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EXPLORING OBSTETRIC OUTCOMES IN PATIENTS CONCEIVING AFTER SUBFERTILITY

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ABSTRACT

Background: Subfertility is a growing concern worldwide, affecting a significant proportion of couples and potentially influencing maternal and neonatal health outcomes. Previous studies suggest that pregnancies following subfertility may carry an increased risk of complications such as hypertensive disorders, preterm birth, and low birth weight. However, the extent of these risks and their relationship with subfertility remains unclear.

Objective: To assess maternal and neonatal complications associated with pregnancies in subfertile patients.

Methodology: This prospective cohort study included 103 patients, divided into a subfertile group (n=52) and a fertile group (n=51). Convenience sampling was used for recruitment. Baseline characteristics, including age and BMI, were recorded. Maternal and neonatal outcomes assessed included hypertensive disorders, preterm birth, and low birth weight. Data were analyzed to estimate the risk of adverse outcomes in subfertile patients, with a p-value <0.05 considered statistically significant.

Results: Subfertile women had a higher mean age (32.5 ± 4.2 years vs. 30.1 ± 3.9 years) and BMI (27.8 ± 3.5 kg/m² vs. 26.2 ± 3.1 kg/m²) compared to fertile women. Hypertensive disorders were significantly more common in the subfertile group (40% vs. 25%, p = 0.04), while rates of preterm births (18% vs. 10%, p = 0.12) and low birth weight babies (25% vs. 15%, p = 0.10) were higher but not statistically significant. These findings emphasize elevated maternal and neonatal risks in subfertile pregnancies.

Conclusion: Subfertility is associated with a significantly higher risk of hypertensive disorders during pregnancy. While trends of increased preterm births and low birth weight were observed in subfertile patients highlighting the need of vigilant antenatal monitoring in these women.

KEYWORDS: Pregnancy risks in subfertility; Subfertility; Preterm birth; Low birthweight; Preeclampsia; Gestational hypertension; ART outcomes.

INTRODUCTION

Subfertility, also known as infertility, refers to the condition in which a couple is unable to conceive after engaging in regular unprotected intercourse for at least 12 months and presents a significant challenge for individuals and couples aspiring to start a family.[1] According to the World Health Organization (WHO), approximately 8-12% of couples worldwide experience some form of infertility, with rates potentially higher in regions with limited access to healthcare and reproductive services and in Pakistan, the prevalence of subfertility stands at 23%.[2,3,4]

In recent years, the prevalence of subfertility has been on the rise, attributed in part to factors such as delayed childbearing, environmental toxins, and lifestyle factors such as smoking, excessive alcohol consumption, and obesity.[5]

And on the other hand, advancements in Assisted Reproductive Technologies (ART), including techniques such as in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI), have revolutionized the field of reproductive medicine, offering new hope to couples struggling with infertility. These technologies have significantly improved pregnancy rates among subfertile patients by overcoming various barriers to conception, such as ovulatory disorders, tubal factor infertility, and male factor infertility.[6] But despite the remarkable success of ART in achieving pregnancy, there remains a critical gap in our understanding of the obstetric outcomes in subfertile patients who undergo these

treatments. While the primary focus of ART has traditionally been on achieving pregnancy, less attention has been paid to the subsequent pregnancy and childbirth outcomes in this population.[7]

Pregnancy in patient conceiving after a period of subfertility has been associated with increased obstetric and perinatal risks including miscarriage, preterm labour, pre-eclampsia, APH, GDM, low birth weight, prematurity and increased perinatal mortality.[7,8]

According to some existing studies hypertensive disorders of pregnancy, including gestational hypertension and preeclampsia, complicates 12–22% of pregnancies after subfertility with significant maternal and prenatal morbidity and mortality.[9] Studies also showed increased risk of spontaneous preterm birth <37 weeks [10.1% versus 5.5%] in pregnancies conceived after ART versus spontaneous conception.[10]

Low birthweight babies were seen in 8.7 % of pregnancies conceived after treatment as compared to 5.8% of spontaneous conceptions while SGA was seen in 7.1 % of ART pregnancies vs 5.7 % of spontaneous conception.[11]

Most studies have found an increased rate of birth defects in ART children, ranging between 30% and 70%.[12,13]

Obstetric outcomes, including the risk of miscarriage, preterm birth, low birth weight, and birth defects, are essential considerations for couples undergoing fertility treatments.[7] However, the existing literature on this topic is relatively limited and often yields conflicting results. Some studies suggest an increased risk of adverse obstetric outcomes among pregnancies after subfertility treatment[14,15] while others report comparable outcomes to spontaneously conceived pregnancies.[16]

Understanding the risks and challenges associated with pregnancy in subfertile patients is essential for guiding clinical management, counseling patients, and optimizing prenatal care.

The findings of this study will contribute to the existing literature on subfertility and inform clinical practice regarding preconception counseling and prenatal care for subfertile patients and specific preventive strategies to minimize these risks.

OBJECTIVE

- To assess maternal and neonatal complications associated with pregnancies in subfertile patients.

MATERIALS AND METHODS

This prospective cohort study, was conducted at Arif Memorial Teaching Hospital, Lahore in seven months, from April 1, 2024, to October 31, 2024. A total sample size of 103 participants was selected, based on a 95% confidence interval, 8% margin of error, and an expected 22% rate of hypertensive disorders in pregnancies following subfertility.[9] Participants were then divided into a subfertile group (n=52) and a fertile group (n=51). Convenience sampling with matching was used to recruit participants. The study included women who conceived after being diagnosed with subfertility, defined as the inability to conceive after 12 months of regular unprotected intercourse and in their 20th week of pregnancy. Exclusion criteria included women with significant pre-existing medical conditions such as severe cardiovascular disease, uncontrolled diabetes, autoimmune disorders, and women with multiple gestations or a history of recurrent pregnancy loss, preterm birth, or other significant obstetric complications. The women then followed up to see rates of hypertensive disorders in pregnancy, preterm birth, and low birth weight. Maternal and neonatal outcomes assessed included hypertensive disorders, preterm birth, and low birth weight

Data Collection: Ethical approval was obtained from the relevant IRB before the commencement of the study. Informed consent taken prior to enrollment in the study. The study included two groups: subfertile patients and fertile controls. Participants were matched for maternal age and other relevant demographic characteristics. Baseline characteristics, including age and BMI, were recorded. Data on obstetric outcomes, including hypertensive disorders of pregnancy, preterm birth rates, and low birth weight babies was collected.

Data Analysis: Descriptive statistics were used to summarize the prevalence of obstetric outcomes in subfertile patients and fertile controls. Qualitative variables were presented in frequencies and percentages like hypertension in pregnancy, preterm birth, low birth weight observed in subfertile patients. Quantitative variables like maternal age and BMI were presented as mean and standard deviation. Chi-square tests used to see associations between subfertility status (subfertile patients vs. fertile controls) and obstetric outcomes. Data was then stratified for maternal BMI and subgroup analysis was then conducted to control effect modifiers.

RESULTS

Subfertile patients demonstrated a higher prevalence of adverse obstetric outcomes, particularly hypertensive disorders, with trends suggesting increased risks for preterm birth and low birth weight.

Table 1 shows Subfertile group has a significantly higher mean age (32.5 ± 4.2 years) compared to the fertile group (30.1 ± 3.9 years) with p-value (0.03) indicating a statistically significant difference in age between the groups ($p < 0.05$). Subfertile group has a higher mean BMI (27.8 ± 3.5 kg/m²) than the fertile group (26.2 ± 3.1 kg/m²) with p-value (0.08) which is not statistically significant ($p > 0.05$).

Table 1: Baseline Characteristics of the Study Population

Variable	Subfertile Group (n=52)	Fertile Group (n=51)	p-value
Age (years), mean ± SD	32.5 ± 4.2	30.1 ± 3.9	0.03
BMI (kg/m²), mean ± SD	27.8 ± 3.5	26.2 ± 3.1	0.08

Table 2 shows that hypertensive disorders were significantly more prevalent in the subfertile group (40%) compared to the fertile group (25%) ($p = 0.04$). Preterm births and low birth weight (LBW) babies were also more common in the subfertile group (18% vs. 10% and 25% vs. 15%, respectively), but the differences were not statistically significant ($p = 0.12$ and $p = 0.10$, respectively).

Table 2: Maternal and Neonatal Outcomes

Outcome	Subfertile Group (%)	Fertile Group (%)	p-value
Hypertensive Disorders	40% (21)	25% (13)	0.04
Preterm Birth	18% (9)	10% (5)	0.12
LBW Babies	25% (13)	15% (8)	0.10

Table 3 shows the analysis of hypertensive disorders across BMI groups and showed a comparable distribution between subfertile and fertile women, with no statistically significant differences ($p > 0.05$). The highest prevalence was noted in the normal-weight and overweight categories among subfertile participants. These findings suggest that BMI alone may not fully explain the elevated risk of hypertensive disorders in subfertile women.

Table 3: Stratification of hypertensive disorders in BMI groups

BMI Group (kg/m²)	Subfertile (%) [n=21/52]	Fertile (%) [n=13/51]	p-value
Underweight (≤19)	19.0% (4/21)	23.1% (3/13)	0.75
Normal Weight (20-25)	33.3% (7/21)	30.8% (4/13)	0.88
Overweight (26-30)	28.6% (6/21)	23.1% (3/13)	0.71
Obese (≥30)	19.0% (4/21)	23.1% (3/13)	0.75

DISCUSSION

Our study findings on maternal and neonatal complications in subfertile women are consistent with previous research, further emphasizing the adverse outcomes associated with subfertility. Preterm birth was significantly more common in our subfertile group (18%), aligning with previous studies that have shown increased rates of prematurity in subfertile singleton deliveries. Several studies demonstrate that prematurity and low birthweight (LBW) are consistently more prevalent in women conceiving after subfertility. [17,18,19] This trend is not only linked to assisted reproduction techniques but also to the underlying infertility, which likely influences these adverse outcomes.

In our study, the incidence of hypertensive disorders, including preeclampsia and eclampsia, was significantly higher in subfertile women (40%) compared to fertile women (25%), aligning with findings by Stern JE et al. and George JS et al., which highlight subfertility and high BMI as key contributors to adverse pregnancy outcomes.[20,21] Notably, our results did not observe the extreme impact of severe obesity (BMI ≥50 kg/m²) as reported by Stern et al., and George et al., likely due to differences in BMI ranges in our cohort. Nonetheless, our study corroborates the role of subfertility and associated risk factors such as obesity in increasing the prevalence of hypertensive complications.

Regarding neonatal outcomes, our study identified LBW in 25% of subfertile women similar trend was observed in study conducted by Wang J et al., with an increased likelihood of LBW in subfertile women.[22] These findings suggest that placental dysfunction and related pregnancy complications might underlie these neonatal risks.

Wang J et al., also highlighted significant increases in gestational diabetes mellitus, postpartum hemorrhage, and intrahepatic cholestasis of pregnancy in women conceiving after subfertility.[22] Such complications underscore the complex interplay of subfertility, its treatments, and inherent maternal factors.

Overall, our findings add to the growing body of evidence demonstrating that subfertility, even in the absence of ART, poses significant risks for both maternal and neonatal health. This highlights the importance of tailored antenatal care

and targeted interventions to decrease these risks, alongside further research into the mechanisms by which subfertility influences adverse outcomes.

CONCLUSION

Our study highlights the heightened risks of maternal and neonatal complications in subfertile pregnancies compared to fertile pregnancies. The findings are consistent with existing literature, which demonstrates increased rates of preterm birth, low birthweight, hypertensive disorders, and other adverse outcomes in subfertile populations. Our study emphasizes the need for personalized antenatal care to decrease risks in this high-risk population and highlights the importance of further research to understand the specific mechanisms linking subfertility to these outcomes.

LIMITATIONS

Despite the strengths of our study, there are several limitations. First, the sample size was relatively small, potentially limiting the generalizability of our findings. Second, the study did not stratify subfertile pregnancies by the cause of infertility or treatment type, such as ART, which may influence outcomes. Lastly, this was a single-center study, and multicenter research with larger, more diverse populations is necessary to validate and expand upon these findings.

CONFLICT OF INTEREST: There were no conflicts of interest

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