histaminase was done by volumetric method of Kapeller and Adler and activity of enzyme was expressed in per manganate unit (P.U.).

Observations

Group I: Histaminase was estimated in

Group I: Histaminase was estimated in 45 healthy non-pregnant women of different parity in different menstrual phases. Table II shows serum histaminase in this group.

No correlation was observed between age, parity and histaminase activity. Average serum histaminase was slightly higher in post menstrual phase as com-

pared to premenstrual and menstrual phases.

Group II: This included 50 normal pregnant women in each trimester of pregnancy. Significant rise in histaminase was detected between 6-8 weeks of pregnancy. This rise continued till 28 weeks of pregnancy and then gradually declined till term. Rise was much steeper after 16 weeks as compared to rise during first trimester. Table III shows details of observations in these cases.

Group III

(a) *Threatened Abortion*: Comparatively low histaminase levels were found in cases of threatened abortion in 80% cases (Table IV).

TABLE II
Histaminase Activity in Non-pregnant Cases

Phase of menstrual cycle	No. of Cases	Histamine in P.U./ml.		
		Range	Mean	r t p
Menstrual	15	0-.20	.056	r = .0649
Postmenstrual	15	0-.14	.048	t = .344
				(28)
Bremenstrual	15	0-.20	.062	p = .05
Total	45	.054 ± .067 P.U./ml.		

TABLE III
Histaminase Activity in Normal Pregnancy

Period of gestation (in weeks)	No. of Cases	Histaminase levels (P.U./ml.)					
		Range	Mean ± S.D.				
6 - 8	27	.0-0.08	0.179 ± .099	t ₁ (55)	= 6.36	P ₁	.05
9 - 12	23	.2-0.50	0.275 ± .090				
13 - 16	13	.3-0.50	0.400 ± .082	t ₂ (34)	= 5.0607	P ₂	.05
17 - 20	14	.5-1.70	0.900 ± .357				
21 - 24	13	.8-1.50	1.150 ± .206				
25 - 28	10	.8-2.20	1.825 ± .401				
29 - 32	9	.5-1.50	1.170 ± .332	t ₃ (49)	= 12.069	P ₃	.05
33 - 36	17	.8-1.20	0.917 ± .139				
37 - 40	24	.3-1.40	0.733 ± .214	t ₄ (52)	= 16.263	P ₄	.01

TABLE IV
Comparison of Mean Histaminase Activity in Threatened Abortion
and in Normal Pregnancy

Period of gestation in weeks	Mean histaminase level in threatened abortion (P.U./ml.)	Mean histaminase level in normal pregnancy (P.U./ml.)	t	P
6 - 8	.050 ± .010	0.179 ± .099	t(29) = 3.491	P .05
9 - 12	.123 ± .112	0.275 ± .090	t(24) = 2.681	P .05
13 - 16	.466 ± .261	0.400 ± .082	t(16) = 0.236	P .05
17 - 20	.400 ± .141	0.900 ± .357	t(16) = 2.585	P .01
21 - 24	.637 ± .117	1.150 ± .206	t(17) = 5.552	P .05
25 - 28	.816 ± .202	1.825 ± .401	t(11) = 4.108	P .05

Re-estimation at weekly interval were made in 40 cases. Table V shows results and prognostic significance of histaminase on re-estimations.

(b) *Toxaemia of Pregnancy*: Table VI denotes comparison of histaminase activity in cases of toxaemia of pregnancy and in control cases.

TABLE V
Results of Reestimation in Cases of Threatened Abortion

No. of estimations	No. of cases	Detor-ation	Same activit.	Increasing activity	Rate of Cases	
					Abor- ted	Conti- nued
I	6	—	—	—	6	—
II	20	10	4	6	11	9
III	12	6	2	4	6	6
IV	2	—	—	2	—	2

TABLE VI
Comparison of Mean Histaminase Values in Toxaemia of Pregnancy
and in Normal Pregnancy

Period of gestation in weeks	Mean histaminase activity in normal pregnancy (P.U./m.)	Mean histaminase activity in toxaemia of pregnancy (P.U./ml.)		
		Mild to moderate pre-eclampsia	Severe pre-eclampsia	Eclampsia
29-32	1.170 ± .332 (9)	.875 ± .224 (6)	.450 ± .071 (8)	.150 ± .071 (3)
33-36	0.917 ± .139 (17)	.825 ± .173 (7)	.350 ± .200 (12)	.450 ± .346 (5)
37-40	0.733 ± .214 (24)	.450 ± .020 (2)	.533 ± .200 (5)	.700 ± .460 (2)
Total No. of cases	50	15	25	10

Note: Figure in parenthesis indicate the number of observations whose mean is there.

(c) *RH-Incompatibility*: Serum histaminase was estimated in 10 cases of Rh-incompatibility. Six cases were primi-gravida and 4 cases were 2nd gravida. All of them had a negative Coomb's test. Serum histaminase ranged from .8-1.2 PU/ml. with a mean of .94 PU/ml. No significant difference was observed when compared with control cases of same duration of pregnancy.

(d) *Postmaturity*: Serum histaminase was measured in 10 cases of postmaturity. The duration of pregnancy in these cases ranged from 292-299 days. Serum histaminase ranged from .5-8 PU/ml. with an average of .59 PU/ml.

(e) *Missed Abortion*: Only 5 cases of clinically suspected missed abortion were studied. All these cases revealed a very low serum histaminase as compared to normal cases.

nancy. The test of enzyme activity for study of placental function is a newer concept. It has now been established by various studies in the last 30 years that there is a tremendous rise in histaminase activity during normal pregnancy. The chief source of enzyme is said to be human placenta hence it has been studied to see if it could be used as a reliable index of placental function.

Minimal histaminase activity was observed in non-pregnant females. There was slight rise in premenstrual phase as compared to post menstrual phase. It seems that progesterone after ovulation may have something to do with rise in histaminase activity as has been reported by Swanberg (1950) and Ahlmark and Swanberg (1953).

A definite rise in enzyme activity was observed as early as 6-8 weeks. A

TABLE VII
Histamine Activity in Missed Abortions

Sl. No.	Expected Size of uterus (in weeks)	Actual Size of uterus on examination (in weeks)	Serum histaminase activity in missed abortion (p.u./ml.)	Serum histaminase activity which must be present according to period of amenorrhoea (p.u./ml.)
1.	16	10	0.12	0.400
2.	20	12	0.15	0.900
3.	16	8	0.10	0.400
4.	28	16	0.35	1.825
5.	22	10	0.20	1.150

Mean \pm S.D. .13 \pm .097 P.U./ml.

Discussion

Management of high-risk pregnancy is still a challenging problem in front of an Obstetrician. In these cases there are increased chances of I.U.D., still birth and dysmature babies. This has given rise to the need of studying the placental function so that a better foetal salvage could be achieved by timely termination of preg-

gradual rise was seen upto 16 weeks. After 16 weeks, the rise in enzyme activity was rapid till 28 weeks and after that it gradually decreased till term, though at term histaminase was found to be about five times higher than in early pregnancy.

The average serum histaminase was found significantly reduced in 80% cases of threatened abortion. The cases in

which it was found to be normal, had reported to hospital soon after occurrence of slight bleeding. The cases who revealed either an increase in histaminase activity or a stationary histaminase activity on re-estimation continued their pregnancy while those who revealed a deterioration ultimately aborted. Similar have been observation of Sanyal *et al* (1972) and Nobutanious *et al* (1974).

Lower histaminase activity was seen in cases of toxæmia as compared to cases of normal pregnancy of same duration. A marked reduction in histaminase was seen in cases of severe toxæmia and in all cases of eclampsia except in 1 case who had normal histaminase activity and was admitted soon after first fit. No further fits occurred in this case, and she delivered an alive baby after 6 hours. Re-estimations were made in 20 cases. All these cases despite a definite improvement in clinical condition did not show a rise in histaminase activity. Hence it seems that greater the duration and severity of toxæmia higher is the redirection in histaminase. Sen and Sanyal (1969) and Weingold (1968) have reported significant reduction in histaminase activity in cases of toxæmia of pregnancy.

Histaminase was found normal in 10 cases of Rh incompatibility. This may be due to the fact that all of them had a negative coomb's test.

In all the 10 cases of postmaturity it was found slightly towards the lower side of the range (.59-.73), though the number of cases is too small, it seems that even with this duration of post maturity placental function was slightly reduced.

All the cases of missed abortion exhibited a gross reduction in histaminase,

though it was higher than in non-pregnant cases. This was of definite diagnostic value in all these cases.

Conclusions

1. Non-pregnant ladies in child bearing age have got minimal histaminase activity.

2. In normal pregnancy there is significant rise in histaminase by 6-8 weeks of gestation. Gradual rise in histaminase continued till 28 weeks and then slightly declined till term. Hence it can be used as a pregnancy test in early gestation.

3. In 80% cases of threatened abortion serum histaminase was low on first estimation. Increase in histaminase activity on re-estimation reveals goods prognosis.

4. Reduction in histaminase activity in toxæmia of pregnancy was found directly proportional to the severity and duration of disease.

5. Serum histaminase has proved to be a simple and reliable method of evaluating placental function.

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