

Clinical Dynamics of Anemia in Pregnancy: A 16-week Cross-sectional Study of Pregnant Women Who Attended Antenatal Clinic of Federal Medical Center, Keffi, Nasarawa State, Nigeria

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Abstract Background: Anemia in pregnancy is a global public health burden. It is the commonest medical disorder of pregnancy and a major cause of maternal and perinatal morbidity and mortality in most developing countries including Nigeria. Aim: To determine the prevalence of anemia and red cell morphological patterns amongst pregnant women attending antenatal clinic of Federal Medical Center, Keffi, Nasarawa State, Nigeria. Materials and Methods: This was a prospective, analytical study involving 415 women at the antenatal booking clinic for a period of 16 weeks. The Packed Cell Volume (PCV) also known as hematocrit, red cell morphology, HIV status and genotype of each pregnant woman were determined. Their biodata, obstetric and medical histories, and results of the routine investigations were documented with structured questionnaires and analyzed with statistical package for social science (SPSS) software (version 20, Chicago 11, USA). Continuous variables were presented as mean and standard deviation (mean±SD), while categorical variables were presented as numbers and percentages. Comparative analysis was done with chi-square test and the level of significance was set at p < 0.05. The association between anemia and some social factors was tested using t-test. Results: Mean age of respondents was 29.7 ± 5.3 years, mean BMI was 28.0 ± 7.2 kg/m², and mean parity was 1.9 ± 1.7 . Mean packed cell volume was 32.7±3.1% and 42.5% of the women were anemic. Specifically, 29.0% and 13.5% of the women had mild and moderate anemia respectively. The commonest blood picture was microcytic hypochromia and normocytic hypochromia suggesting iron-deficiency anemia. Anemia was significantly and independently related to educational level (p=0.00) and socio-economic class (p=0.00). Conclusion: Every pregnant woman should be encouraged to obtain antenatal care, where hematinic supplements can be given for prophylaxis of iron-deficiency anemia. Appropriate clinical investigations, treatment of fever and management of HIV should be instituted for pregnant women attending antenatal care whenever and wherever necessary.

Keywords: Anemia, iron-deficiency anemia, dimorphic anemia, red cell morphology, pregnancy, antenatal clinic, risk factors, prevalence

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1. Introduction

The importance of good hemoglobin concentration during pregnancy for both the woman and the growing fetus cannot be overemphasized. Being a driving force for oxygen for the mother and fetus, a reduction below acceptable levels can have adverse effects on both [1]. Traditionally, anemia is defined as a decrease in the ability of blood to carry oxygen due to a decrease in the total number of erythrocytes (each having a normal quantity of hemoglobin), a diminished concentration of hemoglobin per erythrocyte, or a combination of both [2]. A hemoglobin concentration of <11.0g/dl or packed cell volume (PCV) of <33.0% is regarded as anemia during pregnancy by the World Health Organization (WHO) [3].

The World Health Organization (WHO) divides anemia in pregnancy into mild anemia (hemoglobin, 10-10.9g/dl), moderate anemia (hemoglobin, 7-9.9g/dl), and severe anemia (hemoglobin <7g/dl) [3]. However, in the tropics, a pregnant woman is said to be anemic when the hemoglobin concentration is <10g/dl or PCV is <30% [4]. It is one of the most intractable public health problems in developing countries and the most common medical complication in pregnancy in Sub-Saharan Africa, more so with the advent of the HIV/AIDS pandemic [5].

It has been estimated that the global prevalence of anemia in pregnancy is 41.8% [5]. By WHO's criteria, 1.62 billion people are anemic, with pregnant women most affected after pre-school age children (47.4%) [5]. In Africa, the prevalence of anemia in pregnant women is commonly estimated to be between 52.8%-61.3% [5]. Among non-pregnant women, this is 43.4%-51.6% and in pre-school age children, the estimate is between 64.3%-71.0% [5]. The greatest burden of anemia is borne by Asia and Africa where it is estimated that 60% and 52% of women respectively, are anemic and between 1% and 5% are severely anemic (Hb <7g/dl) [6,7].

The high prevalence and the etiological factors responsible for anemia in pregnancy are multiple and their relative contributions are said to vary by geographical area and by season [8,9]. Malaria is endemic in Nigeria and is a common cause of febrile illness and anemia among pregnant women [10,11], although there is good evidence of the effectiveness of simple interventions such as iron supplementation, long lasting insecticidal nets and intermittent preventive treatment for malaria [12].

Hookworm infection has long been recognized among the major causes of anemia in poor communities, but the understanding of the benefits of the management of hookworm infection in pregnancy has lagged behind the other major causes of anemia [13]. An epidemiological study in 1995 highlighted the paradox presented to public health workers that an estimated one-third of all pregnant women in developing countries were infected with hookworm [14].

Tobacco (*Nicotiana tabacum*) is harmful to the kidneys of pregnant Wistar rats and distorts the histological architecture of the kidneys. Ingested tobacco impairs the blood-clearing function of the kidneys as serum creatinine and urea levels are elevated in the blood. In addition, tobacco ingestion by Wistar rats during gestation reduces the birth weight of their pups [15].

Anemia in pregnancy is associated with significant maternal, fetal and neonatal morbidity and mortality [9,16]. The consequences of anemia in pregnancy include maternal complications like pregnancy-induced hypertension, *abruptio placentae*, puerperal venous thrombosis, cardiac failure, infections (urinary tract infections, puerperal sepsis), postpartum hemorrhage (PPH), and maternal mortality. Positive correlative relationships between asymptomatic hyperuricemia, increased albuminuria, decrease in glomerular filtration rate (GFR), dyslipidemia, systolic blood pressure, glycated hemoglobin (HbA₁C), inflammatory processes, and kidney damage indicate the heterogeneity of renal pathogenicity [17,18,19,20].

Fetal complications include intrauterine growth restriction (IUGR), prematurity, preterm labour, preterm premature rupture of membranes, and increased perinatal mortality. Mild forms of anemia have been related to permanent cognitive damage by decreasing attention span and shortening memory. Children born with anemia have intelligence quotients (IQs) that are two points lower per every 1g/dl decrease in hemoglobin than other children [21]. Anemia has devastating costs to individual and national productivity. Women with anemia during pregnancy have decreased work capacity. They may be unable to earn their livelihood if the work involves manual labor [21,22].

Anemia in pregnancy is a public health concern with its associated negative impact on pregnancy and its outcome. Many of the causes and predisposing factors are preventable; therefore, knowledge of the prevalence and associated socio-demographic factors in the environment will enhance patients' management resulting in improved feto-maternal well-being with reduced maternal and perinatal mortality and morbidity. This study, therefore, aimed to determine the prevalence of anemia and the red cell morphological patterns among pregnant women attending antenatal clinic.

2. Materials and Methods

2.1. Study Area

This research was conducted in the antenatal clinic of the Federal Medical Center (FMC), Keffi, a sub-urban town in Keffi Local Government Area (LGA) of Nasarawa State, Nigeria. FMC, Keffi is a tertiary-care health institution with 277 bed spaces. It came into existence in April 2000, and serves as a major referral center. It is a training institution for clinical resident (postgraduate) doctors. The Antenatal Clinic is a service unit of the Department of Obstetrics and Gynecology which provides services such as health education, nutritional counseling, immunization, screening and treatment of common diseases during pregnancy.

2.2. Study Population

The research was a prospective, analytical study that was conducted over a period of 16 weeks from October 2018 to January 2019 (over four months). The study population comprised of pregnant women attending the antenatal clinic during the period of the study.

2.3. Sample Size

The sample size was calculated using the Kish Leslie formula for cross-sectional studies [3].

$$n = \frac{Z^2 P Q}{d^2}$$

Where:

n is the desired sample size; **Z** is the standard normal deviate usually set at 1.96, which corresponds to the 95% confidence interval; **P** is the proportion of the prevalence of anemia during pregnancy, which is 43.5% based on a previously done similar study at Bingham University Teaching Hospital, Jos, Plateau State, Nigeria by Bassi *et al* [1]; **Q** is complementary proportion equivalent to 1-P; that is, 1-0.435 equal to 0.565, **d** is the degree of

accuracy desired (absolute precision), which is 5.0% (0.05).

Thus,

$$n = \frac{1.96^2 \times 0.435 \times 0.565}{0.05^2}$$
$$n = \frac{0.944}{0.05^2}$$
$$n = 378$$

At an average booking rate of 52 pregnant women per week, from the review of the previous year's record in which a total of 2,800 pregnant women booked for antenatal care (ANC). A total of 378 respondents were needed for the study. However, a 10% attrition rate was applied bringing the sample size to 415. These respondents were pregnant women who were on the attendance list at every booking clinic. The pregnant women were picked randomly and only pregnant women with one fetus at their first antenatal visit, and willing to participate in the study were included in the study.

The following women were excluded: pregnant women with more than one fetus, pregnant women at their follow-up antenatal visit, those who had received a blood transfusion in the index pregnancy, women already receiving treatment for anemia in pregnancy before their booking visit, pregnant women with multiple gestations, and pregnant women with a history of antepartum hemorrhage in the index pregnancy.

2.4. Study Procedure

A semi-structured interviewer-administered questionnaire was used to obtain information from the pregnant women who gave written consent. The questionnaires were administered by the researcher and trained research assistants in the Department of Obstetrics and Gynecology to ensure that the necessary information was obtained. Each pregnant woman in the study was allotted to one of the five social classes based on her level of education and her husband's occupation according to a scoring system designed by Olusanya et al [23]. The social class for single or separated women was based on their occupation and their educational status. Social classes 1 and 2 represent the upper class made up of the elites, the professionals like the doctors, lawyers, bankers, those in managerial positions, and so forth. Class 3 represents the middle class of nurses, clerks, technicians, artisans, and so forth, while classes 4 and 5 represent the lowest rung on the socio-economic ladder.

Blood samples were collected from the women and clinical examinations were conducted on each of the samples. Using the micro method of hematocrit estimation, the packed cell volume was estimated [24]. Women with PCV <33% (Hb <11g/dl) were given free tablets of iron and folic acid for two months, they were also counseled for further investigations into the cause and characteristics of their anemia. The red cell morphology was determined using Leishman's staining technique as reported by Dayyal [25]. Microcytic hypochromic morphology was considered consistent with iron deficiency, while a

macrocytic blood picture was considered megaloblastic anemia. A combination of the two was interpreted as dimorphic anemia. The results of the other routine investigations (HIV screening and genotype) were retrieved from the laboratory and entered into the questionnaire.

2.5. Quality Control

The Packed Cell Volume measurement and red cell morphology were analyzed by the researchers and the clinical hematologist dedicated to the study. Another clinical hematologist not dedicated to this research, randomly selects specimen samples for cross-checking and quality control, at intervals. This was aimed at reducing intra- and inter-observer errors and ensuring quality control.

2.6. Data Analysis

Data were analyzed using the statistical package for social sciences (SPSS) version 20 (Chicago 11, USA). Descriptive statistics were computed for all relevant variables. Comparative analysis was done with a chi-squared test and the level of significance was set at p<0.05. The association between anemia and demographic characteristics was tested using chi-square.

2.7. Ethical Consideration

Ethical clearance was sought and obtained from the Health Research Ethics Committee of the FMC, Keffi. In designing this study, the following ethical issues were put into consideration: signed consent form from participants, confidentiality of information obtained, and beneficence of participants.

3. Results

Four hundred (400) of the 415 samples were analyzed, 10 samples were missing while 5 samples were clotted. The findings of this study are represented in four tables. Table 1 shows the socio-demographic characteristics of the pregnant women. The mean age of the women was 29.7 ± 5.3 years with a range of 17 to 43 years. The mean parity was 1.9 ± 1.7 children with a range of 0 to 9 children. Forty-nine percent (49%) of the women acquired tertiary level of education, while 29.75% and 31.75% of them were in the middle and lower social classes respectively.

Table 2 shows the clinical characteristics of the women. Most of the women 274 (68.5%) booked for antenatal care in the second trimester. Among the pregnant women with previous delivery experience, the mean inter-pregnancy interval was 1.8 ± 1.1 years with a range of 0.8 to 10.0 years. A total of 318 (45.25%) of the women had experienced fever in the course of the index pregnancy. 31 (7.75%) of the women were HIV seropositive, while 59 (14.75%) had the sickle cell trait. 1.5%, 40.5%, and 27% of the women were underweight, overweight and obese respectively.

Socio-demographic characteristics	Options	Frequency, n (%)
Age (year range)	<20	2 (0.5)
	20-24	66 (16.5)
	25-29	127 (31.75)
	30-34	123 (30.75)
	35-39	70 (17.5)
	≥ 40	12 (3.0)
	Total	400 (100)
	Mean age = 29.7±5.3	
Marital status	Married	397 (99.25)
	Single	2 (0.5)
	Widow	1 (0.25)
	Total	400 (100)
Parity	0	93 (23.25)
	1-4	276 (69.0)
	≥5	31 (7.75)
	Total	400 (100)
	Mean age = 1.9±1.7	
Educational level	No formal	13 (3.25)
	Primary	38 (9.5)
	Secondary	153 (38.25)
	Tertiary	196 (49.0)
	Total	400 (100)
Social class	1	56 (14.0)
	2	98 (24.5)
	3	119 (29.75)
	4	107 (26.75)
	5	20 (5.0)
	Total	400 (100)
Occupation	Professional	23 (5.75)
	Skilled labour	152 (38.0)
	Unskilled labour	225 (56.25)
	Total	400 (100)
Husband's	Professional	62 (15.62)
occupation	Skilled labour	196 (49.37)
	Unskilled labour	139 (35.01)
	Unskined labour	137 (33.01)

Table 1. Socio-demographic characteristics of the women at booking,

red cells, and 129 (32.25%) had microcytosis. Majority of the women with normal red cell morphology (normocytosis and normochromia) were not anemic and were 94.79% and 87.87% respectively. However, 5.21% and 12.13% of them respectively had anemia. Also, the majority (85.5%) of those with microcytic hypochromic red cell morphology were anemic.

Clinical characteristics	Options	Frequency, n (%
Trimester	First	72 (18.0)
	Second	274 (68.5)
	Third	54 (13.5)
	Total	400 (100)
Inter-pregnancy interval	<2 years	172 (43.0)
	≥ 2 years	228 (57.0)
	Total	400 (100)
Miscarriage/Ectopic	Yes	130 (32.5)
	No	270 (67.5)
	Total	400 (100)
Bleeding during previous	Yes	17 (4.25)
pregnancy	No	
		383 (95.75)
	Total	400 (100)
Fever	Yes	181 (45.25)
	No	219 (54.75)
	Total	400 (100)
Genotype	AA	341 (85.25)
	AS	59 (14.75)
	Total	400 (100)
HIV	Yes	31 (7.75)
	No	369 (92.25)
	Total	400 (100)
BMI	<18.5	6 (1.5)
	18.5-24.5	124 (31.0)
	25-29.5	162 (40.5)
	≥30	108 (27.0)
	Total	400 (100)

Table 3 shows the association between the red cell morphology of the women and anemia. The mean packed cell volume was $32.7\pm3.1\%$ with a range of 21% to 40%. 170 pregnant women (42.5%) were anemic: the majority (68.24%) of the anemic women had mild anemia, 31.76% had moderate anemia and none had severe anemia. 211 (52.75%) women had normocytosis, 50 (12.5%) women had dimorphic red cells, 159 (39.75%) had hypochromic

Table 4 details the association between sociodemographic characteristics of pregnant women at booking and anemia in the study population. Pregnant women below 20 years had the highest prevalence of anemia. There was an inverse relationship between the prevalence of anemia and the level of education of the women ($x^2 = 17.6$, p = 0.00). Anemia was significantly more common in women of lower social class ($x^2 = 14.5$, p = 0.00).

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RBC Morphology	Options	Non-anemic (%)	Anemic (%)	<i>p</i> -value	\mathbf{X}^2
Normocytosis	No	30 (15.88)	159 (84.12)	0.00*	245.1
	Yes	200 (94.79)	11 (5.21)		
Normochromia	No	20 (12.42)	141 (87.58)	0.00*	224.1
	Yes	210 (87.87)	29 (12.13)		
Dimorphic	No	215 (61.43)	135 (38.57)	0.00*	17.7
	Yes	15 (30)	35 (70)		
Hypochromia	No	210 (87.14)	31 (12.86)	0.00*	217.9
	Yes	20 (12.58)	139 (87.42)		
Microcytosis	No	220 (81.18)	51 (18.82)	0.00*	100.0
	Yes	10 (7.75)	119 (92.25)	0.00*	192.8
Macrocytosis	No	225 (57.54)	166 (42.46)	0.01**	0.014
	Yes	5 (55.56)	4 (44.44)	0.91**	0.014

Table 3. Association between red cell morphology pattern of the women and anemia

*Statistically significant p values; **statistically insignificant p values.

 Table 4. Association between socio-demographic characteristics of pregnant women at booking and anemia in the study population, n=400

Characteristics	Options	Non-anemic (n)	Anemic (n)	<i>p</i> -value	\mathbf{X}^2
Age (years)	< 20	1	1		
	20-24	34	32	0.78**	2.5
	25-29	71	56		
	30-34	77	46		
	35-39	40	30		
	≥ 40	7	5		
	Total	230 (57.5%)	170 (42.5%)		
Marital status	Married	229	168		
	Single	1	1	0.50**	1.4
	Widow	0	1		
	Total	230 (57.5%)	170 (42.5%)		
Parity	0	58	35	0.55**	1.2
	1-4	155	121		
	≥5	17	14		
	Total	230 (57.5%)	170 (42.5%)		
Educational levels	No formal	6	7	0.00*	17.6
	Primary	15	23		
	Secondary	80	73		
	Tertiary	132	64		
	Total	230 (57.5%)	170 (42.5%)		
Social class	1	29	21	0.00*	14.5
	2	51	47		
	3	69	50		
	4	73	34		
	5	8	18		
	Total	230 (57.5%)	170 (42.5%)		

*Statistically significant p values; **statistically insignificant p values.

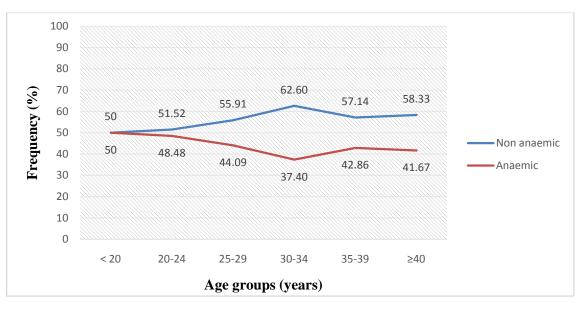


Figure 1. Association between age groups of the pregnant women at booking and the prevalence of anemia

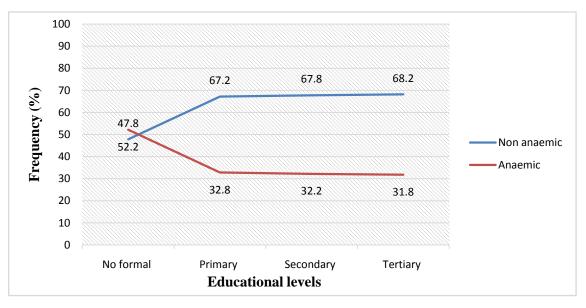


Figure 2. Association between educational levels of the pregnant women at booking and the prevalence of anemia

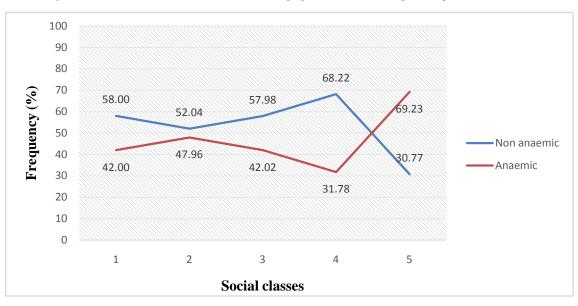


Figure 3. Association between social classes of the pregnant women at booking and the prevalence of anemia

4. Discussion

The diagnosis of anemia during booking among pregnant women is paramount as it enables an individual to plan an intervention to prevent the complication of anemia, especially considering the prevalent high maternal and perinatal morbidity and mortality associated with anemia in pregnancy in the tropics [1,26,27,28]. Data from the literature in developing countries have reported a prevalence of anemia in pregnancy that ranged from 35.0 to 75.0% [5,29], with a high incidence and severity occurring among primigravidae living in malaria endemic areas [29].

The prevalence of anemia among pregnant women in this study was 42.5% which is in the middle range when compared to findings from other studies in Nigeria [4,22,28,30,31] and from countries in South Eastern Africa [7,32]. This finding is similar to the 40.01% anemia prevalence rate among pregnant women in Nigeria, recorded in the World Health Organization's global database on anemia [5]. This finding is also similar to the findings from Bassi *et al* in Jos, Plateau State, Nigeria [1], 40.4% seen in Enugu, Southeast, Nigeria [33], 41.9% in Jamitown Southeast Ethiopia [32,34,35] but lower than the findings of 54.6% and 58% in Abakaliki [22,31], 56.4% and 58.36% in Maharashtra and Telangana, India [36,37], and 54.6% seen in Derna city, Libya [38].

The high prevalence of anemia in this study is probably related to the low socio-economic status of the women, which may have an impact on their nutritional status and health-seeking behavior [3,39]. The prevalence of anemia in this study is lower than the 56.0% quoted by WHO for the prevalence of anemia in Africa based on the 1988 data implying that after 30 years, the situation has improved, though still unacceptably high [39]. The prevalence was higher than the 17.0% seen in Kano, Northwest, Nigeria [40], 25.2% in Aymiba, Northwest Ethiopia [32,34,35], 35.3% in Surulere, Lagos, Southwest, Nigeria [4], 20.7% in Benin-city, Southsouth Nigeria [41].

Most of the women in this study had anemia of mild to moderate severity with none being severely anemic. Mild anemia was the dominant degree of anemia seen in this study, and this is in keeping with the other findings in Nigeria [1,2,6,7]. There was no case of severe anemia in this study, and this was in consonant with the findings in Enugu, Southeast Nigeria and Ibadan, Southwest, Nigeria [42]. However, severe anemia was seen in Benin, (Abeokuta and Sagamu combined) areas of Nigeria with a prevalence rate of 2.8% and (1.7%) respectively [41,42], both in different geo-political zones of Nigeria. Severe anemia in these studies was seen in pregnant women with sickle cell anemia and in chronically ill patients or in the immuno-compromised [41,42].

The mean PCV in this study was 32.7%. By WHO standards, this is anemia. In this study, the incidence of anemia among the various age groups has no significant variation (p=0.78). This insignificant variation of anemia among the age groups agrees with the finding of the study done in Port-Harcourt, Nigeria [30] and in other African countries [7,9].

This study further showed that there was no association between anemia and the number of children observed (p=0.55). This finding is supported by the findings of

previous reports in Port-Harcourt, Nigeria, and former Zaire (now Democratic Republic of Congo) [30,43]; but contrary to a report from Tanzania [44]. The incidence of anemia during pregnancy is expected to be higher as the number of pregnancies increases because of the re-occurring depletion of iron stores. In fact, multiparity especially when the pregnancies have occurred in a rapid sequence, is traditionally regarded as a cause of anemia in pregnancy.

However, the present study showed no consistent relationship between an increasing number of children and the incidence of anemia. Possibly, the experience gained from the first pregnancy followed by increased awareness and good dietary practices, as well as increased interaction with other pregnant women at the antenatal clinic, might counterbalance the effects of multiparity. This study also did not observe any relationship between the prevalence of anemia and increasing gestational age, suggesting that all pregnant women were susceptible to anemia throughout the gestational period. In order to avoid anemia during pregnancy, receiving early antenatal care would serve as an important preventive measure. The same result was observed in a previous study conducted in Nigeria, India and Gondar [9,30,32,40].

It was interesting to note that despite the high level of education of most of the pregnant women in this study, the majority of them were still in the middle to low social class as also noted by Bukar *et al* in their studies [10]. This is because, though majority of the husbands of these women were in the skilled labor class, a significant percentage of them were in the unskilled labor class and only about a quarter were professionals. About 56.3% of the pregnant women were in the unskilled labor class.

The low socio-economic status of the women may have a significant impact on their nutritional status and healthseeking behavior. Women with low socio-economic status tend to consume diets that are low in micronutrients, animal protein, and vitamins but high in carbohydrates and phytates which interfere with intestinal uptake of iron and other trace minerals such as zinc and calcium [45]. This indicates that economic empowerment of women would play a very important role in reducing the prevalence of anemia in the environment.

Approximately 57.0% of the parous women in this study had an inter-pregnancy interval of greater than 2 years. The high level of education of the women as well as the fact that a large proportion of them were civil/public servants may contribute to this trend. Normocytic hypochromia and microcytic hypochromia blood pictures were the most common morphological types of anemia seen in this study, and are characteristic of iron-deficiency anemia.

In developing countries, anemia in pregnancy is commonly believed to result from nutritional deficiencies, especially iron. The gold standard for making a diagnosis of iron-deficiency anemia which is the examination of stained bone marrow aspirate for hemosiderin is invasive. Serum ferritin measurement on the other hand is costly and largely not available in most centers in Nigeria and is elevated in the presence of an inflammation which is not uncommon in the Nigerian environment.

A blood picture suggestive of iron deficiency was found to complicate 97.6% of all cases of anemia in this study. This is higher than the 64.0% reported by Vanderjagt *et al* [46]. The high percentage of iron deficiency in this study could be a result of the large proportion of women of low socio-economic class. The need for iron increases greatly during the second and third trimesters of pregnancy and it was during this period that 82.0% of the pregnant women booked for antenatal care.

5. Conclusion

Anemia in pregnancy is still highly prevalent in developing countries. The high prevalence of anemia (42.5%) in pregnant women is an indicator of the failure of national and WHO programs to address this problem. This study has also revealed that the most important risk factors for anemia in pregnancy are educational levels and socio-economic status of the pregnant women. The common red cell blood pictures among the anemic pregnant women were microcytic hypochromia and dimorphic hypochromia, which are indicative of iron-deficiency anemia.

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Conflict of Interest

The authors guarantee responsibility for everything published in this manuscript, as well as the absence of a conflict of interest and the absence of their financial interest in performing this research and writing this manuscript. This manuscript was written from an original research work and has never been published, neither is it under consideration for publication elsewhere.

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