MATERNAL MEASLES ANTIBODY LEVELS AMONG SOUTH INDIAN INFANTS LESS THAN 9 MONTHS OF AGE – A CROSS – SECTIONAL STUDY

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ABSTRACT

BACKGROUND
Infants are protected against measles infection by passive transfer of maternal anti-measles antibodies. Studies from the West have shown a steady decline in these antibody titers over increasing age.

AIM
This study is aimed to determine the maternal measles antibody titers (MMAT) at various ages in infants below nine months of age.

MATERIALS AND METHODS
Cord blood of thirty babies consecutively born at term and peripheral blood of 24, 27 and 36 infants at 4, 6 and 9 months of age respectively were assayed for MMAT using standardised lab methods.

RESULTS
Eighty three percent of babies at term had MMAT in the protective range. But subsequently there is a steady decline in MMAT and none of the infants in the study had protective levels of MMAT at 9 months of age.

CONCLUSION
With such rapid decline in MMAT during infancy, the position of measles vaccine at nine months in national immunisation schedule needs to be revisited.

KEYWORDS
Measles, Measles antibody titres.

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INTRODUCTION: Measles is an infectious illness caused by a virus belonging to paramyxovirus family. The global mortality associated with this illness is 26 lakhs each year, predominantly affecting children aged less than five years.[1] In spite of the availability of a cheap and effective live vaccine, this disease continues to affect children from developing countries like India. The WHO recommends measles vaccine at 9 months of age, based on observational studies that demonstrated poor seroconversion if given earlier in life. This sub-optimal seroconversion was attributed to the persistence of high levels of passively acquired anti-measles antibodies from the mother.[2] Antibody levels are likely to be higher in mothers who have had natural infection rather than vaccination.

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Studies in western countries have demonstrated earlier waning of antibody levels in babies born to vaccinated mothers. This study aimed to determine anti-measles antibody levels at various ages below 9 months in a developing country.

METHODS: This is a cross-sectional study done at the PSG Institute of Medical Sciences, Coimbatore. Infants below 9 months of age, who were born at term and required blood sampling for any reason, were included in the study. Those infants whose mothers had received blood transfusion during pregnancy or were HIV positive and those infants with history of viral exanthema clinically suggestive of measles, on steroid therapy or suspected immunodeficiency or with history of blood, blood product transfusion or immunoglobulin administration were excluded. None of these babies were premature at birth and their mothers were born after the implementation of universal immunisation program.

Two mL venous blood was collected from all the subjects, centrifuged at 3000 rpm for 10 minutes. The serum was separated and stored in Eppendorf tubes at -

20^0C. Anti-measles IgG antibody was assayed using ELISA technique (Demeditec, Germany). The optical density values of samples were plotted against standard curve and their values were obtained. Anti-measles IgG antibody levels less than 8 mIU/mL were considered negative, 8 to 12 mIU/mL as equivocal, while values more than 12 mIU/mL were positive. Statistical analysis was made using SPSS software version 16.

RESULTS: A total of 117 subjects were enrolled in the study and among them, there were thirty consecutively born term newborn babies whose cord blood was sampled for the estimation of anti-measles antibody levels. Of the remaining 87 infants there were 24, 27 and 36 infants at 4 months, 6 months and 9 months of age respectively. The mean age of the study participant's mothers was 25±3.9 years and the mean birth weight of the thirty term newborns was 3022±764 g. The mean measles antibody titer values (MMAT) in cord blood of the term newborns was 67.29 mIU/mL (range 8 to 200). 25(83%) newborns had protective levels of antibody at birth, while 3(10%) had equivocal and 2(7%) were below the desired levels.

Among the 24 infants at 4 months of age, the MMAT was 12.25±12.70 mIU/mL. In this age group, only 12(50%) of the subjects had protective levels of antibody, while 2(8.3%) had equivocal and 10(41.6%) were below the desired levels. Among 27 and 36 infants at 6 months and 9 months of age, the MMAT were 1.96±2.96 mIU/mL and 1±0.74 mIU/mL respectively. None of these infants had antibody levels in protective range suggesting their vulnerability to measles infection, if exposed beyond 6 months.

Age group (in Months)	Number of subjects	% protected	MMAT (mIU/mL)
Term Neonates	30	83	67.29±64.14
4	24	50	12.25±12.70
6	27	Nil	1.96±2.96
9	36	Nil	1±0.74

Table 1: Proportion of babies with protective levels of antibodies and the MMAT at various ages

DISCUSSION: Measles infection in infants less than 9 months is being increasingly recognised in practice, but often under reported. The significant antibody decay or declining levels of measles antibodies after second dose of Measles-Mumps-Rubella vaccine (MMRV) has been well documented by Davidkin I et al in their 20-year followup study on MMR vaccine recipients.[3] The present study was aimed at identifying the transplacentally transferred maternal measles antibody levels in infants less than 9 months of age in the era of universal immunisation and from a community with high vaccination rates.

In our study, we found that 83% of cord blood samples from term infants showed protective levels of MMAT while 7% showed negative or low protective levels of MMAT even at birth. This observation was similar to that of Rau et al where 81% of term infants had protective levels and 19% had equivocal levels of MMAT.[4] The authors also reported that 51% of infants had undetectable MMAT at 5 months of age showing that there is an exponential decay of transplacentally acquired anti-measles antibody levels as the infant crosses 5 months of age. A similar proportion of infants had negative MMAT (41%) at 4 months in our study. Alarmingly, none of the babies in our study had protective levels of MMAT at 6 and 9 months of age. Harter HK et al in a study from Nigeria have reported that the MMAT value in newborns was only 30 mIU/mL and that protective levels of antibody was seen in only 32% at 3 months, 17% at 4 months and 2% at 6-9 months of age.[5] A similar study by Chowdhury JP et al from Bangladesh found that seropositivity declined from 94% at 3 months to 25% at 9 months of age.[6] The result of all these studies correlate well with our study, which shows early and rapid decline of transplacentally acquired anti-measles antibodies to sub-protective levels by 5 months of age.

In France, where measles vaccine coverage is more than 85% since 2004, Gagneur A et al in their prospective multicentric trial observed a dramatic decline in the MMAT from birth to 9 months of age and concluded that 90% of infants in their study were not protected against measles beyond 6 months.[7] This was because by the 1990s most women in developed countries had received measles vaccine and studies showed that vaccinated women passed on lower amounts of antibodies compared to naturally infected women.[8] A US study found that more than 90% of infants of vaccinated mothers were susceptible to measles by 7 months compared with 65% of infants of women who had natural infection.[9] In Canada, comparative figures of measles susceptibility were 50% and 15% respectively at 8 months.[10]

In the study by Leuridan E et al, the median duration for the presence of maternally derived measles antibodies was 2.61 to 3.78 months in babies born to mothers who were natural measles infection whereas 0.97 months in babies born to mothers who were vaccinated against measles and not had clinical infection.[11] Also at 6 months of age, more than 99% of infants of vaccinated women and 95% of infants of naturally immune women had lost maternal antibodies. This study again highlights that passive transfer of measles antibody in vaccinated mothers might not be adequate as from a measles infected mother and decay of MMAT will be rapid in the latter.[10] Our study was conducted in a tertiary care centre located in Southern India where immunisation rates have been consistently high in the past two decades and on par with western world. With such low levels of MMAT in infants beyond 6 months of age, re-scheduling measles vaccine around 6 months of age would be more rational. The limitations of the present study are that it is not a longitudinal one where the same cohort was to be sampled at various ages. Also most of the mothers in our study could not produce documentary proof of vaccination even though they claimed to have received the measles vaccine.

CONCLUSION: In conclusion, our study shows that while most term neonates had protective levels of transplacentally acquired measles antibodies at birth, none had protective levels at and beyond 6 months age. The early loss of measles antibodies in infants has implications

on the timing of measles vaccine in the community. Further longitudinal studies are required to confirm our findings and verify seroconversion following early measles vaccination.

REFERENCES:

1. Measles WHO Factsheet, Updated November 2015. http://www.who.int/mediacentre/factsheets/fs286/en/
2. Galazka Ak, Lauer BA, Henderson RH, et al. Indications and contraindications for vaccines used in the expanded program on immunization. Bull WHO 1984;62(3):357-366.
3. Davidkin I, Jokinen S, Broman M, et al. Persistence of measles, mumps, and rubella antibodies in an MMR-vaccinated cohort: a 20-year follow-up. J Infect Dis 2008;197(7):950-956.
4. Rau ATK, Dhulia A, Wilson CG, et al. Transplacentally transmitted antimeasles antibodies in term and preterm infants. Indian paediatr 2002:39(3):282-288.
5. Harter HK, Oyedele OJ, Dietz K, et al. Placental transfer and decay of maternally acquired antimeasles antibodies in Nigerian children. Pediatr infect Dis J 2000;19(7):635-641.
6. Chowdhury JP, Mondol M, Uddin MJ, et al. Study on measles antibody status in children below nine months of age and its implication on measles vaccination. JAFMC Bangladesh 2008;4(2):5-9.
7. Gagneur A, Pinquier D, Aubert M, et al. Kinetics of decline of maternal measles virus-neutralizing antibodies in sera of infants in France in 2006. Clin Vaccine Immunol 2008;15(12):1845-1850.
8. Dubois F, Waldman RJ, Mann GF. Loss of maternal measles antibody during infancy in an African city. Int J Epidemiol 1989;18(1):264-266.
9. Pabst HF, Spady DW, Marusyk RG, et al. Reduced measles immunity in a well vaccinated population. PediatrInf Dis J 1992;11(7):524-525.
10. De Serres G, Joly JR, Fauvel M, et al. Passive immunity against measles during the first 8 months of life of infants born to vaccinated mothers or to mothers who sustained measles. Vaccine 1997;15(6-7):620-623.
11. Leuridan E, Hens N, Hutse V, et al. Early waning of maternal measles antibodies in era of measles elimination: longitudinal study. BMJ 2010;340:c1626.