NEUTROPHIL ALKALINE PHOSPHATASE ACTIVITY IN PREGNANCY AS A METHOD FOR MONITORING FOETAL PROGNOSIS

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Valentini *et al* (1954) were first to describe increase in leukocyte alkaline phosphatase (NAP) activity in pregnancy. The NAP activity is known to rise gradually with advancement of pregnancy and it returns to normal limits by sixth week postpartum (Pritchard 1957; Quigley *et al* 1960; Polishuk *et al* 1970).

The regulation of NAP activity is influenced by ovarian and piltuitary hormones is shown by Gordon and Hunter (1965). It was further suggested by Polishuk *et al* (1970), that the activity depends on the balance between the two hormones oestrogen and progesteron produced by the placenta.

The aim of present study was to determine NAP activity in pregnancy, labor and puerperium and to evaluate its correlation with pregnancy outcome.

Material and Method

Two hundred and seventy-nine determinations of NAP activity in 110 normal pregnant women were studied during various trimesters of pregnancy along with control group.

The control group included 10 healthy male and 10 healthy non-pregnant females in various phases of menstrual cycle.

NAP activity was determined after fixation and staining the blood films by Kaplow method (Kaplow 1955), one hundred consecutive segmented and band-form granulocytes were graded from 0 to 4 according to the intensity and quantity of precipitated dye within the cytoplasm, through pale pink to heavy granular black precipitate. The sum of the grade represents the NAP score and possible range is from 0-400.

Result and Discussion

Normal Control

The average score of 10 male was 65 comparing favourably with Kaplow's (1955) control group, and that of non-pregnant women was in mean range of 68-102 Highest peak NAP activity was observed at midmenstrual period i.e. 13th and 14th day of 28 days cycle.

Polishuk *et al* (1968) observed increased in NAP activity midmenstrually with rise of BBT. Similar observation was reported by Gordon and Hunter (1965). Both considered peak oestrogen rise at mid-cycle responsible for it.

Pregnancy

During the first trimester the average score of 30 women was 130 with a range of 102-165 ± 17.7 (Table I), high values were obtained as early as 5th week. A

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score above 102 was considered as positive for pregnancy. Quigley *et al* (1960) and Harer and Quigley (1971) considered a score of 80 as positive for pregnancy.

In 4 cases the pregnancy was doubtful clinically and vaginal cytology was negative, but NAP showed raised activity and all 4 were later confirmed to be cases of pregnancy—intrauterine pregnancy (3 cases) and ectopic (1 case). Quigley *et al* (1960), Climie *et al* (1962), Joshi and Gupta (1967), Harer and Quigley (1971) had all confirmed its value as a test for early pregnancy, while Beal *et al* (1958) considered NAP monitoring as a doubtful test in diagnosing early pregnancy. NAP activity was studied in 59 women in the second trimester, the average score was 156.3 ± 25 with a range of 117-206. There was a significant increase in activity after 26 weeks of pregnancy and this rise was progressive till term (the normal course) and thereafter if pregnancy was prolonged, it showed a decline (Table I). The decline of activity was also observed after first postpartum day (Table II). In establishing the range of activity one case who developed s/s of toxaemia, one of stillbirth and one of low birth weight infant were excluded, but the nature of curves for clinical interest have been recorded in Fig. 1.

NAP activity swings up during labour and remains high for first 24 hours and then starts declining (Table II). Similar pattern was observed by Pritchard (1957) Quigley *et al* (1960) and Efrati *et al*

TABLE I

NAP Activity in Relation to Duration of Gestation in Normal Pregnancy

Duration of getsation	No. of cases	Range of NAP Score	Mean	SD
1st trimester	21	102–149	103.1	14.00
2nd trimester	59	117–206	156.3	22.82
3rd trimester				
28 weeks	14	140–215	173.6	21.56
30 weeks	18	150–221	190.4	20.00
32 weeks	21	145–264	198.1	33.00
34 weeks	31	150–282	208.3	36.55
36 weeks	31	169–283	216.8	36.33
37 weeks	14	174–285	232.5	28.98
38 weeks	24	174–292	241.8	32.25
39 weeks	22	182–301	252.2	37.25
40 weeks	17	178–310	263.9	45.43
41 weeks	7	161–284	184.6	34.55

TABLE II

NAP Activity During Labour and Pueperium

Type	Negative control 1st 24 hrs. of labour		Positive controls between 2nd—6th Postpartum day				
Postpartum day	Before heating	After heating	2	3	4	5	6
No. of. cases	10	10	4	4	4	4	4
NAP Score	306.6	0	293	216	192	177	156

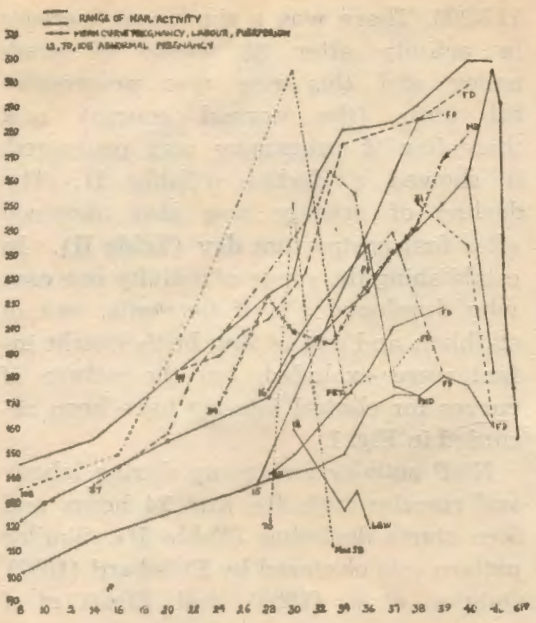

Fig. 1

(1964), while Polishuk *et al* (1970) and Elder *et al* (1971) found a rise up-to 26-28th week and 30th week respectively. Beal *et al* (1958) found no difference in activity in early and late pregnancy.

Nature and Regulation NAP Activity

The study of 10 negative control in which NAP was done before heating and after heating for 15 minutes at 65°C, shows absence of alkaline phosphatase in slide after heating (Table II), proving it to be heat-labile and different from heat stable alkaline phosphatase which is of placental origin. Similiar was the observation of Polishuk *et al* (1970), and Elder *et al* (1971a and 1971b).

The neutrophil alkaline phosphatase is under the influence of hormones is proved by study of Valentine *et al* (1954), Gordon and Hunter (1965), Polishuk *et al* (1970). The latter believe that NAP activity might be an expression of relationship between oestrogen and progesterone and possible corticoids effect of the placenta. Ryan (1962) and Robertson and Maxwell (1963) upheld the same opinion.

In the present series no variation in NAP activity was found with variation in age, parity of mother. Similar was the observation of Beal *et al* (1958) (Table III).

Pregnancy Outcome

With single estimation inspite of the reading being in normal range, an error of 23% was observed i.e. out of 35 cases that reported for delivery, 27 delivered normally. In the remaining 8 cases, foetal distress occurred in 4, premature pain in 1 and premature delivery in 3 cases. As observed in Table I there is a marked variation in absolute values between individual at a specific time of pregnancy and therefore it becomes difficult to pick-up the abnormal values.

In groups of 3 and serial estimation normal curve was observed in 17 and 21 cases, while abnormal curve was in 5 and 17 cases respectively. In group of serial we

TABLE III

Relationship of Mean NAP Score With Age and Parity of Mother in Various Periods of Gestation

Age	Duration of Pregnancy			Parity	Duration of Pregnancy		
	1st	2nd	3rd		1st	2nd	3rd
16–20	117	156	219	0	128	163	213
21–25	112	155	291	I	132	161	207
26–30	127	167	210	II	128	166	197
31–35	—	145	190	III	—	173	227

excluded 3 abnormal cases as mentioned earlier. The prediction accuracy was higher with serial than with three estimation (Table IV) i.e. 94.4% 86.6% in normal group and 84.5%, 50% in abnormal group.

TABLE IV
NAP Activity in Relation to Pregnancy Outcome

Type of Curve	3-Estimation		Serial Estimation		Single Values
	Normal	Abnormal	Normal	Abnormal	
No. of cases	17	5	21	14 + 3	49
No. of cases Not reported for delivery	2	1	2	4	14
Normal delivery	13	2	18	4	27
Foetal distress	1	2	1	5	4
Premature pain	—	—	—	4	1
P.N.D.	1	—	—	1	3
Percentage of accuracy	86.6%	50%	94.7%	80% (84.6%)	87.7%

3 + (Abnormal cases included for clinical interest).

The study of pattern of NAP activity in abnormal group showed following variation: (Fig. 1).

(a) Values persistently on higher side of range-Case No. 47.

(b) Values persistently on lower side of range-Case No. 27.

(c) Fluctuation in form of peak rise or fall-Case No. 16, 37, 39, 101.

The peak rise was followed by premature pain in 4, toxaemia in 1 (excluded from analysis) at 2-4 week's interval, after this, if values settled to normal and showed a progressive rise within the normal range then foetal prognosis was good case No. 39, 101.

Three cases which were excluded from normal group, showed interesting curve (Fig. 1) case No. 12 had low birth weight infant and showed values on lower side with persistent fall. Case No. 70 had macerated still birth. The curve showed a sudden rise from and then fall to, below normal values. Case No. 108 showed marked degree of fluctuation. The peak rise at 28 weeks (NAP score 306) was followed by a fall, sign and symptoms of toxaemia of pregnancy developed at 32 weeks, foetal distress in labour required caesarian. Such fluctuation cannot be observed if the observation is less than 4, as evident by case No. 15—of sudden rise, Case No. 31 of sudden fall. In both cases foetal distress occurred.

Summary

NAP activity during normal pregnancy was studied in 110 cases. The NAP activity during normal pregnancy showed a marked variation in activity, but a consistent progressive curve was observed with advancement of pregnancy. The activity declined gradually after delivery, or if pregnancy prolonged.

The study of pattern was helpful in isolating abnormal cases clinically not detectable. In these cases foetal prognosis was poor. Thus it can be concluded from the study that higher degree of reliance can be placed on serial estimation of NAP activity during antenatal management.

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