Research

Self-reported adherence to iron-folic acid supplementation and its associated factors among pregnant women attending antenatal care in Tamale Metropolis, Ghana

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Background

This study assessed self-reported adherence to iron-folic acid supplementation and its associated factors among pregnant women attending antenatal care in Tamale Metropolis, Northern Ghana.

Methods

This was a health facility-based cross-sectional design. A total of 389 pregnant women attending antenatal care (ANC) were consented and recruited to participate in the study, using systematic sampling. Data were collected using a questionnaire on socio-demographic characteristics, obstetric factors, iron-folic acid (IFA) supplements, and adherence (self-reported). Respondents who consumed ≥70% (5/7 per week) of IFA tablets were considered to be adherent and vice-versa. Logistic regression models were used to determine factors associated with IFA adherence.

Results

IFA adherence was 41% among the respondents. Using multivariate logistic regression, secondary education [AOR=1.37, (95% CI= 1.18-1.82)], having \geq 4 ANC visits [AOR=1.44, (95% CI= 1.28-1.67)], urban residence [AOR=1.59, (95% CI= 1.36-1.97)] and receiving IFA supplements at a health facility [AOR=1.98, (95% CI=1.02-3.83)] were associated with higher IFA adherence.

Conclusion

Iron-folic acid adherence was low (41%). Education, residence, ANC visits and supply of IFA supplements at the health facility attended were associated with IFA adherence. Barriers to IFA adherence were mainly forgetfulness, unavailability of IFA, and perceived side effects.

INTRODUCTION

Despite decades of public health interventions, anaemia in pregnancy remains a major health problem worldwide, affecting about 41% of pregnant women and accounting for 20% of the maternal mortality burden in sub-Saharan Africa (SSA) (Gupta and Gadipudi 2018; McLean et al. 2009). An estimated 50% or more of anaemia cases in pregnant women are attributable to iron deficiency, with folate or vitamin B12 deficiency, infections like malaria and human immune deficiency Virus (HIV), and certain inherited disorders such as sickle cell disease and thalassaemias, accounting for the remaining cases (Gupta and Gadipudi 2018). Pregnant women are at greater risk of iron deficiency anaemia (IDA) due to increasing nutrient demands during pregnancy which may be difficult to meet through dietary means. In Ghana, 42% of women of reproductive age (15-49 years) and 45% of pregnant women are anaemic (Ghana Statistical Service 2015).

Iron deficiency anaemia contributes to a range of negative effects on maternal and child health; increased risk for perinatal morbidity and mortality, low birth weight, preterm delivery, and low Activity, Pulse, Grimace, Appearance and Respiration (APGAR) scores (Allen 2000). Addi-

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tionally, the effect of IDA on poor mental development in infants and young children has been well-documented (Chang et al. 2013). Folic acid deficiency during conception and early pregnancy increases the risks for preterm delivery, infant low birth weight, neural tube defects, and foetal growth retardation, among others (Scholl and Johnson 2000; Sengpiel et al. 2014).

The utilization of iron-folic acid supplementation remains low in many developing countries, despite its effectiveness (Yakoob and Bhutta 2011) and WHO's recommendation of daily oral iron-folic acid (IFA) consumption among pregnant women in most low-income settings (Abdullahi et al. 2014; WHO 2012). Yet IFA supplementation adherence is key in preventing and controlling anaemia and neural tube defects (Guterres 2007).

WHO recommends giving all pregnant women 30- 60 mg elemental iron and 0.4 mg of folic acid daily for six months. In some anaemia endemic settings, an additional three months are recommended (Anlaakuu and Anto 2017; WHO 2016). A pregnant woman who reports that she consumed \geq 70% (5/7) of the combined IFA tablets or 5/7 of the separate iron and folic acid tablets supplied in the preceding week is commonly described as being adherent (Arega Sadore, Abebe Gebretsadik, and Aman Hussen 2015).

Although anaemia among pregnant women was 59% nearly a decade ago (Project 2014), consumption of the ideal number of IFA supplements was found to be low (21%), particularly in the Northern Region, Ghana. Thus, the Ghana National Nutrition Policy highlights the need for IFA supplementation during pregnancy and within six (6) weeks postpartum (Ghana Ministry of Health 2017). Nonadherence was one of the main causes of national iron supplementation failure at the time (Ghana Statistical Service 2015), so it was recommended that identifying, and addressing gaps including health workers' practices, IFA availability management and modifying individuals' behaviour were called for (Project 2014). However, few studies have been conducted on IFA supplementation adherence in Northern Ghana in the past decade. Thus, this study assessed self-reported adherence with iron-folic acid supplementation and its associated factors among pregnant women attending antenatal care at Tamale Central Hospital, Northern Ghana.

METHODS

STUDY SETTING AND DESIGN

A health facility-based cross-sectional study was conducted in the Northern Regional capital of Tamale, Ghana at Tamale Central Hospital. Data were collected from October - November 2019. The Tamale Central Hospital is one of the three (3) main referral hospitals in the Northern Region. It serves people from the local community and referrals from other parts of the Northern zone of Ghana. Comprehensive health services and nutrition programs are provided in this hospital including maternal health services. Health providers at antenatal care administer full range of ANC services including IFA supplementation to pregnant women who visit the facility.

STUDY POPULATION AND SAMPLING

The study population was pregnant women who visited Tamale Central Hospital for routine ANC services for at least a second ANC and had either received IFA supplementation or purchased IFA tablets for at least a month before the interview date. Additionally, they had to meet the following criteria: they were not severely ill, had their maternal health record book available, and agree to share their personal and health-related information with the study team. The interviews were administered immediately before women received ANC services. Eligible study respondents were selected using systematic sampling. The study team estimated the number of ANC service users for the previous two consecutive months, which was 1218. The study population was divided by the desired sample size of 389 (see below), resulting in a sampling interval of 3. On each day of ANC session, the first respondent was selected from the first four (4) pregnant women using a simple random sampling technique. Then on the same day, every third pregnant woman among the eligible respondents was invited for consent and enrolment.

SAMPLE SIZE DETERMINATION

The sample size was determined based on a similar previous study (Sajith et al. 2016), which estimated the prevalence of IFA supplementation adherence to be 64%, using Cochran's (1999) formula ($n=Z^2pq/e^2$) (Robb 1963). The n is the minimum sample score for a normal distribution (z=1.96) for a 95% confidence interval, p is the prevalence of IFA supplementation adherence (64%), q= (1-p) is the proportion of non-adherence and e is the margin of error (e=0.05). After adjusting for an estimated 10% non-response, a total sample size of 389 was determined.

DATA COLLECTION AND QUALITY CONTROL PROCEDURES

A structured, paper-based, interviewer-administered questionnaire was developed by reviewing different existing literature. It consisted of 32 close-ended questions categorized into; socio-demographic characteristics (6), obstetric characteristics (5), knowledge of anaemia (9), knowledge and supply of IFA tablets (8) and IFA supplementation adherence (4). The data collectors included one staff midwife and two final year Bachelor of Science students in Community Nutrition, University for Development Studies, Tamale. All data collectors had previous experience in data collection on maternal and child health as well as nutrition-related indicators. They were trained over two days on the study, covering all study methods, objectives, questionnaire, and interviewing skills. The research team pretested the questionnaire and interviewing skills at the Tamale West Hospital, Ghana. The research team identified minor errors and made relevant modifications to the questionnaire. All administered questionnaires were regularly checked to determine the completeness and consistency of responses. Pill count was conducted for those who brought their IFA tablets to the ANC clinic to validate their self-reports on the number of IFA tablets consumed in the preceding one week. However, pill count was not used in the estimation of IFA supplementation adherence in this study.

DATA ANALYSIS

Our dependent variable was IFA supplementation adherence. This was determined using the self-reported number of IFA tablets consumed during the preceding week (7 days). Pregnant women who consumed ≥70% (5/7 tablets) of the recommended dose of IFA tablets in the preceding 7 days were considered to be adherent (Arega Sadore, Abebe Gebretsadik, and Aman Hussen 2015). The independent variables were socio-demographic characteristics (age, education status, marital status, residence, occupation, and religion of pregnant woman), obstetric and health-related characteristics (gravidity, parity, gestational age during the interview, gestational age at first ANC visit and number of ANC visits), knowledge of anaemia, and knowledge of IFA supplementation and supply. The knowledge on anaemia was determined by summing up all the correct ("yes" or "no") responses for heard of anaemia and currently anaemic/history of anaemia and 24 Likert scale items (4 each on causes, signs, and symptoms, prevention and complications of anaemia, foods rich in iron and foods that prevent the absorption of iron). Similarly, knowledge and supply of IFA supplements was assessed by summing up all the correct ("yes" or "no") responses for heard of IFA supplementation, received information on IFA, supplied with IFA supplementation, expectant mother to take IFA supplementation as soon as pregnancy is confirmed and throughout pregnancy, IFA supplementation in pregnancy prevents anaemia and IFA supplementation during pregnancy prevents birth defects and four (4) Likert scale item on the type of information received on IFA supplementation.

Data were entered, cleaned, and analysed using the statistical package for social sciences (SPSS) version 21.0 (windows version) by an experienced graduate nurse. The findings were presented using tables, frequencies, and percentages. Binary logistic regression analyses were performed to identify factors associated with IFA supplementation adherence for each independent variable and crude odds ratio with 95% confidence intervals were obtained. Subsequently, multivariable logistic regression analysis was performed to determine predictors of IFA supplementation adherence among pregnant women. The model included independent variables that showed a significant association with the dependent variable in the binary logistic regression. Hosmer and Lemeshow's goodness-of-fit test was used to check the appropriateness of the data for multiple logistic regression.

ETHICAL ISSUES

The study team informed the pregnant women that the answers are purposely for the research. They were also assured that all ANC services will still be provided if they chose not to participate in the study. This was to ensure that the pregnant women freely and voluntarily consented, enrolled and participated without fear of not being attended to properly. The current study was part of a larger survey in Northern Region, Ghana. Approval for the study was obtained from the Navrongo Health Research Centre Institutional Review Board (ID: NHRCIRB356).

Permission to conduct this study was also sought from the Northern Regional Health Directorate of the Ghana Health Service (GHS), and the Tamale Central Hospital, as well as the head of the ANC Clinic. Participation in this study was purely voluntary. The respondents were informed that they can withdraw at any time without losing any benefits. Consent was obtained from each respondent before the interview was conducted. The respondents below 18 years of age were included only if they provided informed consent and assent and people adults who accompanied them provided informed consent on their behalf. Pregnant women below 18 years without accompanying adults were excluded. The data collection tool was anonymised.

RESULTS

SOCIO-DEMOGRAPHIC CHARACTERISTICS OF RESPONDENTS

Out of an initial sample size of 389, 99% (384) participated in the study. Of this number, 75% were between 19 and 29 years of age. Further characteristics of the sample are shown in <u>Table 1</u>.

OBSTETRIC AND HEALTHCARE-RELATED CHARACTERISTICS OF STUDY RESPONDENTS

53% of the respondents were primigravida. At the time of the study, 37% were in their 1st trimester of gestation, and about three-quarters (73%) started ANC visit during 1st trimester of pregnancy. Other obstetric characteristics are recorded in <u>Table 2</u>. Regarding knowledge of the respondents, about 73% of respondents of the pregnant women knew about anaemia, 81% knew about IFA supplementation, and 78% had received IFA supplementation information at ANC (<u>Table 2</u>).

IFA SUPPLEMENTATION ADHERENCE OF STUDY RESPONDENTS

IFA supplementation adherence was determined by the self-reported number of iron-folic acid tablets that were provided to and taken by sample women. Only 157 (41%) consumed \geq 70% (\geq 5/7 tablets per week) of the recommended doses of IFA supplements.

As shown in Figure 1, several reasons accounted for nonadherence; more than half (56%) of the underlying reasons were forgetfulness (33%) and unavailability of IFA supplements at the health facility (23%).

FACTORS ASSOCIATED WITH IFA SUPPLEMENTATION ADHERENCE AMONG PREGNANT WOMEN

In a bivariate logistic regression model, four (4) factors were found to be significantly associated with IFA supplementation adherence. The odds of IFA adherence were higher among those with secondary education [COR=3.5,

Table 1. Sociodemographic characteristics of pregnant women receiving ANC services at Central Hospital (n=384)

Frequency (%)

2(0.5)

289(75.3)

93(24.2)

58(15.1)

68(17.7)

143(37.2)

115(29.9)

339(88.3)

45(11.7)

129(33.6)

255(66.4)

85(22.1)

71(18.5)

81(21.1)

33(8.6)

114(29.7)

299(77.9)

80(20.8)

5(1.3)

Table 2. Obstetric and healthcare service-relatedfactors of pregnant women (n=384)

Variables	Frequency (%)	
Gravidity		
Primigravida	204(53.1)	
Multigravida	179(46.9)	
Gestation during interview		
1 st trimester (<13 weeks)	143(37.2)	
2 nd trimester (13-27 weeks)	135(35.2)	
3 rd trimester (≥28 weeks)	106(27.6)	
Gestation at 1st ANC visit		
1 st trimester (<13 weeks)	285(74.2)	
2 nd trimester (13-27 weeks)	66(17.2)	
3 rd trimester (≥28 weeks)	33(8.6)	
Number of ANC visits		
<4	232(60.9)	
4+	150(39.1)	
Knowledge of anaemia	281(73.2)	
Knowledge of IFA supplementation	311(81.0)	
Received IFA supplementation information at ANC	299 (77.9)	
Received IFA supplements at ANC visit (s)	303(78.9)	

Muslim Christian Traditionalist

Others=farmer, daily labourer

Variables

19-29

≥30

None

Primary

Tertiary

Secondary

Marital status Married

Not married

Employment status Unemployed

Government employee

Residence Rural

Housewife

Trader

Others

Religion

Urban

Age in years ≤18

Educational status

(95% CI= 1.53-8.03)] compared to women with no formal education. Similarly, the odds of IFA adherence were higher among pregnant women with urban residence [COR=1.58, (95% CI= 1.03-2.92)]. The odds of IFA supplementation adherence were nearly double among pregnant women who had \geq 4 ANC visits [COR=1.85, (95% CI= 1.08-3.17)]. Furthermore, pregnant women who received IFA tablets during ANC visit at the health facility had lower odds of adherence [COR=0.47, (95% CI= 0.23-0.98)] compared to respondents who purchased their IFA supplements (p<0.05 in each case; see <u>Table 3</u>).

Respondent's marital status, occupation, gravidity, gestation age (weeks) at first ANC visit, gestation age during the interview, knowledge of anaemia, knowledge of IFA supplementation and received IFA information during ANC were not significantly associated with IFA adherence.

As shown in Table 4, in a multivariate logistic regression model using Hosmer and Lemeshow's goodness-of-fit, pregnant women who had secondary education had higher odds [AOR=1.37, (95% CI= 1.18-1.82)] of being IFA supplement adherent compared to no formal education. However, those who had urban residence had lower odds [AOR=0.59,

(95% CI= 0.36-0.97)] of being IFA supplement adherent. Those with \geq 4 ANC visits had higher odds [AOR=1.44, (95% CI= 1.28-1.67)] of being IFA supplement adherent. And respondents who received IFA supplements during ANC visits at the health facility had higher odds [AOR=1.98, (95% CI = 1.02-3.83)] of being adherent.

DISCUSSION

This study assessed self-reported adherence with iron-folic acid (IFA) supplementation and its associated factors among pregnant women attending antenatal care at Tamale Central Hospital in Northern Ghana. Out of the 384 respondents, less than half (41%) self-reported adherence. This finding is similar to studies on self-reported consumption of IFA in other countries such as Eritrea (33%, Kamau, Mirie, and Kimani 2018), and Ethiopia (44%, Digssie et al., 2017). According to the 2014 Ghana Demographic and Health Survey report, 59% of pregnant women were IFA supplement adherent (Ghana Statistical Service 2015).

Many factors have repeatedly been shown to hamper adherence with the IFA supplementation. In the present study, the primary reasons for non-adherence among pregnant women who missed doses of the iron-folate supplement were forgetfulness (33%), unavailability of IFA in the health facility (23%), fear of side effects (18%), unawareness of IFA importance (12%), fear of big foetus (9%) and fear of side-effects (5%). This is consistent with research findings elsewhere which reported that forgetfulness (30.5%), and the occurrence of side effects (35%) (Tarekegn

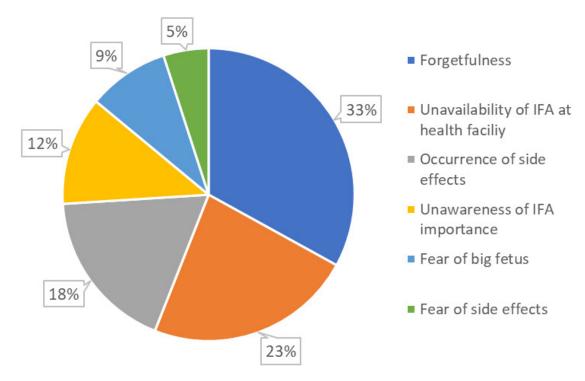


Figure 1. Reasons for IFA non-adherence among pregnant women in Tamale Central Hospital, Ghana

et al. 2019), as well as fear of foetal size increase (30.1%; Kassa et al. 2019) were the underlying reasons why pregnant women missed doses of the IFA supplements.

The present study revealed that maternal education was an independent predictor of adherence with iron-folate supplementation. Expectant mothers with secondary education had higher odds of being IFA supplement adherent [AOR=1.37, (95% CI= 1.18-1.82)] than those with no education. A recent study in Ethiopia also found that formal education increased the likelihood of IFA adherence among pregnant women (Beressa et al. 2022). Similarly, findings from western Iran (Siabani et al. 2018) and Northeast Ethiopia (Boti et al. 2018) reported that attaining secondary school and above education increased the likelihood of IFA supplement adherence.

Pregnant women who were resident in urban areas had higher odds of IFA adherence [AOR=0.59, (95% CI= 0.36-0.97)] areas, consistent with other findings in Ghana (Ghana Statistical Service 2015), Ethiopia (Gebre 2015), and Nigeria (Onyeneho et al. 2016). Usually, urban dwellers have access to more information and educational materials, which may influence their IFA consumption habits. Additionally, in urban settings there is easier access to IFA supplements in health facilities and the open market, unlikely rural populations, especially populations who travel long distances to access antenatal services.

The number of ANC visits during pregnancy also predicted adherence to IFA supplementation; pregnant women who made \geq 4ANC visits had higher odds of adherence [AOR=1.44, (95% CI= 1.28-1.67)]. The same findings have been reported in Kenya (Kamau, Mirie, and Kimani 2018), Ethiopia (Kiwanuka et al. 2017), and Uganda (Tarekegn et al. 2019). The ANC remains the primary channel for the delivery of IFA and the reinforcement of key messages that enhance adherence.

The supply of IFA at the ANC is associated with its adherence among pregnant women. Pregnant women who received free IFA at the ANC had higher odds of adherence [AOR=1.98, (95% CI = 1.02-3.83)]. Our finding is similar to those of (Seck and Jackson 2008) who reported that IFA adherence was significantly higher in expectant mothers who received free IFA tablets in a health facility than those who merely received a prescription (86% vs 48%; p<0.0001). This may be due to economic factors as some women may find it economically burdensome to purchase iron-folic acid tablets from the open market.

STRENGTHS AND LIMITATIONS OF THE STUDY

A major strength of this study is that, to the best of our knowledge, it is the first to assess IFA supplementation adherence and associated factors in the setting of Northern Ghana. The study also used less expensive and simple data collection methods. Nevertheless, the research team used well-trained data collectors and checked completed interviews regularly to determine consistency as well as to eliminate errors.

However, the findings of this study should be interpreted in the light of the following limitations. First, it was conducted using self-reported data from respondents, making it prone to social desirability and, to a small extent, recall biases. Secondly, the study failed to use gold-standard methods for assessing adherence through pill count (Kassa et al. 2019; Tarekegn et al. 2019), stool examination (Young et al. 2000) and biochemical methods (Hartman-Craven et al. 2009). Finally, with our study design it is difficult to es-

Table 3. Bivariate reg	ression between IFA adherer	nce and sociodemographic	and maternal health factors

Sociodemographic	Adherence	Non-adherence		
	N =158	N=226	COR (95%CI)	P-value
Educational status				0.023 ^a
None	12(7.6)	46(20.4)	1.00	
Primary	22(13.9)	46(20.4)	1.88(0.75-4.71)	0.179
Secondary	69(43.7)	74(32.7)	3.5(1.53-8.03)	0.003a
Tertiary	55(34.8)	60(26.5)	2.33(0.92-5.87)	0.074
Marital status				0.098
Married	145(91.8)	194(85.8)	1.00	
Not married	13(8.2)	32(14.2)	0.51(0.23-1.13)	0.960
Residence				0.044a
Rural	41(25.9)	88(38.9)	1.00	
Urban	117(74.1)	138(61.1)	1.58(1.03-2.92)	0.044a
Occupation				0.317
Unemployed	31(19.6)	54(23.9)	1.00	
Housewife	22(13.9)	49(21.7)	0.68(0.28-1.33)	0.216
Government employee	40(25.3)	41(18.1)	1.03(0.48-2.22)	0.943
Trader	50(31.6)	64(28.3)	1.16(0.59-2.29)	0.672
Others ^b	15(9.5)	18(8.0)	1.68(0.64-4.40)	0.293
Gravidity				0.916
Primigravida	83(52.5)	121(53.5)	1.00	
Multigravida	75(47.5)	105(46.5)	0.97(0.51-1.84)	0.916
Gestation during interview				0.530
1s trimester (<13 weeks)	45(28.5)	98(43.4)	1.00	
2nd trimester (13-27 weeks)	62(39.2)	73(32.3)	1.39(0.78-2.49)	0.263
3rd trimester (≥28 weeks)	51(32.3)	55(24.3)	1.28(0.64-2.59)	0.484
Gestation at first ANC visit				0.341
1st trimester (<13 weeks)	119(75.3)	166(73.5)	1.00	
2nd trimester (13-27 weeks)	28(17.7)	38(16.8)	1.34(0.68-2.62)	0.401
3rd trimester (≥28 weeks)	11(7.0)	22(9.7)	0.61(0.24-1.59)	0.314
Number of ANC visits				0.026a
<4	75(47.5)	159(70.4)	1.00	
4+	83(52.5)	67(29.6)	1.85(1.08-3.17)	0.025a
Knowledge of anaemia			. ,	0.237
No	29(18.4)	74(32.7)	1.00	
Yes	129(81.6)	152(67.3)	1.40(0.78-2.51)	0.266
Knowledge of IFA supplementation	. ,		. ,	0.449
No	14(8.9)	59(26.1)	1.00	
Yes	144(91.1)	167(73.9)	1.52(0.52-4.45)	0.449
Receiving information on IFA supplementation at ANC	·······	,		0.289
No	17(10.8)	68(30.1)	1.00	0.207
Yes	141(89.2)	158(69.9)	1.73(0.63-4.74)	0.289
Receiving IFA supplements at ANC		200(0,)	2	0.207
No	15(9.5)	65(28.9)	1.00	5.0450
110	13(7.3)	00(20.7)	1.00	

^aP<0.05

^bOthers= daily labourer or farmer

Variables	Non-adherence	Adherence		P-value
	N=226	N=158	AOR (95% CI)	
Educational status				<0.001*
None	46(20.4)	12(7.6)	1.00	
Primary	46(20.4)	22(13.9)	0.74(0.37-1.44)	0.371
Secondary	74(32.7)	69(43.7)	1.37(1.18-1.82)	0.013*
Tertiary	60(26.5)	55(34.8)	1.22(0.72-2.06)	0.468
Residence				0.036*
Rural	88(38.9)	41(25.9)	1.00	
Urban	138(61.1)	117(74.1)	1.59(1.36-1.97)	0.036*
Number of ANC visits				<0.001*
<4	159(70.4)	75(47.5)	1.00	
4+	67(29.6)	83(52.5)	1.44(1.28-1.67)	<0.001
Receive IFA supplement at ANC				<0.001*
No	65(28.9)	15(9.5)	1.00	
Yes	160(71.1)	143(90.5)	1.98(1.02-3.83)	<0.001*

Table 4. Multivariate regression between IFA adherence and selected sociodemographic and maternal health factors

*P<0.05

tablish causality between exposures and outcome (IFA consumption).

CONCLUSION

We found that iron-folic acid adherence was low (41%) among pregnant women receiving ANC services at Tamale Central Hospital. We found maternal education, residence, ANC visits, and source of IFA supplements were associated with adherence. Thus, stakeholders should ensure that IFA supplements are regularly available at the health facility. Healthcare providers should reinforce the benefits of IFA supplements and monitor their consumption during ANC and home visits.

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ABBREVIATIONS

ANC: Antenatal Care, AOR: adjusted Odds Ratio, APGAR: Activity, Pulse, Grimace, Appearance and Respiration, COR: crude Odds Ratio, GHS: Ghana Health Service, IDA: Iron Deficiency Anaemia, IFA: Iron-Folic-Acid, NHRC-RB: Navrongo, Health Research Centre Institutional Review Board, WHO: World Health Organization.

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AUTHORS' CONTRIBUTIONS

Conceptualization: Matthew Y. Konlan, Martin N. Adokiya. Data curation: Matthew Y. Konlan, Hilarius A. K. Abiwu, Martin N. Adokiya. Formal Analysis: Matthew Y. Konlan. Writing – original draft: Matthew Y. Konlan. Methodology: Matthew Y. Konlan, Martin N. Adokiya. Writing – review & editing: Hilarius A. K. Abiwu, Martin N. Adokiya.

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COMPETING INTERESTS

The authors have no conflicts of interest to declare.

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