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Routine Placental Histopathological Examination: Provides Answers in Neonatal Management

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Abstract: Placental abnormality may affect the fetus adversely. The purpose of this study was to identify the prevalence of placental histopathological examination in a private hospital setting and analyse the placental histopathology findings for high-risk pregnancies. A retrospective cross-sectional study was conducted at the Mater Hospital in Sydney from January 2018 to June 2020. The placental histopathology was classified as per the 2014 Amsterdam Placental Workshop Group criteria, enabling uniformity for analysis. There were 5594 live births during the study period. Of these, 5% (256/5594) were low birth weight (LBW). Placental histopathology was conducted for 8% (443/5594) of the live births and 59% (152/256) of LBW births. The LBW group was subclassified into small for gestation (SGA) (n=66) and non-SGA (n=86) to analyse differences in placental abnormalities between the two groups. Of SGA, 82% (54/66) had placental abnormality compared to 76% (65/86) for non-SGA. Intervillous fibrin deposits ($p=0.013$) and smaller placental weight ($p=0.008$) were more common in the SGA; whereas the placental inflammatory-immune process was more common in the non-SGA. Original placental histopathology reports did not employ the objective Amsterdam classification system, thereby risking subjective or variable interpretation by clinicians. In conclusion, placental histopathology plays an important role in neonatal management. A quality improvement project may improve the prevalence of placental histopathological examination.

Keywords: Low Birth Weight (LBW), Placental Histopathology, Placental Vascular Malperfusion

1. Introduction

Placental abnormality may adversely affect the fetus, as the placenta provides oxygen and nutrients, as well as removes waste products from the growing fetus [1, 2]. Therefore, investigations into placental abnormality may be important in the etiology of neonatal sepsis, birth asphyxia, preterm delivery, intrauterine growth restriction (IUGR) and cerebral palsy [3-6]. They could also offer vital clues to the cause of fetal and neonatal deaths and provide physical evidence for medico-legal assessments [7]. Despite these benefits, a comprehensive examination of the placenta is not part of standard practice in many hospitals. This could be due to challenges such as limited storage facilities for placentas, burden on anatomical pathologists, cost to the healthcare

system or simply a lack of specific guidelines for individual hospitals.

Placental examination has been standardised by the 2014 Amsterdam Placental Workshop Group criteria and includes: a) macroscopic examination of placental shape, placental weight, umbilical cord insertion, umbilical blood vessels, placental abruption and umbilical membrane; b) histopathological examination to identify placental infarction, calcification, and signs of inflammation; and c) microbiological examination to isolate specific bacterial or viral infections in neonates [8].

We undertook this study at the Mater Hospital in Sydney, Australia, with the aim of identifying the prevalence of placental histopathological examination for live births in a private hospital setting. We particularly focused on those with low birth weight (LBW) since LBW is one of the most common pregnancy complications and is associated with increased risk of still birth and cerebral palsy (CP) [9]. The Mater Hospital is a private multispecialty hospital with a Level 5 maternity service that allows preterm deliveries up to 32 weeks gestation [10]. There are 2500–3000 deliveries annually.

At the time of the study, the placental histopathological examinations were conducted at the discretion of the clinicians (obstetrician and/ or neonatologist) at the hospital's affiliated pathological laboratory.

2. Method

2.1. Study Design

The retrospective cross-sectional study was conducted from January 2018 to June 2020 for all live birth deliveries that had placental histopathological examination. The study also included an itemised placental histopathology analysis of the LBW infants. The LBW infants were subclassified into small for gestational age (SGA) and non-SGA. Low birth weight is defined as birth weight less than 2500g [11]. Small for gestational age is a birth weight<10^{th} percentile and non-SGA is a birth weight>10^{th} percentile.

2.2. Data Source

We retrieved data from the hospital electronic database that stores patient records.

2.3. Study Selection

Cases of all gestational ages, including both singletons and multiples, were included if following criteria were met:

1. Live birth at the Mater Hospital;
2. Placental histopathology report available.

2.4. Data Extraction

Data was extracted using the investigator-designed extraction form based on key variables in the published literature, which included: neonatal birth weight; gestational age; diagnosis; and a placental histopathology report. The placental histopathology reports were categorized by the primary investigator into the 2014 Amsterdam Placental Workshop Group criteria, to enable uniformity and standardisation of the analysis [8, 12].

2.5. Statistics

The demographics of the SGA and non-SGA groups were compared using chi-squared tests of independence and independent sample *t*-tests. The placental histopathological classifications of the SGA and non-SGA groups were compared using chi-squared tests of independence or Fisher's exact tests where subcategories had $n<5$. A p-value of<0.05 was considered statistically significant.

3. Results

There were 5594 live births in the 30-month study period, of which 5% (256/5594) were LBW infants (Figure 1). Placental histopathological examination was available for 8% (n=443/5594) of live births and 59% (n=152/256) of LBW infants. Of the 152 LBW infants, 66 were SGA and 86 were non-SGA. The patient characteristics are shown in Table 1. Both SGA and non-SGA groups were homogenous except for the gestational age; average gestation for SGA was 37 weeks and for non-SGA it was 34 weeks ($p<0.001$).

Seventy eight percent (119/152) of the LBW infants had placental abnormality and, of these, 82% (54/66) were SGA and 76% (65/86) were non-SGA (Table 1). As per the 2014 Amsterdam Placental Workshop Group criteria, the placental abnormalities fell into three broad categories: vascular lesions; inflammatory process; and other placental processes [8, 12]. Twenty nine percent (34/119) had one type of placental abnormality while 71% (84/119) had more than one type (Table 2).

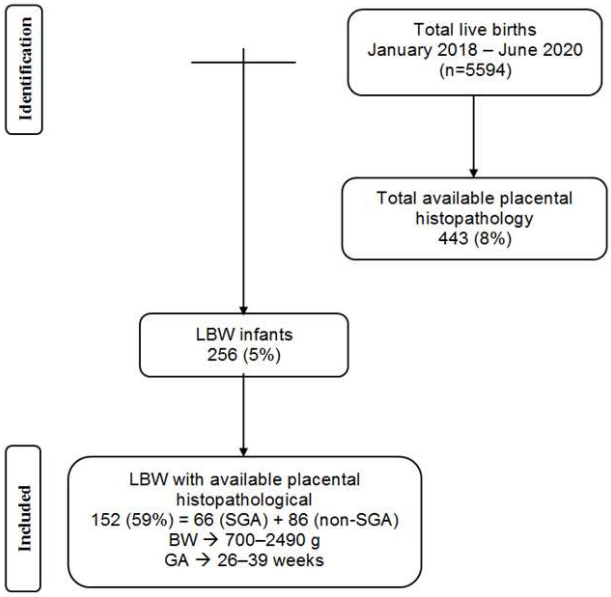

Figure 1. *Patient demographics.*

BW – birth weight; GA – gestational age;
LBW – low birth weight; SGA – small for gestation

Table 1. *Demographics – SGA vs non-SGA.*

	SGA	**non-SGA**	***p* value**
n (%)	66 (43%)	86 (57%)	
Gestational age – average (range; weeks)	37 (26–39)	34 (27–36)	<0.001
Birth weight – average (range; grams)	2224 g (700–2490 g)	2133 g (1020–2490 g)	0.052
male (%): female (%)	26, 40 (39%: 61%)	37, 49 (43%: 57%)	0.653
Placental abnormalities	54/66 (82%)	65/86 (76%)	0.355
one abnormality	15/54 (28%)	19/65 (29%)	0.861
>1 abnormality	39/54 (72%)	46/65 (71%)	

SGA – small for gestation

Table 2. *Placental histopathological classification: 2014 Amsterdam Placental Workshop Group criteria.*

		SGA	**non-SGA**	***p* value**
1	Placental vascular processes			
	a. Maternal stromal-vascular lesions			
	I. Developmental	2/66 (3%)	3/86 (4%)	1.000
	II. Malperfusion	21/66 (32%)	25/86 (29%)	0.715
	1) Placental infarction	10/21 (48%)	12/25 (48%)	0.979
	2) Syncytial knots	10/21 (48%)	6/25 (24%)	0.094
	3) Distal villous hypoplasia	2/21 (10%)	6/25 (8%)	0.260
	4) Fibrin deposition	0	2/25 (8%)	0.493
	III. Loss of integrity	6/66 (9%)	10/86 (12%)	0.613
	b. Fetal stromal-vascular lesions			
	I. Developmental	3/66 (5%)	1/86 (1%)	0.580
	II. Malperfusion	31/66 (47%)	32/86 (37%)	0.226
	1) Intervillous fibrin deposit	8/31 (26%)	1/32 (3%)	0.013
	2) Intervillous thrombus	5/31 (16%)	8/32 (25%)	0.384
	3) Dystrophic calcification	12/31 (39%)	8/32 (25%)	0.243
	III. Loss of integrity	2/66 (3%)	0	0.187
2	Placental inflammatory-immune processes	8/66 (12%)	21/86 (24%)	0.108
3	Other placental processes			
	a. Abnormal cord insertion	5/66 (8%)	6/86 (7%)	0.888
	b. Single umbilical artery	2/66 (3%)	3/86 (4%)	1.000
	c. Small placental weight	23/66 (35%)	14/86 (16%)	0.008
	d. Large placental weight	0	4/86 (5%)	0.133

4. Discussion

Placental histopathology is integral to diagnosis and management in obstetric and neonatal care [13, 14]. However, the discretionary logistics and costs of placental storage and histopathological examination places a burden on the healthcare system, which limits the number of placentas clinicians send to the pathologists. At the Mater Hospital there was no provision for routine storage of the placenta and the decision to order placental histopathological examination was by the clinician on a case-by-case basis. However, in the case of an obvious risk factor, such as low birth weight, preterm delivery, multiple births etc., a higher number of placental histopathology tests were ordered, suggesting cases were missed if there wasn't an apparent risk factor.

The placental histopathological examination was much higher for the LBW infants compared to overall infants (59% versus 8%). Low birth weight could be due to prematurity or growth retardation, or both. Placental analysis was reported separately for SGA and non-SGA LBW infants because growth-retarded infants have a worse prognosis due to poor catch-up growth rate [15]. Incidentally there were more preterm infants in the non-SGA group ($p<0.001$).

Placental vascular malperfusion was the most common placental histopathological abnormality in both groups. Small for gestation and non-SGA infants had similar placental histopathological abnormality, except that intervillous fibrin deposit was more common in the SGA group ($p=0.013$), suggesting increased placental vascular flow abnormality as one of the causes of growth retardation [16]. Likewise, more SGA infants had smaller placental weight compared to non-SGA infants ($p=0.008$) [17, 18].

The limitations of this study include an inherent selection bias, as the request for placental examination was based on individual clinician discretion rather than on standardised criteria. Another limitation was that the placental histopathology report did not precisely follow the 2014 Amsterdam Placental Workshop Group criteria classification system, which left the interpretation open to the clinicians.

The results of this study led to significant knowledge translation strategies and practice change being considered at

the Mater Hospital in Sydney. This includes developing a placental storage and management policy that outlines specific criteria for ordering placental pathological examination. In addition, the hospital is considering routine storage of placentas for 48 hours, which is particularly important in neonatal sepsis as it allows the placenta to be sent for histopathological examination, to explore the possibility of chorioamnionitis.

5. Conclusion

Information regarding placental abnormality could be a missing link in neonatal management. Therefore, placental histopathological examination should be included as standard practice where clinically indicated.

This study was the subject of a quality improvement project that aimed to improve the incidence of placental examination. The next step in continuous quality improvement would be to devise and implement a standard placental histopathology report, to facilitate correct interpretation and clinical application of the placental histopathological findings by the clinician.

Conflict of Interest

The authors have no conflicts of interest to disclose.

Financial Disclosure

There are no financial relationships relevant to this article to disclose.

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