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STATISTICAL MODELLING OF HAEMOGLOBIN LEVEL IN UNDER FIVE YEARS OLD CHILDREN IN NIGERIA

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ABSTRACT

Haemoglobin concentration is a clinical indicator that examines or measures the presence or otherwise of an anaemia in an individual subject particularly due to iron deficiency. Normal Haemoglobin distributions vary with age, sex, life style, race/ethnicity, socio-economic status, regional difference, drug related issues and clinical characteristics including guidelines, and protocols. Issues arising from the recent spikes in the number of new-borns who were anaemic have attracted attention globally and these are of great concern particularly in Sub-Sahara Africa in which Nigeria has huge share of statistics. Hence, this study examined haemoglobin levels in under 5 children in Nigeria and the set of factors driven it from various statistical approaches. These models were: linear regression model (LM), Linear mixed model (LMM) and multilevel model (MM). This study used dataset of children included in the Nigeria Malaria Indicator Survey, 2015. The results of LM, identified two significant predictors of under 5 children haemoglobin level, also only three predictors were significant under LMM. The random effect of household number under LMM setting had higher variability than the state as random effect. In MM with state and household number as random effects, area of residence of the child, head of household wealth index, and the age of the child were all significant. The estimates of MM produced smaller standard errors compared to LMM. This implies that multilevel model is more competitive than other models considered in this study. Therefore, it could be applied to predict the haemoglobin level of under 5 children in Nigeria.

Keywords: Haemoglobin, Multilevel analysis, Predictors, Variability, Anaemia, Nigeria

INTRODUCTION

The issue of anaemia is a global phenomenon which has received less attention in recent times especially in the developing nations where larger proportion of the population lives below 2 (US) dollars per day (World Bank, 2019). These nations lie mostly in the Sub-Sahara Africa (SSA) and are the most hit globally with highest records of disorder due to nutritional deficiency (Parbey *et al*., 2019). Recently, some studies have attributed the rise in this menace to poverty as spikes in the number of cases are rampart among those with lower levels of economic conditions while other studies have attributed it to deficiency in intake of iron-related supplements, poor dietary diversity and nutritional imbalance, thereby affecting the haemoglobin level and causing anaemia in young adults and children (WHO, 2011). In addition to the above stated causes of anaemia, it can coexists with a number of other causes like malaria, tuberculosis, parasitic diseases and chronic medical conditions (WHO, 2008).

Haemoglobin (Hb) is the oxygen carrying pigment (mainly protein) in the red blood cells usually from the lung to tissues and carries the deoxygenated blood back to the lung from the tissues. The reduction in the circulating haemoglobin as a result of destruction or loss of erythrocyte (red blood cells) and possibly due to impaired synthesis of haemoglobin can result into anaemia(Otto *et al*., 2017). Hence, an anaemia is a situation in which the number of red blood cells is insufficient to meet the body physiological needs (WHO, 2011). It represents a scenario which marked by a low haemoglobin level(Mohammed, Habtewold, & Esmaillzadeh, 2019). A haemoglobin concentration below 130g/l in males, less than 120 g/l in non-pregnant females and Hb level less than 110g/l for under five children is considered anaemic(FMoH/NPC, 2016). The common causes of anaemia include but not limited to, iron deficiency, nutritional imbalance, parasitic diseases and some underlying medical illnesses or comorbidity conditions in individual subject (WHO, 2011).

Globally, there are about one out of every three individuals that are anaemic (Dey & Raheem, 2016; Mohammed *et al.*, 2019). Anaemia is the major cause of reduction in quality of life through impairment of capacity of body functions and always accompany unhealthy outcome especially with an individual that has comorbidity conditions with other chronic diseases (Salako, Brieger, & Afolabi, 2001). Generally, Women of childbearing age are more susceptible to anaemia as a result of blood loss due to regular monthly menstruation, pregnancy, childbirth, and even during breastfeeding. These conditions make them prone to infections as their immune systems are supressed during these periods (Adu-Prah & Tetteh, 2015). Also, children of age less than 59 months are not exempted from this category as anaemia is more prevalent among this age group. The cognitive development together with the physical and social life of these children are at risk with anaemia. There are about 293.1 million under five that are anaemic globally. Unfortunately, over 198.4 (67.7%) millions of this cases are in the shores of Africa (Id, Ali, Ali, & Fisha, 2019). Nigeria has about 68.3% prevalence of anaemia among under 5 children and 49.8% among women of reproductive age (15 to 49 years) in 2016 (Worldbank, 2019). Although several studies existed in literature on haemoglobin level and anaemia globally (Dey & Raheem, 2016), few of such studies were from SSA nations including Nigeria (Ughasoro, Emodi, & Okafor, 2015). Hence, this study intends to fill this gap by serving as a reference material and possibly providing way forward in mitigating this trend. Therefore, the present study adopted Linear mixed and multilevel models to explore haemoglobin level in Nigeria.

METHODS

Data and Model Variables

The data used for this study were sourced from Nigeria Malaria Indicator Survey, 2015 for selected household across thirty-six (36) states of Nigeria and Federal Capital territory, Abuja. 2015 (https://dhsprogram.com/data/dataset/Nigeria_mis_2015.cfm). The outcome variable was haemoglobin level (as a measure of the risk of anaemia) while the set of explanatory variables are: Age of the respondent; sex (male or female); education (no education, primary, secondary and higher education), wealth index (poorest, poor, middle, rich and richest) (constructed via principal component analysis using some economic indicators or household variables)(FMoH/NPC, 2016). The details description of these variables in relation to anaemia based on related-studies is given in Table 1.

Table 1: Variable description and classification

Variable	Level/state	Description and relevant information	Source
Age	Quantitative	Age is inversely associated with Hb level as anaemia increased concomitant with age among the older persons while anaemia reduces with age among under five children.	(Id *et al*., 2019; Salive *et al*., 1992)
Residence	Urban Rural	A high Hb level is paramount among urban dwellers (possibly due to socio-economic condition and access to medical infrastructures) while the reverse is true in rural settings. However, the recent literature posited a high prevalence of anaemia in urban area	(Id *et al*., 2019)
Sex of household	Male Female	Literature posited lower level of Hb in female than in male. This is also similar to other health-related reports previously documented in SSA	(Kimberly, Lima, Connor, & Furie, 2013; Loha, Lunde, & Lindjorn, 2012)
Education	Quantitative	A household with at least secondary education is significantly associated with a high Hb level	(Mohammed *et al*., 2019)
wealth index	Qualitative	A rich household is associated with a high mean Hb levels. Hence, anaemia decreases with wealth.	(FMoH/NPC, 2016; Id *et al*., 2019; Mohammed *et al*., 2019)
Family size	Quantitative	A household size dictates susceptibility of individuals to diseases and ill-health conditions like anaemia. A larger household size is likely to bread anaemic individuals than a smaller household size	(Ajadi, Olaniran, Alabi, & Adejumobi, 2012; FMoH/NPC, 2016)

Linear Models

Linear Model is one of the simplest and most well-known models in all of statistics. Its versatility leads to applications in a broad range of disciplines. It attempts to model the mean of a measured n × 1 response vector Y conditioned on observed predictor variables. This leads to the following representation

$Y = X\boldsymbol{\beta} + \varepsilon$ (1)

where X is an n×p matrix of predictor variables and εis a n×1 vector of random errors. In this simplest case, **β** represents a parameter vector of fixed effects. The usual assumptions in this model are independence and constant variance. Either least squares or maximum likelihood can be used to solve the normal equations to solve for the **β** parameter values. Either method leads to the solution: $\boldsymbol{\beta}=(X^T X)^- X^T Y$

where $(X^T X)^-$is the generalized inverse in the case that $(X^T X)$ is not full rank.

Linear Mixed Effects Model

The Linear Mixed Effects (LMM) model is a generalization of the linear model presented in Equation 1. Linear mixed effects models are used when there are correlated responses and the structure of the correlation can be specified in the variance matrix. The correlation arises when there are multiple sources of variability in the n × 1 response vector Y. These different sources of variability must be accounted for in the model. This leads to the following representation,

$Y = X\boldsymbol{\beta} + Z\mathbf{u} + \varepsilon$ (2)

$\varepsilon \sim MVN(0;\Sigma)$

This means that, the ε is multivariate normally distributed with zero mean and variance-covariance matrix of Σ.

$u \sim MVN(0; \Psi)$

This implies that, the u which error associated with random effect is multivariate normally distributed with zero mean and variance-covariance matrix of Ψ.

Where X is an n × p matrix of predictor variables as in the simple linear model. Z is an n × q matrix of known constants, and **β** and **u** are p × 1 and q × 1 vectors of unknown parameters and random variables, respectively. It is very common to assume a constant variance for all the $\varepsilon_i$errors. In this case the covariance matrix for ε can be expressed as $\Sigma = \sigma^2 I$ where I is the identity matrix and σ^2 is variance component. When the joint distribution of (u; ε) is multivariate normal, the mixed effects model has the following properties: $E[Y/X,Z]=X\beta$;

This implies that the conditional expectation of Y dependent given X independent variables and Z random effect variable is equal to Xβ.

$Var[Y/X,Z]= \Sigma+Z\Psi Z^T$

This implies that the conditional variance of Y dependent given X independent variables and Z random effect variable is equal to variance-covariance Σ plus vector Z multiply by random effect variance component multiply by and transpose of Z.

Multilevel Model

In the case of a multilevel model, the Z matrix can be decomposed into pieces representing each of the additional variance components at each of the k levels in the design.

$Y = X\beta + Z_1u_1 + \cdots + Z_ku_k + \varepsilon$ (3)

Consider, a data set with three levels: state, household within state and children within household. Suppose also that we have measurements on a response variable for the j^{th} child in the i^{th} household within the k^{th} state. The full model is

$Y_{kij} = \alpha^*_{kij} + \beta^*_{ki} + \gamma^*_k$ (4)

At each level of the 'hierarchy' let's set up a linear model relating the terms in (1) to a function of explanatory variables, as follows

$\gamma^*_k = \gamma_0 + \gamma_1 w_{1,k} + \ldots + v_k = \sum_{i=0}^{q} \gamma_i w_{i,k} + v_k$ (5)

where v_k is a random variable with $E(v_k) = 0$,& $Var(vk) = \sigma^2_{v_k}$ and γ_i is the state level coefficient for the I^{th} explanatory variable $w_{I,k}$ for state k. Also

$\beta^*_{ki} = \beta_0 + \beta_{1,k} z_{1,ki} + \ldots + \mu_{ki} = \sum_{i=0}^{p} \beta_{1,k} z_{1,ki} + \mu_{ki}$ (6)

where u_{ki} is a random variable with $E(u_{kj}) = 0$, $Var(u_{ki}) = \sigma^2(k)$, and, β_k is the household level coefficient for the I^{th} explanatory variable Z_{ki} for household ki. finally, we have

$\alpha^*_{kij} = \alpha_0 + \alpha_{1,k1} x_{1,k1j} + \ldots + \varepsilon_{kij} = \sum_{i=0}^{r} \alpha_{i,ki} x_{i,kij} + \varepsilon_{kij}$ (7)

where ε_{kij} is a random variable with $E(\varepsilon_{kij}) = 0$, $Var(\varepsilon_{kij}) = \sigma^2$ and $\alpha_{i,ki}$ is the child level coefficient of the I^{th} explanatory variable $x_{I,kij}$ for child kij

Thus we can write the simpler full model, combining (5), (6) and (7), as

$$Y_{kij} = \alpha_0 + \gamma_0 + \beta_0 + \sum_{i=0}^{r} \alpha_{i,ki} x_{i,kij} + \sum_{i=0}^{p} \beta_{1,k} z_{1,ki} + \sum_{i=0}^{q} \gamma_i w_{i,k} + (v_k + \mu_{ki} + \varepsilon_{kij})$$

or as $Y = X\beta + E$. (8)

The model is assumed to be of full rank.

We have

$$\mathrm{Var}(Y_{kij}) = \sigma^2_v + \sigma^2_\mu(K) + \sigma^2(ki)$$

assuming that all covariance between the random variables in (8) are zero. Thus the overall variance of Y can be partitioned into components for state, household and children, hence the term 'variance component' models. We also assume further for simplicity that

$\sigma^2_\mu(K) = \sigma^2_\mu$ and $\sigma^2(ki) = \sigma^2$,

Thus for household we can define the 'intra class coefficient

$\rho_{ki} = (\sigma^2_v + \sigma^2_\mu)(\sigma^2_v + \sigma^2_\mu + \sigma^2)^{-1}$

and for state

$\rho_k = \sigma^2_v(\sigma^2_v + \sigma^2_\mu + \sigma^2)^{-1}$

Ethical Consideration

The data for this study were extracted from an existing and publicly available dataset which were solely information about anonymous human subjects. As such, this does not require ethical approval and clearance.

RESULTS AND DISCUSSION

Socio-Demographics Characteristics of Study Population

Tables 2 present the descriptive statistics of Age of household head, family size, Child age (months) and haemoglobin. The summary statistics revealed that family size ranges from 1 to 21 with an average of about five (5) children per household. The average age of the head of household was 41.14±12.2. years while the haemoglobin level of the under five years old children studied ranges from 3.6 to 15.7.

Table 2: Summary statistics of continuous variables of the sampled households

Continuous Variable	Mean	SD
Age of household head	41.14	12.16
Family size	4.26	2.60
Child age (months)	32.3	15.46
Hb	10.16	1.61

SD: standard deviation; Hb: Haemoglobin

Tables 3 shows that, 3447(66.2%) of the household were in rural area while the remaining 33.8% were urban dwellers. Of 5208 households sampled, 92.9% of the household head are male and 7.1% were female (Table 3).

Table 3: Summary statistics of categorical variables of the sampled households

Categorical variables	Frequency	Percentage (%)
Residence		
Urban	1761	33.8
Rural	3447	66.2
Religion		
Christianity	2301	44.2
Islam	2871	55.1
African traditional	15	0.3
Others	18	0.3
No response	3	0.1
Sex of household head		
Male	4839	92.9
Female	369	7.1

Wealth index		
Poorest	1021	19.6
Poor	2054	39.4
Wealthy	1995	38.3
Wealthiest	138	2.6

Results Based on Different Fitted Models to Haemoglobin Data

This present study fitted four different models to haemoglobin data and various estimates compared. These models are standard linear regression (Model 1), linear mixed model with household number as random effect (Model 2), linear mixed model with state as random effect (Model 3) and multilevel linear model with household number and state as random effects Model 4).

Table 4 displays the parameter estimates and other related statistics using the standard regression model. Two out of all the nine variables included in the model were statistically significant (p<0.05). These variables were area of residence and child age. The results showed that households in rural areas have likelihood of decreasing the level of haemoglobin compared to those living in urban area while the hemoglobin level increased with age.

Table 4: Linear regression model

Variable	Coefficient	Std. Error	t	p> |t|	95%CI
Residence	-6.69	0.47	-14.10	<0.001	(-7.612-5.76)
Religion	0.10	0.09	1.04	0.297	(-0.08,0.28)
Sex of head of household	0.30	0.86	0.35	0.729	(-1.38, 1.97)
Age of head of household	0.011	0.02	0.58	0.560	(-0.03, 0.05)
Wealth index	0.64	0.48	1.34	0.180	(-0.30, 1.59)
Family size	-0.13	0.09	-1.47	0.142	(-0.30, 0.04)
Childage	0.19	0.01	13.33	<0.001	(0.16, 0.21)
Constant	10.03	1.69	6.41	<0.001	(9.72, 10.34)

CI: Confident interval

Table 5 displays the results of a linear mixed regression model with household number as random effect. Three out of the seven fixed effect variables used were significant (p<0.05). Subject area of residence, wealth index of head of household and the age of the child were all significant. Also the random effect which is equal to 2.96 showed that hemoglobin level varies from household to household. The impact of the significant variables on hemoglobin showed that living in rural area have the likelihood of reducing the haemoglobin level. An increased in wealth index increases the level of haemoglobin. Likewise, the results revealed that increase in age increases hemoglobin level.

Table 5: Linear mixed model (Random effect: Household number)

Variable	Coefficient	Std. Error	T	p> |t|	95%CI
Residence	-6.57	0.47	-13.89	<0.001	(-7.49,-5.64)
Religion	0.09	0.09	0.97	0.334	(-0.09, 0.27)
Sex of head of household	0.22	0.85	0.26	0.795	(-1.45, 1.89)
Age of head of household	0.01	0.02	0.59	0.555	(-0.03, 0.05)
Wealth index	1.85	0.20	9.36	<0.001	(1.46, 2.24)
Family size	-0.13	0.09	-1.48	0.138	(-0.31, 0.04)
Childage	0.18	0.01	13.28	<0.001	(0.16, 0.21)
Constant	10.15	1.66	6.77	<0.001	(9.89, 10.41)
Random effect	2.96	1.46			(1.48, 3.18)

Table 6 shows the parameter estimates of a linear mixed regression model with State as random effect. Two out of the seven fixed effect variables used were significant (p<0.05). Area of residence of the subject and the age of the child were significant while other variable like sex of head of household, age of the head of household, family size and wealth index were not significant. Likewise, the random effect variance is 2.98 which implies that the variability between states. The impact of the significant variables on haemoglobin showed that living in rural area reduces hemoglobin level, and increase in age increases hemoglobin level.

Table 6: Linear mixed regression model (Random effect: State)

Variable	Coefficient	Std.error	t	p> |t|	95%CI
Residence	-7.29	0.50	-14.54	<0.000	(-8.27, -6.30)
Religion	0.11	0.09	1.22	0.221	(-0.07, 0.29)
Sex of head of household	0.29	0.84	0.35	0.728	(-1.35, 1.93)
Age of head of household	0.01	0.02	0.71	0.479	(-0.02, 0.05)

Wealth index	0.67	1.01	0.67	0.505	(-1.29, 2.64)
Family size	-0.05	0.09	-0.52	0.600	(-0.22, 0.13)
Childage	0.18	0.01	13.56	0.001	(0.16, 0.21)
Constant	10.23	1.22	6.57	0.009	(9.89, 10.58)
Random effect	2.98	1.43			(2.6, 3.66)

Table 7 shows the result based on the multilevel model with State and household number as random effects. Four out of the seven fixed effect variables used were significant ($p<0.05$). Area of residence, wealth index, family size and the age of the child were all significant. The random effect variances were 0.507 and 0.622 for state and household number respectively. The impact of the significant variables on haemoglobin revealed that living in rural area reduces haemoglobin level, increase in wealth index increases level of hemoglobin, increase in family size in the household reduces haemoglobin level and also increase in age increases haemoglobin level. The haemoglobin level of under five children varies from state to state and household to household.

Table 7: Multilevel model (Random effect: State and household number)

Variable	Coefficient	Std.error	Z	p> |z|	95%CI
Residence	-7.19	0.16	-44.33	<0.001	(-7.5, -6.86)
Religion	-0.11	0.20	-0.57	0.566	(-0.50,0.27)
Sex of head of household	0.17	0.77	0.22	0.829	(-1.34,1.67)
Age of head of household	0.02	0.01	1.80	0.070	(-0.00,0.05)
Wealth index	1.37	0.06	22.86	<0.001	(1.25,1.49)
Family size	-0.16	0.07	-2.24	0.020	(-0.31,-0.02)
Childage	0.19	0.01	13.67	<0.001	(0.16,0.21)
Constant	10.46	1.09	9.65	<0.001	(9.43,10.67)
Random effect(state)	0.51	<0.01			(0.21,0.72)
Random effect (household no.)	0.63	0.65			(0.08,4.82)

Table 8: Intra-class correlation

Model	Intraclass correlation	Intraclass correlation CI
Model 2	0.3027	0.271-0.352
Model 3	0.455	0.334-0.588
Model 4	0.511	0.38-0.641

CI: Confidence interval of Intraclass correlation

Intra-class correlation (ICC) reported the amount of variation unexplained by any predictors in the model that can be attributed to the grouping variable, it clears from Table 8 and figure 1 that multilevel model captured more unexplained variation than linear mixed model.

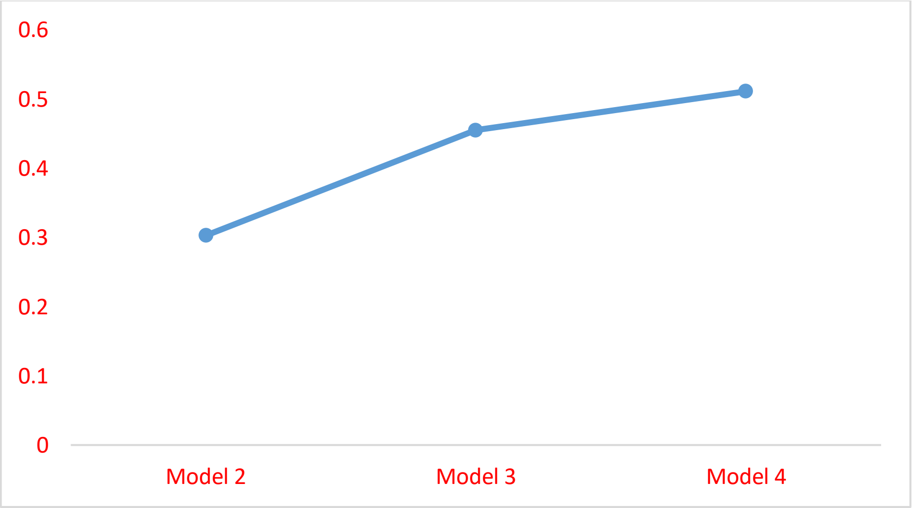

Figure 1: Intraclass Correlation

Table 9: Model efficiency

	Model 1	Model 2	Model 3	Model 4
RMSE	15.32	14.99	24.24	25.03
AIC	43.21	43.20	42.97	42.06
BIC	43.27	43.23	43.02	42.41

RMSE-root mean square, AIC: Akaike Information Criterion, BIC: Bayesian information criterion.

Table 9 and figures 2-4 below indicate that, the model efficiency for various parameters selected for this study. Model 2 and 3 produced better estimate than model 1, model 4 has better estimate than models 2 and 3 based on AIC.

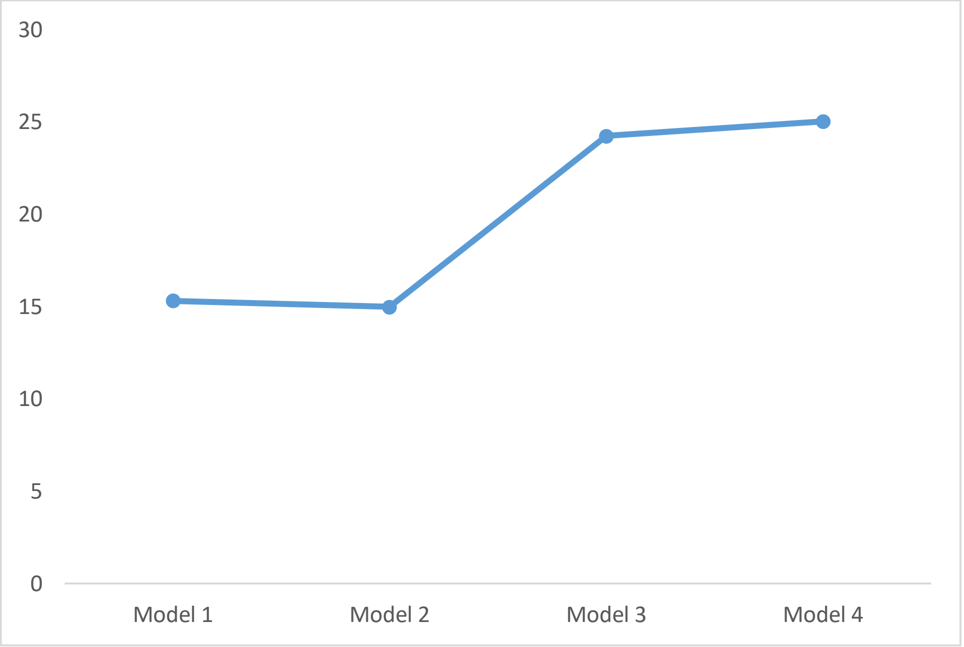

Figure 2: Root Mean Square Error (RMSE)

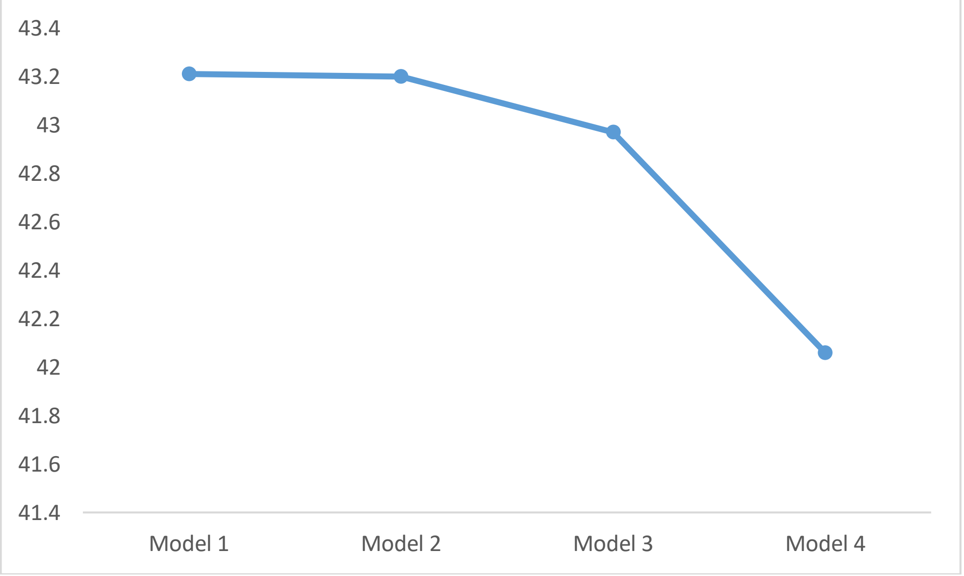

Figure 3: Akaike Information Criterion (AIC)

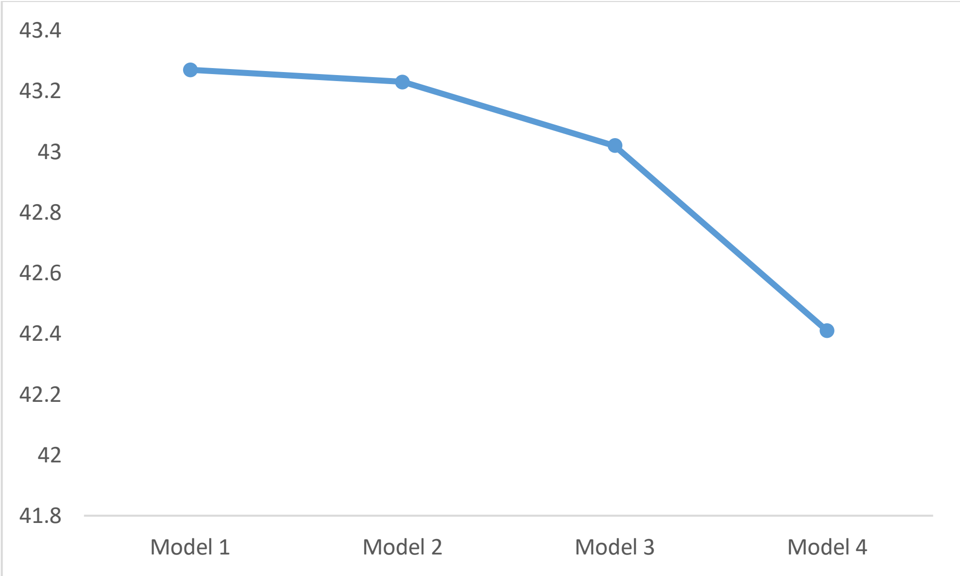

Figure 4: Bayesian Information Criterion (BIC)

Discussion

This current study aimed to determine the influencing factor of Hb level in children aged less than 59 months at household levels in Nigeria. The different models explored in this study identified place of residence, age of a child, family size and wealth index as the influencing variables of Haemoglobin level in children for the population under study. The application of such models were common in literature and authors have frequently applied them in related studies (Mohammed *et al*., 2019).

This study reported a lower value of Hb indicating presence of anaemia among the study subjects. This current result agrees with the high prevalence of anaemia reported in Ethiopia (Mohammed *et al.*, 2019). The authors reported mean Hb level of 10.00 ± 1.63 g/dL,which showed 71.92% anaemia prevalence among the study subjects. The intuitive explanation for this anaemic condition could possibly be due to poor socio-economic conditions of various household under this current study as over 66% of the sample population were rural dwellers. Also, lack of good food additives or supplements rich in iron and bioceuticals could be another possible factor that could be responsible for this huge statistics recorded.

The subject place of residence was found to be associated with the haemoglobin level as in other related studies (Id *et al.*, 2019). This finding suggests that the urban dwellers stand lesser risk of anaemia compared to rural dwellers. This possibility may be due to the level of education and exposure to standard way of lives in the cities and availability of various iron food supplements that can help boost the haemoglobin level of the citizenry. This finding is inconsistent with the one reported in Ethiopia (Mohammsed *et al*., 2019). The authors found the place of residence not associated with level of haemoglobin, however, they identified regions (pastoral and agrarian) to be a significant factor.

Likewise, the current study found age of a child as a significant factor. This results of this current study is in harmony with the findings of Dey and Raheem(2016).Also, socio-economic condition was identified as an influencing factor of Hb level. Children from poor household has lower Hb level compared with those from higher social class. This could be due to the fact that richer households have access to good healthcare facilities and good standard of living. Hence, benefits more from pharmaceutical alternatives and dietary supplements that can enhance iron and Hb level in under five children.

Also, the result based on random effect model revealed an inverse association between family size and hemoglobin level. Hence, an increased in household size leads to reduction in Hb level and vice versa. The intuitive explanation could be that as family size increases, the possibility of a decreased in socio-economic conditions of various households especially among the rural dwellers where majority lives below two (2) US dollar a day. Poverty at household level among the study subjects could be a confounding factor responsible for this result (World Bank, 2019).

Across the three models explored, a multilevel model appeared to be more competitive among all the candidate models considered based on number of significant variables and model efficiency criterion. This current result is consistent with the hierarchical model used by Mohammed *et al*. (2019). The author found hierarchical linear regression analysis more efficient in identifying potential risk factor than common regression models after appropriate adjustment for more confounding variables in the model.

CONCLUSION

Having applied all necessary constraints and model on the hemoglobin data, it is crystal clear that linear multilevel model appears to have a superior competitive edge over all other model settings considered in this study. Therefore, multilevel model could be applied to predict the haemoglobin level of under 5 years old children in Nigeria. Likewise, the decision makers should put strategies in place to curb the menace of anaemia via reduction in poverty and economic hardship among its citizenry. Also, health awareness on the associated risk factors to reduce anaemia.

CONFLICT OF INTEREST

The authors have no conflict of interest regarding this article.

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