ALPHA I-ANTI TRYPSIN ACTIVITY IN PREGNANCY & AFTER PARTURITION

by

NAWAL KISHORE,* M.D.

VEENA RIZVI,** M.B.,B.S.

R. V. SHARMA,*** M.D.

NAWAL KISHORE† M.S., F.A.C.S. (U.S.A.)

and

B. B. SHARMA,†† M.D., M.A. (Toronto)

What factor or factors cause the marked increase of Alpha-I-AT during pregnancy, is not known, but it has been reported by few investigators, that Alpha-I-AT enzyme activity is increased during pregnancy (Lieberman *et al* 1971; Guibaud, *et al* 1975). Faarvang (1959) found the large urinary excretion of trypsin inhibitors, with a return to normal after delivery.

Ganrot and Bjeree (1967) estimated Alpha-I-AT concentration during pregnancy, and found more than twice the normal values at the time of parturition.

The present study is undertaken with a view to observe Alpha-I-Antitrypsin activity during pregnancy and after delivery over 4 weeks.

Material and Methods

Twenty-five healthy pregnant females, from antenatal clinic, Deptt. of Obstetrics and Gynaecology, S.N. Medical College and Hospital, Agra, constituted the material for the present study. Twenty healthy non-pregnant females of matched age groups, served as controls.

Females having any history of lung or liver disease were excluded. The history of the use of oral contraceptives was taken in healthy controls and those females using oral contraceptives, were not included. The detailed history, general examination and routine investigations were made in each subject. All the subjects were asked to visit antenatal clinic on frequent intervals.

Blood samples were collected from these subjects during different trimesters of pregnancy and after parturition over 4 weeks. Three ml blood was collected and serum was separated in dry plain sterilized vials. Alpha-I-Antitrypsin was estimated by Agar-Gel Electrophoresis, using the method of Laurell and Eriksson (1963). The methods for the estimation of Alpha-I-AT and STIC were the same as in our previous study (Sharma *et al* 1974). Subjects having less than 190 mg% alpha-I-AT and STIC < 0.80/ml, was labelled as enzyme deficient subjects. It is based on the work of Lieberman (1973).

*Lecturer in Physiology.

**Previously Demonstrator in Physiology.

***Reader in Physiology.

†Prof. & Head of the Dept. of Obst. & Gynaecology.

††Principal & Chief Superintendent, Prof. & Head of the Department of Physiology.

S.N. Medical College, Agra.

Accepted for publication on 12-5-1978.

Results

Mean values of Alpha-AT in 20 healthy females were 276 mg% with a range of (202-346 mg%). STIC values were in the range of 1.08-1.26 with a mean of 1.18/mg inhibited trypsin (Table I).

TABLE I

Mean, S.D. and Range of Alpha-AT Activity in 20 Controls

	Mean	± S.D.	Range
Alpha-1-AT (mg%)	276	±49	202-346
STIC (1 ml)	1.18	±0.12	1.08-1.26

Alpha-I-AT and STIC were increased linearly during pregnancy and both were significantly ($P < .001$) higher than the values of controls (Table II).

Discussion

It has been known since long time that human serum has anti-trypsin activity. Jacobsson (1955) showed that about 90% of the inhibitory capacity was localised in Alpha-1-globulin and rest 10% in Alpha-2 Band. It has a wider range of activity against various proteolytic enzymes and recently its deficiency has been recognised with lung and liver diseases.

In the present study, Alpha-1-Anti-trypsin was estimated in 20 healthy pregnant females and mean levels were 276 mg%. The deficiency of the enzyme was not seen in any case in present series.

Laurell (1963) and Lieberman (1973) reported its values between 200-500 mg% in healthy subjects. Sharp (1976) also found its value approximately 2 mg/ml.

TABLE II

Mean Values of Alpha-I-AT and STIC IN 22 Pregnant Females During Different Trimesters of Pregnancy

Enzymes Values	1st trimester	2nd trimester	3rd trimester
(i) Alpha-1-AT (mg%)	292 ± 33.5	310 ± 56	338.7 ± 42.0
(ii) STIC (ml)	1.22 ± 0.11	1.24 ± 0.20	1.27 ± 0.16
	P <.05	P <.01	P <.001

After delivery, the concentration decreased significantly and within 4 weeks, the values touched almost normal levels.

Further it was noticed that the concentration of the enzyme and STIC values were higher in pregnant females than healthy controls. There was a linear rise in the

TABLE III

Mean Values of Alpha-1-AT Activity During 4 weeks after Parturition

	1st week	2nd week	3rd week	4th week
Alpha-1-AT (mg%)	306 ± 23.7	294.5 ± 53.0	281 ± 42	272 ± 55.9
SITC/ml	1.23 ± 0.11	1.22 ± 0.16	1.20 ± 0.08	1.16 ± 0.14

Further, it was also observed that Alpha-1-Anti-trypsin activity was raised significant in primipara than multipara pregnancies $P < 0.05$.

levels of the enzyme in relation to the duration of pregnancy. In 1st trimester mean levels were 292 mg%, and they were 310.4 mg and 338.7 mg%, in 2nd

and 3rd trimesters of pregnancy respectively.

Thus it is confirmed that the enzyme activity is altered during pregnancy and it was almost in the linear proportion of the duration of pregnancy. It was also observed that after pregnancy even in first week, the levels of Alpha-1-AT fall significantly ($P < .01$). The levels of the enzyme and STIC touched the normal values within 4 weeks after parturition. Thus, it seems that the enzyme activity tends to decrease after delivery and return towards normal range.

In the past, many other investigators made similar observations. Faarvang (1963) reported the excretion of trypsin inhibitors in the urine almost double during pregnancy. Ganrot and Bjeree (1967) reported almost double concentration of the enzyme during pregnancy and 6 weeks after the parturition, the concentration was normal. Our results are almost similar to these reports. We also found significant rise in the enzyme values, but not to the extent as earlier investigators have reported. Normal values of the enzyme returned within 4 weeks, instead of 6 weeks.

It is well known that trypsin inhibiting capacity is affected by Diethyl stilbestrol therapy (Lieberman *et al*, 1971). They found that even heterozygous deficient subjects responded very well to this therapy.

Recently, Guibaud *et al* (1975) studied alpha-1-AT levels in the amniotic fluid during various gestational weeks. They also reported the variations of the enzyme levels in pregnancy.

Faarvang (1963) stated that the responsible factor for increasing the enzyme levels is release of "Gluco-corticoids" in pregnancy. Thus, it seems that due to "State of Stress" the enzyme activity is

TABLE IV

During Different Trimester of Pregnancy *After Parturition*

Type	No.	1st Tr.	2nd Tr.	3rd Tr.	1st week	2nd week	3rd week	4th week
I	Pri.	(9) 302.6 ± 35	320 ± 44	347.8 ± 38	312.4 ± 32	301 ± 41	289.3 ± 28	281.4 ± 46
	Alpha—I							
II	At 1 mg%	284.0 ± 23	296.7 ± 16	328 ± 27	298 ± 33	286 ± 27	275.5 ± 31	269.3 ± 19
	MW (13)							
	SITC							
I	(1 ml)	1.22 ± 0.16	1.25 ± 0.12	1.30 ± 0.20	1.24 ± 0.076	1.22 ± 0.12	1.19 ± 0.12	1.18 ± 0.14
	(9) P							
II	MW (13)	1.20 ± 0.11	1.22 ± 0.13	1.26 ± 0.9	1.21 ± 0.11	1.18 ± 0.16	1.16 ± 0.092	1.15 ± 0.92

I—Primipara.
II—Multipara.

increased. In the present series it was also found that the increase in the enzyme concentration was in linear fashion and after delivery, as the stress was over, the enzyme values were within normal limits. Further, Alpha-1-Anti-trypsin enzyme activity was more increased in primipara, where the factor of stress was more visible (Table IV).

It is equally possible that with stress, the effect of sex hormones may be responsible for this effect. The status of hormones changes with the advancement of pregnancy. Lieberman (1971) has already confirmed the effect of sex hormones on trypsin inhibiting capacity.

Extensive work is required to confirm the exact mechanism, responsible for this effect.

Summary

Alpha-1-Anti-trypsin (Alpha-1-AT) activity was measured in 22 healthy pregnant females, during different trimesters of the pregnancy and after parturition, over 4 weeks.

There was a significant rise in Alpha-1-AT concentration in serum, during pregnancy, and this rise was in a linear fashion. There was an abrupt fall after delivery, and within 4 weeks the enzyme concentration was within normal limits.

The possible mechanism for this relationship has been explained and further work is indicated.

References

1. Eriksson, S.: Acta. Med. Scand. Supp. 432: 1, 1965.
2. Faarvang, H. G.: Endocrinol. 30: 285, 1959.
3. Faarvang, H. G. and Lauritsen, O. S.: Nature. 199: 290, 1963.
4. Ganrot, P. O. and Bjeree, B.: Acta. Obst. & Gynec. Scand. 46: 290, 1967.
5. Guibaud, S., Bonnet, M. and Thoulon, N. M.: Obst. & Gynec. 45: 34, 1975.
6. Jacobsson, K.: Scand. J. Clin. Lab. Invest. 7: (Suppl. 14) 65, 1955.
7. Laurell, C. B. and Eriksson, S.: Scand. J. Lab. Invest. 15: 132, 1963.
8. Lieberman, J., Mittman, C. and Kent, J. R.: J. Am. Med. Assoc. 217: 1998, 1971.
9. Lieberman, J.: Med. Clin. North Am. 57: 691, 1973.
10. Sharp, H. L.: Gastroenterology. 70: 610, 1976.
11. Sharma, B. B., Nawal Kishore, Brij Kishore, Hazra, D. K., Mittal, V. P. and Sharma, R. V.: J.A.P.I. 22: 541, 1974.