Original Article

Effect of Gestational Age and Nutrition on Transplacental Transfer of Measles Antibody

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Abstract:

A cross sectional study was done to find out the role of gestational age and nutrition on transplacental tranfer of measles antibody. The study was made on pregnant women admitted for delivery from July 2008 to June 2009 in Sylhet M A G Osmani Medical College Hospitals. Sample of venous blood of 94 pregnant mother and 94 cord blood of their newborn babies were collected and processed as per work schedule. Samples were tested by quantitative ELISA method for measles antibody. It was observed that baby of full term mother and good nutrition had higher antibody levels. Protein and haemoglobin level was taken as nutritional indicator.

Keywords:

Measles IgG, Transplacental transfer, Nutrition, Gestational age.

Introduction:

Measles is one of the most common communicable diseases and was one of the major killers of infants in the world particularly in developing countries. It has no animal reservoir and no vector is involved in its spread[1]. Live attenuated vaccine is highly protective in preventing the disease[2].

There occurs transplacental transfer of measles IgG and attack of measles depends on the IgG level of the baby. Maternal antibody passes the placenta & the infants are usually protected during the first 6-9 months of life.

Mother with higher antibody level, transplacental transfer is higher which can give protection against measles up to 9-12 months. Placental transfer of measles antibody occurs more in 3rd trimester (after 36 wks) which can give protection against measles. Premature & many preterm infants may fail to reach the detectable antibody level at birth, leaving them more susceptible to infection than full term infants[3].

Over 99% of the 1 million deaths of children are less than 5 years of age in developing countries & 70% of them are caused by infectious diseases[4].

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It has been noted in earlier studies that death rate of acute measles infection is higher in malnourished population[5]. Most of the deaths due to measles in tropical countries occur within second year of life, the age at which protein energy malnutrition is most prevalent[6].

Malnutrition including anaemia diminishes the immune response to virus allowing great proliferation of the virus & subsequent damages to the host & causes prolonged immune suppression. Secondary bacterial infection like *Streptococcus pneumoniae* & other bacterial infection follow in the wake of this intense immune suppression often killing or miming the child[7].

Maternal IgG antibodies enter the fetal circulation through the placenta. IgG transport from mother to fetus begins at about 16 weeks gestation & increases as gestation proceeds. But the bulk of immunoglobulin is actively transported through the placenta from 30 to 32 weeks gestation and onwards so that the full term infant has an IgG level equal to or slightly greater than the maternal levels[8]. Accordingly preterm infants are endowed relatively poorly with maternal antibodies.

Unfortunately not all subclasses of IgG are transferred equally across the placenta. IgG 2 & IgG 4 are transferred in very small amounts. Preterm infants born prior to 30 weeks gestation are deficient in all classes of IgG[9].

Infants born to vaccinated mother acquire a lower level of measles antibody that disappears at an earlier age than the infants born to mothers who have natural measles infection[10]. This low titre & inefficient transfer of passive immunity may complicate the overall protection of infants against measles in this region[11]. Poor nutrition and rapid loss of maternal antibodies in developing countries prompted suggestion for review of the existing immunization practices for measles[12].

Bangladesh is the most densely populated country in the world. Malnutrition is one of the major public health problems and it is one of the leading causes of morbidity and mortality in Bangladesh. According to Gomez classification[13] 2.5% of Bangladeshi are suffering from sever malnutrition. 35.1% from moderate malnutrition. Prevalence of anaemia in pregnancy in Bangladesh is 47% in rural area and 40% in urban area[14].

Estimation of haemoglobin and serum total protein are standard laboratory measures and good indicators that can give idea about overall nutritional status[15].

In developing countries, a mother may be malnourished & may not have good titres of measles antibodies; Children born to such mother's can suffer from measles as early as 6 months of life. Hence during epidemics of measles the vaccine can be given as early as 6 months. In case of high antibody level measles vaccination can be delayed up to usual schedule at 9 months or even 15months to receive a dose of MMR vaccine[16].

In this study, measles antibody level in mother and baby determined by ELISA method. Highly protective level is 200mIU/ml or above. Moderately protective level is 120-200mIU/ml and below 120 is not protective[17]. For determination of time of vaccination measles IgG antibody level in mother and placental transfer to baby is very important[18]. Lower the level, vaccination time is earlier, higher the level, vaccination time is later. But if a measles vaccine is administered when maternal antibodies are still present, the immune response of the child is either inhibited or weaker than that of a child with no maternal antibodies[19].

Therefore in determining the age of vaccination, countries must balance the consequences of an older age (lack of protection in the early months of life) and a younger age (reduce effectiveness). Many countries, where morbidity and mortality due to measles are uncommon in infants, choose an older age for vaccination such as 12 months to15 months[20].

The study will reveal the effect of maternal nutrition and gestational age on the measles antibody level in the newborns, which were not well documented before in Bangladesh.

Materials & Methods: Type of study; Comparative cross sectional study.

Place & duration of study: Department of microbiology, Sylhet MAG Osmani Medical College, Sylhet from 1st July 2008 to 30th June 2009.

Study population: Pregnant mothers admitted at Sylhet MAG Osmani Medical College hospitals & their newborn babies.

Sample size: 94 mothers & their offspring's cord blood.

Data collection Procedure:

1. Pregnant women admitted for delivery in Sylhet MAG osmani medical college hospitals & their offspring cord blood after delivery.

2. Detailed history from mother was taken. Particulars of the patients were recorded including age, residence, housing, sanitation, monthly family income, naturally immune history, vaccination history, gestational age and birth weight were taken.

Collection of Samples: 02 ml venous blood & 02 ml cord blood were taken in two properly labeled different test tubes. The samples were allowed to clot at room temperature and then centrifugation at 2,000 rpm for 10 min. Serum were separated & stored at -20º C .

Laboratory Procedure:

- ELISA (Enzyme Linked Immunosorbant Assay) the ELISA test kits used for detection of measles antibody were purchased from Human, Weisbaden, Germany.
- Serum total protein level was measured by colorimetric assay using RANDOX TP, manufactured by Randox Laboratory, UK.
- Haemoglobin was estimated by cyanomethhaemoglobin method, manufactured by Randox Laboratory, UK.

Statistical Analysis:

Analysis of the test result was carried out by using the SPSS (Statistical Package for social science) win version 12.0 and the statistical method like mean, SD, t-test, Linear regression test were applied.

Resuits:

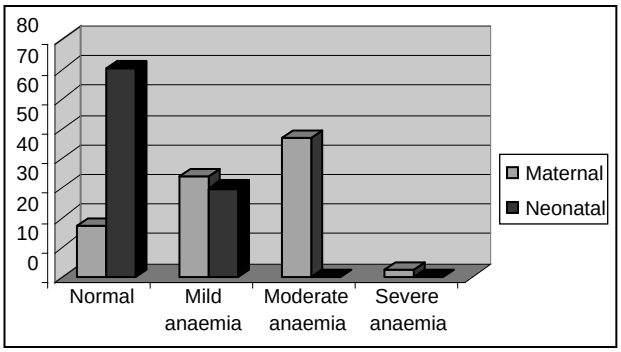
Out of 94 mothers, naturally immune 35.1%, non-immune 11.7%, not known about measles 53.2%. Vaccinated 33.3%, non-vaccinated 44.7%, not known 22.3%. Non-vaccinated means naturally immune mother also. (Table1)

Table 1: Distribution of mothers according to history of measles &vaccination status

	History of measles		Measles vaccination	
	Frequency (n)	Percentage (%)	Frequency(n)	Percentage (%)
Yes	33	35.1	31	33.3
No	11	11.7	42	44.7
Not known	50	53.2	21	22.3
Total	94	94	100	100

Most 78 (83%) of the mothers included in the study were anaemic, only 16 (17%) having normal haemoglobin level (11-13.5 gm/dl). 32 (34%) of them were mildly anaemic (Haemoglobin level <11gm/dl), 44 (46.9%) were moderately anaemic (Haemoglobin level <10gm/dl) and only 2 (2.1%) were severely anaemic (Haemoglobin level <7gm/dl)[21] (Figure 1).

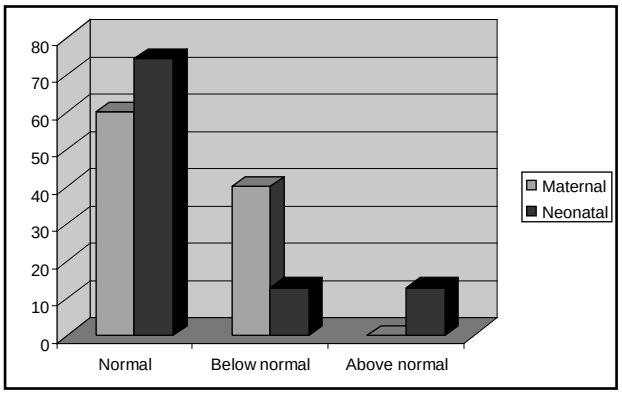
Figure 1: Maternal and neonatal haemoglobin level



Most 66 (70.2%) of the newborns had normal haemoglobin level (14-16.6 gm/dl), only 28 (29.8%) were born with anaemia (haemoglobin level <14 gm/dl)[2].

Majority 56 (60%) of the mothers had normal serum protein level and 38 (40%) had serum protein level below normal. About three fourth 70 (74.4%) of the newborns had serum total protein level within normal range (4.6-7.4 gm/dl). Among the rest 12 (12.8%) had protein level below normal (< 4.6 gm/dl.) and 12 (12.8%) above normal level (> 7.4 gm/dl) (Figure 2).

Figure 2: Maternal and neonatal serum protein level



The geometric means of haemoglobin, serum total protein & measles antibody level in mothers and newborn babies. All levels were found higher for the children than mothers due to haemodilution effect during pregnancy (Table 2).

Table 2: Geometrics means of maternal and neonatal haemoglobin, serum total protein & measles antibody levels

Criteria	Maternal (Mean ± SD)	Neonatal (Mean ± SD)
Haemoglobin level (gm/dl)	9.13±0.95	13.46±1.68
Total protein level (gm/dl)	6.03±0.96	6.14±1.10
Measles antibody titre (mIU/ml)	161.12±4.96	171.26±4.37
Total	94	94

The geometric means of measles antibody titre, total protein level and haemoglobin level in relation to birth weight of babies. The mean levels of IgG and total protein were found significantly lower for the low birth weight babies in t-test. The haemoglobin level was also lower but not significant (Table3).

Table 3: Relation of birth weight with geometric means of measles antibody titre, serum total protein and haemoglobin level

	Birth weight		t-value
	≥2.5 kg	<2.5 kg	
Measles anti-body level (mean ± SD)	179.99±38.33	134.41±44.13	-3.99*
Total protein level (mean ± SD)	6.20±1.21	5.52±0.89	-2.26**
Haemoglobin level (mean ± SD)	14.04±1.61	13.76±1.53	-0.662

*** indicates p<0.001, ** indicates p<0.01

The geometric means of measles antibody titre, total protein level and haemoglobin level in relation to gestational age of newborn babies. The mean levels of IgG and total protein were found significantly (applying t-test) lower for the babies who born before 37 weeks of gestation. The haemoglobin level was also lower but not significant (Table 4).

Table 4: Relation of gestational age with geometric means of measles antibody titre,serum total protein and haemoglobin level

	Gestational age		t-value
	≥37 wks	<37 wks	
Measles antibody level (mean ± SD)	176.37±40.51	133.77±40.66	-3.113***
Total protein level (mean ± SD)	6.15±1.21	4.50±0.69	-1.86**
Haemoglobin level (mean ± SD)	14.01±1.61	13.77±1.50	-0.49

*** indicates p<0.001 ** indicates p<0.01

The study revealed significant positive relationship (r^2 = 0.0081) between protein level of mother and measles antibody level. Linear Regression model shows a positive trend (regression coefficient, B=11.26) of measles antibody level of babies on serum protein level of mother (Figure 3).

Figure 3: Fitted Linear Regression between neonatal measles antibody level and maternal serum protein level.

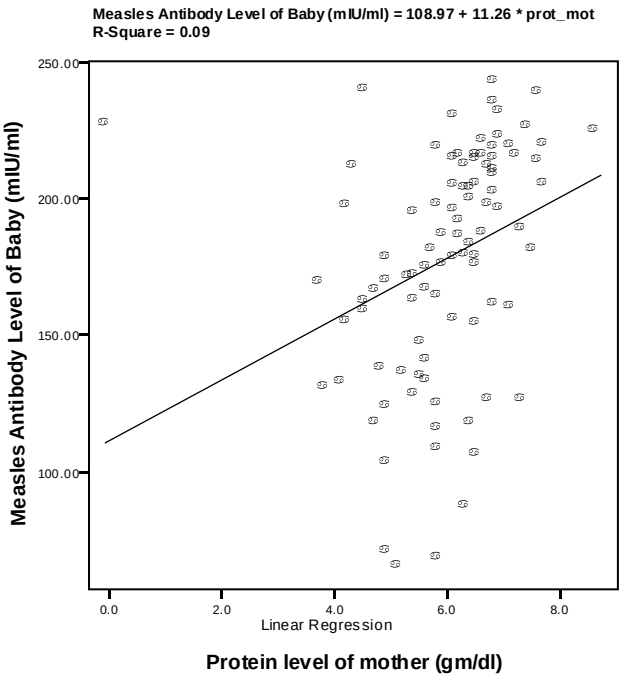


Table shows the results of multiple linear regression models which indicate that maternal measles antibody level; serum protein level, birth weight and gestational age have significant impact on neonatal measles antibody level. But maternal haemoglobin level is not significantly associated (Table-5).

Table 5: Impact of several variables on neonatal measles antibody level:

Multiple linear regression analysis

Variables	Regression coefficient (β)	Standard error	t-value	Significance (p value)
Maternal measles antibody level (mIU/ml)	0.469	0.073	6.459	0.000***
Maternal serum protein level (gm/dl)	6.847	2.898	2.362	0.020*
Maternal haemoglobin level (gm/dl)	-0.705	2.259	-0.312	0.756
Birth weight of newborns (Kg)	27.006	8.626	3.131	0.002**
Gestational age of newborns (weeks)	4.482	2.108	2.126	0.036*

*** indicates p<0.001, ** indicates p<0.01, * indicates p<0.05

Discussion:

Present study is a cross sectional comparative research work carried out in department of microbiology, Sylhet MAG Osmani Medical College, to evaluate status of measles IgG of naturally immune & vaccinated mother and the cord blood of their offspring and to determine the role of gestational age, nutrition on antibody level & transfer. The study, though on a limited scale, could provide vital information which could be used to design further study in the field for settling the best timing of measles vaccination in our country.

Table 3 shows relationship of antibody titre with the birth weight of baby. It was observed that higher birth weight of baby had a higher antibody titre.

In our study (Table-4) gestational age, measles antibody level and total protein level of baby significantly higher in term infant than the pre term. The mean level of IgG for term babies was observed176.37 mIU/ml, while the level for the pre-term babies was found only 133.77 mIU/ml.There is significant relationship in case of measles antibody ($p<0.01$) and total protein level ($p<0.10$) with gestational age. Measles antibody titre of baby is higher in full-term group than the pre term group[22,23]. This implies that gestational age is an important determinant of transfer of IgG from mother to fetus[24].

Malnutrition is a significant underlying factor in more than half the deaths of young children in developing countries. Malnutrition impairs the immune response, also depressed cell mediated immunity to measles resulting more frequent & prolonged attack of measles[25]. There is relationship between antibody titre and nutritional status of mother. Higher antibody level observed incase of good nutritional condition of mother. Protein and haemoglobin level is an indicator of nutritional status [26]

It is not practicable to give vaccination by determining the IgG titre of mother and baby. In this study it is observed that healthy mother with good nutrition and history of measles, full term baby with normal weight and no history of infection will give good protective level of antibody titre and give protection against measles up to 9-12 months. In such cases vaccination will be given at 9-12 months. In case of vaccinated mother lower protective titre level will give protection against measles up to 5-6 months. In such cases vaccination time better is fixed at 5-6 months. Unhealthy mother with no/doubtful history of measles and vaccination, pre term low birth weight baby antibody titre is below the protective level, vaccination is required to be given within few weeks if one is to avoid outbreak of measles in those group.

Conclusion:

Measles vaccination is one of the most effective public health interventions available to date for preventing the attack of measles and save millions of children from its

associated morbidity and mortality. The most important factor affecting the success of measles immunization is the time of disappearance of passively transferred maternal antibodies from baby. In evolutionary terms, it is this maternal antibody which protected the newborn infants during the early parts of life through the ages from the scourge of measles. Multiple factors e.g. nutrition, gestational age, birth weight etc. influence the quantity and quality of antibodies. As a result, many young infants are exposed to a period of several months during which the titre of maternal antibodies falls below protective level. But may interfere with antibody production in response to measles vaccine. During this window of vulnerability, young infants may develop measles. Continued monitoring of measles antibody levels in premature and full term infants, adjustment of vaccination schedules and implementation of novel vaccination strategies could improve protection from measles. Results from this study indicate towards undertaking large scale study to find out the appropriate time for immunization against measles.

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