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Original Research Article

Insights into Placental Pathology: Analyzing Patterns and Fetal Outcomes in 205 Livebirths at Bugando Medical Centre, Mwanza, Tanzania

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Abstract: ***Background*:** The placenta facilitates vital nutrient exchange between fetus and mother, offering insights into fetal and maternal health. Despite its significance, research on placental histopathology in Tanzania is scarce. This study investigates placental features, maternal factors, and their impact on fetal outcomes at Bugando Medical Centre from January to May 2022. ***Methods*:** This 5-month cohort study included 205 mothers delivering at BMC. Fetal outcomes were evaluated at birth and after seven days, with maternal characteristics recorded at delivery. Participants were from the twenty-eighth week of gestation, excluding those with intrauterine fetal death or multiple pregnancies. Data on placental histology, maternal factors, and fetal outcomes were collected systematically, while statistical analysis employed STATA version 15, utilizing descriptive statistics. ***Results*:** In this study of 205 placentas, participants had a median age of 29 years and a mean gestational age of 38 weeks. Histopathological patterns were present in 61% of placentas, with acute inflammation (22%) and maternal vascular malperfusion (20.8%) being most common. Favorable outcomes were observed in 81% of newborns, while 19% experienced poor outcomes, including 1.9% early neonatal deaths. Most placental lesions were mild (53.6%), with severe pathology in 2.9% of cases. Acute inflammation correlated with various admission reasons, especially neonatal sepsis (60%). Maternal vascular lesions were associated with prematurity (63.6%) and birth asphyxia (40%). Chronic inflammation was more prevalent among low-birth-weight infants (18.8%), while very low birth weight was common in cases of maternal vascular lesions (68.8%). ***Conclusion*:** The majority of placentas showed normal or mild pathology, associated with positive fetal outcomes. Further research is needed to understand placental changes and their impact on maternal-fetal health.

Keywords: Placental histopathology, placental patterns, livebirths, fetal outcomes.

INTRODUCTION

The placenta is a crucial organ that plays a significant role in fetal development and pregnancy outcomes. It functions as the interface between the mother and the fetus, facilitating the transfer of nutrients, gases, and waste products necessary for optimal fetal growth and development [1]. Abnormal placental development and function can have immediate consequences on the outcome of a pregnancy and influence the lifelong health of the offspring [2]. The placenta also serves as a mastermind behind different fetal and maternal processes, with its rapid growth and pleiotropic functions extending beyond pregnancy to fetal programming before birth [3]. Compromised placental function can lead to pregnancy complications such as miscarriages, pre-eclampsia, fetal growth restriction, and poor perinatal outcomes [2]. Therefore, understanding the molecular processes governing

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placental development and function is crucial for pregnancy outcomes and lifelong health span [4].

The pathological examination of the placenta is highly useful in providing valuable information to obstetricians, neonatologists, pediatricians, and families, explaining adverse outcomes, managing subsequent pregnancies, and assessing newborn risk for short- or long-term sequelae [2]. Placental examination can aid in diagnosing conditions such as chorioamnionitis and fetal growth restriction, which are associated with adverse outcomes and high disease-related morbidity in children [5]. Additionally, placental examination can provide important information about the effect of maternal abnormalities on the placenta, the cause of preterm delivery, fetal growth restriction, or fetal neurodevelopmental damage [6]. Furthermore, it has been shown that placental examination can significantly contribute to determining the cause of death in perinatal cases, and can help in planning and more effective prenatal monitoring of future pregnancies [7]. Overall, the clinical utility of placental examination is recognized, and there is a need for increased awareness and conformity to guidelines to improve its application for better patient care [8].

The major placental pathological patterns known to cause fetal compromise in livebirths include uteroplacental vascular lesions, chronic inflammation, coagulation, maternal vascular mal-perfusion, acute and chronic inflammation, fetal vascular mal-perfusion, and maternal vascular mal-perfusion [9, 10]. These patterns have been associated with adverse birth outcomes, such as preterm birth, fetal growth restriction, and neonatal encephalopathy [9]. It is important to note that there is no single uteroplacental or villous lesion that results in fetal growth restriction, but rather the accumulation of placental injury over time [11]. Additionally, the occurrence of placental pathologies varies with gestational age, and their clinical manifestations vary during pregnancy [10]. Further research is needed to understand the causal pathways by which placental histopathology is translated into fetal compromise and its attendant neonatal and pediatric sequelae [11].

Neonatal deaths due to placental pathology in Tanzania are a significant concern, with studies indicating a potential association between placental pathologies and adverse perinatal outcomes [12]. Placental pathologies such as fetal thrombotic vasculopathy (FTV) have been linked to adverse outcomes, including stillbirth and low birth weight [13]. Additionally, low placental weight has been associated with an increased risk of adverse perinatal outcomes, including low Apgar scores, neonatal death, respiratory distress, and seizures [14]. Furthermore, inflammatory lesions in the placenta, such as chorioamnionitis, have been linked to fetal and neonatal morbidity and mortality [15]. These findings highlight the importance of understanding and addressing placental pathologies to improve neonatal outcomes in Tanzania. However, it is important to note that while these studies provide valuable insights, further research is needed to confirm and expand upon these associations.

The classification of placental pathology into mild, moderate, and severe categories is based on various criteria, including macroscopic and histological abnormalities, as well as their correlation with clinical outcomes. Macroscopically visible abnormalities of the placenta, such as large haemangioma, can cause complications in the mother, fetus, and neonate, while most histological abnormalities represent reactions to alterations in maternal or fetal blood flow through the placenta [16]. In cases of severe pregnancy complications and thrombophilia, placentas with increased rates of vascular lesions are associated with more severe clinical outcomes, such as lower gestational age at delivery, birth weight, and placental weight [17]. It is crucial to investigate the presence of placental pathology in our local population of women who deliver live births and subsequently encounter fetal complications, in order to ascertain the evidence available.

The rates of early neonatal deaths in Tanzania have been a significant concern. A hospital-based retrospective survey from 2006 to 2015 reported an increase in overall hospital-based neonatal mortality rates, reaching 10.4 deaths per 1000 live births in 2015, with the majority of neonatal deaths (87.5%) occurring in the first week of life [18]. Hence, the primary objective of this study was to identify placental histopathological patterns and their connection with adverse fetal outcomes during the perinatal period. Understanding these established patterns of fetal outcomes and maternal characteristics can aid in the selective screening of individuals for placental histopathological examination, prompting timely intervention. This approach is crucial for elucidating the underlying causes of poor fetal outcomes attributed to pathology rather than intervention.

METHODS AND MATERIALS

This longitudinal study spanned seven days with a duration of five months, from January 2022 to May 2022. It was carried out at Bugando Medical Centre, encompassing various departments including Obstetrics and Gynecology, the labor ward, neonatology unit, operating theatre, and central pathology laboratory. The neonatal ward consists of both a premature unit and an intensive care unit. Bugando Medical Centre is a tertiary and a teaching hospital for Catholic University of Health and Allied Health Sciences in the Lake Zone, caters to a population of 14 million and averages 400 deliveries per month.

The Obstetrics and Gynecology department comprises the labor ward, postnatal ward, antenatal ward, and general gynecological ward, with a total bed

capacity of 135, including 16 beds for high-dependence units. Additionally, there is one dedicated operating theatre for obstetrics.

Inclusion criteria encompassed women from the twenty-eighth week of gestation with a live fetus who were admitted for labor and delivery, while exclusion criteria comprised cases of intrauterine fetal death and multiple pregnancies. Convenience sampling was employed, resulting in a total of 205 participants included in the final analysis.

Placentas obtained from recruited women underwent meticulous collection and processing in accordance with established protocols and standard operating procedures (SOPs). They were then fixed in neutral buffered formalin (10%) and preserved for a duration of 10 to 14 days. Maternal socio-demographic and clinical data were meticulously recorded using a standardized, pretested questionnaire. Information pertaining to placental histology, maternal factors, and fetal outcomes was systematically gathered utilizing a structured tool. Histological examination of the placenta was conducted by two independent pathologists, who arrived at a consensus regarding the final diagnosis. Statistical analysis was performed using STATA version 15, employing descriptive statistics such as frequency, mean, and standard deviation.Data quality assurance was maintained by adhering strictly to the provided protocol and SOPs.

RESULTS

Out of the initial 224 participants screened for eligibility, 9 were lost to follow-up, and 10 cases had poorly fixed slides. Consequently, a total of 205 participants were included in the final analysis.

Maternal Socio-Demographic and Clinical Characteristics

Among the 205 participants, ages ranged from 14 to 43 years, with the predominant age group falling between 26 and 33 years. The median age was 29 years with a standard deviation of ±4 years. The majority of participants (60%) had a gravida of 2-4. Additionally, 12 participants (5.6%) had a history of previous preterm delivery, while 14 participants (6.8%) had experienced previous prenatal death. Additional maternal demographic details are presented in Table 1.

Table 1: Social demographic characteristics and maternal clinical profile

Variable	Number (205)	Frequency %
Age		
14-19	5	2.44
20-34	163	79.51
>34	37	18.05
Education		
Illiterate	16	7.80
Literate	189	92.20
Occupation		
Small scale farmers	50	24.39
Self-employed	11	4.85
Employee	52	25.36
Housewife	92	45.85
Gravidity		
1	56	27.32%
2-4	123	60%
>4	26	12.68%
Frequency of Antenatal visits		
<4	28	13.66%
≥4	177	86.34%
Mode of delivery		
Vaginal delivery	118	57.56%
Caesarian Section	87	42.44%
Maternal conditions		
Premature rupture of membrane	7	3.41%
Hypertension	17	8.29%
Urinary tract Infection	2	0.98%
Others*	10	4.88%
Normal	168	82.44%
History of preterm delivery		
Yes	12	5.8%
No	193	94.2%
History of perinatal death		
Yes	14	6.8%
No	191	93.2%

*Flue -1, cough -1, sinusitis -2, gastritis -2, anemia -1, vaginal candidiasis -2, diarrhoea -1.

Fetal Outcomes Characteristics

Of the 205 live births, 15.1% of neonates were premature, with 14 (6.8%) being extremely premature, born between 28 and 33 weeks of gestational age. The most frequent reasons for neonatal admission included birth asphyxia (7.3%), prematurity (5.3%), and meconium aspiration (2.1%). Additionally, there were 4 cases (1.9%) of early neonatal death. Further findings are detailed in Table 2.

Table 2: Newborn characteristics

Variable	Number	Percentage
Gestation age at birth		
Preterm (28weeks to 36 weeks)	31	15.1%
Term (≥37 weeks)	174	84.9%
Gestation age		
28-33 weeks	14	6.8%
34-36 weeks	17	8.3%
37-40 weeks	149	72%
>40 weeks	25	12%
Birth weight by clusters		
Normal(≥2.5kg)	173	84.4%
Low birth weight (≥2kg to <2.5kg)	16	7.8%
Very low birth weight (<2kg)	16	7.8%
Neonatal admission diagnosis		
Birth asphyxia	15	7.3%
Prematurity	11	5.3%
Meconium aspiration	6	2.9%
Sepsis	5	2.4%
Not Admitted	168	81.9%
Seventh Day status		
Live	201	98.1%
Death	4	1.9%
Fetal admission to NICU		
Yes	37	19.1%
Not Admitted	168	81.9%

Placental Histopathological Patterns

The most common pathological patterns identified were acute and chronic inflammation, observed in 47 (22.9%) and 21 (10%) cases, respectively. However, the majority of placental lesions were mild in severity, accounting for 110 (53.6%) cases, while 6 (2.9%) were categorized as severe placental pathology. Additional findings are outlined in Table 3.

Table 3: Placental histopathological patterns

Placenta histological patterns.	Number(n)	Percentage (%)
Lesion type		
Acute inflammation	47	22.9%
Chronic infection	21	10.0%
Maternal vascular mal-perfusion	41	20.8%
Fetal vascular mal-perfusion	17	8.3%
No Lesion	79	38.5%
Placenta lesions severity		
Mild	110	53.6%
Moderate	10	4.9%
Severe	6	2.9%
No	79	38.6%
Number of lesions		
No lesion	79	38.5%
Single	107	52%
Mixed	15	7.3%

Placental Histopathological Patterns among Preterm and Term Newborns

There are variations in placental histopathological patterns concerning gestation age, reasons for admission, delivery method, and birth weight. These patterns offer insights into potential relation between placental pathology and various factors impacting neonatal health and delivery outcomes. Acute

inflammation cases were predominant with diverse admission reasons, with the highest percentage noted for neonatal sepsis (60%). Maternal vascular lesions were commonly linked to prematurity (63.6%) and birth asphyxia (40%). Chronic inflammation was highest among infants with low birth weight (3 cases, 18.8%), while very low birth weight was commonly in placental maternal vascular lesions (11 cases, 68.8%). Further details are provided in Table 4.

Table 1: The placental histopathological pattern and fetal outcomes

	*Placental histopathological pattern			
Newborn	**Acute inflammation**	**Chronic inflammation**	**Maternal vascular lesion**	**Fetal vascular lesion**
Gestation age				
28-33 weeks	0	0	9(64.3%)	4(28.6%)
34- 36 weeks	0	7(41.2%)	6(35.3%)	00
37-40 weeks	42(28.2%)	10(6.7%)	23(15.4%)	12(8.1%)
>40 weeks	5(20.8%)	4(16.7%)	3(12.5%)	1(4.2%)
Admission				
Birth asphyxia	1(6.7%)	1(6.7%)	**6(40%)**	3(20%)
Prematurity	00	00	**7(63.6%)**	2(18%)
meconium	2(33.3%)	00	00	00
neonatal sepsis	**3(60%)**	1(20%)	1(20%)	00
Delivery				
vaginally	40(33.9%)	13(11%)	12(10.2%)	7(5.9%)
Caesarian	7(8.1%)	8(9.2%)	29(33%)	10(11.5%)
Birth weight				
Normal	44(26.3%)	17(10.1%)	27(15%)	13(7.7%)
Low weight	2(12.5%)	**3(18.8%)**	3(18.8%)	3(18.8%)
Very low	1(6.3%)	00	**11(68.8%)**	1(6.3%)

*In this table, 79 placentas with no lesions have been excluded. Additionally, the frequency numbers may vary due to the presence of mixed lesions in some of the placentas.

DISCUSSION

This study at Bugando Medical Centre in Mwanza, Tanzania, examines placental pathology in 205 live births, highlighting acute and chronic inflammation, maternal and fetal vascular mal-perfusion's impact on fetal outcomes. Despite early neonatal deaths typically linked to poor intrapartum monitoring, placental factors also contribute. Intrauterine inflammation severity correlates with higher neonatal morbidity rates, including sepsis, intraventricular hemorrhage, chronic lung disease, and necrotizing enterocolitis [19]. Histological placental examination, especially for mal-perfusion, is vital in understanding pathways to fetal and neonatal deaths, identifying at-risk fetuses, and reducing mortality and premature delivery risks [20]. Encouraging histopathology use in tertiary hospitals can enhance neonatal health understanding in Tanzania and Africa.

Maternal Socio-demographic and Clinical Characteristics:

The maternal demographic profile revealed a diverse range of ages, with the majority falling between 26 and 33 years. Additionally, a significant proportion had multiparity, with a notable history of preterm delivery and perinatal death. These factors may influence placental health and subsequent fetal outcomes. Similarly in previous studies have shown that multiparity and a history of adverse pregnancy outcomes such as preterm delivery and perinatal death can have a significant impact on placental health and subsequent fetal outcomes [21, 22]. Monitoring and managing these risk factors are crucial for improving perinatal outcomes in future pregnancies.

This study highlights the occurrence of preterm births and extremely premature neonates, as well as the common reasons for neonatal admission, such as birth asphyxia, prematurity, and meconium aspiration. Furthermore, the incidence of early neonatal death underscores the importance of understanding placental pathology in predicting and managing adverse fetal outcomes. Previous studies have suggested that understanding placental pathology is crucial for predicting and managing adverse fetal outcomes. Histological examination of the placenta can provide insights into the etiology of preterm birth and neonatal morbidity, guiding interventions to improve neonatal care and outcomes [23-25].

Placental Histopathological Patterns:

Examination uncovered a range of lesions, with acute and chronic inflammation predominating. This likely reflects increased exposure to infectious agents, limited healthcare access, and broader socioeconomic challenges impacting maternal and fetal health outcomes, as seen in prior research [26, 27]. Placental infection is frequently linked to acute placental inflammation, while maternal hypertension is often associated with chronic inflammation of the placenta.

This observation may explain our findings in this study, where 8% of mothers exhibited maternal hypertension and 3% experienced premature rupture of membranes. Studies have shown that a significant proportion of placentas from pregnancies complicated by preterm PROM exhibit acute inflammatory lesions, with varying clinical characteristics and outcomes [28]. Chronic inflammatory lesions of the placenta have been reported in association with maternal hypertension and have been linked to adverse pregnancy outcomes, including fetal growth restriction, preeclampsia, and preterm labor [29]. Nonetheless, most lesions were mild, underscoring the importance of early detection and intervention to mitigate adverse fetal outcomes.

The results of our study reveal notable variations in placental histopathological patterns across different factors such as gestational age, reasons for admission, delivery method, and birth weight. These patterns offer valuable insights into potential relationships between placental pathology and various factors impacting neonatal health and delivery outcomes.

We found that acute inflammation cases were predominant, with diverse reasons for admission, and notably, the highest percentage was common with neonatal sepsis (60%). Maternal vascular lesions, on the other hand, were commonly linked to prematurity (63.6%) and birth asphyxia (40%) as reported in other studies [30] . The relationship between acute inflammation of the placenta and neonatal sepsis is complex and multifactorial. Research suggests that acute inflammation of the placenta such as chorioamnionitis, is indeed associated with neonatal sepsis. Chorioamnionitis is an acute inflammation of the membranes and chorion of the placenta typically due to ascending polymicrobial infection, and it has been linked to significant adverse neonatal outcomes, including severe neonatal sepsis [31].

Furthermore, chronic inflammation was most prevalent among infants with low birth weight, with three cases (18.8%) identified, suggesting a potential association between chronic placental inflammation and low birth weight. Interestingly, very low birth weight infants were frequently seen in placental maternal vascular lesions, with 11 cases (68.8%) observed. These findings highlight the intricate nature of placental pathology and its potential influence on neonatal health and delivery results. They suggest a correlation between placental pathology and early neonatal outcomes, underscoring the importance of comprehensive microscopic evaluations of the placenta in high-risk pregnancies, rather than solely relying on intrapartum monitoring as the primary method of reducing adverse perinatal outcomes. This approach guarantees optimal care for newborns and provides solace to mothers affected by early neonatal deaths, thereby enhancing management and care strategies for both mothers and infants.

Clinical Implications and Future Directions: Understanding the relationship between placental pathology and fetal outcomes is crucial for improving prenatal care and reducing adverse pregnancy outcomes. Further research is warranted to elucidate the underlying mechanisms driving placental pathology and its impact on maternal-fetal health.

Study Strength

The study's strengths lie in its comprehensive examination of a significant number of placentas, providing a robust dataset for analysis. Additionally, the inclusion of detailed demographic and clinical information about the participants, such as age and gestational age, enhances the validity and depth of the findings. Furthermore, the identification of various histopathological patterns and their correlation with fetal outcomes adds valuable insight into the complex dynamics of maternal-fetal health. The study's ability to highlight correlations between specific placental lesions and adverse outcomes contributes to our understanding of potential risk factors. Overall, these strengths bolster the study's credibility and contribute to its significance in advancing knowledge in the field of obstetrics and neonatology.

Study Limitation

This study's single-center design may limit its generalizability, and while a substantial number of placentas were analyzed, a larger sample size would bolster statistical power. There's a possibility of selection bias due to convenience sampling methods, which might not fully represent all demographic groups. Additionally, inconsistencies in interpreting placental histopathology among pathologists could impact the accuracy of lesion identification and classification. Furthermore, the study predominantly emphasizes fetal outcomes, thus offering a less comprehensive evaluation of maternal health.

CONCLUSION AND RECOMMENDATION

The majority of the placentas studied showed either normal histology or only mild pathology, which aligned with positive outcomes for the fetuses. Conversely, only a small fraction of cases led to unfavorable outcomes. While this research provides crucial insights, it underscores the necessity for deeper exploration into the intricate mechanisms driving placental histopathological alterations and how they precisely impact the health of the fetus. This calls for additional studies to unravel the complexities surrounding these changes and their implications for maternal-fetal well-being.

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generously volunteered their time to take part in this study.

Authors Contribution

We extend our sincere gratitude to the team members who contributed their expertise and efforts to this research project. NH played a pivotal role in conceptualization, validation, investigation, resource procurement, original draft writing, visualization, and oversaw data collection, analysis, and interpretation. DM provided valuable contributions in writing, reviewing, and editing, along with supervising aspects of the project. RK's insightful reviews and supervision greatly enriched the study. OO and CM were instrumental in investigating and interpreting pathological reports. AH's contributions in validation, resource allocation, and supervision were invaluable. EN significantly contributed to conceptualization, validation, investigation, resource management, visualization, writing, literature review, and data analysis and interpretation, as well as providing supervision throughout the study.

Data and Materials Availability

The dataset utilized and/or analyzed during the present study are available upon request from the corresponding author.

Privacy and Ethical Considerations

This study received approval from the joint review board of the Catholic University of Health and Allied Sciences and Bugando Medical Centre, with clearance permit number CREC/516/2022. Additionally, permission was obtained from hospital management. All study participants provided informed consent, and data extraction and analysis adhered meticulously to relevant guidelines and regulations. Robust anonymization measures were diligently implemented to ensure confidentiality and privacy.

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