SERUM PROTEIN BOUND IODINE STUDIES DURING PREGNANCY

by

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Litzenberg (1939) first drew attention to the importance of thyroid in reproduction. Heinemann, *et al* (1948) reported that early in pregnancy the precipitable or protein bound iodine in the serum rose to concentrations in the upper range of normal or even to levels that outside of pregnancy are characteristic of hyperthyroidism. Engstram (1951), Mann *et al* (1964) and Russel (1953) have also shown that the protein bound iodine of serum rises early in pregnancy and returns to normal within a few days after delivery. The rise has been detected as early as the third to sixth week of gestation and from then on it remains high until shortly after parturition. It was postulated that if the protein bound iodine does not increase, the pregnancy was likely to end in abortion within the first four months. However, Singh and Morton (1956) and others have shown that the rise in protein bound iodine does not occur in all cases and the values during pregnancy are subject to considerable fluctuation in contrast to more stable values found in non-pregnant women. They also had not confirmed low protein bound iodine values in cases of abortion. But recently, Kock *et al* (1966) have found that in cases of abortion, within ten days preceding expulsion of products of conception, the protein bound iodine levels were significantly lower. Such conflicting views prompted us to undertake the following study of estimating protein bound iodine levels (P.B.I.) during normal pregnancy and its role in various complications of pregnancy, especially in abortions.

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Material and Methods

In all, 78 cases have been taken up for this study at the Sassoon General Hospitals, Poona. These include 24 cases of normal pregnancy. Estimations were done in all the trimesters of pregnancy and also during labour. A few cases were followed up in the

puerperium. The series also includes ten healthy normal non-pregnant euthyroid women who were investigated as a control. Cases of abnormal pregnancy were studied to see if there was any variation in the P.B.I. levels. These include 27 cases of abortion, five cases of toxaemia of pregnancy, four cases of twin pregnancy, three cases of hydramnios, four cases of intra-uterine death of the foetus and one case of vesicular mole.

Before starting the investigations all patients were thoroughly examined and investigated to exclude any pathology, such as thyroid disease or any other systemic disease. Patients were advised not to take any expectorants or any other iodine containing drugs, any medications like antibiotics, tranquilisers, anti-convulsants which might affect the concentrations of P.B.I. Also patients suffering from vomiting, colds or any other virus infection were excluded from this study as they tend to alter the values.

Procedure

All the estimations were done by the modified chloric acid digestion method, as described by Kulkarni and Desai (1962).

To 1 ml. of serum, 10 ml. trichloracetic acid was added, drop by drop, and allowed to settle for 10 minutes and then centrifuged for 10 minutes and later washed twice with 10 c.c. of trichloracetic acid.

To the washed precipitate, 0.2 c.c. of 0.5% solution of potassium chromate and 5 c.c. of chloric acid were added and mixed thoroughly. Two test tubes, each containing a solution of 0.5 ml. of trichloracetic acid, 0.2 ml. of potassium chromate and 5 ml. of chloric acid, were taken to serve as blank and a standard. All the test tubes were heated in a paraffin bath gradually to reach a temperature of 120-125°F and maintained till digestion was over. The completion of the process was judged by the reduction of contents to 1 ml. These were allowed to cool to room temperature and later the volume was made up to 5 ml. in each of the test tubes by the addition of distilled water.

Four cc. aliquots were taken from each of the test tubes. To one of the two blank digests, was added 0.4 ml. of standard iodine solution containing 0.04 ugm. iodine, and to the standard and test digests 0.4 ml. of distilled water was added so as to equalise the volume in all the test tubes. To each of the test tubes, 0.5 ml. of 10% sodium chloride and 2 c.c. of arsenous acid reagent was added. Fifteen minutes after the addition of arsenous reagent, 0.5 ml. of ceric acid reagent was added and time noted. Readings were taken at an interval of exactly 2, 4, 6 and 8 minutes after the addition of ceric acid reagent on the kelt Summeron photoelectric colorimeter set with filter No. 42 (violet).

Readings were plotted against the interval of time.

P.B.I. was calculated as under:—

$$\frac{\text{Serum P.B.I. in Ugm. \%}}{} = \frac{\text{Slope of test—slope of blank}}{\text{Slope of standard—slope of blank}} \times 5$$

Observations:

(1) *P.B.I. levels in non-pregnant women* (Table 1)

All the ten women were in the age group of 18-35 years and compare well with the age of the pregnant cases. Except one, the others were all unmarried. The average P.B.I. level was 4.62 ug.% (3.8 to 5.8).

TABLE I

Serum Frotein Bound Iodine Level in Non-Pregnant Patients

S. No.	Reg. No.	Age in years	Previous obstetrical history	P.B.I. in ugm. %
1	119	20	Unmarried	4.8
2	121	18	Unmarried	5.4
3	131	18	Unmarried	5.4
4	120	25	Unmarried	5.8
5	13	35	Unmarried	3:8
6	14	24	Unmarried	4.0
7	15	22	Unmarried	3.8
8	16	20	Unmarried	5.4
9	17	24	Unmarried	4.0
10	124	28	2nd F.T.N.D.	3.8

(2) *P.B.I. Levels in Normal pregnancy*

These patients were in the age group of 16-35 years and were in the parity group of I and V. Of these 24 cases, estimations were done in 18 cases in the first trimester and of these only 11 cases came for regular follow-up during pregnancy and labour. In seven cases the estimations were done in the second and third trimesters only and of these four were followed during labour.

The mean protein bound iodine levels were:

(1) 5.16 ugm.% (2.9-8.7) in the first trimester.
(2) 5.80 ugm.% (4.3-7.8) in the second trimester.
(3) 6.0 ugm.% (4.3-6.8) in the third trimester and
(4) 6.13 ugm.% (4.8-7.2) during labour.

All the above values denote that the P.B.I. level rises steadily during pregnancy and the maximum rise was observed during labour. Though the initial value was only slightly more than the non-pregnant level, a steady rise was observed in the subsequent trimesters. There is practically a rise of 1.51 ugm.% during labour as compared to the non pregnant level.

However, some irregular patterns were observed in the above study. In one case the level was only 2.9 ugm.% in the first trimester, although the level went up to 4.3 ugm.% later. The values were far below the average first trimester level; yet, no complications occurred during pregnancy. However, in the same case the level shot up to 6.2 ugm.% during labour. In another case the initial value was 8.7 ugm.% even though the patient had no symptoms of thyroid disease. This level dropped to 6.8 ugm.% subsequently but without any complication. Likewise, in another four cases the initial values were higher with a subsequent

TABLE II

Serum P.B.I. Levels in Normal Pregnancies and Deliveries

S. No.	Reg. No.	Age yrs.	Para	Previous obstetrical history	Serum P.B.I. values in ugm. %				
					Antenatal trimesters			Intra natal	Post natal 6 weeks
					I	II	III		
1-	2	16	Primi	Primigravida	8.7	7.8	6.8	6.8	..
2	2	25	2nd	1 F.T.N.D.	5.8	..	5.1	5.8	..
3	14	25	2nd	1 F.T.N.D.	4.0	5.8	6.5	6.6	4.3
4	24	29	5th	4 F.T.N.D.	4.7	5.4	6.4	..	..
5	25	30	4th	2 F.T.N.D. 1 stillbirth.	2.9	4.3	4.8	6.2	..
6	35	18	3rd	2 F.T.N.D.	6.1	5.8	..	5.4	..
7	52	23	2nd	2 F.T.N.D.	3.5	4.5	6.1	6.5	..
8	54	30	5th	4 F.T.N.D. (1 Anencephalic)	5.4	6.4	6.4	..	..
9	60	23	2nd	1 F.T.N.D.	5.3	4.8	4.4	..	4.4
10	78	30	3rd	2 F.T. still birth	4.8	..	5.2	5.7	..
11	57	21	Primi	..	6.3	6.4	5.4	..	..
12	26	26	4th	1 F.T. 2 F.T.C.S.	..	6.1	6.7	6.8	4.7
13	30	20	Primi	..	..	7.5	6.0	6.4	..
14	33	20	Primi	..	..	4.5	6.6	..	..
15	39	26	2nd	1 F.T.N.D.	..	4.6	6.4	6.6	..
16	51	30	4th	2 F.T.N.D. 1 Premat .D.	..	5.9	6.4	4.9	..
17	43	28	3rd	1 Premat. 1 F.T.N.D.	..	73	5.2	..	..
18	11	16	Primi	..	3.2	..	..	5.6	..
19	58	28	5th	4 F.T.N.D.	3.6	..	..	6.3	..
20	63	26	4th	1 F.T.N.D. 2 abortions.	5.3	..	..	6.0	..
21	66	26	3rd	2 F.T.N.D.	5.0	..	..	6.5	5.8
22	68	35	3rd	1 F.T.N.D. 1 Premature	7.6	..	..	7.2	6.2
23	80	22	2nd	1 abortion	3.0	..	..	6.2	4.6
24	70	30	5th	1 F.T.N.D. 3 abortion.	5.7	..	..	4.8	..
					5.16	5.80	6.0	6.13	5.83

fall later, though in all these the levels were not lower than the average for that period of pregnancy. In two cases the levels were as low as 4.4-4.8 ugm.% during third trimester and labour but without any adverse effect. No significant correlation was found between the P.B.I. level and age and parity of the patient.

Six cases came for follow up in the purperium and the average P.B.I. level was 5.83 ugh.%. This value was higher than the average first and second trimester levels seen during pregnancy.

P.B.I. Levels in Abortions:

Of the twenty-seven cases that were studied, seven were admitted as threatened abortions, two as inevitable and the rest were incomplete abortions.

The period of gestation was between 6-10 weeks in 12 cases, 10-20 weeks in seven and in three it was 20-24 weeks. In the threatened abortions group, the protein bound iodine level ranged from 1 ugm.% to 7.6 ugm.% (mean 4.57 ugm.%). In the inevitable and incomplete groups it ranged from 2.8 to 5.2 ugm.% On

TABLE III

Serum P.B.I. Levels in Abortions

S. No.	Reg. No.	Age	Gravida	Previous obst. history	Gestation in weeks	Type of abortion	Serum PBI (ugm. %)	Course of pregnancy
1	5	12	2nd	1 abortion	12	Threatened	3.9	Aborted
2	138	20	Primi.	..	10	,,	4.3	,,
3	134	22	4th	3 abortion	10	,,	5.6	,,
4	139	..	3rd	2 abortion	10	,,	7.6	..
5	136	25	3rd	2 abortion	22	,,	5.6	Continued on proluton.
6	123	20	2nd	1 F.T.N.D.	12	,,	4.0	Aborted
7	76	25	3rd	1 abortion	10	,,	1.0	Do.
8	106	28	3rd	2 F.T.N.D.	20	Inevitable	4.6	Do. on the same day.
9	132	27	3rd	2 F.T.N.D.	8	Incomplete	3.9	Do.
10	90	29	3rd	1 F.T.N.D. 1 abortion.	20	,,	3.8	Do.
11	96	26	4th	3 F.T.N.D.	6	,,	4.9	Do.
12	114	20	Primi	..	12	,,	3.0	Do.
13	115	16	,,	..	8	,,	4.8	Do.
14	116	28	2nd	1 abortion	10	,,	5.2	Do.
15	117	32	9th	6 F.T.N.D. 1 Prem stillbirth 1 abortion.	10	,,	3.5	Do.
16	133	21	4th	3 F.T.N.D.	8	,,	4.6	Do.
17	135	20	2nd	1 abortion	8	,,	3.7	Do.
18	140	45	8th	5 F.T.N.D. 2 abortion.	6	,, (septic).	2.8	Do.
19	141	29	4th	3 F.T.N.D.	16	,,	3.8	Do.
20	2	19	2nd	1 abortion	12	,,	3.8	Do.
21	95	22	2nd	1 F.T.N.D.	14	,,	5.3	
22	107	16	Primi	..	16	,,	4.7	
23	109	24	2nd	1 abortion	20	,,	4.4	
24	111	35	4th	2 F.T.N.D. 1 abortion	24	,,	5.2	
25	112	26	2nd	1 abortion	24	,,	5.3	
26	113	38	Primi	20 yrs. Primary sterility.	16	,,	3.8	
27	118	27	Primi	..	8	,,	5.8	
						Mean	4.33 Mgm. %	

the average the P.B.I. level for all the cases was 4.33 ugm.%. This figure approximated to the non-pregnant levels, and is lower than the level for normal pregnancy.

Except in one case of threatened abortion, the pregnancy did not continue in spite of bed rest and treatment. In that case the pregnancy was 22 weeks and the P.B.I. level was 5.6 ugm.%. Three patients had previous 2 or 3 consecutive abortions at the same period of pregnancy and the P.B.I. level in them was 5.6-7.6 ugm.%. In spite of this high level two of them aborted this time. But in another case of repeated abortions the level was only 2.8 ugm.%. In another case who had a previous stillbirth and abortion the P.B.I. level was also low, i.e. 3.5 ugm.%. In as many as 9 cases the levels were more than 5.16 ugm.% (average for normal pregnancy), yet, abortion occurred in all the cases. These findings indicate that while the levels were low in cases of abortions, there is no relation between the initial

value and the completion of abortion. However, in none of threatened abortions who had a initially low value, the pregnancy could be salvaged.

There were three other cases of habitual abortions which ultimately went to term with bed rest and progesterone. None of them were admitted with the symptoms of abortion. In one case the initial level was only 3 ugm.% but, this rose upto 6 ugm.% subsequently. In the other two the initial levels were 4.8 ugm.% and 5.7 ugm.% but, the levels were maintained and increased during labour. Thyroid therapy was not given to these cases during pregnancy.

Comparing these three cases with above three cases of habitual abortion, who subsequently aborted, one cannot come to any conclusion as to critical level when abortion is likely to occur during pregnancy.

P.B.I. Levels in cases of twin pregnancy

Of the four, two patients were admitted in the third trimester and the other two during course of labour.

In one case the initial level was 4.2 ugm.% but, this subsequently went up to 7.6 ugm.%. In the rest the levels were that of normal pregnancy and this raises a doubt of the possible role of foetus and placenta for the raised P.B.I. levels during pregnancy.

P.B.I. Levels in cases of toxaemia of pregnancy

All the five were between the age of 20 and 30 years and were in the parity group of two and six. None of them gave a previous history of toxaemia. They were between 28 and 34 weeks at the time of admission.

In two cases the levels were as low as 3.1-3.5 ugm.% and in two others the levels were high, 7.1-7.6 ugm.%. The average level was 5.34 ugm.%. All these patients responded to treatment of toxaemia and ultimately went to term. The P.B.I. levels have no bearing on cases of toxaemia of pregnancy.

P.B.I. Levels in cases of hydramnios

Both the cases were admitted in the third trimester. X-ray of the

TABLE IV

Serum P.B.I. Levels in Twin Pregnancy

S. No.	Reg. No.	Age	Gravida	Previous obst. hist.	Gestation in weeks	Serum P.B.I. ugm. %	Course in pregnancy
1	86	37	6th	5 F.T.N.D.	24 36	4.2 7.6	Delivered normally. Both babies well.
2	89	20	Primi.	..	During Labour	5.0	Delivered both babies normal.
3	127	32	9th	3 F.T.N.D.	34	6.3	Delivered premature babies.
4	128	24	2nd	1 F.T.N.D.	During Labour.	6.3	Delivered normal twins.
Mean						5.88	

TABLE V

Serum P.B.I. Levels in Pregnancies with Toxaemias

S. No.	Reg. No.	Age	Gravida	Previous obst. hist.	Gestation in weeks	Serum P.B.I. ugm. %	Course of pregnancies
1	75	30	6th	5 F.T.N.D.	30	7.1	F.T.N.D. on 18-5-69.
2	10	30	4th	3 F.T.N.D.	28	3.5	Continuing pregnancy.
3	9	25	2nd	1 F.T.N.D.	30	5.2	Induction of labour.
4	98	20	2nd	1 Premature still birth.	32	7.6	Continuing pregnancy.
5	83	30	6th	4 F.T.N.D. 1 abortion.	34	3.1	Delivered premature baby.
Mean						5.34	

TABLE VI

Serum P.B.I. Levels in Pregnancies with Hydramnios

S. No.	Reg. No.	Ags in yrs.	Gravida	Previous obst. hist.	Gestation weeks	Height of uterus	Serum P.B.I. ugm. %	Course of pregancies
1	99	16	Primi	..	36	36	5.5	Delivered F.T F.T. Baby.
2	105	40	9th	8 F.T.N.D.	34	36	4.6	Delivered premature male baby.
Mean							5.05	
Range	16–40						4.6 to 5.5	

abdomen did not reveal any congenital malformations.

The P.B.I. levels were 5.5 ugm.% and 4.6 ugm.% respectively but, these were lower than the average normal for that period of pregnancy. One of them had a premature labour but no significant correlation can be drawn from these values.

P.B.I. Levels in cases of intra-uterine death of the foetus

In all these cases there were confirmatory radiological signs of intra-uterine death.

In one case the initial level was 5.9 ugm.% at 22 weeks but it subsequently fell to 3.2 ugm.%, when she came and delivered a stillborn baby

TABLE VII

Serum P.B.I. Levels in Pregnancies with Intrauterine death of the Foetus

S. No.	Reg. No.	Age	Gravida	Previous obst. history	Gestation in weeks	Height of Uterus	Serum P.B.I. ugm%	Course of pregnancy
1	69	25	2nd	1 Premature still birth.	22 during labour	22	5.9	Still birth
						26	3.2	Rh incompatibility
2	104	20	Primi.	..	30	26	4.0	Still birth, Induced labour.
3	122	20	Primi.	..	34	30	6.1	Still birth.
Mean							4.8	

due to Rh- incompatibility. In the other two, the levels were 4 ugm.% and 6.1 ugm.% respectively. These two values cannot be discussed as the initial values were not available.

P.B.I. values in vesicular mole

The patient, a 7th gravida, with a history of 10 weeks' amenorrhoea and slight bleeding was admitted as a case of threatened abortion. The uterus on examination was about 16 weeks' size and subsequently the diagnosis was confirmed when the patient expelled the mole.

TABLE VIII

Serum P.B.I. Levels in Vesicular Mole

S. No.	Reg. No.	Age	Gravida	Previous obst. Hist.	Gestation in weeks	Height of uterus	Serum P.B.I.
1	91	25	7th	5 F.T.N.D. 1 Abortion.	10	16	2.8

The P.B.I. level was only 2.8 ugm.%. This very low level is significant, more so in a case which normally has high HCG levels.

Discussion

Pregnancy affects virtually all aspects of thyroid hormone economy. The thyroid is enlarged, accompanied by hyperplasia of glandular tissue and increased vascularity. These changes cause some alterations in the physiological role of the thyroid during pregnancy. The serum protein bound iodine is raised during pregnancy and also the thyroid binding protein of plasma, particularly alpha globulin. The thyroid uptake of I^{131} is distinctly elevated. The B.M.R. progressively increases to as high as + 25%. Probably these changes are essential for the maintenance of pregnancy just as the changes in the pituitary function and the H-ion concentration.

But, all these changes are not associated with the signs of hyperthyroidism or demonstrable rise in oxidative processes. This is probably because the rise with capacity for binding is such that the concentration of free thyroxine in the serum is usually no higher than in normal women. It is possible that thyroxine is available to tissues only in the free form.

Of the various methods of estimating thyroid function, the study of protein bound iodine level in serum (serum precipitable iodine) is a reliable one and one commonly used. The values for the non-pregnant state were 1-3 ugm.% for hypothyroid, 3-7 ugm.% for euthyroid and 7-12 ugm.% for hyperthyroid patients. Beginning as early as the sixth week of pregnancy this level rises sharply in mother's plasma and at 12 weeks of gestation the value reaches the level of 6 ugm.% (Mann *et al* 1951), and from then on it remains high ranging from 6.2-11 ugm.% and the majority will have an upper limit of normal, i.e. nearly 8 ugm.%. These values remain elevated until after delivery. The rise occurs whether pregnancy is uterine or ectopic.

Many explanations have been put forward to explain the rise in the protein bound iodine level during pregnancy. (1) It may be due to the high circulating oestrogen level, which

causes an increase in the thyroid binding capacity. (2) Probably the placenta elaborates a thyroid stimulating principle but search for this hormone has been unrewarding. (3) It was thought to be due to an increase in the basal metabolic rate. This is not accepted as B.M.R. which is one measurement of oxidative process is not elevated before the latter part of pregnancy, whereas the rise in the protein bound iodine occurs 3-6 weeks after conception and is not correlated to a rise in B.M.R. Moreover, B.M.R. does not denote an increased activity of thyroid, but seems to be related to the need for extra oxygen, created by the enlargement of the uterus and growth of the foetus. (4) The high P.B.I. values in the latter weeks may indicate that the foetus may complement maternal thyroid function. Fisher (1964) observed that infants have significantly higher thyroid secretion rates than adults. Zondek (1940) noticed improvement of thyroid function during the latter part of pregnancy in a myxoedematous patient and a relapse to hypothyroid state after delivery, and stated that a thyroxine-like compound crosses the placenta. Kelly and Skudden (1960) confirmed the enlargement of the foetal thyroid in endemic goitre areas. But, other studies have shown that there is a low concentration of T-4 binding protein in foetal plasma as compared with maternal plasma and the values are very low. Studies of Andreoli and Robbins (1962) on young foetuses gave very low values. But as term approaches significant maternal foetal transfer occurs and a rise in the TBG capacity occurs in the foetus. However, the placenta appears to be impermeable to T-4, since the foetal P.B.I. after maternal T-4 load is low. (5) The high levels of hydroxy-corticoids in pregnancy may decrease the rate of peripheral utilization of thyroid hormone resulting in increase of P.B.I. level.

Whatever might be the cause, high levels of P.B.I. are found in pregnancy, which shows that there is a rise in the active circulating thyroid hormone. But this rise does not affect the tissue metabolism, nor is it associated with hyperthyroidism as in non-pregnant women. This seems to denote that the pregnant woman tolerates a greater concentration of hormone in her serum and this altered concentration does not cause a corresponding rise in cellular metabolism.

Of the various methods of estimating P.B.I., the alkaline fusion method described by Barker *et al* (1951) and the chloric acid digestion method described by O'Neal *et al* (1953) were the ones commonly used. Kulkarni and Desai (1962) modified the chloric acid method of O'Neal *et al* to suit the Indian conditions. The values for the general population by this method are a little low as compared with those of other investigators (Table 9). The levels in the non-pregnant women in the present study, 4.62 ugm.% (3.8-5.8), though slightly low, are, however, comparable to the values obtained by Sen and Banerjee (1958) by the alkaline fusion method.

All workers noted a steady but definite rise in the P.B.I. level during normal pregnancy. Williams (1968) gives a range of 7.12 ugm.% and Mann *et al* (1951) give the range of 5.5-9.5 ugm.% for P.B.I. levels

TABLE IX

Normal Serum P.B.I. Values by Different Investigators

Investigations	Year	Method of digestion	Range	Average
Barker Et al	1951	Alkaline fusion method	3.5–8	5.1
Zak et al	1952	Chloric acid method	3.5–11.1	7.3
O'Neal et al	1953	Chloric acid method	4.0–7.3	5.2
Bodansky et al	1958	Chloric acid method	..	6.2
Sen and Banerjee	1958	Alkaline fusion method	3.46–6.6	4.4
Kulkarni and Desai	1962	Chloric acid method	2.4–5.1	3.7

during pregnancy. In the present study the average values ranged from 5.16 ugm.% in the first trimester to 6.12 ugm.% during labour. There is a difference of 1 ugm.% between the two and 7.51 ugm.% (if the non-pregnant value is taken). Thus, while these values are definitely lower as compared with others (Table 10) yet a steady rise has been obtained throughout pregnancy.

If the pregnancy is to be completed P.B.I. level should not be below 6 ugm.% after pregnancy has proceeded approximately 16 weeks (Mann *et al* 1951). This suggests that if this concentration is not reached in this period, abortion is more likely to occur. The average P.B.I. level of 4.33 ugm.%, in the abortion cases in the present series, is also low as this figure approximated to the level in the non-pregnant patients. Heinemann *et al* (1948) gave figures ranging from 2.8 to 5.8 ugm.% in cases of abortion. In their opinion failure of adjustment typical of pregnancy will cause premature termination. However, in 9 of our cases the P.B.I. levels were more than the

TABLE X

Serum P.B.I. Level in Pregnant Women by Different Investigators

Year	Investigator	P.B.I. Values Range (Percentage)	Average (percentage)
1948	Heinemann, M. Johnson, C. E. Mann, E. B.	6.2 to 11.2	8.2
1964	Mann, E. B., Reid, W. A., Jones, W. S.	5.5 to 9.5 ugm.	7.1 (7.6)–1.8 in first trimester. 7.4 (7.9–1.6) in third trimester.
1951	Mann, E. B. Heinman, M. Johnson, Leary, D. C. & Peters, J.P.	5.6 to 10 ug.	
1966	Kock, H., Vankessel, H., Stolte, L.	6.8 to 8.4 ug.	
1963	Harvey, Rose et al	5 to 13 ug.	8.2-1.5 ug.
1969	Hankock, et. al	4.5 to 11.5 ug.	7.7 ug. 8 ,, 8.3 ,,
1969	Mestman	6.7 to 7.8 ug.	7.6
1969	Present Series	2.9 to 8.7 ug.	5.16 5.8 6 6.13

average for normal pregnancy. This shows that high levels do not insure against abortion. Probably, the abortion in such cases occurred due to other causes. However, in none of the cases with low P.B.I. levels admitted with symptoms of abortion, the pregnancy could be continued with treatment. Failure of the P.B.I. to rise in those who miscarry may indicate two things: (1) that there is a defect in the ovum or its implantation and (2) that the stimulus for the P.B.I. to rise is lacking. The secreting activity of the thyroid and proper utilisation of the thyroid hormone is essential for the continuation of pregnancy. In three cases of habitual abortion with low initial values, the abortion did not occur but subsequently the level of P.B.I. increased. In these cases the stimulus to cause a rise in the P.B.I. progressively manifests itself with treatment. In three other cases of habitual abortion admitted with symptoms like bleeding, even though the values were high, abortion still occurred. That shows that when once symptoms of abortion occur probably indicating the death of embryo, nothing can save the pregnancy. In such cases of abortion with low P.B.I. levels, it was observed that even though thyroid was given, it only raised the P.B.I. levels but did not prevent the abortion. Thus, as many workers think, the low P.B.I. levels in cases of abortion may be as explained above possibly due to withdrawal of the stimulus after the death of the foetus. Koch *et al* (1966) observed similar low levels 10 days before the occurrence of abortion.

All the levels were that of normal pregnancy in the four cases of twin pregnancy. That shows that unlike in the metabolism of steroids, the presence of a second foetus and placenta do not alter the levels of P.B.I.

In cases of toxemia, the values were low in two cases but in the other two the levels fell in the range of normal pregnancy. In all these cases the pregnancy went to term with treatment. This condition probably appears not to modify the P.B.I. levels as to cause any untoward complication.

In both the cases of hydramnios the values were lower than the average for that period of pregnancy. Though one of them had a premature delivery, yet no correlation could be drawn from these values.

In one case of intra-uterine death, the P.B.I. level dropped from the initial 5.9 ugm.% to 3.2 ugm.%. In the same case the cause of foetal death was due to Rh-isoimmunisation which shows that a significant fall does occur when the foetus dies. But in the other two cases the values were not low. The initial values in these cases were not known—as they were admitted after foetal death had occurred.

The P.B.I. level in the case of vesicular mole was 2.8 ugm.% which is very low. This is contrary to the observations of Knock *et al* (1966) who quote a high P.B.I. level of 12 ugm% and an increased thyroid uptake of I^{131} in molar pregnancy. Since the oestrogen level is not altered during molar pregnancy, they suggest that abnormal chorionic tissue elaborates a thyroxine stimulating principle such as seen in some cases of choriocarcinoma. The above finding cannot be substantiated by our case.

While it is believed that higher concentrations of HCG in early weeks of normal pregnancy have no significant effect upon the serum P.B.I. level (Williams) yet our cases of vesicular mole, abortions and foetal death possibly suggest that the degenerating chorion may actively lower the P.B.I. level.

Summary and Conclusion

(1) Serum protein bound iodine level estimations were done in 78 cases.

(2) These included 24 cases of normal pregnancy, 27 cases of abortion, 5 cases of toxaemia, 4 cases of twins, 3 cases of hydramnios, three cases of intra-uterine death, 1 case of vesicular mole and 10 cases of normal non-pregnant women.

(3) Estimations were done by the modified chloric acid method.

(4) The average P.B.I. level in normal non-pregnant women was 4.6 ugm.%.

(5) The level during the first trimester was 5.16 ugm%, second trimester 5.80 ugm%, third trimester 6 ugm.% and 6.13 ugm% during labour.

The rise of levels of P.B.I. in first and second trimesters is not significant but if we take the level during labour it is 1.51 ugm% higher than the non-pregnant level which is statistically significant.

(6) (a) The average level in abortion is 4.33 ugm%. Level is low and approximates the non-pregnant levels.

(b) In 9 cases of abortion the levels were higher than pregnancy level.

(c) In none of the cases with low P.B.I. level admitted with symptoms of abortion could the pregnancy be continued with treatment.

(d) In three cases of habitual abortions even though the initial values were low—the pregnancy continued and subsequently the values increased.

(e) But in three other cases with symptoms of abortion, like bleeding, the pregnancy terminated.

(f) The low P.B.I. levels in cases of abortion were probably due to the withdrawal of the stimulus after death of the foetus.

(7) No significant alteration in P.B.I. levels were observed in cases of toxaemia, twin pregnancy and hydramnios.

(8) A definite drop in the P.B.I. level occurred in a case of intra-uterine death of the foetus.

(9) The P.B.I. level in the case of vesicular mole was very low, i.e. 2.8 ugm.%. This is contrary to other reports which quote a high level in such cases.

(10) Low values in cases of abortion due to foetal death, in case of vesicular mole and in cases of intra-uterine death of the foetus possibly suggest that the degenerating chorion may actively lower the P.B.I. level.

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