

EFFECT OF SEVERITY OF ANAEMIA ON THE HUMORAL IMMUNITY IN PREGNANCY

By

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SUMMARY

Investigations regarding the effect of severity of anaemia on the humoral immunity in pregnancy was carried out on 245 women including 50 nonpregnant controls. The pregnant women were divided into 2 groups. Group A consisted of 110 pregnant non-anaemic women with Hb > 11 gm% and group B (85) anaemic women with Hb < 11 gm%. Group B was further subdivided into 3 categories depending upon the degree of anaemia (i) Hb levels 11-8.1 gm% (ii) Hb levels 8-5.1 gm% and (iii) Hb < 5.1 gm%. The present study clearly shows that mild anaemia (Hb 11-8.1 gm%) has no effect ($p > .05$) on the serum immunoglobulin levels. In moderate anaemia (Hb 8-5 gm%) there is lowering of the serum IgG & IgA levels ($p < .001$). In severe anaemia (Hb < 5 gm%) there is significant lowering of all the immunoglobulin levels (IgG, A & M) resulting in significant suppression of humoral immunity, which in turn could be a potent cause for infant mortality and morbidity in our country.

Introduction

Nutrition is an essential part of the mosaic of factors that determine the natural history and biological gradient of health especially in the developing world. It has been recognized that anaemia is a major nutritional problem and its prevalence is as high as 50-90% in the third trimester of pregnancy (Ramalingaswamy, 1963). Anaemia is also associated with obstetrical outcomes including increased susceptibility to infection (Chandra *et al*, 1977), intrauterine

growth retardation, prematurity and low birth weight (Prema *et al*, 1981).

Cohen and Hansen (1962) found that the turnover of globulins remains relatively unaffected by malnutrition. However Chandra (1975) proposed that Haemoglobin levels less than 8 gm% is associated with immune depression. Chandra (1970) observed a significant correlation between cord IgG levels and birth weight in human neonates. Fetal growth retardation was associated with a significant reduction in the transfer of IgG from mother to the foetus. However Mohanlaxmi *et al* (1986) found no correlation between maternal nutrition and fetal biochemical levels of Haemoglobin,

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iron, protein and albumin. Hence the effect of anaemia on the maternal immune response and the cord IgG levels remains controversial.

The present study was undertaken to evaluate the effect of maternal Haemoglobin levels on serum Immunoglobulins.

Material and Methods

The present study was conducted in department of Obstetrics and Gynaecology, University Hospital, Banaras Hindu University in collaboration with the UGC Immunodiagnostic Training and Research Centre, department of Pathology, Institute of Medical Sciences, Banaras Hindu University. The material included 195 randomly selected patients attending the antenatal clinic during the period between April 1987 to Feb. 1988 and 50 age and socioeconomically matched nonpregnant controls selected from the attendants of the patients. Any woman giving history of infection, major or minor within the past 3 months of the study was excluded.

The pregnant women were divided into two main groups depending upon the presence or absence of anaemia. Anaemia in pregnant women defined as Hb < 11.0 gm% and in non-pregnant women as Hb < 12 gm% (WHO, 1974).

Groups

Group A—110 non-anaemic normal pregnant women with uncomplicated pregnancy (Hb > 11 gm%).

Group B— 85 anaemic mothers with uncomplicated pregnancy (Hb < 11

gm%). The anaemic mothers were subdivided into three groups depending upon the degree of anaemia. (i) Hb 11-8.1 gm%, (ii) 8.0-5.1 gm%, and (iii) Hb < 5 gm%.

Group C—25 normal non-pregnant controls (with Hb > 12 gm%).

Group D—25 anaemic non-pregnant controls (with Hb < 12 gm%).

A detailed clinical history was taken and general, systemic, obstetric examinations, and ultrasonography were carried out. Routine investigations included Hb%, serum iron levels, TLC, DLC, ESR, routine urine and stool examinations. Samples for immunoglobulin estimations were taken at different gestational age according to the trimester of pregnancy. In the 1st trimester samples were taken between 8-10 weeks of pregnancy, in 2nd trimester samples were taken 18-22 weeks of pregnancy, in 3rd trimester samples between 28-32 weeks and then samples were taken during the 1st stage of labour.

Serum IgG, A and M estimations were carried out by single radial diffusion technique as described earlier (Gupta *et al*, 1975). W.H.O. serum No. 67/97 served as a control and nonspecific antisera were obtained from Behringwerke, West Germany.

Observations

A total of 245 cases in the age groups of 15-45 years were studied. Table I shows the distribution of cases according to the trimester of pregnancy.

Table II shows that 57.65% of the

TABLE I
Distribution of Cases

Group	No. of cases	Percentage
(A) Normal pregnant mothers		
1. 1st trimester of pregnancy	28	11.44
2. 2nd trimester of pregnancy	25	10.20
3. 3rd trimester of pregnancy	28	11.44
4. During labour	29	11.84
(B) Anaemic pregnant mothers		
1. 1st trimester of pregnancy	20	8.16
2. 2nd trimester of pregnancy	20	8.16
3. 3rd trimester of pregnancy	20	8.16
4. During labour	25	10.20
(C) Non pregnant nonanaemic controls	25	10.20
(D) Non pregnant anaemic controls	25	10.20

anaemic pregnant women had mild anaemia with Hb 11-8 gm%, 36.4% had moderate anaemia with haemoglobin levels between 8-5.1 gm% and 5.88% had severe anaemia with Hb < 5 gm%.

Table III and IV show variations in immunoglobulin levels.

Serum IgG levels

In non-anaemic pregnant women (Group A) the mean serum IgG levels were highly significantly raised (range 1000-2300 gm%, mean 1596.00 ± 248.10 gm%, $p < 0.001$) as compared to age and socio-economically matched controls. There was a gradual but statistically insignificant ($p > 0.05$) fall from the 1st to 3rd trimester which become highly significant ($p < 0.001$) during labour (Mean 1319.64 ± 318.95 mg%).

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In anaemic pregnant women having Hb% < 11.0 gm% (group B) the range of serum IgG was 1000-2100 mg%, with a

mean of 1280.00 ± 212.70 mg%. This value though comparing well with the control was highly significantly lower ($p < .001$) than non-anaemic pregnant mothers (group A).

Further analysis of the anaemic mother showed that in (i) women with Haemoglobin 11-8.1 gm% the mean serum IgG level was 1476.04 ± 248.00 mg% which was not significantly different from those of nonanaemic mothers ($p < .05$, Mean 1596.00 ± 248.10 mg%), (ii) In women with Hb 8-5.1 gm% the mean serum IgG levels was 1136.99 ± 99.82 mg% which was significantly lower ($p < .001$) than the levels in non-anaemic mothers, and (iii) in anaemic mothers with Hb < 5 gm% the serum IgG levels fell further (Mean 970.00 ± 85.89 mg%, $p < .001$).

Trimester wise analysis of serum IgG levels in women with Hb 11.0-8.1 gm% compared well with the result obtained in the non-anaemic mothers. In women with Hb < 8 gm% (i.e. 8-5.1

TABLE II
Serum Iron Levels in Different Groups and Distribution According to the Haemoglobin Levels

Group	Mean serum iron (ugm/dl)	Haemoglobin levels in grams per cent				
		14-12.1	12-11.1	11-8.1	8-5.1	5
(A) Normal pregnant women						
Ist trimester (N=28)	90.62 ± 23.96	6 (21.43%)	22 (78.57%)			
IIInd trimester (N=25)	90.71 ± 23.11	10 (40.00%)	15 (60.0%)			
IIIrd trimester (N=28)	83.90 ± 19.44	9 (34.14%)	19 (67.86%)			
During labour (N=28)	84.68 ± 21.53	3 (10.71%)	25 (89.29%)			
(B) Anaemic pregnant women						
1. Ist trimester (N=20)	49.61 ± 13.57			8 (40%)	11 (55%)	1 (5%)
2. IIInd trimester (N=20)	50.13 ± 9.45			12 (60%)	7 (35%)	1 (5%)
3. IIIrd trimester (N=20)	46.13 ± 8.45			12 (60%)	6 (30%)	2 (10%)
4. During labour (N=25)	46.36 ± 12.0			17 (68%)	7 (28%)	1 (4%)
(C) Normal non pregnant control (N=25)						
	90.30 ± 14.11	25 (100%)				
(D) Anaemic nonpregnant controls (N=25)						
	53.27 ± 11.38			15 (60%)	10 (40%)	—

Anaemia defined as Hb < 11 gm% in pregnant women and Hb < 12 gm% in non pregnant women (WHO 1974)

TABLE III
 Immunoglobulin in the Different Groups

Immunoglobulin estimated	Group		Control (mg%) (N=25)	Ist trimester (mg%)	IIrd trimester (mg%)	IIIrd trimester (mg%)	During labour (mg%)
IgG	Normal pregnant women (N=110)	Range	1000-1450	1000-2200	1100-2300	1050-2400	1000-2100
		Mean	1296.00	1544.44	1452.97	1418.96	1319.64
		S.D.	±133.09	±312.97	±312.47	±312.47	±318.95
	Anaemic pregnant women (N=85)	Range	900-1600	1050-2100	1000-1800	1050-1900	1050-1800
		Mean	1210.68	1288.09	1277.27	1280.54	1306.00
		S.D.	±215.19	±334.27	±256.68	±268.75	±250.96
IgA	Normal pregnant women (N=110)	Range	120-230	100-300	100-30	100-320	120-350
		Mean	224.40	208.80	192.40	199.28	124.14
		S.D.	±47.00	±95.49	±67.78	±85.05	±84.90
	Anaemic pregnant women (N=85)	Range	120-330	100-350	100-300	100-350	100-280
		Mean	234.80	181.11	193.63	206.84	187.20
		S.D.	±62.99	±59.25	±74.61	±97.75	±75.42
IgM	Normal pregnant women (N=110)	Range	80-230	100-300	100-300	100-260	120-350
		Mean	150.00	152.61	166.24	155.63	230.53
		S.D.	±45.00	±59.94	±76.67	±88.41	±110.045
	Anaemic pregnant women (N=85)	Range	100-200	100-270	100-300	120-350	120-350
		Mean	155.20	215.88	205.5	154.23	188.46
		S.D.	±32.42	±107.73	±87.50	±62.04	±68.97

gm% group and < 5 gm% group) the mean 1st trimester values of 1177.27 ± 112.61 mg% and 850.00 mg% respectively which were significantly lower ($p < .001$) as compared to non-anaemic pregnant women, there was no further significant variation in 2nd and 3rd trimester values. However the fall in IgG levels observed in non-anaemic mothers during labour was not observed in anaemic mothers with Hb between 8-5.1 gm% and Hb < 5 gm%.

Serum IgA levels

Serum IgA levels in normal pregnant women in all the trimesters of pregnancy were not significantly different from control levels (Table III).

In anaemic pregnant women the mean serum IgA levels were significantly lower ($p < 0.01$) in the 1st trimester (118.11 ± 59.25 mg%) as compared to non-anaemic pregnant women (208.80 ± 95.49 mg%). In successive trimesters there was no further significant change.

Further analysis showed that in anaemic women (I) with Hb between 11-8.1 gm% the mean serum IgA value (208.29 ± 80.05 mg%) which was not significantly different from normal pregnant women. However, the levels in (ii) women with Hb 8.0-5.1 gm% and (iii) < 5 gm% were 168.38 ± 99.82 mg% and 134 mg% respectively which were significantly lower ($p < .01$) than those of non-anaemic pregnant women.

Serum IgM levels

In normal pregnant women serum IgG levels (152 ± 59.44 mg%) compared well with normal controls ($150.00 \pm$

45.00 mg%). There was no change in IgM levels during different trimesters of pregnancy ($p > .05$). However a significant rise ($p < .01$) in IgM levels (Mean 230.53 ± 110.045 mg%) was seen during labour.

In anaemic pregnant mothers the mean serum IgM levels were significantly higher ($p < .01$) in the 1st trimester (215.88 ± 107.73 mg%) as compared to the control values (155.20 ± 32.42 mg%). The rise persisted into the 2nd trimester (205.5 ± 87.50 mg%) where as in the 3rd trimester the values come down to the control levels, again there was a significant rise ($p < .01$) during labour (188.46 ± 68.90 mg%).

Further analysis showed that the above trend was maintained in (i) women with Haemoglobin 11-8.1 gm% and (ii) 8-5.1 gm%. However, in (iii) women with Hb < 5 gm% there was a significant fall ($p < .01$) in serum IgM levels which persisted through all the trimesters and during labour.

Discussion

There are controversial reports regarding the effect of anaemia on the humoral immunity. Various workers (Amino *et al*, 1978; Bagchi *et al*, 1980; and Gupta *et al*, 1984) observed that anaemia had no effect on the serum immunoglobulins in healthy adults. Observations in depressed lymphocyte function were reported in children with iron deficiency anaemia of Hb < 10 mg% (Chandra *et al*, 1975; McDougall *et al*, 1975). However none of these workers have correlated humoral immunity with the degree of anaemia in pregnancy. Prema *et al* (1982) investigated the

TABLE IV

Levels of Immunoglobulin in Relation to the Degree of Anaemia in Anaemic Pregnant Women

Group	Hb in gm% 11-8.1			Hb 8-5. 1 gm%		
	No.	IgG (mg%)	IgA (mg%)	IgM (mg%)	No.	IgG (mg%)
Control	15	1256.66 ± 183.09	220.00 ± 64.91	148.00 ± 36.88	10	1145.00 ± 106.58
Ist trimester	8	1606.26 ± 288.36	215.00 ± 70.91	198.74 ± 69.78	11	1177.27 ± 112.61
IInd trimester	12	1150.00 ± 189.50	214.16 ± 80.05	219.15 ± 82.95	7	1158.33 ± 73.60
IIInd trimester	11	1450.00 ± 213.20	211.66 ± 82.33	196.25 ± 45.38	6	1071.43 ± 99.42
During labour	17	1385.29 ± 248.60	198.82 ± 72.82	160.00 ± 32.78	7	1121.42 ± 80.92
	48	1476.04 ± 248.60	208.29 ± 80.05	189.55 ± 69.78	31	1136.99 ± 98.82

effect of severity of anaemia on the cell mediated immunity in pregnant women and reported a suppression of CMI when the Hb fell below 8 gm%.

The present study shows that mild degree of anaemia (Hb 11-8.1 gm%) in pregnant women has no significant effect ($p > .05$) on the levels of serum immunoglobulins. However moderate anaemia with Hb 8-5.1 gm% has a suppressant effect on the humoral immunity. When the Hb fell below 8 gm% there was a statistically significant ($p < .001$) fall in the levels of serum IgG & IgA. However, the serum IgM levels were raised in this group ($p < .01$). In anaemias with Hb < 5 gm% there was significant lowering of serum IgG (970.00 ± 85.89 mg%) IgA (134 mg% ± 84.81 mg%) and IgM levels (94.00 ± 193 mg%) showing thereby the profound illeffect of severe

anaemia on the humoral immunity, which inturn could be a potent cause for infant mortality and morbidity in our country.

References

1. Amino, N. Z. and Tanizawa, O.: *Obstet. Gynec.* 52: 412, 1984.
2. Bagchi, K., Mohanram, M. and Reddy, V.: *Brit. Med. Jr.*, 280, 1249, 1980.
3. Chandra, R. K.: *J. Pediatr.*, 37, 361, 1970.
4. Chandra, R. K.: *J. Pediatr.*, 81, 1194, 1970.
5. Chandra, R. K.: *Am. J. Dis. Child.*, 129: 450, 1975.
6. Chandra, R. K.: *Ciba Found. Symp.*, 51: 249, 1977.
7. Cohen and Hansen, J. D. L.: *Science*, 23: 351, 1962.
8. Gupta, R. M., Gupta, I. M., Gupta, V. M. and Marwah, S. M.: *Ind. J. Med. Res.* 63: 1058, 1975.

Hb <5 gm%

IgA (ng%)	IgM (mg%)	No.	IgG (mg%)	IgA (mg%)	IgM (mg%)
236.00 ± 73.82	236.00 ± 73.82	—	—	—	—
175.45 ± 78.08	175.45 ± 79.92	1	850	100	130
171.45 ± 78.02	180.00 ± 58.02	1	950	160	80
170.00 ± 48.80	170.00 ± 89.22	2	1000 ± 70.70	140.00 ± 84.61	125.00 ± 7.07
152.85 ± 66.07	187.14 ± 73.19	1	1050	130	110
168.38 ± 9.99	178.00 ± 79.82	6	970.00 ± 85.89	134.00 ± 84.81	94.00 ± 19.3

9. Gupta, R. M., Sharma, D. and Agrawal, K.: *J. Asian Med.*, 27: 470, 1984.
10. Mac Dougall, L. G., Anderson, T., Mc-mol, G. M. and Katz, J.: *J. Pediatr.* 86: 833, 1975.
11. Mohanlaxmi, T. K., Kethamani, C. R., Madhavan and Jaya, J.: *Obstet. Gynec. India*, 674, 1986.
12. Prema, K., Nelakumari and Ramalakshmi, Nutr. Rep. Intel. 23: 637, 1981.
13. Prema, K., Ramalakshmi, B. A., Mr-dhavapeddi, R. and Babu, S.: *Brit. J. Obstet. Gynec.* 89: 222, 1982.
14. Ramlingaswamy, V. *Lancet* (ii) 733, 1969.