

Medical Science

To Cite:

Młynarska J, Górny A, Chwiejczak J, Kościan J, Szczerkowska K, Wójcik A, Obrębski M, Seroka A, Mitkowska M, Rybicka M. Anorexia Nervosa and pregnancy complications: Review. *Medical Science* 2024; 28: e34ms3334

doi: <https://doi.org/10.54905/disssi.v28i146.e34ms3334>

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Peer-Review History

Received: 08 February 2024

Reviewed & Revised: 12/February/2024 to 18/April/2024

Accepted: 22 April 2024

Published: 27 April 2024

Peer-review Method

External peer-review was done through double-blind method.

Medical Science

pISSN 2321-7359; eISSN 2321-7367



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Anorexia Nervosa and pregnancy complications: Review

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ABSTRACT

The substantial interplay between anorexia nervosa (AN) and pregnancy, both psychologically and physiologically, exerts significant impacts on the health of both the mother and the baby. As AN is the most prevalent eating disorder globally, particularly impacting young women of childbearing age, numerous studies have investigated the correlation between maternal health events and outcomes for newborns during pregnancy, childbirth, and the postpartum period. This review aims to discuss the potential risks of AN-affected pregnancies to both the mother and the baby, along with the prevalence of the associated health problems, referring to recent studies. The analysis concentrated on studies that included women either currently experiencing an active stage of the disease or those with a history of AN.

Keywords: Anorexia nervosa; pregnancy; labor complications; postnatal period

1. INTRODUCTION

Anorexia nervosa DSM-5 criteria include restriction of caloric intake, leading to significantly low body weight, feeling fear of weight gain or becoming fat, ongoing behavior that interferes with weight gaining, being disturbed by one's body weight or shape, self-esteem influenced by body mass or shape, or persistent lack of recognition of the seriousness of low body weight (Substance and Mental Health Services, 2016). The lifetime prevalence of AN in women is 0.8-6.3% (Silén and Keski-Rahkonen, 2022). The disease mainly affects young women of childbearing age (Linna et al., 2013). It is a significant issue, affecting 1% of women in the reproduction age group (Smink et al., 2012; Pan et al., 2022).

The peak prevalence of AN among females occurs around the age of 15 (Van-Eeden et al., 2021). Young women aged 15-19 years make up approximately 40% of all cases. The incidence rate remains high in 20-24 years and 25-29 years

groups (Van-Son et al., 2006). According to one of the latest meta-analyses investigating the eating disorders prevalence and related factors in pregnancy, the incidence of AN during pregnancy demonstrated a notable rise in statistical significance compared to the period before conception (Çiçekoğlu-Öztürk and Taştekin-Ouyaba, 2024). The prognosis for the AN patients remains poor. Approximately 20% of them develop a chronic course of the disease (Arcelus et al., 2011).

The mortality rate of AN is the highest among all mental disorders (Harris and Barraclough, 1998). According to the recent meta-analysis of 36 studies, the mortality rate of AN patients was 5.1 per 1000 person-years (Arcelus et al., 2011). The studies indicate, that approximately 15% of pregnant women are estimated to have experienced an eating disorder at some stage in their lives, while around 5% are affected by an eating disorder during pregnancy (Bye et al., 2021). As AN is a significant health concern within the reproductive population, our goal was to specify and emphasize the potential health complications specific to AN-affected pregnancies in the following paragraphs.

2. MOTHER

AN may lead to malnutrition and result in a range of severe health consequences. The somatic complications include cardiovascular, gastrointestinal, endocrine, musculoskeletal, dermatological, neurological, immunological, and electrolyte disorders (Meczekalski et al., 2013). While the prevalence of amenorrhea is high among AN women, fertility issues may occur in this group of patients. The fertility of patients previously hospitalized for AN is diminished even to one-third when compared to the general population (Brinch et al., 1988). Women with a history of AN are also more likely to seek professional consultation due to fertility issues (Easter et al., 2011). However, it seems that this issue is reversible in patients who have recovered from AN. The meta-analysis of 5 long-term follow-up studies found, that pooled odds of childbirth rates between the patients who have recovered from AN and the no-AN population were not statistically significant (OR = 0.75, 95% CI: 0.43–1.29, $p = 0.41$) (Chaer et al., 2020). It is not recommended to initiate fertility treatment in underweight patients (Kasahara et al., 2020).

Current data regarding the correlation between AN and maternal obstetric outcomes are incompatible. Anemia stands out as one of the most common complications associated with pregnancy (Sifakis and Pharmakides, 2000). It is more common among pregnant women with AN. The case-control studies investigating the complications of women with AN found that the relative ratio (RR) for anemia was 2.1 (95% CI 1.3–3.2) Mantel et al., (2020) and the adjusted odds ratio (OR) was 2.39 (95% CI 1.20–4.76) Linna et al., (2014) when compared to women with no previous history of AN. Low body mass in pregnant women, which is a serious concern in patients with a history of AN, is associated with anemia (Hu et al., 2022). Other adverse outcomes during pregnancy, which are more likely to occur in AN women, are acute liver failure with a relative risk of 1.90 (95% CI 1.12–3.21) in comparison with no-AN Ante et al., (2020), hyperemesis with RR 2.1 (95% CI, 1.8-2.5) Mantel et al., (2020) and antepartum hemorrhage with OR 1,22 (95% CI 0,95-0,57) Ante et al., (2020) or RR 1.6 (95% CI, 1.2-2.1) Mantel et al., (2020) or RR 1.70 (95% CI 1.09–2.65) Eagles et al., (2012), depending on the study.

Moreover, the elevated risk of antepartum hemorrhage is more pronounced in active vs previous disease (Mantel et al., 2020). The risk for precipitate labor was found to be 1.43 times greater (95% CI 1.12–1.82) in the group of women previously hospitalized from AN compared to controls (Ante et al., 2020). On the other hand, gestational diabetes (GD) tends to occur less often in women suffering from AN. Individuals with AN were found to have a significantly lower likelihood of developing GD (RR 0.57, 95% CI 0.44–0.73) (Ante et al., 2020). Another study discovered no statistically significant difference in rates of GD between the AN group and the non-AN group (Linna et al., 2014). Many studies report, that AN is associated with preterm labor (Micali et al., 2016; Baer et al., 2023).

The 2023 population-based study that women diagnosed with AN experienced a greater occurrence of preterm delivery, with the adjusted OR 5.31 (95% CI 3.02 to 9.32, $P < 0.001$) than a cohort of women without AN, matched for age, race, medical insurance type, and income quartile (Feferkorn et al., 2023). The 2020 Japan study does not confirm this association, as the positive association between the history of AN and preterm birth was not observed after adjustment for pre-pregnancy BMI and gestational weight gain (OR = 0.202, $P = 0.11$), or in the matching analysis with pre-pregnancy BMI and gestational weight (OR = 1.87, $P = 0.37$) (Kasahara et al., 2020). Particularly, low body mass in pregnant women is associated with preterm delivery (Kosa et al., 2011; Verma and Shrimali, 2012). In the case-control study, which investigated the obstetric results in AN and no-AN groups, gestational weight gain below the recommended level mediated 38.89% of the excess in preterm births (Baer et al., 2023).

According to a 2023 meta-analysis, findings between AN and preterm birth and miscarriage are not statistically significant (Milembamane et al., 2023). The current data on the association between cesarean section (CC) and AN are incompatible. The authors of

the longitudinal study of AN and bulimia nervosa (BN) found, that women, who were experiencing active eating disorders during pregnancy had more significant risk for delivery by cesarean sections (CC) than women with no symptoms during pregnancy (Franko et al., 2001). Linna et al., (2014) found no statistically significant contrast in the rates of elective CC between women currently experiencing active AN and those without a history of AN. The study conducted by Ante et al., (2020) did not discover any association between the rate of CCs in women with AN and those without AN as well.

Based on the current state of knowledge, there is no doubt, that breastfeeding plays an essential role in maintaining and improving infant health (Binns et al., 2016). Nevertheless, mothers with any subtype of eating disorder are prone to encounter challenges related to breastfeeding, and that can affect both the mother's and child's well-being (Waugh and Bulik, 1999; Reba-Harrelson et al., 2010). Mothers with AN tend to discontinue breastfeeding earlier compared to mothers without AN (Torgersen et al., 2010). Breastfeeding might be challenging and demanding, requiring extra lactational assistance, particularly in AN mothers (Mitchell and Bulik, 2006). When discussing comorbidities of AN in pregnant women, it is essential to acknowledge its impact on the psychiatric state.

The prevalence of substance use disorder among pregnant women with AN is recorded at 2.7%, contrasting with the rate of 1.5% among pregnant women without AN (Ante et al., 2020). Moreover, pregnant women with active symptoms of eating disorders (including AN) face an increased risk of both perinatal anxiety and depression (Easter et al., 2015; Chan et al., 2019). The presence of depression alongside eating disorders increases the likelihood of postpartum depression (Mazzeo et al., 2006). Women with previous or active AN experience the symptoms of depression after giving birth more often (Franko et al., 2001).

3. BABY

Infants born to pregnancies of women with AN are at a higher risk of experiencing complications during both the fetal and neonatal periods. There is a significant association between maternal malnutrition and heightened risks of adverse birth outcomes. The pregnancy outcomes are highly dependent on the consumption of nutrients, such as complete proteins, lysine, omega-3 fatty acids, folate, and iron, which may be deficient in individuals with active AN (Ramachandran, 2002; Wu et al., 2004). Prenatal and early perinatal periods undeniably influence future life. The prenatal and early perinatal environment may affect the development by inducing fetal epigenetic programming processes (Micali et al., 2009). The environment determines which genes are available for later transcription. Reports suggest, that psychosocial and neuroendocrine factors, frequently present in AN mothers, such as increased levels of stress and malnutrition may also affect the neurodevelopment of the babies.

However, additional research is needed to evaluate the efficacy of psychological interventions in improving maternal and fetal well-being and preventing long-lasting health issues in offspring (Rondó et al., 2003). An essential adverse fetal outcome reported in babies of women with a history of AN is intrauterine growth restriction (IUGR). In the fetal and neonatal population, IUGR is a significant yet often undetected cause of various morbidity and mortality. It is a condition when a fetal growth rate falls below the standard growth potential for the specific infant (Sharma et al., 2016). Mothers with AN were more likely to deliver babies with IUGR, with an RR of 1.54 (95% CI 1.11-2.13) (Eagles et al., 2012). IUGR was found to be more prevalent in babies of women with AN also in another study with the OR 2.59 (95% CI 1.43–4.71) (Linna et al., 2014).

Multiple complications in newborns of AN mothers are more prone to occur compared to newborns of mothers with no history of AN. Maternal AN predicts lower birth weight. The proposed mechanism suggests that malnutrition affects placental development and may result in vascular dysfunction (Triunfo and Lanzone, 2015). Newborns born from pregnancies affected by AN were more prone to be small for gestational age at birth (SGA) with the OR 2.90 (95% 1.98-4.26) Micali et al., (2016) or OR 4.69 (CI 2.6 to 8.41, $P < 0.001$) Feferkorn et al., (2023), depending on the study. In the case-control study examining obstetric outcomes in both the AN and no-AN groups, mothers' gestational weight gain below the recommended level contributed to 40.44% of the additional occurrences of low-birthweight infants (Baer et al., 2023).

Another finding regarding infants born from pregnancies, whether marked by previous or active AN, is the increased likelihood of microcephaly. Microcephaly is 1.9 times more likely to occur in newborns of mothers with AN compared to those without the disorder (RR 1.9, 95% CI 1.5-2.4) (Mantel et al., 2020). The next concern arises from the occurrence of cardiovascular and respiratory disorders in neonates born from pregnancies affected by AN. The OR for cardiovascular disorder is 1.27 (1.03–1.56) and 1.16 (1.02–1.31) for respiratory disorder (Ante et al., 2020). Newborns born to mothers with AN also face an increased risk of perinatal death (stillbirth or death during the neonatal period) as well as intensive care unit for neonates (NICU) admission. The ORs for the following adverse

outcomes in AN mothers' babies are 1.99 (1.20–3.30)- for stillbirth, 1.16 (0.48–2.78)-for newborns' death before discharge, and 1.33 (1.09–1.62)- for NICU admission.

Ante et al., (2020), Brinch et al., (1988) described a six-fold increase in the anticipated rate of perinatal death in AN cases, primarily attributed to prematurity (Brinch et al., 1988). The infancy stage is crucial in shaping the future growth and development of the baby. Babies born to mothers with AN experience feeding difficulties more frequently. After adjusting for relevant confounding factors, infants born to women with AN were more likely to experience feeding difficulties between the ages of 0 and 6 months in comparison with infants born to women with no psychiatric disorders (Micali et al., 2009).

The Norwegian cohort study assessed weight-for-length (WFL) trajectories in children aged birth to 12 months born to mothers with and without eating disorders (including AN) (Perrin et al., 2015). The authors found that the offspring of mothers reporting any eating disorder presented a reduced WFL growth rate from birth to 12 months compared to children of mothers without eating disorders, even after accounting for relative birth weight and certain confounding factors known to impact growth. Knowing that the growth trajectories observed from infancy to early childhood are associated with the risk of chronic diseases in adulthood, that may be a severe concern (Perrin et al., 2015; Reilly et al., 2005; Singhal and Lucas, 2004).

4. CONCLUSION

The significant interaction between AN and pregnancy, both psychologically and physiologically, has notable effects on the health of both the mother and the baby. Continuing regular screening tests to identify eating disorders in the pre-conception period and during pregnancy may aid in implementing specific preventive measures for high-risk groups, thereby protecting the health of both mother and child. Furthermore, evaluating nutritional status through scale assessment and providing treatment for malnutrition could help prevent various adverse effects in high-risk individuals. It is important to provide a collaborative treatment involving obstetricians, mental health specialists, and dietitians, and it is essential to obtain the agreement of the women involved in such collaboration. It is worth making an effort as weight gain during pregnancy has a shielding effect on harm avoidance. We suggest an early discussion about fertility and potential pregnancy complications with women who were diagnosed with AN.

Authors' Contribution

Julita Młynarska- Conceptualization, writing- rough preparation, methodology, investigation

Aleksander Górny- Conceptualization, methodology

Justyna Chwiejczak- Resources, writing- rough preparation

Jan Kościan- Resources, investigation

Karolina Szczerkowska- Conceptualization, writing- rough preparation

Anna Wójcik- Methodology, data curation

Michał Obrębski- Conceptualization, data curation

Anna Seroka- Visualization, data curation

Maria Miłkowska- Writing - Review and editing, supervision

Maria Rybicka- Formal analysis, supervision

Project administration- Julita Młynarska

Informed consent

Not applicable.

Ethical approval

Not applicable.

Funding

This study has not received any external funding.

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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