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Placenta Histomorphological Analysis in Women with Polycystic Ovary Syndrome

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Abstract:
The purpose of this research was to examine the effect of low and high body mass index on the materno-placento-fetal features of pregnant women with PCOS using histomorphology. PCOS is a prevalent endocrinopathy that affects women of childbearing age. PCOS and obesity have a number of common symptoms. The purpose of this study was to compare the placental macroscopic or microscopic examination, foetal birth weight or pulse, maternal TSH and Hb level, and other maternoplacento-fetal features between pregnant women with PCOSand those without the condition. The findings show that PCOS placentas vary in size, shape, umbilical cord insertion, fibrosis, hematoma, calcification, and villitis regardless of the mother's body mass index.

1. Introduction

Stien and leventhal syndrome, most commonly known as PCOS, affects 5–20% of reproductive-aged women worldwide. Hyperandrogenism, irregular menstruation, polycystic ovaries, persistent anovulation, and impaired fertility are all symptoms of polycystic ovary syndrome (PCOS), a complicated endocrine condition. The most prevalent endocrine condition in females is polycystic ovary syndrome. Oligomenorrhea or amenorrhea, hirsutism, acne, and rapid hair loss on the scalp are the hallmark symptoms of this disease.[1]

High triglyceride and low high-density lipoprotein (HDL) levels, as well as elevated serum creatinine protein and increasing plasma homocysteine levels, have all been linked to an increased risk of cardiovascular disease in women with polycystic ovary syndrome, according to a number of studies. The syndrome encompasses four different phenotypes, since the current diagnostic criteria necessitate the presence of at least two of these characteristics.hyperandrogenism, oligoanovulation, and polycystic ovary syndrome (i) (complete) Patients with (ii) hyperandrogenism and oligoanovulation polycystic ovarian syndrome, (iii) hyperandrogenism and ovulatory polycystic ovarian syndrome, and (iv) oligoanovulation and nonhydrogenic polycystic ovarian syndrome.

However, PCOS affects pregnant women negatively. Both the mother and the unborn child are at increased risk when the pregnant woman has PCOS. Maternal difficulties include things like high blood pressure throughout pregnancy, miscarriages, preeclampsia, GDM, preterm birth, and difficult caesarean sections. Premature delivery, intrauterine growth restriction (IUGR) - low birth weight infants, and infants born with a high risk of spontaneous admission to the neonatal intensive care unit are all examples of complications that may arise during pregnancy. In

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pregnancy, the placenta plays a crucial function and is considered a highly specialised organ.[2]

Although only present during pregnancy, it plays a critical role in the healthy development of the foetus by ensuring it receives sufficient oxygen and nutrients, eliminating waste products such as carbon dioxide, and shielding the developing embryo from harmful environmental factors such as xenobiotics, infections, and maternal diseases. This dynamic endocrine organ has unparalleled sensitivity to both maternal and foetal stimulation.[3]

Due to the placenta's central role in reflecting changes in maternal and foetal tissues, we utilised a placental sample to examine the effects of PCOS on the placenta and, via it, the foetus. The placenta, as stated by, is a singular component that must be examined in order to probe and appreciate the intrauterine environment. It also keeps track of everything that can have an impact on the pregnancy's outcome. Similarly, suggested looking at the placenta for clues to diagnosis, prognosis, and treatment since it represents maternal and foetal pathophysiology.[4]

Thus, it seems that placental examination may ultimately aid in the creation of a careful technique for the treatment of pregnancies afflicted by polycystic ovary syndrome. Macroscopic and microscopic analyses of placentas from healthy and PCOS pregnancies are used for this purpose.

The placenta plays a critical role in the development of the embryo and the maintenance of the pregnancy. The placenta is essential for the fetus's growth and development within the mother's womb. The researchers wanted to evaluate how placental histological abnormalities and other pregnancy problems fared among women with PCOS. Over the last several decades, the reproductive health of women with PCOS, namely the pregnancy result, has received a great deal of attention from the scientific community.[5]

Seventeen percent to thirty-five percent of reproductive-age women suffer with polycystic ovary syndrome, making it the most common endocrine disorder. Some research suggests that even in the absence of pregnancy, women with polycystic ovary syndrome (PCOS) have a higher risk of metabolic complications. Several recent studies pregnant women with polycystic ovary syndrome had an increased risk of complications including high blood pressure during pregnancy, preeclampsia, gestational diabetes mellitus, and preterm birth, according to a meta-analysis of a small number of studies. Many complications during pregnancy may be traced back to the placenta. Ovarian insufficiency and elevated androgen levels are only two symptoms of polycystic ovary syndrome.[6]

Women of all ages, both during and after childbearing, might be affected by polycystic ovary syndrome (PCOS), which has recently been established as a condition with metabolic difficulties. Macroscopic and microscopic analyses of pregnant women with PCOS or PCOS plus obesity have shown distinct differences in placental morphology. Microscopically, there was no alteration and the pregnancy went well; nevertheless, the placenta of a woman with PCOS weighed less, had less volume, and was smaller than average. Microscopic abnormalities, including chronic villitis and necrosis, were seen in the placentas of women with polycystic ovary syndrome and body mass index in a separate investigation.[7]

2. Material and Methods

A. Altered placentation in polycystic ovary syndrome

A total of 120 placentas from women with PCOS were analyzed in this cross-sectional investigation. Over the period of 35 months, researchers gathered data. Women in the 25–40 age range were selected for the research. The study's sample size was determined to be optimal for its purposes. Pregnant women with polycystic ovary syndrome had their placentas compared to those of obese women of the same age. Sixty patients' medical histories were collected.

During a study period of 35 months, placentas were collected from the OB/GYN department of a university hospital and submitted to the histopathology lab for analysis. Overnight, the placentas sent to the pathology lab were fixed in 10% formalin. Placentas were subjected to a thorough analysis the next day. The placenta was dissected and samples collected from the abnormal areas for standard histopathology analysis. The tissue fragments were treated through various stages of tissue

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processing in an automated tissue processor using graded alcohols to create microscopic slides. Microscopic alterations were seen in the placentas of all 120 women who had their placentas examined to rule out abnormalities.

"ANOVA was utilized to do group comparisons for the statistical analysis, and p values of less than 0.05 were regarded to be significant."

B. Effects of maternal and foetal body mass index in women with polycystic ovary syndrome

Between April 2020 and April 2021, researchers from Institute of Medical Sciences, Lucknow, and General Hospital, Haryana, conducted the retrospective study. The research was given the go light by the university's ethics board. Women with PCOS who wanted to have a family were included in this research. Consent once full disclosure has been acquired in writing. The women's ages ranged from 20 to 35. Women who were already suffering from diabetes, hypertension, or a thyroid condition during pregnancy were also included in this analysis.

Rotterdam requirements were included into PCOS's definition of the ESHRE-ASRM. Normal participants were pregnant ladies who had no problems. The features of women who were obese were then determined by measuring their BMI. According to guidelines established by the World Health Organisation, both overweight and normal weight were specified in pregnant women. Placentas from women who gave birth to a singleton at both were obtained for this research; those who gave birth at term after a healthy pregnancy were included as a comparison group. In this prospective research, 60 women with PCOS and 60 women without PCOS were compared. All individuals had their blood for thyroid stimulating hormone, haemoglobin, and foetal pulse checked before delivery. Then, all babies' weights were recorded just after they were born.

The placenta was removed from the mother as soon as possible after birth, cleaned under running water, labelled, and then preserved in 10% formalin for a night before being utilised in further research. The placenta was analysed both macroscopically and grossly. The placenta was measured for its mass, length, and thickness.

All of the data was recorded and analysed statistically. "The data was shown using a mean and standard deviation format. Bonferroni's "t" test was used to determine whether there was a statistically significant difference between the means of the control and study groups after two-way analysis of variance. If the probability value was less than 0.05, it was deemed significant."

3. Results

A. Altered placentation in polycystic ovary syndrome

Placenta gross anatomy:

One hundred and twenty placentas were submitted to the histology lab, and the results showed that 51 of the women had PCOS alone, whereas 9 had PCOS and a body mass index (BMI) of 25 or higher. The placental gross features of those nine PCOS people are larger in size and have a few patches of necrosis when compared to PCOS patients with BMI less than 25. Large-scale changes highlighted in table.

Table1: Normal and PCOS placental parameters in women with and without a BMI of 25 kg/m2 are compared

Parameters	ControlsBMI <25>25		CasesBMI <25>25		PValue
Placental weight	480+_9.5	493+_8.6	452+_11.6	487+_7.6	P <0.05
Placental length	17.7+_0.3	17.5+_0.3	16.7+_0.4	16.8+_0.2	P <0.05

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Placental width	16.3+_0.4	15.9+_0.4	16.1+_0.9	16+_0.5	P <0.05
Placental thickness	2.3+_0.06	2.2+_0.05	2.7+_0.07	2.7+_0.05	P <0.05

Table2: Placental comparison between normal and PCOS pregnancies with BMI 25 and 25 kg/m2

Variable	**Category**	**Controls -BMI**			**Cases -BMI**		
		N	**<25**	**>25**	**N**	**<25**	**>25**
Placentalposition	Anterior	24	12	12	24	12	12
	Posterior	36	15	21	36	06	30

Table3: Placental comparison between normal and PCOS pregnancies with BMI 25 and 25 kg/m2

Variable	**Category**	**Control-BMI**			**Cases-BMI**		
Placentalshape	Round	36	15	21	25	17	08
	Oval	24	12	12	12	0	12
	Irregular	0	0	0	23	01	22

Structures at the nanoscale: Histological abnormalities in PCOS placentas were seen in all nine cases where the mother had a body mass index (BMI) of 25 or above, but in only 16 of 53 cases when the mother had a BMI of 25 or lower.

Table4: Observing the microscopic placental alterations.

Microscopic changes	**PCOS placentas>25BMI**	**PCOSplacentas <25BMI**
Villousedema	9	2
Fibrinoidnecrosis	9	11
Dialatedblood vessels	9	5

B. Effects of maternal and foetal body mass index in women with polycystic ovary syndrome

Placentas of various shapes and sizes, as well as fibrosis and hematoma for PCOS. Normal placentas have a central umbilical chord, which also show the

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surfaces of the foetus and the mother**.**Evidence of calcification and villitis was observed to be significantly higher in PCOS samples compared to normal placental samples.

"No statistically significant difference was seen between the normal and PCOS groups (P=0.078). There was a statistically significant split between the two BMI groups (25 and >25; P=0.011). No statistically significant relationship could be found (P=0.255) between the groups and BMI." There was no statistically significant difference between the BMI categories among the normal (P=0.292), however there was among those with PCOS (P=0.013). There was no significant difference between the normal and PCOS categories of body mass index (P=0.068 and P=0.603, respectively). This demonstrates that PCOS patients with lower body mass index had smaller placentas.

There was a statistically significant difference between the two groups (normal and PCOS). There was no statistically significant difference in any dimension between the two BMI groups (25 and >25). There was no statistically significant difference between the groups when considering both length and thickness as a function of body mass index. There was no statistically significant difference between the normal and PCOS groups with regard to BMI, and the same was true for the PCOS group. While there is a statistically significant difference between the normal and PCOS BMI categories in terms of thickness (P=0.001), there is no difference in terms of length (P=0.082). This demonstrates that PCOS patients with a higher body mass index had shorter placentas and thicker placentas.

There was a huge disparity (P0.001) between the control and PCOS groups. When comparing the two groups of BMI (25 and >25), there was a significant difference (P=0.036). The interaction between groups and BMI was not statistically significant (P=0.005). Body mass index (BMI) categories did not differ substantially between the normal and the overweight (P=0.589), but they did differ significantly between the overweight and those with polycystic ovary syndrome (PCOS; P=0.001). The group with normal body mass index did not differ from the others (P=0.070), whereas the group with PCOS does (P0.001). BMI was shown to have a positive effect on TSH levels in pregnant women with PCOS.

"It was shown that there were statistically significant differences between the normal and PCOS groups (P=0.018). The difference between the 25 and >25 BMI categories was not statistically significant (P=0.693)." In terms of body mass index, there is a statistically significant split between the groups (P=0.021). When comparing the normal BMI categories to the PCOS BMI categories, no significant difference was found. A statistically significant difference (P=0.004) exists between the normal and PCOS categories of BMI, while no similar difference exists between any of the other BMI categories. Both PCOS and excess weight are associated with decreased Hb levels.

Foetal heart rate did not change significantly between the two groups, but birth weight did (P0.001). Foetal pulse and birth weight were significantly different across the BMI groups. There is a statistically significant difference between the groups while controlling for BMI. Foetal pulse and birth weight did not change significantly between BMI categories in the normal group, but they did in the PCOS group. Foetal pulse and birth weight vary significantly (P0.001) between the normal and overweight/obese BMI categories, however there is no difference between the PCOS and normal BMI categories. This demonstrates that maternal obesity is associated with increased foetal heart rate and foetal weight in PCOS.

Table5: Values are presented as Mean + SE and compared between normal and PCOS in the 25 and > 25 BMI categories.

S. No.	Factors	Weight (g)	Length (cm)	Thickness (cm)	TSH	Fetal birth weight (Kg)	FETAL PULSE	HB (mg/dL)

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	Groups	BMI							
1	Normal	< 25	480.0 + 9.6	17.77 ± 0.3	0.973 ± 0.13	2.3 ± 0.06	2.94 ± 0.06	148.11 ± 1.09	10.15 ± 0.17
1	Normal	< 25	480.0 + 9.6	17.77 ± 0.3	0.973 ± 0.13	2.3 ± 0.06	2.94 ± 0.06	148.11 ± 1.09	10.15 ± 0.17
2	Normal	> 25	493.6 + 8.6	17.54 ± 0.3	0.877 ± 0.11	2.24 ± 0.05	2.92 ± 0.05	150.09 ± 0.99	10.63 ± 0.16
3	PCOS	< 25	452.2 + 11.7	16.72 ± 0.4	1.353 ± 0.16	2.71 ± 0.07	2.43 ± 0.07	154.00 ± 1.34	9.98 ± 0.21
4	PCOS	> 25	487.6 + 7.7	16.63 ± 0.2	2.006 ± 0.10	2.73 ± 0.05	2.95 ± 0.05	157.85 ± 0.87	9.74 ± 0.14
A	Significance within Groups		P = 0.078	P= 0.009	P= 0.001	P= 0.001	P= 0.001	P= 0.096	P=0.018
B	Significance within BMI category		P = 0.011	P= 0.857	P= 0.529	P=0.036	P=0.001	P=0.059	P=0.693
C	Between groups and BMI		P = 0.255	P= 0.609	P= 0.345	P=0.005	P=0.001	P=0.001	P=0.021
D	Significance within Normal: <25&>25		P = 0.292	P= 0.609	P= 0.246	P=0.589	P=0.840	P=0.183	P=0.046
E	Significance within PCOS : < 25 and > 25		P = 0.013	P= 0. 822	P= 0.830	P=0.001	P=0.001	P=0.001	P=0.190
F	Significance within < 25 : Normal and PCOS		P = 0.068	P=0.05 0	P=0.001	P=0.070	P=0.001	P=0.001	P=0.004

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G	Significance within > 25 : Normal and PCOS	P = 0.603	P=0.082	P=0.001	P=0.001	P=0.684	P=0.094	P=0.958

Our research shows that PCOS is associated with problems in the maternal, placental, and foetal compartments regardless of body mass index. Increases in body mass index were also seen to have an impact on normals, although one that was much less compared to the impact on normals with normal BMI. This leads us to the conclusion that PCOS pregnant women should strive to keep their body mass index (BMI) within the healthy range.

4. Discussion

In this study, we compared the macroscopic & microscopic placental features of women with PCOS to those of a healthy, low-risk reference group. Further, a sub-analysis compared PCOS women who had a pregnancy complicated by PIH, PE, or GDM versus those who had a normal delivery. After controlling for potential confounding variables, we discovered that placentas from women with PCOS had a substantially higher frequency of many histological abnormalities compared to the control group. The majority of these variations did not reflect an inherently greater incidence of pregnancy complications among women with PCOS.

Females in the Netherlands have a prevalence of obesity ranging from 10–15%. According to This disparity in BMI may explain why we observed more placental inflammation. To those who share PCOS. Obesity has been demonstrated to alter PCOS symptoms and, by extension, placental features; however, the changes may be too small to be statistically significant in our PCOS sample, which is quite thin.[9]

Through measuring BMI beforehand, macroscopic and microscopic examination of the placenta and umbilical cord, assessment of placental weight, placental length, and placental thickness, assessment of foetal characteristics like foetal pulse and foetal birth weight, and quantification of maternal characteristics like TSH and haemoglobin level, the current study is the first to evaluate the impact of BMI on the materno-placento-fetal characteristics together in PCOS condition.[10-11]

Macroscopic examination of the placenta in PCOS shows abnormalities such as fibrosis, haemorrhage, and eccentric placement of the umbilical cord, and there is no discernible difference in BMI categories between PCOS and normal.[12-13] Similar to how studies have shown that normal mothers' placentas have a central cord insertion and a normal placenta shape, anaemic mothers' placentas have an eccentric cord insertion and an irregular shape intrauterine growth restriction, congenital abnormalities, etc. have all been linked to abnormal umbilical cord insertion. Consistently, we have shown that PCOS people have both low Hb and poor foetal birth weight compared to normal. According to the research there was no statistically significant difference in foetal birth weight between normal of both BMI and PCOS of BMI>25, showing the prevalence of insulin tolerance and the accompanying impact on foetal weight.[14-15]

5. Conclusion

Our current research aimed to better understand the influence of PCOS on the placenta by examining the modifications it causes, and we did so by correlating our findings with maternal and foetal features. Since PCOS and obesity go hand in hand, we aimed to learn how BMI affects placental and maternofetal features in both PCOS and non-PCOS pregnant women. The placental changes and foetal birth weight results in the current research show that pregnant women having PCOS are at the greatest risk of prevailing unfavourable materno-fetal outcomes.

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