The effects of maternal haemoglobin as an indicator of maternal nutritional status on, maternal measles antibodies of mother-infant pairs at birth

*Baba UA[1], Ashir GM[2], Mava Y[3], Gimba MS[2], Abubakar R[2], Ambe JP[2]

1. Department of Paediatrics, Federal Medical Centre, Yola, Adamawa state, Nigeria; formerly, Department of Paediatrics University of Maiduguri Teaching Hospital (UMTH),Maiduguri, Borno state, Nigeria.
2. Department of Paediatrics, UMTH, Maiduguri, Borno state, Nigeria.
3. Department of Paediatrics, Bengham University, Jos, Plateau state Nigeria; formerly, Department of Paediatrics, UMTH, Maiduguri, Borno state, Nigeria.

Abstract

Background: Maternal measles antibodies (MMA) are actively transferred through the placenta from mother to foetus. A relationship could exist between MMA of mother-infant pairs and maternal nutritional indicator (haemoglobin).

Objectives: This study reviewed the effects of maternal haemoglobin (Hb) on MMA of mother-infant pairs at birth.

Methods: One hundred and fifty three mother-infant pairs were enrolled in this study using the systematic random sampling method. Means of maternal Hb and MMA of mother-infant pairs were compared using the Student t test. Correlation coefficients of maternal Hb and MMA of mother-infant pairs were also determined. Multivariate analysis of variable (MANOVA) and covariates (MANCOVA) was used to investigate the effects of maternal Hb (fixed factor), gestational age, maternal age, birth weight (covariates) on combined MMA of mother-infant pairs (dependent factors). Benferroni adjusted Univariate linear regression was used to investigate the dependent variables separately.

Results: There were 78 (51%) males and 75 (49%) females. The (mean ± SD) MMA of mother-infant pairs at birth were 134.66 ± 93.31 (95% CI, 119.76 – 149.56) U/ml, and 187.49 ± 85.01 (95% CI, 173.91 - 201.07) U/ml, and their correlation was significant (p = 0.025). Ninety one (59.5 %) mothers had low Hb, 62 (40.5 %) had acceptable Hb levels. The overall mean maternal Hb was 11.01 ± 1.00 (95% CI, 10.85 – 11.17) g/dl . A positive significant correlation was observed between maternal Hb and MMA of the newborn-infant (p = 0.031). The MANOVA showed a statistically significant difference between maternal Hb on the combined dependent variables (p =0.033); however, results for the dependent variables using the Benferroni adjusted Univariate analysis was significant for only MMA of the infants, (p = 0.009).

Conclusion: There was a significant association between aacceptable levels of maternal Hb and high MMA of the newborn-infants. Therefore, these newborn infants start out with higher MMA that could give them better protection against measles during infancy.

Keywords: Maternal haemoglobin, maternal measles antibodies, Maiduguri, Nigeria.
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Introduction

Measles is one of the most common communicable diseases and one of the major killers of infants in the world particularly in developing countries. Live attenuated measles vaccine is highly protective in preventing measles.[1] Transplacental transfer of maternal measles antibodies (MMA) may protect infants against measles during infancy.[2] Sadly, the transplacental transfer of MMA in mother-infant pairs is affected by numerous factors that may include poor nutrition.[3] Measles is high in malnourished population most especially those found in tropical countries of the world.[4, 5] Possibly due to high prevalence of malnutrition associated with these countries.[4, 5] Low haemoglobin (Hb) anaemia as an indicator of malnutrition causes diminished immune response to measles virus (MV), and this could lead to decreased levels of measles antibodies in a population.[6]

Poor nutrition and rapid loss of MMA in developing countries prompted suggestion for review of the existing immunization practices for

***Corresponding author:**
Dr. Baba Usman Ahmadu
Department of Paediatrics
Federal Medical Centre Yola
Adamawa State, Nigeria
PMB 2017, Yola, Adamawa State, Nigeria.
Phone: +2348033668948
E-mail: ahmadu4u2003@yahoo.com

measles.[7] Malnutrition is one of the major public health problems and it is one of the leading cause of morbidity and mortality in Nigeria.[8, 9] This may not be unconnected to high poverty rate existing in Nigeria.[8] Different methods of estimating malnutrition in countries yielded high proportions of individuals with malnutrition. For instance, in Maiduguri, the prevalence of malnutrition was put at 36% using the modified Wellcome's classification.[9] Other workers using the Gomez classification, however, documented 47% cases of malnutrition elsewhere.[1] Estimation of Hb is a standard laboratory measure and good indicator that can give an idea about overall nutritional status of individuals in a community.[10] Whereas the prevalence of malnutrition could vary from place to place, dearth of knowledge still exist world-wide on the extent to which maternal malnutrition affects MMA in mother-infant pairs particularly in our setting that is measles endemic.

Therefore, this work looked at the effects of maternal Hb as an indicator of maternal nutrition on MMA of mother-infant pairs at birth. To the best of our knowledge there is no study on this subject matter especially in North-Eastern Nigeria and the country at large.

Methods

Study area

The study was carried out at the Department of Paediatrics and Obstetrics unit of the University of Maiduguri Teaching Hospital (UMTH), Nigeria. The UMTH is a tertiary centre located in North-Eastern Nigeria and a centre of excellence for infectious diseases and immunology. It also serves as a referral site for the six North-Eastern States of Nigeria and the neighboring countries of Chad, Cameroon and Niger Republics.

Study design

The study was a hospital-based comparative cross sectional study of mother-infant pairs recruited from the labour ward of the UMTH.

Ethical issues

The study protocol was reviewed and authorised by the Medical Research and Ethics Committee of UMTH, and informed consent from parents was also obtained. Parents had unlimited liberty to deny consent without any consequences and confidentiality was maintained.

Sample size/Subject selection

The minimum sample size was determined using a statistical formula, which detects differences between two means when using paired sampling units: the effect size was set at 0.2, alpha level at 0.05 and power at 90%.[11] However, 45% of the calculated minimum sample was added to maximize power. Therefore, the sample size for this study was one hundred and fifty-three mother-infant pairs. Consenting women who delivered vaginally at the UMTH were enrolled for this study. Severely sick pregnant women, those diagnosed with ante-partum haemorrhage, those delivering stillborns and mothers who had received blood transfusion during pregnancy were excluded.

Data collection procedure

Mother-infant pairs were enrolled in this study using the systematic random sampling method where the first of every three mother-infant pair was picked at the labour ward. Where the first mother did not fulfil the inclusion criteria, the immediate next mother that qualified was selected. On enrolment of the mother-infant pairs, study proforma were administered to the mothers to collect information on their bio-data, pregnancy history and antenatal care history. Dubowitz Score was used to access the gestational age (GA) of the newborn infants at birth, [12] and their birthweight (BW) was measured using the basinet weighing scale that has a sensitivity of 50 grams. Newborn infants with GA less than 37 completed weeks were classified as preterm, those from 37 completed to less than 42 completed weeks were term, and those with 42 completed weeks or more were post term. [12, 13] Newborns weighing > 3.99 kilograms were classified as macrosomia, those weighing 2.5 – 3.99 kilogram as normal and those < 2.5 kilogram were termed low BW.[13]

Collection of Samples

Three millilitres (mls) of venous blood were obtained from the mothers on admission using sterile disposable five mls syringe under aseptic technique. Of the three mls of maternal venous blood drawn, one ml was placed in ethylenediaminetetracetic acid (EDTA) bottle. This blood was used for the estimation of haemoglobin (Hb) concentration in grams per decilitre (g/dl) using the micro-haematocrit method.[14] Low Hb is defined as Hb < 11g/dl, while acceptable Hb is Hb > 11g/dl.[15] The remaining two mls of maternal venous blood were placed in sterile plain bottles and serum was separated

after centrifuging the blood samples at 5000 revolutions per minute (rpm) for five minutes. The sera obtained from maternal blood samples were used for the analysis of MMA using enzyme linked immunosorbent assay (ELISA).

Three millilitres of blood samples were also obtained from the umbilical cord of the newborn infants for the estimation of MMA. This was done after centrifuging the blood samples and the subsequent separation of the serum of the newborn cord blood. All blood samples collected were stored in a refrigerator at -20°C until the time of MMA assay.

Statistical analysis

Statistical analyses were performed by use of SPSS statistical software version 16, Illinois, Chicago USA. Values were expressed as percentages, mean ± standard deviation (SD) and range. Means of maternal Hb and MMA of mother-infant pairs were compared using the Student t test. Correlation coefficients of maternal Hb and MMA of mother-infant pairs were also determined. Preliminary checks were conducted to ensure that there was no violation of the assumptions of normality, linearity, homogeneity of variances, homogeneity of regression slopes, and reliable measurement of the covariate. Multivariate analysis of variance (MANOVA) and covariates (MANCOVA) was used to investigate the effects of maternal Hb (fixed factor), GA, MA, BW (covariates) on combined MMA of mother-infant pairs (dependent factors). Benferroni adjusted Univariate linear regression model was used to investigate the dependent variables separately. A p value < 0.05 was considered significant. Tables were used appropriately for illustration.

Results

One hundred and fifty three mother-infant pairs were enrolled in this study. There were 78 (51%) males and 75 (49%) female newborn infants giving an approximate male to female ratio of 1.04:1. Thirteen (8.5%), 138 (90.2%) and 2 (1.3%) newborn infants were preterm, term and postterm deliveries. Similarly, 17 (11.11%), 130 (84.97) and 6 (3.92%) newborn infants were low BW, normal and macrosomic deliveries. Table 1 shows the mean and range values of the study group. Maternal age ranges from 17 to 37 years, the mean MMA of mother-infant pairs was 134.66 ± 93.31 (95% CI, 119.76 – 149.56) U/ml and 187.49 ± 85.01 (95% CI, 173.91 - 201.07) U/ml respectively in a ratio of 1:1.3. Correlation of these MMA was significant (r = 0.182, p = 0.025) as shown in table 2.

Table 1: Mean and range values of the study group

Parameters	Mean ± SD	95% CI	Range
GA (weeks)	38.78 ± 1.83	38.49 – 39.07	30 - 43
MA (years)	23.58 ± 4.9	22.78 – 24.38	17 - 37
BW (Kg)	3.06 ± 0.57	2.97 – 3.15	1.25 – 4.60
MMA (U/ml)	134.66 ± 93.31	119.76 – 149.56	-
MMA of Newborns (U/ml)	187.49 ± 85.01	173.91 - 201.07	-

SD = Standard deviation, CI = Confidence interval, GA = Gestational age, MA = Maternal age, BW = Birth weight, MMA = Maternal measles antibodies

Table 2: Correlation of maternal haemoglobin and maternal measles antibodies of mother-infant pairs

		Maternal Hb (g/dl)	Mothers MMA (U/ml)	Newborns MMA (U/ml)
Maternal Hb (g/dl)	r		0.036	0.174
	p		0.658	0.031*
Mothers MMA (U/ml)	r			0.182
	p			0.025*
Newborns MMA (U/ml)	r			
	p			

Hb = Haemoglobin MMA = Maternal measles antibodies *= p value < 0.05 (significant)

Of the 153 (100 %) mothers that participated in this study, 91 (59.5 %) were found to have low Hb (< 11g/dl), and 62 (40.5 %) had acceptable Hb levels (> 11g/dl). The overall mean maternal Hb was 11.01 ± 1.00 (95% CI, 10.85 – 11.17) g/dl. Table 3 shows the comparison between maternal Hb and mean MMA of mother-infant pairs. The mean MMA of mother-infant pairs were higher for mothers who had acceptable Hb and low for mothers having low Hb. However, the differences in mean MMA was only significant in newborn infants of mothers with acceptable Hb and low Hb (p = 0.002).

A positive correlation also existed between maternal Hb and MMA of mother-infant pairs. However, this correlation was only significant for maternal Hb and MMA of the newborn infants (r = 0.174, p = 0.031) table 2.

Table 4 shows a statistically significant difference between maternal Hb on the combined dependent variables: F = 3.490, p = 0.033; Wilks' Lambda= 0.955; partial eta squared= 0.045. No significant difference was observed between the covariates (GA, MA and BW) on combined dependent variables. When the results for the dependent variables were considered separately, the only difference to reach statistical significance using a Bonferroni adjusted alpha level of 0.04, was the relationship between maternal Hb and MMA of the infants: F = 7.027, p = 0.009, partial eta squared = 0.045 (table 5). No significant difference was observed between the covariates and the dependent variables separately.

Table 3: Comparison between maternal haemoglobin and mean maternal measles antibody of mother-infant pairs

Maternal Hb (g/dl)	Mean maternal measles antibodies ± SD (U/ml)		
	Mothers	Newborn infants	p value
Acceptable Hb (g/dl) (Hb > 11g/dl)	127.21± 63.38	227.40 ± 29.98	0.000*
Low Hb (g/dl) (Hb < 11g/dl)	117.32 ± 59.19	175.98 ± 53.29	0.005*
p value	0.651	0.002*	

Hb = Haemoglobin *= p value < 0.05 (significant)

Table 4: Multiple tests of effect of maternal haemoglobin, maternal age, gestational age, birth weight on maternal measles antibodies of mother-infant pairs at birth

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Intercept	Pillai's Trace	0.010	0.737[a]	2.000	147.000	0.480	0.010
	Wilks' Lambda	0.990	0.737[a]	2.000	147.000	0.480	0.010
	Hotelling's Trace	0.010	0.737[a]	2.000	147.000	0.480	0.010
	Roy's Largest Root	0.010	0.737[a]	2.000	147.000	0.480	0.010
MA	Pillai's Trace	0.001	0.075[a]	2.000	147.000	0.927	0.001
	Wilks' Lambda	0.999	0.075[a]	2.000	147.000	0.927	0.001
	Hotelling's Trace	0.001	0.075[a]	2.000	147.000	0.927	0.001
	Roy's Largest Root	0.001	0.075[a]	2.000	147.000	0.927	0.001
GA	Pillai's Trace	0.008	0.584[a]	2.000	147.000	0.559	0.008
	Wilks' Lambda	0.992	0.584[a]	2.000	147.000	0.559	0.008
	Hotelling's Trace	0.008	0.584[a]	2.000	147.000	0.559	0.008
	Roy's Largest Root	0.008	0.584[a]	2.000	147.000	0.559	0.008
BW	Pillai's Trace	0.002	0.179[a]	2.000	147.000	0.836	0.002
	Wilks' Lambda	0.998	0.179[a]	2.000	147.000	0.836	0.002
	Hotelling's Trace	0.002	0.179[a]	2.000	147.000	0.836	0.002
	Roy's Largest Root	0.002	0.179[a]	2.000	147.000	0.836	0.002
Maternal Hb	Pillai's Trace	0.045	3.490[a]	2.000	147.000	0.033*	0.045
	Wilks' Lambda	0.955	3.490[a]	2.000	147.000	0.033*	0.045
	Hotelling's Trace	0.047	3.490[a]	2.000	147.000	0.033*	0.045
	Roy's Largest Root	0.047	3.490[a]	2.000	147.000	0. 033*	0.045

a. Exact statistic Gestational age, b. Design: Intercept + MA +GA +BW +Maternal Hb

MA = Maternal age, BW = Birthweight, Hb = Haemoglobin *= p value < 0.05 (significant)

Table 5: Univariate tests of between-subjects effects

Source	Dependent Variable	Type III Sum of squares	df	Mean square	F	Sig.	Partial Eta Squared
Corrected Model	MMA	14450.362[a]	4	3612.591	0.408	0.802	0.011
	Newborn MMA	52111.333[b]	4	13027.833	1.843	0.124	0.047
Intercept	MMA	542.409	1	542.409	0.061	0.805	0.000
	Newborn MMA	9007.171	1	9007.171	1.274	0.261	0.009
MA	MMA	1151.523	1	1151.523	0.130	0.719	0.001
	Newborn MMA	44.804	1	44.804	0.006	0.937	0.000
GA	MMA	10339.637	1	10339.637	1.169	0.281	0.008
	Newborn MMA	82.501	1	82.501	0.012	0.914	0.000
BW	MMA	2099.622	1	2099.622	0.237	0.627	0.002
	Newborn MMA	1323.611	1	1323.611	0.187	0.666	0.001
Maternal Hb	MMA	1727.031	1	1727.031	0.195	0.659	0.001
	Newborn MMA	49681.788	1	49681.788	7.027	0.009*	0.045
Error	MMA	1309085.964	148	8845.175			
	Newborn MMA	1046450.902	148	7070.614			
Total	MMA	4097939.000	153				
	Newborn MA	6476906.000	153				
Corrected Total	MMA	1323536.327	152				
	Newborn MMA	1098562.235	152				

a. R Squared = .011 (Adjusted R Squared = -.016 b. R Squared = .047 (Adjusted R Squared = .022)
*= p value < 0.05 significant, Hb = Haemoglobin, GA = Gestational age, MA = Maternal age
BW = Birth weight, MMA = Maternal measles antibodies

Discussion

Present study revealed a high MMA in mother-infant pairs at birth, with newborn infants having higher levels of MMA than their corresponding mothers. This is similar to the observations that were made in Lagos, Nigeria three decades ago and from other studies conducted in other parts of the world.[1, 16, 17] Active placental transfer of MMA from mothers to their foetuses could be the likely explanation for the newborn infants having higher MMA than their mothers.[18] The high levels of MMA that was found in the study population could be as a result of the boosting effect of MMA by MV, stemming from the fact that measles is endemic in our setting.[7, 17, 18]

Whereas, acceptable maternal Hb yielded higher mean MMA, low maternal Hb was associated with low MMA of mother-infant pairs in this work. Maternal Hb, in fact, was found to contribute significantly towards newborn-infants having much more MMA than their mothers. This conformed to the observation made by other authors' in both developed and resource poor countries of the world.[17-19] The transfer of macromolecules from mother to their foetuses via the placenta in most cases is a reflection of maternal nutrition. The placenta exerting activating mode of action towards preferential concentration of some macromolecules in the foetus.[19] In this regard, MMA being macromolecules would be better passed from mother to foetus where maternal Hb is acceptable relative to mothers with low Hb since maternal Hb is a good indicator of maternal nutrition.[1]

Apart from being a good indicator of mother's health and nutrition, maternal Hb also has a long-term health benefit in babies. This could include newborn infants starting out with high levels of MMA.[1, 17-18] The present study showed that infants of mal-nourished mothers (low Hb) are more prone to measles. Reason being that, these newborn infants are delivered with lower MMA; these antibodies may not last long enough to protect them against measles during infancy.[18] The low MMA in infants whose mothers have low Hb are further cleared by overwhelming and recurrent infections among other causes, thereby, making these children highly vulnerable to measles and its complication chief amongst them malnutrition.[18, 20] Growth faltering and developmental delay subsequently sets in in those who continue to be malnourished following measles in this vulnerable group.

Even though the mean MMA of mother-infant pairs of cohorts having low maternal Hb was low compared to subjects whose mothers had high (acceptable) Hb, their mean MMA was, nonetheless, protective in present study. Similar finding was made by victor et al, [18] in the year 2000. Mothers that were found with low Hb in this study could still be producing measles antibodies probably from exposure to MV. Moreover, some workers have found that humoral immunity is not impaired even under acute nutritional stress.[21] This means that, mothers with low Hb as seen in our study could respond to MV challenge by producing high levels of MMA, which are transferred to their babies.

Maternal age, GA and BW did not significantly affect MMA of mother-infant pairs in this work. Other workers had reported similar findings with respect to MA and BW, however, GA age was found to vary directly with MMA in mother-infant pairs. [1, 16-18] The possible explanation for our observation may be that most of the mothers are very young in their twenties, majority of the newborn infants are term and with normal BW. The transfer of MMA in mother-infant pair across the placenta occurs maximally from the third trimester of pregnancy that is from 28 weeks of gestation onward. [1, 16, 17] The least GA in this study was 30 weeks and since the study was not primarily design to compare MA, GA and BW with MMA of mother-infant pairs, our finding in this regard is anticipated.

Most developing and sub-Saharan countries like Nigeria are saddled with malnutrition and high cases of measles. The scourge of measles and its complications, such as malnutrition in children from these poor nations could be reduced if mothers thought of health values like adequate nutrition. These would ensure acceptable Hb levels in mothers, which could in turn generate high levels MMA. Information obtained from this study may be of public health benefit because policy makers can use this work as a platform to improve on the existing maternal health practices geared towards improving maternal nutrition. By improving maternal nutrition, higher levels of MMA could be generated, which could prevent infants from measles.

Conclusion

Mothers with acceptable Hb gave birth to newborn infants with higher levels of MMA compared to the low levels of MMA observed in newborns whose mothers had low Hb. Thus, newborn infants of mothers with acceptable Hb in the current work have better protection against measles.

Limitations

This work was performed at the UMTH, which makes it a uni-centered study. This is a setback because caution is needed in generalizing the results of this research. Data on MA, GA and BW were skewed towards very young MA, term deliveries and normal BW. These could be another drawback because skewed distribution of data is a shift from normal population distribution that may interfere with the interpretation of results.

Recommendations

In order to eliminate measles in children in our setting, there is need for relevant authorities to re-strategize and implement maternal health practices like adequate nutrition. The girl child should be educated and be well informed on good nutritional habits. This will help in generating acceptable maternal Hb and high levels of MMA needed to protect infants against measles during the child bearing age of the girl child. Studies of this kind in the future should include mother-infant pairs from multiple health centers in order to have a representative cross-section of the study population. Furthermore, a study design that accommodates all MA groups within the child bearing age, GA groups and BW groups in greater frequencies is also recommended in order to improve the power of the relationship between these variables and MMA.

Contributors

BUA, AGM, MY, and AJP conceived and designed the study; all authors assessed and interpreted the data and wrote the draft of the report. All authors were involved in the critical revision of the paper.

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