

Could Birth Weight to Placental Weight Ratio Predict Postpartum Haemorrhage and Neonatal Intensive Care Unit Admission?

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ABSTRACT

Objective: To evaluate the usability of the ratio of birth weight to placental weight [fetoplacental ratio (FPR)] in predicting postpartum haemorrhage (PPH) and neonatal intensive care unit (NICU) admission.

Study Design: Prospective observational study.

Place and Duration of Study: Bursa Yuksek Ihtisas Training & Research Hospital, Bursa, Turkey, between July 2020 and July 2021.

Methodology: Women who were supposed to have an uncomplicated delivery with a live, single, term pregnancy without any concomitant disease, were included in the study. Patients with PPH were accepted as the study group and patients without PPH were the control group. For NICU requirement, babies who were admitted to NICU were the study group, and babies who did not require NICU were the control group. The fetoplacental ratio was calculated by dividing the newborn weight to placental weight and evaluated in the prediction of NICU admission and PPH.

Results: The number of patients included in the study was 812. Approximately 7% of women had postpartum haemorrhage. The FPR was found as an independent predictor for PPH by nearly 3.5 fold. Women who experienced PPH had heavier placenta and lower fetoplacental ratio. Patients whose babies were admitted to NICU also had lower FPR with statistically significant differences.

Conclusion: The fetoplacental ratio could be a promising predictor for PPH and NICU admission in the postpartum period. Since novel studies are needed using ultrasonographic measurements during antenatal surveillance to predict PPH or NICU admission.

Key Words: Birth weight, Neonatal intensive care unit, Placental weight, Postpartum haemorrhage, Cesarean birth, Vaginal birth, Fetoplacental ratio.

How to cite this article: Elmas B, Simsek D, Dincgez B, Ozceltik G, Urun C, Akin HY. Could Birth Weight to Placental Weight Ratio Predict Postpartum Haemorrhage and Neonatal Intensive Care Unit Admission?. *J Coll Physicians Surg Pak* 2022; **32(12)**:1557-1562.

INTRODUCTION

The placenta is the most important and the biggest organ of the fetus. It is essential for fetal growth and continuity of pregnancy. Placental weight, ultrasonographic measurements such as placental length, volume, thickness, blood flow doppler parameters, and placental magnetic resonance imaging evaluations were investigated in several studies whether the usefulness in the prediction of maternal or neonatal outcomes.¹⁻³ Birth weight to placental weight ratio which is also called fetoplacental ratio (FPR) is one of these parameters exposing the placental efficiency.

It is well-known that the placenta has the ability to enlarge or reduce weight for compensation. That might be considered as the insurance to prevent short-term adverse outcomes for both the mother and the fetus. Contemporary studies have stated that FPR could have been related to long-term consequences such as cardiovascular disease, mortality, and hypertension.^{4,5} Besides the use of FPR for long-term consequences, the alteration and association in various diseases such as gestational diabetes mellitus, preeclampsia, small for gestational age (SGA), intrauterine growth restriction, and stillbirth have been exposed. Inadequate placental implantation, placental villous immaturity, placental infarct or edematous placenta were accused of alteration in that disease.⁶⁻⁹ Evaluating the neonatal outcomes have also reflected the relationship between adverse outcomes like low APGAR scores and FPR. The basis of the problem could be the placental invasion problems that impair the nutritional transport from mother to fetus.

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Received: August 10, 2022; Revised: November 03, 2022;

Accepted: November 18, 2022

DOI: <https://doi.org/10.29271/jcpsp.2022.12.1557>

World Health Organisation (WHO) has clarified that about 808 women died every day in 2017 due to complications of pregnancy. The major cause of maternal death is haemorrhage.¹⁰ Definition of PPH has revised in 2017 by the American College of Obstetricians and Gynecologists to cumulative blood loss ≥ 1000 mL or bleeding associated with signs/symptoms of hypovolemia within 24 hours of the birth process regardless of the delivery route.¹¹ Besides the definition of PPH, the authors specify that the measurement of PPH is difficult, and the real amount of PPH is much more than it is predicted by the physician. Thus, it is a better evaluation to determine the degree of the haemorrhage *via* haemoglobin levels or the symptoms of the patients. In a healthy adult, loss of up to 15% of blood volume can be asymptomatic which is determined as class 1 however, class 2 haemorrhage is the loss of 15-30% of blood volume that has manifested clinically symptomatic.¹² Uterine tonus and tissue factor are the major determinants of PPH. Considering both factors are related to the fetus and the placenta, FPR could be a promising predictor for PPH.

Admission to the neonatal intensive care unit (NICU) and PPH in term pregnancies are unexpected circumstances if the newborn is appropriate for gestational age and the mother had no concomitant diseases. Prediction of the NICU admission or PPH is precious in these patients for the rapid intervention or the transfer to fully equipped hospitals such as NICU or blood component transfusion. There is no adequate test or marker to predict these issues during antenatal surveillance. Besides, there were no appropriate studies investigating the correlation between FPR and PPH, NICU admission.

The objective of this study was to evaluate the usability of the FPR which could be calculated in the early postpartum period in predicting NICU admission or PPH in women who gave birth to a newborn with an appropriate gestational age at term.

METHODOLOGY

An observational case-control study was conducted prospectively in Bursa Yuksek Ihtisas Training & Research Hospital, Bursa, Turkey, which was university-affiliated research and training hospital after the approval from the local Ethics Committee.

Patients who had a live, single, and term pregnancy (gestational age between 37-40 weeks due to the last menstruation period or first-trimester ultrasonography) were included in the study.

Two analyses were performed in this case-control study. First the role of FPR in PPH. For this analyses, patients with PPH were accepted as the study group and patients without PPH were accepted as the control group. Second, NICU requirement was assessed. In this analysis, babies who were admitted to NICU were the study group, and babies who did not require NICU were the control group. The FPR was compared between the study and control groups, and then the predictive role of FPR was evaluated for NICU admission and PPH.

Patients' characteristics including age, gravidity and parity were recorded. Women with any concomitant disease that complicated the pregnancy (including systemic disease of the patient, any fetal abnormalities such as fetal anomaly or ultrasonographic disorders like oligohydramnios and polyhydramnios) were excluded from the study. After the delivery, the birth weight and the placental weight were weighed with an electronic scale. The placentas were weighted with the membranes and the umbilical cord which was necessary for umbilical cord blood sampling.

After admission to the delivery unit, blood samples for complete blood count (CBC) and fibrinogen were obtained. The samples for CBC examinations were collected in 2 mL tubes with EDTA and analysed using an automated haematology analyzer (Mindray BC-6800 Plus, Shenzhen, China) within 1 hour. The CBC tests were repeated at the postpartum 24th hour. Women whose blood haemoglobin level has decreased at least 15% were assumed as experienced PPH. Plasma fibrinogen levels were measured using a Clauss fibrinogen assay (Siemens Healthcare Diagnostics).

Neonatal outcomes were evaluated in terms of; birth weight, APGAR 1st and 5th minutes scores, baby gender, and admission to NICU. The particular indication of the NICU admission was not evaluated because the aim was to determine the number of take-home babies during hospital discharge of the women. The FPR was calculated by dividing birth weight by placental weight. The relation between FPR, PPH, and NICU admission was evaluated.

Shapiro-Wilk test was performed to assess the normality of the distribution of the variables. Mann-Whitney-U test was used to compare non-normally distributed continuous variables between two groups while the student t-test was used to compare normally distributed ones. For categorical variables, Chi-square, and Fisher exact test were used for group comparisons. The descriptive statistics were expressed as mean \pm standard deviation for normally distributed variables, median (minimum-maximum) for non-normally distributed variables, and frequency or percentages for categorical variables. Spearman correlation coefficient was calculated for determining the relationship between FPR and the sociodemographic findings of patients. Logistic regression analysis was performed to evaluate the independent risk factors for NICU admission and PPH. Statistical analysis was carried out by using SPSS Version 21.0. (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp.) and Medcalc version 19.5.6 software. And p-value < 0.05 was considered as statistically significant.

RESULTS

The number of women who were investigated for the relationship between FPR and PPH was 725. Eighty-seven women were excluded from the PPH evaluation due to missing blood sample examination. The numbers of women who delivered *via* vaginal route and cesarean section were 534 and 191 respectively.

Table I: Characteristics of the NICU patients and the comparison of the groups.

	NICU (+) (n=74)	NICU (-) (n=738)	p
Age (years)	26 (18-43)	26 (16-44)	0.518 ^a
Gravidity (n)	3 (1-7)	2 (1-12)	0.369 ^a
Parity (n)	1 (0-3)	1 (0-3)	0.622 ^a
Delivery route (n,%)			<0.001 ^{a,b}
Vaginal	41(55.4%)	553 (74.9%)	
Cesarean	33 (44.6%)	185 (25.1%)	
Birth weight (gram)	3055 (2580-3960)	3250 (2500-4000)	0.003 ^a
Baby gender (n,%)			0.520 ^b
Male	42 (56.8%)	390 (52.8%)	
Female	32 (43.2%)	348 (47.2%)	
Placental weight (gram)	600 (390-850)	580 (365-950)	0.116 ^a
APGAR 1 st minute score	9 (5-9)	9 (7-9)	<0.001 ^a
APGAR 5 th minute score	10 (7-10)	10 (8-10)	<0.001 ^a
Fetoplacental Ratio (FPR)	5.2 (4-7.8)	5.6 (4-7.9)	<0.001 ^a

A p-value of <0.05 was considered significant (*). a: Mann-Whitney U test, b: Chi-square test.

Table II: Clinical characteristics of the patients who gave vaginal birth and the comparison of the groups.

	PPH (+) (n=28)	PPH (-) (n=506)	p
Age (years)	25 (17-34)	26 (16-44)	0.389 ^a
Gravidity (n)	1 (1-5)	2 (1-9)	0.001 ^a
Parity (n)	0 (0-2)	2 (0-3)	0.003 ^a
Birth weight (gram)	3235 (2660-4000)	3245 (2500-4000)	0.853 ^a
Baby gender (n,%)			0.845 ^b
Male	16 (57.%)	270 (53.4%)	
Female	12 (42.9%)	236 (46.6%)	
Placental weight (gram)	607.5 (516-815)	580 (365-900)	0.020 ^a
APGAR 1 st minute score	9 (7-9)	9 (5-9)	0.435 ^a
APGAR 5 th minute score	10 (8-10)	10 (7-10)	0.397 ^a
NICU requirement (n,%)	1 (3.6%)	37 (7.3%)	0.712 ^c
Fetoplacental Ratio (FPR)	5.22 (4.12-5.96)	5.57 (4.05-7.75)	0.002 ^a

A p-value of <0.05 was considered significant (*), a: Mann-Whitney U test, b: Chi-square test, c: Fisher exact test.

Table III: Clinical characteristics of the patients in terms of PPH who gave cesarean section and the comparison of the groups.

	PPH (+) (n=22)	PPH (-) (n=169)	p
Age (years)	28.5 (18-42)	28 (18-43)	0.660 ^a
Gravidity (n)	2 (1-7)	2 (1-12)	0.239 ^a
Parity (n)	1 (0-2)	1(0-3)	0.934 ^a
Birth weight (gram)	3230 ±379.2	3244.2 ±358.2	0.862 ^b
Baby gender (n,%)			0.155 ^c
Male	8 (36.4%)	93 (55%)	
Female	14 (63.6%)	76 (45%)	
Placental weight (gram)	577.5 (459-755)	550 (397-875)	0.081 ^a
APGAR 1 st minute score	9 (8-9)	9 (7-9)	0.955 ^a
APGAR 5 th minute score	10 (9-10)	10 (8-10)	0.955 ^a
NICU requirement (n,%)	4 (18.2%)	24 (14.2%)	0.538 ^c
Fetoplacental Ratio (FPR)	5.45 ±0.37	5.87 ±0.85	0.018 ^a

A p-value of <0.05 was considered significant (*), a: Mann Whitney U test, b: Student t-test, c: Chi-square test.

The number of women who gave birth at term, without any concomitant disease and the baby with appropriate for gestational age included in the study was 812. Seventy-four babies with a rate of 9% were admitted to NICU. Comparison of the patients whose newborns were admitted to NICU and not exposed delivery type ($p < 0.001$), birth weight ($p = 0.003$), APGAR 1st minute score ($p < 0.001$), and APGAR 5th minute score ($p < 0.001$) differed statistically different. The median value of FPR was 5.2 (1.23) in the NICU(+) group, whereas 5.6 (1.10) in the healthy group ($p < 0.001$). Table I has demonstrated the comparison of the groups and the values of the variables.

The correlation analysis depicted that there was no correlation between FPR and patients' age ($p = 0.368$), gravidity ($p = 0.883$) and parity ($p = 0.789$).

Logistic regression analysis was performed to evaluate the role of age, gravida, APGAR scores, delivery type, birth weight, baby gender, and FPR on NICU admission. FPR ($p < 0.001$) and APGAR 5th minutes scores ($p = 0.030$) were related to two-fold increased NICU admission risk and delivery type was related to nearly three-fold increased risk ($p < 0.001$).

Twenty-eight women with a rate of 5.2% experienced PPH in the vaginal birth group. Women who had PPH had heavier

placental weight and a lower FPR. These parameters differed statistically significantly. Evaluation and the comparison of the variables were demonstrated in Table II.

To evaluate the risk factors for PPH in women who gave vaginal birth, logistic regression analysis was performed. In the analysis, nulliparity and FPR were found to be independent predictors of PPH. Nulliparity increased the PPH risk by nearly 3.7 fold ($p=0.005$), while 1 unit change in FPR increased the risk by nearly 2.2 fold ($p=0.008$).

Women who underwent cesarean section were evaluated in terms of PPH individually. Twenty-two of 191 patients with a rate of 11.5% experienced PPH. Patients who experienced PPH had lower FPR ratio. The evaluation of the variables was demonstrated in Table III.

The correlation analysis has revealed that FPR was not correlated with age ($p=0.846$), gravidity ($p=0.463$), parity ($p=0.589$), prepartum fibrinogen levels ($p=0.266$), prepartum platelet levels ($p=0.310$), APGAR 1st minute scores ($p=0.340$), and APGAR 5th minute scores ($p=0.325$) scores in cesarean section patients. Logistic regression analysis was also evaluated for risk assessment. Only FPR was found as an independent predictor for PPH in women who underwent cesarean section ($p=0.011$) and FPR increased the risk of PPH by nearly 3.5 fold.

The FPR and placental weight have been evaluated individually in terms of anaemia, fetal gender, and parity whether there was a statistical difference through these parameters. Placental weight ($p=0.175$) and FPR ($p=0.182$) did not differ statistically difference between male and female babies. However, placental weight differed statistically different in nulliparous patients ($p=0.033$), and FPR differed significantly in patients with maternal anaemia ($p=0.026$).

DISCUSSION

Placental weight and the measurements such as chorionic disc area, and placental morphometries have been considered valuable indicators for maternal and neonatal outcomes.^{13,14} The placenta is the major organ of the fetus, whereas FPR could provide invaluable information about the newborn and the mother. Recent studies have focused on the association between FPR and SGA, intrauterine growth restriction, admission to NICU, or low APGAR scores.¹⁵⁻¹⁷ It was stated in the results of these studies, the placenta could enhance its size and weight more than the fetus *via* the adaptive mechanism as compensation especially, in the hypoxic milieu. The present study revealed that the FPR could be a predictive marker for fetuses who would be admitted to NICU.

The recent studies had similar conclusions however, in these studies the authors have included the women with SGA and preeclampsia.¹⁵⁻¹⁷ In the present study all babies were appropriate for gestational age and without any concomitant maternal or fetal disease. This is the strength of the study.

The FPR was lower in patients whose babies have been admitted to NICU and that differed statistically difference. The birth weight was lower and the placental weight was higher in these patients, which could mean not only the placenta has enlarged to compensate the pathologic pathways, but also might even mean that placental enlargement has ensured for the fetus to an appropriate weight, however, these compensations might not be enough to accommodate the babies to the extra uterine environment, thus, these fetuses have admitted to NICU. In a contemporary study, the authors have investigated the relationship between the placental weight to birth weight (PW/BW) ratio and neonatal outcomes in term newborns.¹⁸ They stated that the high PW/BW (which means low fetoplacental ratio) was related to adverse neonatal outcomes such as admission to NICU, low APGAR scores, breech presentation, and cesarean section.

The present results were compatible with these results however, these authors did not state the exact value of PW/BW or FPR for predicting these adverse outcomes as we have stated.^{1,18}

The placenta is the source of several hormones. Recent studies examined the relation between fetal gender and FPR. There was no consensus on whether the FPR may differ with fetal gender.^{14,19} In the present study, no statistical difference had detected in FPR in terms of fetal genders.

Postpartum haemorrhage is one of the major causes of maternal morbidity and mortality. In the present study, the main purpose was to investigate the relationship between PPH and FPR. Over 1000 articles have been reviewed which were about PPH. There was only one study that investigated the relationship between the placental weight to fetal weight ratio in the excess postpartum haemorrhage, and maternal and neonatal adverse outcomes. However, the haemorrhage volume was based on visual estimation, and the patients or the fetuses had also concomitant diseases.²⁰

The unique part of the present study was that the patients had no other diseases which may affect PPH or admission to NICU, all babies were appropriate for gestational age, and ultrasonographic views of all placentas were normal. The aim was to evaluate the PPH in unproblematic patients who were supposed to experience any complications. The present results have exposed that FPR could predict excess postpartum haemorrhage in these patients who were full-term and unproblematic. That is essential evidence because if the FPR is lower than the proper threshold level, the physician can utilise the uterotonic agents in high doses or initially prepare the blood components for transfusion. Placental weight was higher and the FPR was lower in patients who experienced excess PPH which was characterised as the minimum 15% decrease of haemoglobin levels. The placenta which was growing at a higher rate relative to the fetus might cause PPH due to increased invasion through the spiral arteries or a larger placenta with a wider

surface could also lead to PPH. A recent study has focused on the relation of maternal anaemia with placental weight or FPR, and concluded as women who had low haemoglobin levels which they identified as below 9 gr/dl, had a higher placental weight and lower FPR.²¹ The present results were similar yet anaemia was also identified as the haemoglobin levels were below 11gr/dl. These patients had heavier placenta weight (did not differ statistically difference) and lower FPR (differed statistically difference). This study's result was in concordance with the previous study, however, the logistic regression analysis had revealed that only nulliparity and FPR are independent predictors for PPH, not the maternal anaemia status. Age, prepartum fibrinogen level which is essential for blood clot stabilisation, prepartum platelet levels, and prepartum haemoglobin levels also did not differ statistically different in the statistical analyses.

The strength of the present study was being prospective design and the inclusion criteria of the patients. Since all women who were supposed not to have problem were included in the study and crucial issues were investigated which could cause serious circumstances such as PPH and NICU admission. The study had two limitations. One of them was the definition of the PPH was determined *via* haemoglobin levels. The haemorrhage could be measured *via* different methods, however, almost every physician needs an objective laboratory result such as haemoglobin level for intervention and diagnosis. The FPR was calculated after the delivery which could reduce the value of prediction NICU admission and PPH, however, FPR might induce early intervention especially, for PPH. On the other hand, the findings of that study might enlighten the newer studies using ultrasonographic evaluations like estimated fetal weight, estimated placental weight or estimated placental volume.

CONCLUSION

FPR provides crucial information about newborn NICU admission and postpartum haemorrhage in women with full-term and newborns with appropriate for gestational age. Decreased levels of FPR in patients with an unproblematic pregnancy could be a predictive marker of NICU admission and PPH. These results might assure the obstetrician to warn for the early intervention or to take action initially. On the other hand, these results would inspire the novel studies such as ultrasonographic evaluations or investigating biochemical indicators to provide these results before the deliveries.

ETHICAL APPROVAL:

The study was approved by the ethics committee of the University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital (Date:10.06.2020- Number:2011-KAEK-25 2020/06-22).

PATIENTS' CONSENT:

Written informed consents were obtained from all partici-

pants before the study was conducted in accordance with the Declaration of Helsinki.

COMPETING INTEREST:

No potential conflict of interest was reported by the authors. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

AUTHORS' CONTRIBUTION:

BE, DS, HYA: The acquisition, analysis and interpretation of data for the work, drafting and revising the manuscript critically for important intellectual content.

GO: Drafting and revising the manuscript critically for important intellectual content.

BD, CU: The acquisition and analysis of data for the work.

All the authors have approved the final version of the manuscript to be published.

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