Maternal Age as a Determinant of Placental Morphology and Morphometry at Term Pregnancy: A Cross-sectional Study of Selected Hospitals in Rivers State, Southern Nigeria

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Abstract
The placenta which is a crucial intermediary in maternal-fetal exchanges, undergoes intricate structural changes throughout gestation, culminating in its fully developed form at term. The potential impact of maternal age on pregnancy and fetal outcomes has generated interest. This study aimed to investigate the intricate relationships between maternal age, and placental morphology and morphometry at term pregnancy. This study was a hospital-based, cross-sectional study with a systematic sampling technique, which meticulously collected and examined 250 placentae postpartum. Rigorous cleansing under running water preceded comprehensive assessments and precise measurements. Detailed maternal histories were obtained to facilitate comprehensive contextual analysis. Descriptive statistics (frequency and percentage) were complemented by inferential analyses (ANOVA and Pearson correlation), with significance level set at \( p < 0.05 \). Among the reviewed placentae \( (n=250) \), statistically significant relationships exist between maternal age and some placental parameters. Notably, maternal age exhibited positive associations with placental thickness \( (p=0.048) \), placental weight \( (p=0.014) \), and the number of cotyledons \( (p=0.028) \). However, no statistically significant relationships were identified between maternal age and placental shape \( (p=0.977) \) or placental diameter \( (p=0.070) \). Maternal age significantly influences pregnancy outcomes. Maternal age affects placental morphometry more than placental morphology.

Introduction
Gametes are ova and sperm cells which are haploid and have one copy of each type of chromosome i.e. 1–22 X or 1–22 Y [27]. The sperm cell must fertilize an ovum \textit{in vivo} or \textit{in vitro} in order for conception (pregnancy) to occur [7]. The influence and effects of hormonal imbalance in females leading to infertility in such females have also been reported in different studies [3, 4]. The placenta, an intricate amalgamation of fetal membrane and maternal uterine tissue (decidua...
basalis), assumes a pivotal role in pregnancy, facilitating vital exchanges between the developing fetus and the maternal environment. This transformation into a functional organ typically occurs around the 13th week of gestation, establishing a dynamic interface crucial for fetal nourishment and waste elimination [40]. Linked to the induction of oxidative stress are major free radicals. Among these major free radicals, superoxide anions, hydroxyl radicals, and hydroperoxyl radicals are of physiological significance. A non-radical of physiological significance is hydrogen peroxide [5, 10, 26, 43]. Characterized by its discoid appearance, the placenta exhibits a complex architecture comprising villous and decidual structures. Notably, it possesses an average diameter of approximately 22cm and a thickness of around 2cm, underscoring its substantial spatial presence within the uterine cavity. Its weight, approximating one-sixth of neonatal birth weight, further emphasizes its significance in maternal-fetal exchanges [12, 38, 41]. While varying in shape, circular or oval configurations predominate at term pregnancy, a reflection of its co-evolution alongside fetal development. As gestation culminates, the placenta transitions from an integral gestational participant to a postpartum entity after the delivery of the fetus [37]. The link between placental anomalies and other systemic disorders, notably metabolic syndrome diseases (MSDs) is still being studied. Gestational diabetes is widely known. MSDs (Hypertension, Adiposity, Diabetes mellitus and Dyslipidemia) are interrelated diseases with very high morbidity and mortality rates [13, 14, 16, 28, 31, 33] and characterized with high levels of blood pressure, glucose and lipid metabolic disorders, asymptomatic hyperuricemia, activation of systemic immune inflammation, fibrogenesis, and contribute to nephropathy [17, 18, 21, 22, 23, 30, 32, 44, 45, 46, 47, 48, 52]. Uremia is also one of the diagnostic clinical pentad for thrombotic thrombocytopenic purpura [25].

MSDs require new and effective treatment options. Dapagliflozin which is a Sodium-Glucose Linked Transporter 2 (SGLT-2) inhibitor and Liraglutide which is a Glucagon-like Peptide 1 Receptor Agonist (GLP-1 RA) have been found to increase the effectiveness of treatment and improve the clinical course of type 2 diabetes mellitus and hypertension in patients with such comorbidities [15, 19, 20, 24, 29, 34, 49, 50, 51]. It has also been reported that coconut water has hepatorenal protective functions against alloxan-induced type 1 diabetes mellitus [11]. Maternal age, a recognized predictor of pregnancy outcomes, introduces intriguing complexities into the realm of placental dynamics. Existing research has unveiled divergent patterns of placental weight across different age groups. Specifically, investigations have documented reduced placental weight among younger parturients (aged 19 years and below), juxtaposed against elevated weight among those aged 30-35 years [6]. Given the placenta's capacity to mirror intrauterine events, this principle extends to encompass maternal age, potentially influencing its structural characteristics [9].

In this context, the aim of this study was to assess the relationship between maternal age and placental morphology and morphometry at term pregnancy. Through a comprehensive analytical approach, the role of maternal age as a determinant shaping placental structure and function will be studied.

Materials and Methods

Study Design

A hospital-based, descriptive, cross sectional study design was employed.

Study Population

The study population comprised of mothers of term neonates delivered in the facilities listed below within the study period.

Sample Size

The study sample size was derived using the formula for quantitative variables [36].

\[
n = \frac{z^2 s^2}{d^2}
\]  

Where \( n \) = the desired sample size when total population >10,000  
\( z \) = the standard normal deviate set at 1.96 which corresponds to a 95% confidence level.  
\( s \) = standard deviation of outcome variable from a similar study; standard deviation of placental weight among term neonates in Nigeria was 0.084kg [2].  
\( d \) = degree of accuracy desired, set at 0.01.

\[
n = \frac{1.96^2 \times 0.084^2}{0.01^2}
\]

\[
n = 0.0271
\]

\[
n = 0.00001
\]

\[
n = 271
\]

Allowance for non-response of 10% = \( \frac{n}{1-0.10} \)

Where \( n \) = minimum sample size (271)  
Non-response = 10% (0.1)

Thus, adjusted sample size = 301

Adjustment for population <10,000 using finite population correction

\[
n = \frac{n}{(1+n/N)}
\]

Where:
n = sample size determined when total population is >10,000 = 301
N = size of population from which sample is to be selected = 1,500

Adjusted sample size = \[\frac{301}{\left(\frac{14.400}{1500}\right)}\] = 250

Hence final sample size of 250 placentae were sampled in this study.

**Sampling Technique**

Proportional size allocation was used to determine the number of parturients to be sampled from each study center for effective representation. A systematic random sampling method which required a sampling interval was employed. The sampling interval was obtained by dividing the estimated number of parturients in the facility within the study period of three months by the size of the sample.

Proportional size allocation:

\[\frac{x_i}{\sum x_i} \times n\] (3)

Where \(n\) is sample size (250)

\(x_i\) = number of term deliveries for 3 months data collection period at the facility

Rivers State University Teaching Hospital: \(240 = \frac{240}{792} \times 250 = 76\)

Obio Cottage Hospital: \(480 = \frac{480}{792} \times 250 = 152\)

General Hospital, Omoku: \(72 = \frac{72}{792} \times 250 = 22\)

Sampling interval = \(\frac{x_i}{n}\)

Rivers State University Teaching Hospital = \(\frac{240}{76} = 3.2 \sim 3\)

Obio Cottage Hospital = \(\frac{480}{152} = 3.2 \sim 3\)

General Hospital, Omoku = \(\frac{72}{22} = 3.3 \sim 3\)

The sampling interval of three (3) for each center was therefore deduced. Hence, every 3rd trimester parturient was sampled. The random start was selected by simple random sampling via balloting after which the sampling interval was followed as with systematic random sampling technique.

**Nature/Source of Data**

The study involved primary data collection. Information was collected directly from each parturient and her placenta was assessed immediately after delivery.

**Methods of Data Collection**

Samples were collected immediately after delivery, washed under running water and examined for completeness. The attached umbilical cord was cut leaving a stump of about 5cm from its insertion. Relevant maternal history was recorded. The following morphological features of placenta were observed and recorded:

1. **Shape**: By inspection.

2. **Number of cotyledons**: By inspection and palpation. The placenta was put on a flat tray with the maternal surface facing upward; then, a gentle pressure was applied on the center of the fetal surface to make the cotyledons visible. Counting was done from end to end. The total numbers of cotyledons were recorded.

3. **Cord attachment**: By inspection and palpation. The placenta was placed on a flat tray with the fetal surface facing upward. The cord attachment was observed and recorded.

4. **Thickness**: The toothpick method was used [1]. A toothpick was inserted through the placenta and measured at five points on each placenta to the nearest centimeter. Each placenta was placed on a flat tray on the fetal surface and divided arbitrarily into three zones by drawing two circles on the fetal surface. These circles cut the radius of the placenta into three equal parts. One measurement was taken from the middle of the central zone while two measurements were taken from the middle zone and another two from the peripheral zone. The mean of all five measurements were calculated and considered the thickness of the placenta.

5. **Weight**: After trimming with running water, the placenta was placed on a sensitive weighing scale with readings taken in kilograms.

6. **Diameter**: The placenta was placed on a flat tray and measured in three planes with a plastic meter rule. The mean of the three planes was considered the diameter of the placenta.

**Data Analysis**

Collected data was analyzed using Statistical Package for Social Sciences (SPSS) version 23. Tables and graphs were used for data presentations as appropriate. SPSS ANOVA was used to assess maternal age and placental shape. Correlation analysis was employed in investigating the relationship between maternal age and placental features. Confidence level was set at 95% and statistical significance was set at \(p<0.05\).

**Ethical Considerations**

Approval for this study was sought from the Research and Ethics Committee of the University of Port Harcourt. Clearance was also sought from Obio Cottage Hospital, Rumubiakani and Rivers State Hospitals Management Board. Approvals were obtained prior to commencement of the study. Written informed consent was obtained from the mothers of the neonates before their inclusion in the study. Participation in the study was voluntary and non-participation in the study did not alter their medical care or treatment. Anonymity was maintained by using research numbers rather than names. Data obtained was held in confidence in keeping with ethical principles.
Results

Table 1 presents the distribution of placental shapes among different maternal age groups. Fisher’s exact test revealed no statistically significant relationship between maternal age and placental shape ($p=0.977$).

<table>
<thead>
<tr>
<th>Maternal Age category</th>
<th>Round n (%)</th>
<th>Oval n (%)</th>
<th>Triangular n (%)</th>
<th>Irregular n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 years</td>
<td>6 (66.7)</td>
<td>3 (33.3)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>9 (100.0)</td>
</tr>
<tr>
<td>20 – 24 years</td>
<td>10 (50.0)</td>
<td>10 (50.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>20 (100.0)</td>
</tr>
<tr>
<td>25 – 29 years</td>
<td>42 (56.0)</td>
<td>29 (38.7)</td>
<td>2 (2.7)</td>
<td>2 (2.7)</td>
<td>75 (100.0)</td>
</tr>
<tr>
<td>30 – 34 years</td>
<td>47 (51.1)</td>
<td>42 (45.7)</td>
<td>2 (2.2)</td>
<td>1 (1.1)</td>
<td>92 (100.0)</td>
</tr>
<tr>
<td>35 – 39 years</td>
<td>28 (54.9)</td>
<td>23 (45.1)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>51 (100.0)</td>
</tr>
<tr>
<td>≥40 years</td>
<td>2 (66.7)</td>
<td>1 (33.1)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>3 (100.0)</td>
</tr>
<tr>
<td>Total</td>
<td>135 (54.0)</td>
<td>108 (43.2)</td>
<td>4 (1.6)</td>
<td>3 (1.2)</td>
<td>250 (100.0)</td>
</tr>
</tbody>
</table>

Note: Fisher’s exact test = 9.072; $p$-value = 0.977

Table 2: Pearson Correlation Between Maternal Age (in Years) and Placental Features among the Parturients

<table>
<thead>
<tr>
<th>Placental measurements</th>
<th>Age (in years)</th>
<th>Pearson Correlation Co-efficient (r)</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thickness (cm)</td>
<td>0.125</td>
<td>0.048*</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>0.156</td>
<td>0.014*</td>
<td></td>
</tr>
<tr>
<td>Diameter (cm)</td>
<td>0.115</td>
<td>0.070</td>
<td></td>
</tr>
<tr>
<td>Number of cotyledons</td>
<td>0.139</td>
<td>0.028*</td>
<td></td>
</tr>
</tbody>
</table>

Note: * Statistically significant

Table 2 displays the Pearson correlation coefficients and $p$-values indicating the relationships between maternal age and various placental features. Placental thickness, weight, and number of cotyledons demonstrated statistically significant positive linear correlations with maternal age ($p<0.05$), while placental diameter exhibited a positive linear correlation that was not statistically significant ($p=0.070$).
Discussion

This study embarked on assessment of the relationships between maternal age and placental morphology and morphometry using such parameters as placental shape, number of cotyledons, thickness, diameter, and weight. While this study did not reveal statistically significant relationships between maternal age and all placental shape parameters, nonetheless, the results require some contemplation. The absence of such an association suggests that placental shape, an attribute established early in gestation, may remain relatively unaltered by maternal age as pregnancy advances towards term. This intriguing insight into placental form underscores the complexity of its developmental trajectory.

This study unveiled an engrossing and statistically significant positive linear correlation between maternal age and key placental parameters. Specifically, a discernible association was observed between maternal age and placental thickness, a metric intricately linked to nutrient and gas exchange. This finding echoes existing literature and underscores the potential impact of maternal age on orchestrating structural adaptations within the placenta to optimize fetal development [40, 41].

Furthermore, this study revealed an analogous significant positive linear correlation between maternal age and placental weight. This compelling observation hints at a compensatory mechanism wherein the placental weight increases with advanced maternal age. Such augmentation in weight may potentially reflect an adaptive response aimed at accommodating heightened nutrient and oxygen demands crucial for optimal fetal growth. This novel finding emphasizes the nuanced cascade of events influenced by maternal age, thus delineating the intricate relationship between maternal age and placental morphometry [6, 9].

Equally noteworthy is the significant positive linear correlation established between maternal age and the number of cotyledons. This observation suggests that advancing maternal age may confer an increase in cotyledon count, potentially amplifying placental perfusion and optimizing nutrient exchange. The implication of these findings lies in the multifold impact of maternal age on placental adaptations, further highlighting the intricate orchestration of these elements to facilitate fetal growth and development.

However, an important observation from this study is the lack of a statistically significant relationship between maternal age and placental diameter. This intriguing outcome can potentially be attributed to previous reports indicating that placental diameter attains near-maximal dimensions by approximately 20 weeks of gestation, exhibiting limited growth thereafter [8]. As this study concentrated on term placentae, this absence of significant relationship might be anticipated. Moreover, the expanded uterine dimensions associated with advanced maternal age might contribute to the detected positive linear correlations, offering a more accommodating milieu for placental expansion [35].

The conspicuous enhancements in placental morphometry, evident through augmented thickness, weight, and cotyledon counts, could plausibly be attributed to a convergence of factors. It is conceivable that heightened trophoblastic invasion and enhanced

\[
\begin{align*}
\text{Age (in years)} & \\
15 & 20 & 25 & 30 & 35 & 40 & 45 \\
\text{Placental diameter (cm)} & \\
10 & 12 & 14 & 16 & 18 & 20 & 22 & 24 & 26 & 28 & 30 \\
\text{Number of placental cotyledons} & \\
10 & 12 & 14 & 16 & 18 & 20 & 22 & 24 \\
& r = 0.115; \ p\text{-value} = 0.070 \\
& y = 0.0455x + 18.493 \\
& R^2 = 0.0133 \\
& r = 0.139; \ p\text{-value} = 0.028 \\
& y = 0.0574x + 16.016 \\
& R^2 = 0.0194
\end{align*}
\]
placental functionality, characteristics reported to intensify with advancing maternal age, substantiate the observed positive correlations. These physiological adaptations may underscore an adaptive strategy aimed at optimizing fetal nutrient supply and waste elimination [39,42]. The impact of maternal age appears more pronounced on placental morphometry than on placental morphology. Further comprehensive investigations are imperative to unravel the complexities of this intricate relationship, thus contributing to a deeper understanding of placental dynamics and their broader implications.

Conclusion
No statistically significant relationships were identified between maternal age and placental shape (p=0.977) or placental diameter (p=0.070). Maternal age significantly influences pregnancy outcomes. Maternal age affects placental morphometry more than placental morphology. These findings underscore the considerable impact of maternal age on fundamental placental attributes such as thickness, weight, cotyledon count, etc.

Acknowledgments
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Conflict of Interest
Authors declare that they do not have any conflict of interest. This manuscript was written from an original, self-funded, research work and has not been published earlier neither is it under consideration for publication elsewhere.

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