

# Placental fetal weight ratios among anemic and non-anemic pregnant women

## Abstract

**Aim:** To establish the placental fetal weight ratio (PFWR) in anemic pregnant women (AW) as well as in non-anemic pregnant women (NW).

**Methods:** This was a matched cohort study conducted in the Yaoundé University Teaching Hospital, Cameroon, from March 1st, 2011 to February 28th, 2013. Women with singletons pregnancies and hemoglobin concentration (Hb) at booking  $<10\text{g/dl}$  (AW) or  $\geq 11\text{g/dl}$  (NW) were recruited and followed up till delivery. All women were taking iron and folic acid. Main variables recorded were Hb at booking and at 36 weeks, birth weight, fetal sex and placental weight. Data were analyzed using SPSS 18.0. The PFWR was obtained by dividing placental weight by birth weight. Data for NW were compared to those for AW. Student t-test and Fisher exact test were used for comparison.  $P < 0.05$  was considered statistically significant.

**Results:** Mean placental weight for male newborns was higher in the AW group than in the NW group ( $492.5 \pm 84.5$  vs  $409.7 \pm 42.4\text{g}$ ,  $P < 0.0001$ ). Female newborns from anemic women also had higher mean placental weight ( $498.8 \pm 72.9$  vs  $408.2 \pm 38.6\text{g}$ , ( $P < 0.0001$ ). No difference in mean placental weight was found between male and female babies either in the AW group ( $492.5 \pm 84.5$  vs  $498.8 \pm 72.9$ ,  $P = 0.58$ ) or in the NW group ( $409.7 \pm 42.4$  vs  $408.2 \pm 38.6$ ,  $P = 0.80$ ). The mean PFWR for NW was 12.4% for male against 12.8% for female babies ( $P = 0.80$ ). The PFWR for male babies was higher in the AW group ( $0.144 \pm 0.019$ ) than in the NW group ( $0.124 \pm 0.0138$ ) ( $P < 0.0001$ ); that of female babies was also higher in the AW group ( $0.157 \pm 0.03$ ) than in the NW group ( $0.128 \pm 0.013$ ) ( $P < 0.0001$ ). The PFWR was lowest when Hb concentration at booking was between 9 and 10 g/dl and highest when it was  $< 5\text{g/dl}$ .

**Conclusion:** Mean placental weight was higher in anemic pregnant women independently of the fetal sex. The PFWR also was higher among anemic pregnant women independently of the fetal sex. The PFWR was inversely proportional to the Hb concentration at booking.

**Keywords:** anemia in pregnancy, placental fetal weight ratio, hemoglobin

Volume 4 Issue 1 - 2018

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**Received:** October 18, 2017 | **Published:** January 19, 2018

## Introduction

According to WHO, anemia in pregnancy (AP) is defined as hemoglobin (Hb) concentration  $<11\text{g/dl}$ <sup>1,2</sup> or  $10.5\text{g/dl}$  in the second trimester.<sup>2</sup> AP is frequent worldwide with a prevalence of 30-65% in Africa according to this definition.<sup>3-5</sup> Because hemodilution may appear early enough and can be so marked in some pregnant women, AP is defined as Hb concentration  $<10\text{g/dl}$  in our setting as also defined by some authors.<sup>6,7</sup> Fetal growth depends on the ability of the placenta to provide oxygen and nutrient to the fetus. Janthanaphan et al.<sup>8</sup> showed that in normal singleton term pregnancy, the placental weight is approximately 1/6 the weight of the fetus.<sup>8</sup> When this ratio is altered, certain conditions must be explored. Placental development is reduced in pre-eclampsia and eclampsia, and in other chronic diseases like diabetes and hypertension while its development is increased in certain conditions or diseases like hyperemesis gravidarum,<sup>9</sup> maternal syphilis, erythroblastosis fetalis and maternal anaemia.<sup>10</sup> Placental growth depends on certain factors which include maternal Hb concentration.

Anemia is capable of inducing placental hyperplasia and hypertrophy,<sup>11,12</sup> explaining why placental weight is frequently increased among anemic pregnant women. Low birth weight

observed among anemic pregnant women is due to decreased oxygen supplementation to the fetus.<sup>13</sup> Severe persistent maternal anemia will, therefore, lead to fetal hypotrophy. This explains why the PFWR is increased for anemic women compared to the ratio for non anemic women. If anemia is progressively corrected, placental hyperplasia might stop at a certain time while the fetal weight is still increasing. The PFWR should, consequently, be lesser than that of anemic women whose anemia has not been corrected. Knowing the PFWR for anemic women might help us estimate the magnitude of anemia present in early gestation. Although placental weight is increased among anemic pregnant women, the magnitude of this increase is not well established. The aim of this study, therefore, was to calculate PFWR in anemic pregnant women according to the degree of anemia present at booking.

## Methods

This cohort study was conducted in the maternity 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 pregnancy and Hb concentration at booking  $<10\text{g/dl}$  and one control of the same parity with a singleton pregnancy and Hb concentration  $\geq 11\text{g/dl}$  (standard definition of normal Hb

concentration in pregnancy) were recruited and both followed up till delivery. Women with gestational diabetes were excluded by using fasting or 75g oral glucose challenge test. Between 24 to 28weeks gestation a fasting blood sugar of >0.92g/l or values of blood sugar of >1.8g/dl or >1.53g/dl one or two hours respectively after oral ingestion of 75g of glucose were suggestive of gestational diabetes. Women with hypertensive diseases of pregnancy (blood pressure 140/90mmHg with proteinuria or not) were also excluded. Eight women with severe anemia (Hb concentration <6g/dl) received blood transfusion until new Hb concentration was 6 to 7g/dl. Thereafter, they were prescribed as other anemic women 100mg of iron supplementation and 1mg of folic acid daily while non-anemic women were prescribed 50mg of iron supplementation and 0.5mg of folic acid daily. Two women received parenteral iron because of intolerance of oral iron therapy. Hb concentration was controlled every two months and at 36weeks gestation. Variables recorded included gestational age at booking (confirmed by an ultrasound scan performed before 20weeks gestation, sometimes under women's request), Hb concentration at booking and at 36weeks gestation, maternal age and gestational age at delivery, birth weight, fetal sex and placental weight. Hb concentration was checked during labor at 35weeks in four women who had preterm deliveries. 5ml of venous blood was collected and Hb concentration was measured on automated cell counter (HumaCount 30TS). Before measuring placental weight, membranes were removed, the cord sectioned at the placental insertion site and fetal blood evacuated from the placenta. The weight of babies and that of placentas were measured immediately after delivery with the same apparatus. The PFWR in each case was obtained by dividing the placental weight by the birth weight. This study received approval from the institutional ethics committee. The necessary sample size was calculated as needing 169 women at least in each group. An informed consent form was obtained from each woman. Data were analyzed using SPSS 18.0. The data for anemic pregnant women were compared to those for non-anemic pregnant women. Student t-test and Fisher exact test were used for comparison. P<0.05 was considered statistically significant<sup>1</sup>.

## Results

During the study period, 16 anemic women were excluded for various reasons while 188 anemic pregnant women (AW) were recruited as cases and the same number of women as controls (NW). Data are shown in Table 1.

Birth weight distribution is shown in Table 2. The mean BW for male babies was 3427.6±533.1g(range 1877-4500) in the AW group (n=89) as compared to 3304.6±358.9g(range 2525-4150) in the NW group (n=90) (P=0.0059). For female babies, the mean BW was 3237.1±444.2g(range 2295-4120) in the AW group (n=99) as against 3189.5±289.5g(range 2752-3692) in the NW group (n=98) (P=0.37).

Table 3 shows placental weight distribution in both groups. Mean placental weight for male was 492.5±84.5g(340-703) in the AW group (n=99) as against 409.7±42.4g(301-520) in the NW group (n=98) (P<0.0001) whilst mean placental weight for female was 498.8±72.9g(225-820) in the AW group (n=89) as against 408.2±38.6g(339-508) in the NW group (n=90) (P<0.0001).

<sup>1</sup>The formula for sample size calculation was  $N = 2 \times (1/f) \times (Z\alpha + Z\beta)^2 / (P_0 - P_1)^2 \times P \times (1-P)$  where f was the assumed percentage of women that might be lost during follow-up (10%),  $Z\alpha = 1.65$  corresponding to a type I error of 5%,  $Z\beta = 1.28$  corresponding to a type II error of 10% or a power of 90%,  $P_0$  the prevalence of low birth weight (LBW) (<2500 g at birth) in anemic women (10%),  $P_1$  the prevalence of LBW among non anemic women (2%) and P is  $(P_0 + P_1)/2$ .

There was no statistically significant difference when comparing the means of placental weights between male and female babies either in the AW group (492.5±84.5 vs 498.8±72.9 respectively, P=0.586) or in the NW group (409.7±42.4 vs 408.2±38.6 respectively, P=0.80). The PFWR for male babies varied between 0.10 and 0.20 with a mean of 0.144±0.0189 in the AW group as against a range from 0.08 to 0.15 with a mean of 0.124±0.0138 in the NW group (P<0.0001) (Table 4), while for female babies it ranged from 0.09 to 0.26 with a mean of 0.157±0.031 in the AW group as against a range of 0.10 to 0.16 with a mean of 0.128±0.013 in the NW group (P<0.0001) (Table 5). The PFWR was lowest when Hb concentration at booking was between 9 and 10 g/dl and highest when it was <5g/dl.

**Table 1** Distribution of some variables among both groups

Variables	Anemic pregnant women mean±SD(Range)	Non-anemic pregnant women mean±SD (Range)	P value
Number	188	188	
Gestational age at booking (weeks)	21.5±7.3 (6-34)	17.8±4.9 (6-29)	<0.0001
Hb at booking(g)	8.9±1.1 (3.4-9.9)	12.3±0.6 (11-14.1)	<0.0001
Maternal age (years)	27.9±5.2 (17-45)	28.3±5.2 (17-41)	0.46
Parity	0-5 (mean 1.4)	0-5 (mean 1.4)	1
Hb at 36weeks(g)	10.8±1.2 (4.7-13.3)	12.2±0.6 (11-13.5)	<0.0001
Gestational age (delivery)	39.9±1.6 (35-43)	39.6±1.3 (36-42)	0.07
Birth weight(g)	3328496.7 (1877-500)	3243.5±328.2 (2327-4150)	0.052
Male babies	89/188(47.3%)	90/188 (47.8%)	0.88
Placental weight(g)	499.7±101.4 (225-820)	408.5±45.2 (301-520)	<0.0001

SD, standard deviation; Hb, hemoglobin concentration

**Table 2** Birth weights distribution according to Hb level at booking

Anemic pregnant women:		Non-anemic pregnant women n=188, Mean Hb Level=12.3±0.6	P
Hb at booking in g/dl(number)	Mean BW (g)±SD	Mean BW (g)±SD	
<5(n=6)	2450.1±133.2		<0.0001
5 to <7(n=4)	3456.2±120.1		0.198
7 to <8(n=9)	3305.6±229.0		0.577
8 to <9(n=54)	3365.1±527.4	3243.5±328.2	0.04
9 to <10(n=115)	3348.4±477.7		0.024
Total (n=188)	3328±496.7		0.052

BW, Birth weight; SD, Standard deviation; Hb, Hemoglobin concentration

**Table 3** Placental weights distribution according to Hb level at booking

Anemic pregnant women:		Non-anemic pregnant women n=188, Mean Hb Level=12.3±0.6	P
Hb at booking in g/dl(number)	Mean placental weight (g)±SD(range)	Mean placenta weight (g)±SD(Range)	
<5(n=6)	460.0±65.6(249-582)	408.5±45.2(301-520)	0.0074
5 to <7(n=4)	574.0±16.2(560-590)		<0.0001
7 to <8(n=9)	546.4±46.6(490-602)		<0.0001
8 to <9(n=54)	526.3±103.7(225-700)		<0.0001
9 to <10(n=115)	483.1±99.2 (295-820)		<0.0001
Total (n=188)	499.8±101.4(225-820)		<0.0001

Hb, hemoglobin concentration; SD, standard deviation

**Table 4** Placental fetal weight ratio among male babies

Anemic pregnant women		Non-anemic pregnant women (n=90)	P
Booking Hb(g/dl)	Mean FPWR±SD(Range)	Mean FPWR±SD(Range)	
5 to <7(n=2)	0.169±0.003(0.16-0.16)	0.124±0.013(0.08-0.15)	<0.0001
7 to <8(n=3)	0.166±0.016(0.15-0.18)		<0.0001
8 to <9(n=25)	0.148±0.014(0.10-0.20)		<0.0001
9 to <10(n=59)	0.140±0.018(0.10-0.17)		<0.0001
Total= 89	0.143±0.0198(0.10-0.20)		<0.0001

Hb, hemoglobin concentration, FPWR, placental fetal weight ratio, SD, standard deviation

**Table 5** Placental fetal weight ratio among female babies

Anemic pregnant women		Non-anemic pregnant women(n=98)	P
Booking Hb(g/dl)	Mean FPWR±SD(range)	Mean FPWR±SD(range)	
3 to <5(n=6)	0.188±0.051(0.14-0.26)	0.128±0.0137(0.10-0.15)	<0.0001
5 to <7(n=2)	0.170±0.006(0.17-0.18)		<0.0001
7 to <8(n=6)	0.165±0.006(0.15-0.17)		<0.0001
8 to <9(n=29)	0.156±0.033(0.09-0.22)		<0.0001
9 to <10(n=56)	0.151±0.027(0.11-0.22)		<0.0001
Total =99	0.157±0.031(0.09-0.26)		<0.0001

Hb, hemoglobin concentration, FPWR, placental fetal weight ratio, SD, standard deviation

## Discussion

There was no difference in maternal age between anemic and non-anemic pregnant women. The gestational age at booking for anemic pregnant women (21.5weeks) was higher than that of non-anemic pregnant women (17.5weeks) ( $P<0.0001$ ). This might be due to the fact that anemic women might have poor income and might still be looking for financial means in order to start their consultation.

Hb concentrations at booking was significantly lower in anemic pregnant women than in the control group ( $P<0.0001$ ). This lower Hb concentration might be aggravated by the hemodilution that could be more pronounced in the anemic women since the mean gestational age at booking was slightly more advanced. Hb concentrations at term was also significantly lower in anemic pregnant women than in the control group ( $P<0.0001$ ) despite high dose of iron and folic acid therapy in the anemic group meaning that to reduce the prevalence of anemia at term, anemia should be corrected before conception.

The mean gestational age at delivery of formerly anemic women was similar to that of the control group (39.9 versus 39.6weeks) with no statistically significant difference ( $P=0.07$ ) meaning that a mean Hb concentration at term of 10.8 might have the same influence on the onset of labor as that above 11g/dl. The proportions of male and female babies were similar in both groups ( $P=0.88$ ) showing that anemia status was not influenced by fetal sex.

The mean placental weight was significantly higher in the AW group independently of fetal sex. This is explained by the fact that anemia can induce placental hyperplasia and hypertrophy.<sup>11,12</sup> The mean BW was also significantly higher in the AW group when compared to that of the NW group. This is explained by the fact that most fetuses were delivered when the Hb concentration at 36weeks was already normalized since AW were on a high dose of iron and folic acid therapy. An increased placental weight with an increased surface area of exchange at a moment when  $O_2$  transport to the fetus is normalized might contribute to an increased  $O_2$  supply to the fetus and therefore to increased fetal weight. This has already been observed by some researchers.<sup>14</sup> Among AW, the mean placental weight for male babies was similar to that of female babies. This shows firstly that placental weight increase among anemic women do not depend on fetal sex and secondly that increased birth weight usually observed among male fetuses is not due to increased placental weight. This similar mean of placental weight in both sexes was noticed among NW. This finding is different from that of some authors who found that placental weight of male was a bit higher than that of female babies.<sup>15</sup>

The PFWR was significantly higher in the AW group than in the NW group either for male or for female babies. This has also been noticed elsewhere.<sup>16</sup> This shows that although both placental and fetal weights are increased in AW, the increase in the weight of placentas was more important than that of fetuses.

The PFWR of NW in our series was 0.124(or 12.4%) for male and 0.128(or 12.8%) for female babies. This value was at bit lower for male babies because placenta weight was almost the same as for female babies ( $P=0.80$ ) while their mean birth weight was a bit higher than that of female babies though not statistically significant ( $P=0.37$ ).

Janthanaphan et al.<sup>8</sup> found that the ratio of placental weight to that of the fetus in normal singleton pregnancies at term was approximately 1/6(or 17%) in Thailand.<sup>8</sup> This large difference is due to the fact that

in our study in contrast to theirs, placental weight was obtained after we have removed umbilical cord and membranes and evacuated fetal blood from the placenta. Fetal adnexae include placenta, umbilical cord whose length varies enough, fetal membranes, and fetal blood found in the placenta whose amount also varies widely.

The PFWR of female babies among AW in our series varied between 0.188(or 18.8%) when the Hb concentration at booking was  $<5$ g/dl and 0.151(or 15.1%) when Hb concentration was 9 to  $<10$ g/dl. As already mentioned above, this ratio was 0.128(or 12.8%) when booking Hb concentration was  $\geq 11$ g/dl. The PFWR of male babies among AW ranged from 0.169(or 16.9%) when booking Hb concentration was 5 to  $<7$ g/dl to 0.140(or 14.0%) when it was 9 to  $<10$ g/dl. This ratio was 0.124 (or 12.4%) when booking Hb concentration was  $\geq 11$ g/dl. The lowest PFWR (14.0% for male and 15.1% for female) was obtained when the mean Hb concentration at booking was 9 to 10g/dl while the highest was obtained when the mean booking Hb concentration was  $<5$ g/dl(0.188 or 18.8% for female). This can be explained by placental hyperplasia and hypertrophy observed among anemic pregnant women, the degree of hyperplasia and hypertrophy depending on the degree of anemia. These observations have already been made by other researchers.<sup>17</sup> We had no male baby delivery from women with Hb at booking  $<5$ g/dl.

We found that the mean placental weight was lowest among AW when the booking Hb concentration was  $<5$ g/dl, although this mean placental weight was significantly higher than that of NW, while the mean birth weight was significantly reduced when the booking Hb concentration was  $<5$ g/dl though the PFWR was the highest. Anemia might have been so severe that placental growth and especially fetal growth were limited in some of these women. The weakness of our study resides in the fact that we had only few pregnant women with booking Hb concentration  $<8$ g/dl. More studies with large sample should be conducted to verify these findings.

## Conclusion

Mean placental weight was higher in anemic pregnant women independently of the fetal sex. The PFWR also was higher among anemic pregnant women independently of the fetal sex. The PFWR was inversely proportional to the Hb concentration at booking.

## Acknowledgements

We wish to thank Mister Domkam Kammogne Irénée for the statistical analysis and also all the doctors and the midwives who contributed in the realization of this study.

## Conflicts of interest

Author declares that there is no conflict of interest.

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