



Original Article



Assessment of Predictors for Placental Weight and Birth Weight Ratios from Deliveries Conducted in Pakistani Tertiary Care Hospitals

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ABSTRACT

Anomalous placental morphology is associated with obstetric complications. To date, published data is not available regarding placental weights from Pakistan. The aim of the study was to obtain a reference value for placental weights in the Pakistani population and examined the predictors of birth weight to placental weight ratio an indicator of placental efficiency.

Objective: To assess the predictors for placental weight and birth weight ratios in singleton pregnancies delivered at a tertiary care hospital in Pakistan. **Methods:** Data were collected prospectively for the study cohort at a tertiary care hospital unit in Islamabad, Pakistan. Placental and birth weight obtained and documented immediately post-delivery. Information about maternal factors was obtained from medical records. A linear regression model was employed to predict the effects of various risk factors on BW:PW. **Results:** Fetal weight varied from 2 to 4.5 kg with a mean of 3.016 ± 0.445 kg whereas mean placental weight was 0.667 kg (SD = 0.175). Fetal placental weight ratio (FPWR) existed in the range of 2.54 to 7.91 (mean = 4.732 ± 1.082). Anemia, $p < 0.001$ and pregnancy-induced hypertension $p=0.001$, can influence the weight of the placenta. **Conclusion:** The average placental weight reference values obtained represented the diverse multi-ethnic population residing in Islamabad, Pakistan. The correlation between placental weight and the birth weight to placental weight ratio offered valuable insights into how the placenta adapted to the various challenges posed by the various stages of pregnancy.

INTRODUCTION

The placenta experiences dynamic morphological transformations during the course of gestation as influenced by a multitude of factors. These changes are essential for the placenta to effectively adapt to the ever-evolving conditions it encounters within the maternal-fetal environment. The intricate nature of its function necessitates a high degree of specialization to meet the demands placed upon it. Ensuring the proper growth and operation of the placenta is crucial for the successful progression of a pregnancy characterized by optimal

maternal and fetal health. Placental abnormalities can cause miscarriages in early pregnancy as well as other pregnancy-related complications in later gestation [1]. Five days following fertilization, placenta formation begins with the trophoblastic layer co-existing with the embryonic layer. Syncytiotrophoblast invades the endometrium, leading to the generation of primary villi. Rapid enlargement of the villous tree leads to the formation of secondary followed by tertiary villi, hence placental formation is mostly complete by the end of first trimester

[2]. Disruptions anywhere during this process alter the placental morphology making the basis of several pregnancies related complications, for instance, early-onset preeclampsia has been shown to be associated with disordered villous development i.e., distal villous hypoplasia along with placental undergrowth (lower placental weight) [3]. It can be hypothesized that subnormal placental weight might be indicative of ongoing pathology. chronic hypertension and preeclampsia were also associated with low placental weight whereas diabetes, anemia, chorioamnionitis, chorangioma, circumvallate placenta, and marginal cord insertion are risk factors of higher weight of placenta [4]. Since placental weight correlates with the birth weight, birth weight to placental weight ratio (BW:PW) can serve as a more useful tool predicting aberrance in placental weight [5]. A large population based study illustrated a strong positive correlation between placental weight and birth weight as well as a consistent increase in placental weight until 41st week of pregnancy [6]. Placental weight and the BW:PW are frequently reduced in cases of fetal growth restriction (FGR) which may be a sign that the placenta has not been able to adapt its nutrient transfer capability according to its size [7]. Previous study demonstrated higher risk of cardiovascular morbidity later in life in neonates with lower BW:PW and relatively larger placentas [8]. Several studies showed maternal body mass index gestational age, lower socioeconomic status, maternal anemia, gestational diabetes, and smoking to be significantly associated with BW:PW. Pre-eclampsia, risk of induced labour, preterm delivery, low birth weight, and stillbirth were all significantly ($p < 0.001$) related to lower placental weight [9-12]. On the other hand, higher placental weight significantly ($p < 0.001$) correlated to an increased risk of caesarean section, post-term delivery, and large for gestational age birth. Apart from these pathological factors discussed above, BW:PW is also influenced by the gender of the baby. Richardson *et al.*, observed that BW:PW was lower in females which indicates reduced placental efficiency, similarly lower oxygen saturation of umbilical artery was seen, representing reduced systemic oxygenation [13]. Fetal oxygenation is thought to play the basic role behind altered morphogenesis of placenta. Hence the factors that influence fetal oxygenation bring changes in weight of placenta. For example, higher the maternal age, lesser the vascular compliance, and greater is the placental weight [14]. Risk of Small for Gestational Age (SGA) fetus correlated well with the lower placental weight and as placental weight crosses 50th centile, SGA risk becomes negligible [15]. Gestational Diabetes Mellitus (GDM), which produced a state of fetal hypoxia, is associated with larger placentas and lower BW:PW [16]. The aim of the study was to obtain a reference value for

placental weights in the Pakistani population and examined the predictors of birth weight to placental weight ratio (BW:PW), an indicator of placental efficiency. To date, published data is not available regarding placental weights from Pakistan. It can be used as reference for population specific weight of placenta to measure pregnancy outcome and predict lifelong health of fetus.

METHODS

This prospective cohort study was conducted in Maternity Child Center Islamabad, a tertiary care maternity unit from December 2021 to November 2022. Sample size was calculated taking the population size of 1200 (100 patients delivered per month in the study settings) and confidence limit of 5% in Epi calculator and turned out to be 339 for a confidence level of 97%. Weights of 363 freshly delivered untrimmed placentas, as well as the fetal weight, were determined using electronic balance in the labor room and operating rooms of the study setting immediately after the delivery and recorded in the form of a hand-written document. All patients with singleton pregnancies delivering either vaginally or by Cesarean section were included. Multiple pregnancies, extremely preterm delivery at less than 24 weeks' gestation, and pregnancies with known fetal anomalies were excluded from the study. Fetal anomalies can impact placental development and fetal growth in ways that are not representative of the general population. These cases were excluded to avoid potential confounding factors and ensure the study's focus on typical pregnancy outcomes. For diagnosis of pregnancy and labor related complications e.g., preeclampsia, GDM, preterm labor, polyhydramnios, oligohydramnios, obstetric cholestasis, pre-labor rupture of membranes, intrauterine growth restriction (IUGR), postpartum hemorrhage (PPH) etc., RCOG and NICE guidelines definitions of the respective complications were used. Maternal anemia was defined as hemoglobin concentration of less than 9g/dL in maternal blood sampled during labor. At least 3 antenatal visits were the prerequisites for 'appropriate antenatal care'. Sample size calculated from the Epi calculator was 339 taking sampling population of 1200, at 97% confidence interval and design effect of 1. Data were collected using consecutive sampling technique. Data were stored and analyzed in statistical package for social sciences (SPSS) version 26.0. Descriptive statistics were used to represent baseline characteristics of the study population. Continuous numerical data was expressed in mean \pm standard deviation form whereas categorical data as percentage and frequencies. Multivariate regression analysis predicted the effects of various risk factors on weight of placenta as well as BW:PW. Pearson correlation was used to determine individual correlation of maternal weight and gestational age with placental weight. The ethical approval was taken from IRB (Ref No, FGPC.1/12/2021/Ethical Committee).

RESULTS

Mean age of the participants was 28.09 ± 4.902 (range = 18-41 years). Most of the patients had parity of 2 or 3 (cumulative percentage of 71.1%). Gestational age at which patients presented were between 33¹¹ to 42 weeks (mean = 38⁶). Mean maternal BMI was $26.21 \pm 4.71 \text{kg/m}^2$. Frequencies of various risk factors are given in the table 1.

Table 1: Frequencies of Risk Factors

Risk Factors	Frequency (%)	Risk Factors	Frequency (%)
Anemia	82 (22.6%)	Preeclampsia	4 (1.1%)
Rh-negative	19 (5.2%)	History of LSCS	21 (5.8%)
Pre-PROM	8 (2.2%)	IUD	2 (0.6%)
Lack of regular ANC	3 (0.8%)	GDM	13 (3.6%)
Oligohydramnios	2 (0.6%)	Obstetric cholestasis	3 (0.8%)
Polyhydramnios	5 (1.4%)	Preterm labor	21 (5.8%)
PIH	15 (4.1%)	PROM	4 (1.1%)
PPH	4 (1.1%)	IUD	2 (0.6%)
MSL	6 (1.7%)	IUGR	2 (0.6%)
Hydrocephalus	1 (0.3%)	DM type II	1 (0.3%)
Breech	5 (1.7%)	Antithrombotics use	1 (0.3%)
CPD	2 (0.6%)	Shoulder dystocia	1 (0.3%)
Post-dated	60 (16.5%)	Malpresentation	1 (0.3%)
Cord prolapse	2 (0.6%)	-	-

Pre-PROM (Preterm Prelabor Rupture of Membranes); ANC (Antenatal Care); LSCS (Lower Segment Cesarean Section); IUD (Intrauterine Death); GDM (Gestational Diabetes Mellitus); PIH (Pregnancy-Induced Hypertension); PROM (Prelabor Rupture of Membranes); PPH (Postpartum Hemorrhage); MSL (Meconium-Stained Liquor); IUGR (Intrauterine Growth Restriction); CPD (Cephalopelvic Disproportion)

Out of 344 newborns, 177 were male and 167 were females. Females have generally less birth weights and their placenta were also lighter than males (Figure 1).

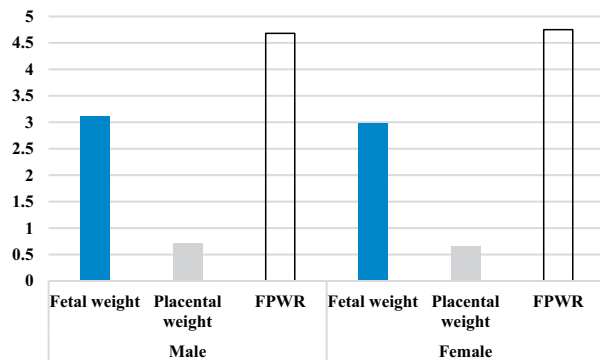


Figure 1: Comparison of Male and Female Placental Metrics

Fetal weight varied from 2 to 4.5 kg with a mean of 3.016 ± 0.445 kilograms whereas mean placental weight was 0.667 kg (SD = 0.175). Fetal placental weight ratio (FPWR) calculated from proportion of weight in kilograms of fetus to placenta, existed in the range of 2.54 to 7.91 (mean = 4.732 ± 1.082). Pearson 'r' of 0.209 showed weak positive

correlation of gestational age and placental weight (Table 2).

Table 2: Correlation of Gender, Placental Weight, FPWR and Fetal Weight

Gender	N	Placental Weight Mean \pm SD	FPWR Mean \pm SD	Fetal Weight Mean \pm SD
Male	177	0.70 ± 0.19	4.68 ± 1.13	3.11 ± 0.42
Female	167	0.65 ± 0.15	4.75 ± 1.01	2.97 ± 0.43

Increasing gestational age showed an increasing trend of placental weight but fetal placental weight ratio (FPWR) remained greatly unchanged with advancing gestational age (Figure 2).

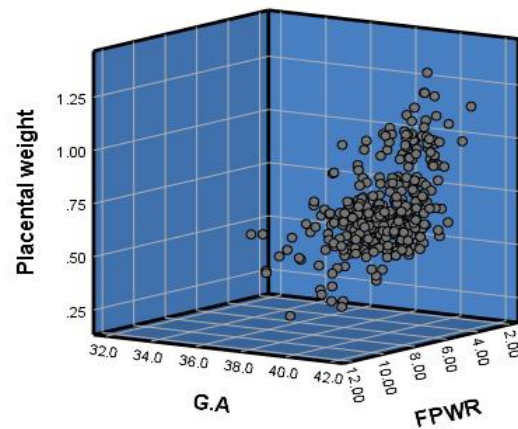


Figure 2: Correlation of Gestational Age Versus Placental Weight Fetal Placental Weight Ratio

Women with lowest BMI 16.40kg/m^2 delivered a 3.3 kg baby with fetoplacental weight ratio of 6.23g while Women with highest BMI 42.4kg/m^2 delivered a 3.6 kg baby with fetoplacental weight ratio of 5.29g (table 3). Maternal BMI exhibited a positive correlation with both birth weight and placental weight ($p = 0.04$ and 0.11 respectively). Placental weight was found positively correlated with oligohydramnios, PPH, obstetric cholestasis, and post-dated pregnancy and it had a negative correlation with PPROM, GDM and IUGR ($p = 0.13$, $p = 0.47$, $p = 0.25$). It suggested that PPROM itself may not directly influence these specific outcomes in the studied population. However, values were statistically insignificant with a mean placental weight of $674.90 \pm 173.93 \text{g}$. The average ratio of birth weight to placental weight was $4.72 \pm 1.07 \text{g}$. There was no significant correlation between GDM and placental weight or birth weight ratios, it could suggest that GDM's impact on fetal growth might not be directly reflected in these ratios. While IUGR affects birth weight, its impact on placental development or the ratio of placental to fetal weight is not straightforward (Table 3).

Table 3: Association of Birth Weight, Placental Weight And Maternal BMI

Variables	BMI	Maternal Age	Fetal Weight	Placental Weight
Mean	26.214	28.07	3.043	0.674
Median	26.000	28.00	3.000	0.630
Standard Deviation	4.717	4.858	0.430	0.173
Minimum	16.40	19	2.0	0.28
Maximum	42.40	41	4.5	1.31

Table 4 cross-tabulated these variables to show the distribution of participants across different age and BMI groups, as well as their FPWR, and presents data on maternal age, Body Mass Index (BMI), and Fetoplacental Weight Ratio (FPWR) for a total of 344 participants. The majority of participants were in the 26-30 years' age group (139 participants), followed by 21-25 years (97 participants). Most participants fall in the 25.1-29 BMI group (105 participants), followed by the 18-23 BMI group (85 participants). The most participants have an FPWR of 4.1-5 (126 participants), followed by 5.1-6 (103 participants). Multivariate regression analysis was preceded by confirmation of homoscedasticity of data. Multivariate analysis predicted the higher placental weight in association with maternal anemia (standardized coefficient = 0.234, CI = 0.055 - 0.140, $p < 0.001$) while lower placental weights with pregnancy-induced hypertension [standardized coefficient = -0.180, CI = (-0.250) - (-0.065), $p = 0.001$]. In multiple regression analysis using FPWR as the dependent variable, maternal anemia presented to be the sole highly significant predictor of placental weight [standardized coefficient = -0.277, CI = (-0.986) - (-0.448), $p < 0.001$], whereas PIH revealed no significance in predictability of placental weight ($p = 0.13$).

Table 4: Maternal Age, BMI and FPWR Cross-Tabulation

Variables	Categories (Years)	BMI Groups					Total
		<18.1	18-23	23-25	25.1-29	>29	
Maternal Age	<21	3	4	3	3	4	17
	21-25	1	25	19	35	17	97
	26-30	5	36	21	39	38	139
	31-35	0	17	7	16	22	62
	>35	1	3	6	12	7	29
Fetoplacental Weight Ratio	<3	1	5	2	0	2	10
	3.1-4	0	24	13	22	22	81
	4.1-5	7	32	19	36	32	126
	5.1-6	1	22	21	36	23	103
	>6	1	2	1	11	9	24
Total		10	85	56	105	88	344

DISCUSSION

Placental weights in this study exhibited a strong correlation with a limited number of risk factors, notably maternal anemia and pregnancy-induced hypertension. Among the 14 patients included in this research, there were

cases of diabetes present, with 13 individuals diagnosed with gestational diabetes (GDM) and one with diabetes mellitus type 2. Analysis revealed that the average placental weights of diabetic patients compared to non-diabetic patients did not show a statistically significant variance, registering at 0.63 and 0.67 respectively ($p = 0.443$) within the study environment. These findings are compatible with the previous study reported that birth weight, birth weight/placental weight ratio (BPW) were higher in the diabetic group whereas placental weight and volume did not differ significantly in the two groups [17]. These results can be projected to the study as the majority of the diabetics who participated had good glycemic control indicated by them in-hospital blood sugar monitoring. Maternal anemia, as operationalized within the parameters of the research, was characterized by a maternal hemoglobin level falling below 10 g/dL over the course of a trimester during pregnancy. The prevalence of anemia within the population under study stood at 22.6%, a finding that demonstrated a strong correlation with increased placental sizes when subjected to multivariate analysis. This observation aligns closely with the conclusions drawn in the investigation conducted by Godfrey and colleagues, thus reinforcing the consistency and reliability of study's results [18]. Several large-scale studies have shown a clear negative correlation between maternal hemoglobin levels and placental size. IDA and maternal nutrition may influence placental weight at birth [19]. However, patients with β -thalassemia minor and erythroblastosis had smaller placentas as well, indicating the possibility of placental insufficiencies arising in such cases. A large Japanese birth cohort study has also revealed that mean placental weight and placental weight to birth weight ratio was higher among smokers compared to non-smoking women [6]. This, again, can be an adaptive response of the placenta to meet the increased oxygen demand in a hypoxic in utero environment. Chronic fetal hypoxia caused by diminished placental blood flow results in a transformation of placental structure. Emerging indicators of placental performance, such as sFLT1: PlGF (representing antiangiogenic soluble FMS-like tyrosine kinase-1 and placental growth factor), are presently being investigated. The examination of these markers, in addition to reduced ACGV (abdominal circumference growth velocity), can potentially function as prognostic tools for fetal growth restriction. The assessment of these parameters may aid in the early detection and management of FGR, thereby improving clinical outcomes for both the mother and the developing fetus [20]. Parameters investigated in placental morphometry through the use of ultrasonography and MRI studies consist of placental diameter, placental volume, placental quotient (which is the volume of the placenta divided by

gestational age), and the placental thickness/volume ratio (PT/PV). A case-control research endeavor delving into the correlation between placental weight and surface area with fetal growth restriction found that a reduction of 10 units in placental weight and surface area resulted in a 21% increase (OR = 1.21, 95% CI, 1.08-1.44) and a 19% increase (OR = 1.19, 95% CI, 1.06-1.41) in the likelihood of FGR occurrence, respectively. This study underscores the significance of examining various morphometric parameters of the placenta and their impact on fetal growth and development, providing valuable insights into the intricate relationship between placental characteristics and adverse pregnancy outcomes such as fetal growth restriction [21]. In this study, increasing gestational age showed an increasing trend of placental weight but fetal placental weight ratio (FPWR) remained greatly unchanged with advancing gestational age whereas Richardson et al. revealed birth/placental weight ratio values increased with progressing gestational age [22]. Placental histopathology in cases with higher FPWR than anticipated in given gestational age revealed maternal vascular stromal lesions and villitis of unknown etiology. Another study conducted by Adeniran et al. showed that placental weight and birth weight increases with gestational age while placental to birth weight ratio (PBWR) increased till 36th week, declined from 37th to 42nd week with a rise from 43rd week [23]. This study demonstrated a positive correlation between maternal BMI and both placental weight and birth weight. Similar findings were observed by Sathasivum et al., Placental weight was positively correlated with birth weight and maternal BMI, but not with newborn sex [24]. However, unexpectedly in the study, mother with lowest BMI i.e. 16.40 kg/m² delivered a 3.3 kg baby with fetoplacental weight ratio of 6.23g. Two cases of intrauterine fetal deaths were reported in the study where mean gestational age happened to be less than those with healthy pregnancies (38.913 versus 36.7; $p = 0.039$) but no relationship could be established between IUFD and FPWR or placental weight. However, previous study indicated that higher placental weight relative to birth weight was associated with an increased risk of neonatal death in preterm infants (aOR, 1.94; 95% CI, 1.40-2.70). For infants born at term, placental weight was not associated with neonatal death. Higher placental weight relative to birth weight was associated with an increased risk of neonatal mortality in term infants with congenital malformations (aOR, 1.82; 95% CI, 1.37-2.41) [25]. An economic history review in Barcelona concluded that even if placenta undergoes adaptive mechanisms to make up for the given conditions, it does less in neutralizing the effect of pathology behind it which explains why both higher and lower placental weights are associated with adverse early neonatal as well as later life outcomes despite the fact that

they underwent adaptive morphological changes [26]. A retrospective cross-sectional study analysis of placental histopathological features and autopsies obtained from intrauterine fetal deaths revealed pathological characteristics in histopathology of 27% of placentas and usually existed with smaller placental sizes [27]. All parameters under study i.e. placental weight (PW), fetal weight (FW), and PW/FW were lower in pregnancies complicated by FGR owing to preeclampsia (PE) compared to FGR without PE or PE without FGR. Placental growth was slower in cases of oligohydramnios. PE in this analysis caused a significant decrease in placental weight. Similarly, the study found pregnancy-induced hypertension to significantly reduce placental weight and as a result decreases PW:BW [28]. In a prospective cohort study conducted at a tertiary care hospital, 430 untrimmed placentas from singleton pregnancies were collected and weighed. This study provided the values of placental weights in centiles at the given gestational ages in the population of Ireland. Although overall placental weight increases with gestational age, proportionately increasing birth weight causes BW:PW ratio to increase as well. Centile distribution presented in this study can be used to categorize placental weights and assess them accordingly. Another study conducted in Nepal shows that the ratio of placental weight to birth weight was 1:6.6 for 158 deliveries and calculated percentiles for birth weights in various placental weight groups [29]. The study is limited to a specific population from a tertiary care hospital in Pakistan, which may not be representative of broader or different populations. Further research is needed to validate the findings across diverse demographic and geographic settings. Expanding the research to include diverse populations from different regions and healthcare settings would enhance the generalizability of the findings. It is imperative for future investigators to ought to center on the examination of antenatal placental morphometry, delving deeper into this aspect to uncover valuable insights. Moreover, delve into the correlation between umbilical and uterine artery Doppler assessments and the BW/PW ratio, shedding light on potential associations. By pursuing these avenues of investigation, a more comprehensive understanding of the intricate dynamics at play in placental development and function can be achieved, leading to advancements in the field of maternal-fetal health. It is crucial for researchers to consider these recommendations to enhance the depth and breadth of knowledge in this critical area of study.

CONCLUSIONS

Current study has revealed the average weight of placenta in Pakistani population and the result of adaptive changes in placenta in response to maternal medical conditions in pregnancy. The positive association between maternal anemia and higher placental weight suggests that anemia management during pregnancy is crucial. The negative association between pregnancy-induced hypertension and lower placental weights highlights the importance of closely monitoring and managing hypertension during pregnancy. The study's insights into the fetoplacental weight ratio (FPWR) can inform clinical practices related to assessing placental efficiency. Researchers were encouraged to conduct further studies pertaining to anatomical and functional modification in placenta in relation to complications of pregnancy.

Authors Contribution

Conceptualization: MM, NF

Methodology: LK, SC, SA

Formal analysis: NWS, HUR

Writing, review and editing: MM, NWS, HUR, NF, LK

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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