

Outcome of Pregnancies among Cameroonian Anemic Women: A Comparative Cohort Study

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Abstract

Objective: To evaluate maternal and fetal outcomes among Cameroonian anemic pregnant women according to the degree of correction of anemia.

Methods: This cohort study was conducted in the Yaoundé University Teaching Hospital, Cameroon, from March 1st, 2011 to February 28th, 2013. Anemic pregnant women (initial Hemoglobin concentration (Hb) <10 g/dl) and non-anemic pregnant women (Hb \geq 11 g/dl) were followed up till delivery. Variables measured were gestational age at the first visit (booking), Hb value at the first consultation and at 36 weeks gestation, pregnancy complications, gestational age at delivery, birth weight (BW) and Apgar score. Data were analyzed using SPSS 18.0. Chi square test or Fisher exact test and t-test were used for comparison. $P < 0.05$ was considered statistically significant.

Results: Hb still less than 9 g/dl at 36 weeks gestation was associated with an increased risk of low BW (RR 7, 95%CI 1.6-30.4), pre-eclampsia (RR 3.3, 95%CI 0.9-11.9) and preterm deliveries (RR 3, 95% CI 0.6-14.6). Mean BW observed among initially anemic women with Hb \geq 10 g/dl at 36 weeks gestation was higher than that found among women of the non anemic group ($P < 0.0001$).

Conclusion: Hb still less than 9 g/dl at 36 weeks gestation was associated with increased risk of low BW while anemia corrected with iron and folic acid before term was associated with a significant increase in BW.

Keywords: Anemia in pregnancy; Maternal outcome; Fetal outcome

Introduction

The World Health Organization defines anemia in pregnancy (AP) as Hb <11 g/dl during the first trimester [1,2]. Given that hemoglobin concentration drops during second trimester due to hemodilution, WHO defines anemia in the second trimester as Hb <10.5 g/dl [2]. AP is a common condition worldwide, its prevalence, according to WHO definition, being reported in Africa to be between 30% and 65% [3-5]. This definition is not being used by all authors. Owing to the fact that no study found significant maternal nor fetal risk when maternal Hb was \geq 10 g/dl [6], AP is defined as Hb concentration <10 g/dl in our setting, as already defined by some authors [7,8]. When untreated, anemia is associated with increased risk of intra uterine growth restriction (IUGR), intra uterine fetal death (IUFD), pre eclampsia, preterm delivery, stillbirth and low birth weight [4,9,10]. A complication of anemia depends on its severity. Maternal and fetal adverse effects are usually observed when Hb concentration is chronically <9g/dl [4,10]. It is estimated that 6.37% of maternal deaths in Africa are anemia attributable maternal mortalities whether from direct or indirect causes [11].

There are many causes of anemia in pregnancy. These causes can be hemorrhagic, hemolytic, aplastic, resulting from chronic diseases, nutritional or physiologic [12,13]. Nutritional causes include iron, folic acid and Vitamin B12 deficiency. Iron deficiency anemia is the most encountered worldwide [1,13]. Hemodilution, a physiologic cause of anemia, may be quite marked in some women, especially in second trimester. Iron supplementation during pregnancy has been shown to be associated with a significant increase in birth weight [14].

Many studies have evaluated pregnancy outcomes in anemic women, but no study has been carried out in Cameroon to evaluate the outcomes of mother and fetus especially when anemia was (being) corrected during pregnancy. The aim of this study was to evaluate pregnancy outcomes in anemic women according to its degree of correction (Hb concentration at 36weeks).

Material and Methods

This matched cohort study was conducted in the maternity ward of the Yaoundé University Teaching Hospital, Cameroon, during a two-year period from March 1st, 2011 to February 28th, 2013. During this period, each woman with a singleton and Hb concentration at the first visit (booking) <10 g/dl was recruited. For each anemic woman, a nonanemic woman of the same parity with a singleton and Hb concentration \geq 11 g/dl who was received at booking immediately after the case was recruited and both were followed up till delivery. When a nonanemic woman was lost during follow up, she was replaced by the one who followed her at booking on the consultation list. Hb \geq 11g/dl cutoff point was used for nonanemic women because all authors agree that these women with Hb \geq 11g/dl are not anemic. All women had normal (routine) follow up.

Women with gestational diabetes were excluded, as well as women lost during follow up. Between 24 to 28 weeks gestation a fasting blood sugar of >0.92 g/l or values of blood sugar of >1.8 g/l or >1.53 g/l one or two hours respectively after oral ingestion of 75 g of glucose were suggestive of gestational diabetes. Eight women with severe anemia (Hb concentration <6 g/dl) received blood transfusions until new Hb concentration values got between 6 and 7 g/dl. Thereafter, they were prescribed as other anemic women, 100 mg of iron supplementation

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and 1 mg of folic acid daily, while non anemic women were prescribed 50 mg of iron supplementation and 0.5 mg of folic acid daily. Women with severe anemia were not excluded because we wanted to observe the severity of anemia on pregnancy outcomes. Two women received parenteral iron because of intolerance to oral iron therapy. Hb concentration was controlled again at 36 weeks gestation.

Variables recorded included maternal age at delivery, parity (deliveries at ≥ 28 completed weeks gestation), gestational age at booking (confirmed by an ultrasound scan performed before 20 weeks gestation), Hb concentration at booking and at 36 weeks gestation, complications observed during pregnancy, gestational age at delivery, mode of delivery, birth weight, fetal sex and placental weight. Hb concentration was checked during labor at 35 weeks in four women who had preterm deliveries. Five ml of venous blood was collected and Hb concentration was measured on automated cell counter (Huma Count 30TS). Before measuring placental weight, membranes were removed, the cord sectioned at the placental insertion site and fetal blood evacuated from the placenta.

Sample size was calculated using the following formula: $N = 2 \times (1/1-f) \times (Z\alpha + Z\beta / P_0 - P_1)^2 \times P \times (1-P)$ where f was the assumed percentage of women that might be lost during follow-up (10%), $Z\alpha = 1.65$, $Z\beta = 1.28$, P_0 the assumed prevalence of low birth weight (LBW) (<2500 g at birth) in anemic women (10%), P_1 the assumed prevalence of LBW among non anemic women (2%) and P is $(P_0 + P_1)/2$. According to this formula, at least 169 women were needed in each group. This study received approval from the institutional ethics committee. An informed consent form was obtained from each woman. Data were analyzed using SPSS 18.0. Data of anemic pregnant women were compared to those of non anemic pregnant women. Fisher's exact test was used to compare categorical variables and t-test to compare continuous variables. We used relative risks with their 95% confidence intervals (CIs) to present the comparison between the two groups. $P < 0.05$ was considered statistically significant.

Results

During the study period, we received 235 anemic women (Hb

concentration <10 g/dl) with singleton pregnancies out of 4150 women, giving an incidence of 5.66%. Seven women with gestational diabetes were excluded and 16 women were lost during follow-up. The remaining 212 women were followed up till delivery. The same numbers of non-anemic pregnant women (Hb concentration ≥ 11 g/dl) were also followed up. Each nonanemic pregnant woman recruited was received at booking immediately after the anemic pregnant woman. Data are shown in Table 1.

At booking, eight women had severe anemia (Hb concentration < 6 g/dl), 11 had moderate anemia (Hb concentration: 6 to < 8 g/dl), and 193 mild anemia (Hb concentration: 8 to < 10 g/dl). Three women with Hb at booking between 3.4 and 6 g/dl whose Hb concentration < 8 g/dl at 36 weeks received blood transfusions until new Hb value was ≥ 10 g/dl.

Complications observed during pregnancy were LBW (<2500 g at delivery), premature delivery (<37 weeks) and pre-eclampsia (blood pressure $\geq 140/90$ mm Hg associated with proteinuria ≥ 300 mg/24h) (Table 2).

Fourteen cases of LBW (6.4%) were also observed in the anemic group (mean Hb concentration 8.9 ± 1.9) as against two (0.9%) among the nonanemic group (mean Hb concentration 11.7 ± 0.6) (RR 7, 95%CI 1.6-30.4, $P = 0.003$).

Ten cases of pre eclampsia (4.7%) were observed in the anemic group (mean Hb concentration 8.5 ± 0.8) and three (1.4%) in the non-anemic group (mean Hb concentration 11.7 ± 0.6) (RR 3.3, 95%CI 0.9-11.9).

Premature deliveries were observed amongst six (2.8%) anemic pregnant women (mean Hb concentration 8.7 ± 0.9), and only two (0.9%) among the nonanemic group (mean Hb concentration 11.7 ± 0.6) (RR 3, 95%CI 0.6-14.6, $P = 0.28$).

Among women who were anemic at booking, mean Hb concentration at 36 weeks gestation was 8.7 ± 0.9 for those who delivered before 37 complete weeks, as against 10.8 ± 1.2 for those who delivered at 37 weeks gestation or above ($P < 0.0001$).

Variables	Anemic pregnant women (range)	Non anemic pregnant women (range)	RR	95% Confidence Interval	P value
Baseline characteristics					
Number of women	212	212			
Gestational age at booking (weeks)	19.5 \pm 7.3 (6-34)	17.8 \pm 4.9 (6-29)			0.0051
Hb at booking (g/dl)	8.9 \pm 1.1 (3.4-9.9)	11.7 \pm 0.6 (11-14.1)			<0.0001
Maternal age (years)	27.9 \pm 5.2 (17-45)	28.3 \pm 5.2 (17-41)			0.46
Parity	0-5 (mean 1.4)	0-5 (mean 1.4)			1
Outcomes					
Hb at 36 weeks gestation (g/dl)	10.8 \pm 1.2 (4.7-13.3)	11.9 \pm 0.6 (11-13.5)			<0.0001
Gestational age at delivery (weeks)	39.9 \pm 1.6 (35-43)	39.6 \pm 1.3 (36-42)			0.07
Cesarean section	12 (5.6%)	16 (7.5%)			0.06
Instrumental delivery (non CS)	12/198 (6.0%)	5/187 (2.7%)	2.2	0.8-6.1	0.09
Episiotomy	33/198 (16.7%)	17/187 (9%)	1.8	1.0-3.1	0.03
Birth weight (g)	3328 \pm 496.7 (1877-4500)	3243.5 \pm 328.2 (2327-4150)			0.039
Male babies	101/212 (47.6%)	99/212 (46.7%)			0.88
Placental weight (g)	499.7 \pm 101.4 (225-820)	408.5 \pm 45.2 (301-520)			<0.0001
Maternal Death	0	0			

RR: Relative risk, CS: Cesarean section

Table 1: Distribution of variables among both groups.

Complications N (%)		Anemic pregnant women (n=212)	Non anemic pregnant women (n=212)	RR	95%CI	P
Maternal	Pre-eclampsia	10 (4.7)	3 (1.4)	3.3	0.9-11.9	0.04
	Prematurity	6 (2.8)	2 (0.9)	3	0.6-14.6	0.28
Fetal	Low birth weight	14 (6.6)	2 (0.9)	7	1.6-30.4	0.003
	Total	30 (14.1)	7 (3.3)	4.2	1.9-9.5	<0.0001

RR: Relative risk

Table 2: Maternal and fetal complications.

Birth weight (gram)	Anemic pregnant women N (%)	Non anemic pregnant women N (%)
<2000	2 (0.9)	0 (0)
2000-2499	12 (5.6)	2 (0.9)
2500-2999	34 (16.0)	47 (22.2)
3000-3499	87 (41.0)	122 (57.5)
3500-3999	55 (26.0)	37 (17.4)
4000-4500	22 (10.4)	4 (1.9)
Total	212 (100)	212 (100)

Table 3: Distribution of birth weights according to anemia status.

Vaginal deliveries occurred in 198 anemic women (93.4%) as against 186 (87.7%) in nonanemic women. The indications for emergency cesarean section in the anemic group were cephalopelvic disproportion (CPD) (6 cases), acute fetal distress (AFD) (4 cases), severe preeclampsia and placenta praevia (one case each). The indications for emergency CS in the nonanemic group were CPD (7 cases), AFD (5 cases), placenta praevia (3 cases) and placenta abruptio (one case). The indications for elective CS were scarred uterus in the anemic group (2 cases), while in the nonanemic group, the indications were scarred uterus (7 cases) and praevia myoma (2 cases).

Main indications for episiotomy were imminent perineal tears and instrumental delivery while those for instrumental deliveries were mainly prolonged second stage of labor and poor maternal compliance when pushing.

Birth weight distribution among both groups is shown in Table 3. In relation to fetal sex, mean birth weight for boys was 3427.6 ± 533.1 g among initially anemic pregnant women (n=101) as against 3304.6 ± 359 g among nonanemic pregnant women (n=99) (P=0.006), while mean birth weight for girls was 3237.1 ± 444.2 g among initially anemic pregnant women (n=111) as compared to 3189.6 ± 289.5 g among non-anemic pregnant women (n=113) (P=0.013).

Among women who were anemic at booking, mean birth weight of babies delivered by women (n=18) whose 36 weeks Hb <9 g/dl was 2742.1 ± 585 g as against 3439.6 ± 439.9 g for babies delivered by women (n=170) whose 36 weeks Hb ≥10 g/dl (P<0.0001). Mean birth weight of babies delivered by women (n=18) whose 36 weeks Hb <9 g/dl was lower than that of babies delivered by women of the nonanemic group (Hb ≥11 g/dl) (2742.1 ± 585.1 g vs 3243.5 ± 328.2 g, P=0.002).

Mean birth weight of babies delivered by initially anemic women (n=170) whose 36 weeks Hb ≥10 g/dl was higher (3439.6 ± 439.9 g) than that of babies delivered by women of the nonanemic group (3243.5 ± 328.2 g) (P<0.0001).

Placental weights varied between 225 and 820 g with a mean of 499.7 ± 101.4 g among anemic pregnant women as against a range of 301 to 520 g with a mean of 408.5 ± 45.2 g among nonanemic pregnant women (P<0.0001). No maternal death was observed during the study period.

Discussion

Hb concentration <10 g/dl was observed in 5.66% of our anemic

pregnant women. This rate is a bit lower than that of 8.6% reported by some authors [7].

Mean gestational age at delivery was similar amongst anemic and nonanemic pregnant women (P=0.07), but anemic pregnant women were more at risk for premature deliveries (RR 3, 95%CI 0.6-14.6), though the difference was not statistically significant. This might be explained by the fact that anemia with resulting hypoxia can induce maternal and fetal stress. This stress stimulates the synthesis of corticotropin-releasing hormone and of cortisol, which are major risk factors for preterm labor, pregnancy-induced hypertension and eclampsia, and premature rupture of the membranes. Cortisol may inhibit longitudinal growth of the fetus [15]. These findings have been made by other authors [7,10,16]. Our rate of premature deliveries among anemic pregnant women (2.8%) is lower than that of 4.1% reported by others [10].

Mean term Hb concentration was significantly lower in the anemic group than in the nonanemic group despite high doses of iron and folic acid therapy (P<0.0001). During pregnancy, there is physiologic hemodilution that may limit the rapid correction of anemia. Moreover, the digestive symptoms observed during the first trimester, or during the first half of pregnancy in some women, may exaggerate the intolerance of oral iron therapy, when the woman is treated with high doses of iron [17]. This means that in order to reduce the prevalence of anemia during pregnancy, anemia should be corrected before conception.

In our series, the complications observed were LBW, pre-eclampsia and preterm birth, although the only statistically significant complication was LBW. The explanations have already been given above. Cesarean section (CS) rate among anemic pregnant women (6.6%) was lower than the 11.8% found in the nonanemic group. This is due to the fact that CSs in the nonanemic group were usually elective for various indications. Although CSs were frequently done among nonanemic pregnant women, there was no statistical significant difference between both groups regarding emergency CSs (P=0.55) or elective CSs (P=0.06). Leading indications for CSs in both groups were cephalopelvic disproportion and scarred uterus. High CS rate among anemic pregnant women has been reported [6].

Episiotomies and instrumental deliveries were more carried out in the anemic group (RR 1.8, 95% CI 1.0-3.1 and RR 2.2, 95% CI 0.8-6.1 respectively). This might be explained by the increased mean birth weight observed in this group (P=0.039). The increased rates of

episiotomies and instrumental deliveries have already been noticed by some authors especially when booking Hb was <7.5 g/dl [6].

Mean birth weight was significantly increased among the initially anemic pregnant women ($P=0.039$), with a difference in mean of 85 g. This was observed among both male fetuses ($P=0.006$), and female fetuses ($P=0.013$). This increase in birth weight can be explained by the increased placental weight observed among initially anemic women. The placenta is the organ through which there is transfer of nutrients and oxygen to the fetus [18,19]. This transfer is maximized when the placenta is well developed. This transfer of nutrients is associated with an increased transfer of oxygen, when anemia has been corrected. A maximum transfer of nutrients is associated with an increased fetal growth, hence, with an increased birth weight, as observed in pregnancies complicated by gestational diabetes [19]. Moreover, higher doses of iron and folic acid in our study, as observed in the anemic group, might have led to rapid correction of anemia in some cases and, therefore, increased birth weight. The increase in mean birth weight among the anemic pregnant women who received iron during pregnancy has been documented by others [20-22].

Nevertheless, there was an increased risk of LBW (RR 7, 95%CI 1.6-30.4, $P=0.003$) among anemic pregnant women, especially when Hb was <9g/dl at 36 weeks gestation, as observed elsewhere [4,9,10]. This might be explained by the fact that, despite the increased placental weight, anemia was so severe that the oxygen transfer to the fetus was limited. Indeed, some researchers think that low birth weight observed among anemic women might be due to decreased oxygen supplementation to the fetus [23]. Women with Hb <9g/dl should either be transfused or receive parenteral iron for a rapid correction of the Hb concentration [24], before 32 weeks for instance, to improve fetal growth. More studies should be carried out to confirm this.

Conclusion

Anemia corrected before term with iron and folic acid was associated with a significant increase in birth weight. Hb still <9g/dl at 36 weeks gestation was associated with an increased risk of LBW. At Hb ≥ 9 g/dl there were few fetal and maternal complications observed. Nevertheless, we should not allow women to have Hb <10 g/dl at term, since studies have shown that anemic women are at a higher risk of dying from post partum hemorrhage [10].

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