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Identification of Common Adverse Outcomes of Pregnancies Diagnosed with Endometriosis: Review of Past Studies

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Abstract

Endometriosis is a progressive stirring disease marked by the appearance of endometrial glands and stroma exterior of the uterus. It affects 8%–10% of reproductive-age women and is linked to developing primary or secondary infertility in 30% of these women. The main objective of this systematic review was to critically analyse the current related literature to explore the maternal and neonatal adverse outcomes of pregnancies diagnosed with endometriosis. Pregnant women with endometriosis are more likely to develop negative pregnancy outcomes and complicated neonatal outcomes, and therefore they may benefit from extra screening and early detection. Therefore, eight studies are critically analysed in terms of study design, sample size, sample type, exclusive criteria, comprehensive criteria, data analysis, and key findings based on data availability to identify common adverse outcomes of pregnancies with endometriosis. After critically analysing the eight studies, authors explored that pregnant women diagnosed with endometriosis are at elevated risk to develop Placenta previa, hypertensive disorders, postpartum hemorrhage, emergency caesareans and preeclampsia as common maternal outcomes and premature birth, Low birth weight and stillbirth as common neonatal outcomes. In conclusion, women with endometriosis are at elevated risk of developing adverse maternal and neonatal outcomes in their pregnancies.

Keywords: Adverse effects, Endometriosis, Maternal outcomes, Neonatal outcomes.

Introduction

Endometriosis is a progressive stirring disease marked by the appearance of endometrial glands and stroma-like lesions outside the uterus (Leyland et al., 2010). Furthermore, it is associated with chronic pelvic pain, which often affects 8%–10% of reproductive-age women, and it is linked to primary or secondary infertility in 30% of these women (Velasco, 2004). However, endometriosis can continue as a minor or non-existent condition in some cases, or it can disappear on its own in others (Ozkan et al., 2008). But, there have been many studies in literature, especially within the past 10 years, showing increasing

evidence of the association between endometriosis and increased risk of pregnancy complications such as placenta Previa, hypertensive disorders of pregnancy (HDP), small for gestational age (SGA), placental abruption, postpartum hemorrhage (PPH) and neonatal complications, such as preterm birth and low birth weight (Chen et al., 2018; Berlac et al., 2017). In America, the effects of endometriosis on perinatal outcomes have remained provocative, while neonatal outcomes such as preterm delivery, low birth weight have been commonly observed (Zullo et al., 2017). However, in Canada, women with endometriosis who had developed pre-eclampsia, gestational hypertension, gestational Diabetic Mellitus (GDM), placenta Previa, and partum hemorrhage, emergency cesareans as maternal complications. Furthermore, neonates had preterm births, low birth weight and even neonatal deaths (Lalani et al., 2018).

Not only in European countries, but also Asian countries such as Japan, placenta previa and post-partum haemorrhage in the endometriosis group were significantly higher with endometriosis women, incidences of preterm birth, GDM, and placental abruption between were noted (Miura et al., 2019). However, in Sri Lanka no exact studies were done related to the research topic, but articles have mentioned major social, public health, and economic ramifications that can be caused to reduce quality of life due to endometriosis because of extreme pain, exhaustion, sadness, anxiety, and infertility. In relation to many of these cases, endocrine and ovulatory abnormalities in women with endometriosis include luteinized unruptured follicle syndrome, compromised folliculogenesis,

luteal phase defect, and premature or multiple luteinizing hormone (LH) spikes, all of which have a significant effect on their pregnancies and outcomes (American Society for Reproductive Medicine, 1996). Invasion and tissue penetration, development of endometriomas or “chocolate cysts”, extreme pelvic adhesions, or pelvic blockage that may damage other organs, as well as pelvic carcinomas, can trigger severe symptomatology (Oxholm et al. 2007).

Furthermore, currently, there is no satisfactory treatment for all endometriosis patients. Endometriosis treatments are problematic because they can reduce pain, increase pregnancy symptoms and outcomes, and also improve infertility, but they do not cure the disorder. However, it can be concluded that having endometriosis may lead to developing serious complications in pregnancies. Consequently, to overcome the possible negative outcomes, clinicians should be aware of the potential endometriosis-related complications, particularly during pregnancy and labor (Farland et al., 2019). The prevalence of endometriosis has been studied in a variety of ways, with diverse estimates reflecting the variations in diagnosis parameters and population size (Berlac et al., 2017). Therefore, increased interest towards endometriosis around the world resulted in finding long-term health and endometriosis-related comorbid conditions in both women and newborns (Farland et al., 2019). Consequently, many research works have been conducted to identify the maternal and neonatal outcomes related to endometriosis and are reviewed with different and occasionally contrastive outcomes. Through this systematic review, the researcher intended to synthesize and

discuss the common possible adverse outcomes of pregnant women diagnosed with endometriosis, and adverse neonatal outcomes associated with endometriosis.

Methods and Materials

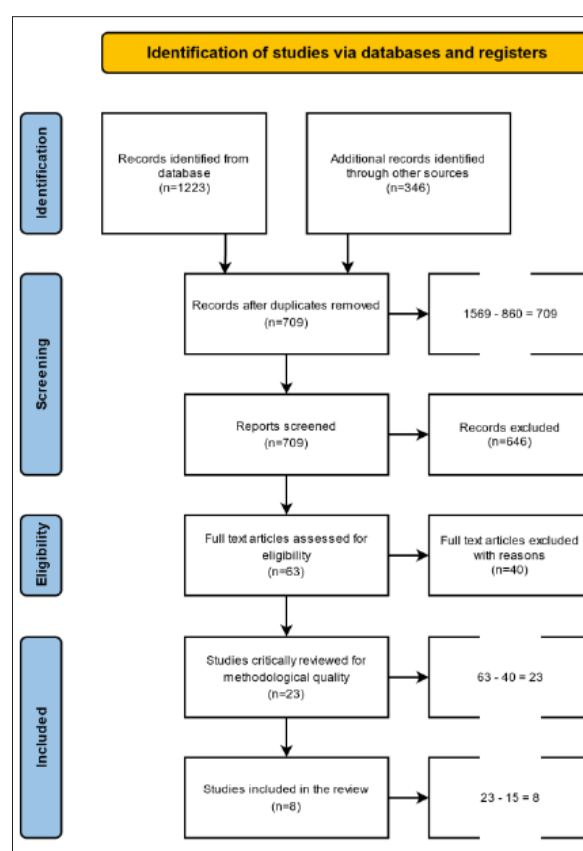
Selection of articles

In the current study, a systematic review method is followed as the study design. Literature from the following online databases like CINAHL, MEDLINE and PUBMED is used as search libraries to collect relevant literature for the topic of maternal and neonatal outcomes of pregnancies diagnosed with endometriosis. Retrospective cohort studies and primarily written articles which are less than 5 years ago were considered and their eligibility criteria for the study are based mainly on the PICO approach, date of publication, and the study design. Articles on the neonatal and maternal outcomes of pregnant mothers with diagnosed endometriosis were considered for the study, and no restrictions were made based on the country, patient's age, and race. Using the keywords 'Endometriosis', 'Maternal outcomes', 'Neonatal outcomes', and 'Adverse effects', a total number of 1569 related articles were found and of which 825 articles from CINAHL, 505 articles from MEDLINE and 239 articles from PUBMED. Out of which articles in duplicates, not in English language or English translations and subsequently further modified and restricted for the search keywords were excluded, reducing the number of total articles. The article's title and abstract were appraised, and the search period was confined to a time span from 2016 to 2020. After the above process, further 646 articles were excluded from the filtered literature, and the number of related articles were reduced to 63. After conducting

a further eligible review of the selected 63 articles, the number of related literatures was further reduced to 23 articles. Eventually, the selected 23 articles from the search databases were subjected to filtering according to their methodological quality and research findings. After the exclusion of all irrelevant articles, 8 research articles were finalised using CASP method for critical appraisal of the systematic review using the PRISM flow chart (Fig. 1).

Figure 1.

PRISMA flow chart of the article selection.



Furthermore, full-text articles in English or translations were considered in the inclusive criteria. The researcher excluded the studies that are not reliably extracted, duplicates, or consist of overlapping data. Furthermore, articles not in the English language and articles with no full-text availability are also excluded.

Results and Discussion

Related literature within 5 years (2016-2021) was taken for research, and a few related literatures over 5 years were taken due to the availability of relevant information. Nevertheless, as with a comprehensive review of observational studies, it is constrained by the nature and variability of the studies used. Most of the papers found during the search process are closely related to the research topic, making it easy for researchers to find the right solution to their current problem. However, control composition was not standardized in most trials, and some studies used a wider range of controls compared to the affected groups.

As a result, there is a risk of reliability and prejudice issues when considering the results. Despite these restrictions, some studies have taken into account or limited the amount of time, equality, and pregnancy. These variables contributed to the heterogeneity of the study, as expected in a systematic empirical sample.

Each study is critically analysed in terms of study design, sample size, sample type, exclusive criteria, comprehensive criteria, data analysis, and key findings based on data availability (Table 1).

Table 1.

Factors influencing on maternal and neonatal outcomes of the eight studies.

Author	Study Design and Focus	Time frame and sample size	Factors influencing on	
			Maternal outcomes	Neonatal outcomes
Shmueli et al. (2017)	Retrospective Cohort Study. To explore the obstetrical and neonatal outcomes of pregnancies complicated by endometriosis	2007 to 2014 Endometriosis group (135) Control group (61400)	Postpartum haemorrhage, emergency	caesareans, placenta Previa. no neonatal complications were noted
Uccella et al. (2014)	Retrospective Cohort Study. To identify maternal and neonatal outcomes of endometriosis specified with the location of the disease	2011 to 2014. Endometriosis group (118) Control group (1680)	Placenta Previa. Hypertensive disorders.	preterm deliveries

Table 1. (Continued)

Pan et al. (2017)	Nationwide population-based longitudinal study. To explore the risk of gestational hypertension and preeclampsia in women with preceding endometriosis.	1998 to 2012 Endometriosis group (2578) Control group (10312)	preeclampsia Hypertensive disorders.	preterm deliveries Low birth weight
Li et al. (2017)	Retrospective Cohort Study. To explore the obstetrical and neonatal outcomes of pregnancies complicated by endometriosis	2011 to 2013 Endometriosis group (98) Control group (300)	Gestational diabetes mellitus placenta Previa postpartum haemorrhage	preterm deliveries
Farland et al. (2019)	Prospective cohort study. to explore the maternal and neonatal outcomes of pregnancies associated with endometriosis	1989 Endometriosis group (8875) Control group (196,722)	Gestational diabetes mellitus Hypertensive disorders	Still birth
Conti et al. (2014)	Multi-centric, observational, and cohort study. To evaluate pregnancy, delivery, and neonatal outcomes in singleton primiparous versus multiparous women with or without endometriosis	Endometriosis group (316) Control group (1923)	Gestational diabetes mellitus	Preterm Delivery Low birth weight
Miura et al. (2019)	Case-control study. Adverse effects of endometriosis on pregnancy	2010 to 2017 Endometriosis Group (316) Control group (1923)	Risk of placenta Previa Postpartum haemorrhage Gestational Diabetic mellitus	Preterm Delivery
Berlac et al. (2017)	National cohort study to assess the obstetrical complications and neonatal outcomes in women with endometriosis	2007 to 2014 Endometriosis group (135) Control group (61,400)	placenta Previa postpartum haemorrhage	no neonatal complications were noted

The results of the eight selected studies lead to the that endometriosis during pregnancy can cause negative pregnancy outcomes for both women and neonates. According to the results, postpartum haemorrhage, emergency caesareans, placenta Previa, Hypertensive disorders, preeclampsia, and GDM are identified as common maternal outcomes of pregnancies diagnosed with endometriosis. Preterm deliveries, low birth weight, and stillbirth are identified as common neonatal outcomes. Therefore, the two main themes emerged after analysing the findings are as follows: (i) Theme 1- Pregnant mothers are at high risk and (ii) Theme 2- Keep awareness of neonates.

Pregnant mothers are at high-risk.

Endometriosis has been linked to several adverse pregnancy outcomes in previous studies (Brosens et al., 2012; Chen et al., 2018). However, Maggiore et al. (2017) published two interesting and detailed studies which displays that the risk of endometriosis-related complications during pregnancy is low. However, this study identified that among the study participants with endometriosis, a high incidence of placenta previa was detected as one of the most frequent endometriosis pregnancy outcomes (Uccella et al., 2014; Farland et al., 2019). These results are in line with the previous research that has stressed the connection between endometriosis and placenta previa (Maggiore et al., 2017). In addition, researchers have found an increase in placenta previa. This is a condition that affects only women with deep infiltrative endometriosis. Pregnant women with endometriosis generally need to be reassured about the course of their

pregnancy (Maggiore et al., 2017). Moreover, current studies show that the women with endometriosis have a higher incidence of emergency caesarean sections and lower vaginal delivery rates for both selective and non-selective purposes. Previously, a similar pattern of emergency caesarean section was observed in several studies, demonstrating the same fact (Exacoustos et al., 2016). Similarly, current studies have observed that obstetric complications such as placenta accreta and postpartum bleeding are significantly associated with endometriosis.

On the other side, obstetrical problems, such as placenta accreta and postpartum haemorrhage, were found to be substantially correlated with endometriosis in the current study. Marcellin et al. (2015) established that the decidua of women with endometriosis can produce endometriosis-like lesions as it encounters the fetal membranes in an in-vitro analysis. Furthermore, this finding may help in explaining the increased risk of placenta accreta and postpartum haemorrhage. In addition, the study found that women with a history of endometriosis were at increased risk of developing gestational diabetes (GDM) or hypertensive pregnancy disorders. The finding was also published in a recent meta-analysis of 12 studies, which found that women with endometriosis had a 26% higher risk of GDM and hypertensive disease than women without endometriosis (Maggiore et al., 2017). Furthermore, the endometriosis disease stage has been linked to heterogeneity in the relationship between endometriosis and hypertensive disorders of pregnancy (Harada et al., 2016). However, the current study shows that the entire population is at increased risk of hypertensive pregnancy disorders, and

the relationship is stronger in the second and subsequent pregnancies (Farland et al., 2019).

In the current study, it was revealed that women with prior diagnosed endometriosis, on the other hand, had a higher rate of Preeclampsia in subsequent pregnancies than women without endometriosis. According to Maggiore et al. (2017), a recent meta-analysis of 13 studies also suggests that women with endometriosis are at increased risk of preeclampsia (95%). Women who have previously had endometriosis are more likely to develop preeclampsia in subsequent pregnancies and should have enhanced maternal and fetal monitoring.

Keep awareness of neonates

Endometriosis causes complicated outcomes in neonates, similar to maternal complications. Women with a history of endometriosis were found to have a higher risk of stillbirth or intrauterine death, preterm birth, and low birth weight; all of which are common neonatal outcomes. According to a recent study, women with endometriosis are at increased risk of preterm birth before 34 weeks of gestation (Farland et al., 2016). Glavind et al. (2017) reported in a recent study in the Aarhus Birth cohort that women with endometriosis are at increased risk of preterm delivery. Endometriosis causes local and systemic inflammation in women (Mu et al., 2018). As Goldenberg et al. (2008) states, inflammation is one mechanism thought to be increasing the risk of preterm birth in the endometriosis groups, compared to the controls. Leyland et al. (2010) contend that endometriosis can cause growth restriction due to insufficient uterine contractility and

improper placentation. Current studies confirm that pregnancy in women with endometriosis is highly associated with low birth weight compared to women without endometriosis. Moreover, the current study shows an increased risk of neonatal death associated with spontaneous abortion and ectopic pregnancy compared with women with no history of endometriosis. A recent meta-analysis discovered that women with endometriosis have a 75% per cent higher risk of spontaneous abortion and a 21% and 29% per cent higher risk of stillbirth, respectively (Lalani et al., 2018). Progesterone resistance in endometriosis patients is thought to cause the deregulation of genes involved in embryo implantation, which could result in pregnancy loss (Vannuccini et al., 2016).

Conclusions

Endometriosis increases a woman's risk of significant negative prenatal, fetal, and neonatal outcomes. The women who have previously been diagnosed with endometriosis are at a high risk of having placenta previa, postpartum haemorrhage, and hypertension disorders as maternal outcomes. On the other hand stillbirth, preterm birth, and Low birth weight were identified as common neonatal outcomes of pregnancies diagnosed with endometriosis. These results inform women previously diagnosed with endometriosis of potential obstetric complications associated with endometriosis and provide prejudices or recommendations during the prenatal period. In addition, close monitoring by health professionals should be continued and prepared to overcome ongoing complications. The neonatal intensive care unit should be notified and prepared before delivery to avoid

unnecessary delays in managing neonatal complications. Finally, even though the purpose of this review was to integrate the available knowledge on this significant topic, it is still unknown how endometriosis worsens pregnancy outcomes.

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