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Unraveling the impact of adenomyosis on obstetrical outcomes: a comprehensive review

Abstract

Objective: Adenomyosis' impact on obstetrical outcomes is investigated with detailed discussion of plausible pathogenesis. Discussion of management strategies to improve outcomes included.

Methods of study: Terms utilized include 'adenomyosis', 'fertility', ' pregnancy', 'obstetrical outcomes', 'preeclampsia, 'fetal growth restriction', 'preterm labor', 'preterm prelabor rupture of membranes, 'in vitro fertilization, 'prelabor rupture of membranes', 'ultrasound', 'small for gestational age', 'cesarean section' Inclusion criteria are English, between January 1990-January 2023, randomized controlled trials, case controls, cohorts, case series, case reports, systematic reviews, and meta-analyses. Exclusion criteria are studies/articles completed prior to 1990, non-relevant, and non-English.

Results: Limited literature exists evaluating the relationship between adenomyosis impact on obstetrical outcomes. However, amongst available literature there exists statistically significant relationship between adenomyosis and adverse obstetrical, neonatal outcomes such as: ectopic pregnancy, placental abruption, pre-eclampsia (PEC), gestational diabetes (GDM), low birth weight (LBW), intra-uterine growth restriction (IUGR), and preterm prelabor rupture of membranes (PPROM). Proposed physiologic mechanisms include disordered anatomic, functional, and immunological environment in the uterus. Proposed management strategies to improve obstetrical outcomes include removal of focal adenomyotic lesions and pre-treatment with GnRH agonists before conception.

Conclusion: Adenomyosis has a multifactorial impact on obstetrical outcomes; treatment modalities do exist to improve the chances of conception and retaining a pregnancy. However, more research is required to not only further substantiate treatment modalities relationship to improve pregnancy; but also to clarify adenomyosis impact on infertility.

Keywords: adenomyosis, obstetrical outcomes, maternal morbidity, pregnancy, adverse obstetrical outcomes

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Abbreviations: PEC, Pre-eclampsia; GDM, Gestational Diabetes; LBW, Low birth weight; IUGR, Intra-uterine growth restriction; FGR, fetal growth restriction; PPROM, preterm prelabor rupture of membranes; PP, placental previa; PA, placental abruption; C/S, cesarean section ; CD, cesarean delivery; SGA, small for gestational age; PPH, post-partum hemorrhage; ART, assisted reproductive technology; IVF, in-vitro fertilization; IVF/ICSI, in-vitro fertilization/intracytoplasmic sperm injection; IVF-ET, in-vitro fertilization-embryo transfer; TVUS, transvaginal ultrasound; GnRHa, GnRH agonist; GnRH-R, gonadotropin releasing hormone receptor; AMH, anti-Mullerian hormone; CPR, cumulative pregnancy rate; HTN, hypertension; PTB, preterm birth

Introduction

Adenomyosis is classically characterized by the presence of both endometrial glands and stroma within the myometrium. This condition, though less commonly discussed than its counterpart, endometriosis, has gained increasing attention in recent years due to its potential implications for women's reproductive health. Adenomyosis can produce the following symptoms: abnormal uterine bleeding, dyspareunia, dysmenorrhea, or infertility; however, about 1/3 of women are asymptomatic.[1] The pathogenicity of adenomyosis remains deeply divided with the following hypotheses: molecular changes in the endometrium contribute to the migration and survival of ectopic endometrial implants versus constant tissue injury and repair on the endometrial-myometrial interface through prior uterine surgery, previous cesarean-sections, and multiple pregnancies.[2] Yet another theory posits that the spread of endometrial tissue through both lymphatic pathways and displaced bone marrow cells could contribute to adenomyosis. Despite the many theories, definitive pathogenesis of this clinical condition continues to remain unclear.

While the impact of adenomyosis on menstrual and pelvic pain symptoms has been extensively explored, its association with obstetrical outcomes remains an area of ongoing investigation. Pregnancy and childbirth are complex processes that require precise coordination between maternal and fetal factors. Any underlying uterine condition, such as adenomyosis, has the potential to influence these outcomes, making it crucial to gain a comprehensive understanding of its effects on obstetric health. It is important to recognize that while adenomyosis may have notable effects on obstetrical outcomes, managing the condition during pregnancy requires a delicate balance between the well-being of the mother and the developing fetus. As such, a multidisciplinary approach involving obstetricians, gynecologists, and maternal-fetal medicine specialists is necessary to provide optimal care for women with adenomyosis throughout their pregnancy journey.

This literature review aims to provide a thorough analysis of existing literature regarding the impact of adenomyosis on obstetrical outcomes. By critically examining relevant studies and data, we seek to shed light on potential associations between adenomyosis and various aspects of pregnancy. Further, it provides detailed explanations as to the specific reasons of obstetrical outcomes from physical uterine distortion to creation of an inflammatory environment destructive for

pregnancy, amongst others. Discussion of management strategies to improve pregnancy outcomes including both non-invasive and surgical methods are detailed in this article. Understanding these connections can empower healthcare providers to offer more personalized and effective care to women with adenomyosis during their reproductive journey.

Materials and Methods

This is a literature review that was conducted utilizing the PubMed, Cochrane, Embase, and Google Scholar databases. Terms utilized include 'adenomyosis', 'fertility', ' pregnancy', 'obstetrical outcomes', 'preeclampsia, 'fetal growth restriction', 'preterm labor', 'preterm prelabor rupture of membranes, 'in vitro fertilization, 'prelabor rupture of membranes', 'ultrasound', 'small for gestational age', 'cesarean section' Inclusion criteria are English, between January 1990-January 2023, randomized controlled trials, case controls, cohorts, case series, case reports, systematic reviews, and meta-analyses. Exclusion criteria are studies/articles completed prior to 1990, non-relevant, and non-English. Additionally, the reference section of salient articles was utilized and included as well in the final literature review (Figure 1).

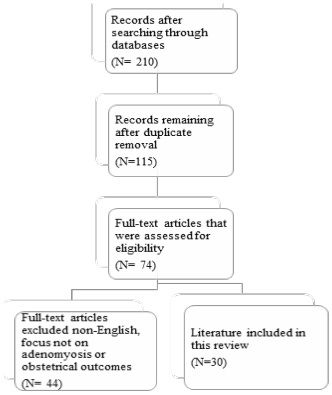

Figure 1 Flowchart of the literature screening and selection.

Results

Literature focusing on adenomyosis' impact on both neonatal and obstetrical outcomes is growing; however, limited data exists (Table 1). Huang's recent meta-analysis found no statistically significant differences between both pregnant women with and without adenomyosis for the following outcomes: rates of ectopic pregnancy, placental abruption, pre-eclampsia (PEC), gestational diabetes (GDM), low birth weight (LBW), and intra-uterine growth restriction (IUGR).[3] However, meta-analyses conducted by both Nirgianakis et al.,[3] and Razavi et al.,[5] found adenomyosis during pregnancy directly linked to poor neonatal and obstetrical outcomes such as preterm delivery, preterm prelabor rupture of membranes (PPROM), spontaneous abortion, fetal malpresentation, PEC, cesarean section (C/S), fetal malpresentation, small for gestational age (SGA), LBW, and post-partum hemorrhage (PPH).[3–23] There has been conflicting information about cesarean section rate as previous studies have not taken into account different aspects of patient care that would result in this mode of delivery such as: prior obstetrical history, socioeconomic status, socio-culture demographics, and structural factors.

Interestingly, small for gestational age (SGA) neonate with a weight of <2500g and <1500g is significantly increased for patients with adenomyosis as directly evidenced by Yamaguchi; however, there have been studies that merely showed only an increased risk without any associated significance.[3,16] Hypertensive disorders of pregnancy, particularly preeclampsia, were another commonly assessed outcome in the current literature as evidenced by Porpora et al.,[20] and the studies mentioned above.[20] Though multiple studies endorse a significantly increased risk of preeclampsia with adenomyosis, one study showed no statistically significant increased risk.[8,13] Interestingly, Shinohara et al.,[21] provided evidence that individuals with diffuse adenomyosis had significantly increased risk of poor obstetrical outcomes mentioned above; however, it is merely the only study that states that individuals with focal adenomyosis did not have statistically different outcomes compared to those without any adenomyosis.[21]

Table 1 Impact of adenomyosis on obstetrical outcomes

Author	Year	Study design	Intervention	Result	References
Dommisse & Tiltman	1992	Prospective Descriptive Study	Placental bed biopsies were obtained at caesarean section in patients with placental abruption	Vascular malformations in the setting of placental abruption was seen.	12
Juang, et al.	2007	Case Control	Types of adverse obstetric outcomes investigated in pregnant patients with and without adenomyosis	Gravid women with adenomyosis were associated with significantly increased risk of PTB[12] and PPROM.[13]	19
Costello, et al.	2011	Retrospective Cohort Study	IVF/ICSI[27] outcome in women with and without adenomyosis.	There was no difference in live birth rate per patient between the two groups.	24
Youm, et al.	2011	Retrospective Case Control Study	Patients undergoing IVF-ET[1] were divided into groups based on myometrial thickness and outcomes were observed.	Myometrial thickening greater than 2.50 cm exerts adverse effects on IVF-ET[28] outcomes (decreased implantation CPR,[2] increased spontaneous abortion rates, and with significantly lower live birth rates). Mild myometrial thickening (2.00–2.49 cm) is associated with adverse outcomes of IVF-ET.[28]	25
Thalluri, et al.	2012	Retrospective cohort study	A single IVF-ICSI[27] cycle in patients with and without adenomyosis.	Adenomyosis group had a statistically significant decreased CPR[29] of 23.6% compared with 44.6% in the non-adenomyosis group.	26
Ballester, et al.	2012	Prospective longitudinal study	CPR[29] in patients with and without adenomyosis undergoing IVF-ICSI[27]	CPR[29] for patient with adenomyosis was 19% and without adenomyosis was 82.4% (p=0.01). Patient over 35 years and anti-Mullerian hormone serum level under 2ng/ml associated with a decreased CPR.[29]	27

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Table 1 Continued...

Author	Year	Study design	Intervention	Result	References
Mochimaru A, et al.	2015	Retrospective Case Control	Types of adverse obstetric outcomes investigated in pregnant patients with and without adenomyosis	Adenomyosis subjects were associated with PTB,[12] PPROM,[13] SGA,[3] and CD[4] as compared with the control group. PPH[5] reported to be increased risk in those with adenomyosis.	14
Exacoustos, et al.	2016	Cohort study	Types of adverse obstetric outcomes investigated in pregnant patients with adenomyosis	When compared with the control group, women with adenomyosis had a higher risk of pregnancy complicated by PTB,[12] PP,[6] PA,[7] and HTN.[8]	17
Hasdemir, et al.	2016	Prospective cohort study	Women with diagnosis of pre-eclampsia with and without adenomyosis	The prevalence of adenomyosis was found to be more common in patients with FGR.[9]	18
Hashimoto A, et al.	2018	Retrospective case control	Types of adverse obstetric outcomes investigated in pregnant patients with and without adenomyosis	Adenomyosis subjects had significantly increased risk of PEC,[10] PTB[12]	13
Shin Y, et al.	2018	Retrospective case control study	Types of adverse obstetric outcomes investigated in pregnant patients with and without adenomyosis	The adenomyosis group was associated with significantly higher rates of PTB,[12] LBW[11] than the non-adenomyosis group. Risks of either outcome are significantly higher in pregnant women with adenomyosis who conceived by assisted reproductive technologies versus those who conceived naturally.	15
Harada, et al.	2019	Prospective Cohort Study	Women with endometriosis and adenomyosis were followed for incidence of obstetric complications	The presence of endometriosis and adenomyosis significantly increased prevalence of obstetrical complications such as PTB,[12] PPROM,[13] PP.[14]	11
Hashimoto A, et al.	2018	Retrospective Case Control	Types of adverse obstetric outcomes investigated in pregnant patients with and without adenomyosis	Adenomyosis subjects were significantly more likely to have a second trimester miscarriage, PEC,[15] placental malposition, and PTB,[12] compared to the control group.	13
Yamaguchi, et al.	2019	Prospective cohort study	Types of adverse obstetric outcomes investigated in pregnant patients with adenomyosis	Adenomyosis was a risk factor for PTB,[12] LBW <2500g,[19] LBW <1500g,[19] and SGA.[16] CD[17] significantly increased in those with adenomyosis.	16
Porpora, et al.	2020	Prospective Cohort Study	Obstetrical outcomes measured in women with and without adenomyosis	A significantly increased relationship was noted with pregnancy-induced hypertension and preeclampsia in the presence of adenomyosis.	20
Shinohara, et al.	2020	Retrospective Case Control Study	Obstetrical outcomes measured in women with and without adenomyosis	The adenomyosis group had significantly higher incidence of PTB,[12] hypertensive disorders of pregnancy, CD,[17] and PPH[15] risk than the control group.	21

[1][12]IVF/ICSI: *In-vitro* fertilization/Intracytoplasmic sperm injection

IVF-ET: *In vitro* fertilization-embryo transfer

[2]CPR, cumulative pregnancy rate

[3]SGA, small-for-gestational age

[4]CD, Cesarean delivery

[5]PPH, Postpartum hemorrhage

[6]PP, Placenta previa

[7]PA, Placental abruption

8HTN, Hypertension

[9]FGR, Fetal growth restriction

[10]PEC, preeclampsia

[11]LBW, low birth weight

[12]PTB, preterm birth

[13]PPROM, preterm prelabor rupture of membranes

[14]PP, placenta previa

[15]PPH, Postpartum hemorrhage

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Further, adenomyosis has a negative impact on patients undergoing assisted reproductive technology (ART). For example, Shin et al.,[15] provided evidence that pregnant women with adenomyosis who conceived via ART had significantly higher preterm birth rate and associated low birth weight neonates.[8,15] Chiang et al.,[22] also provided preliminary evidence that patients with a sonographically diffused enlarged uterus without distinct uterine masses had a higher spontaneous abortion rate when undergoing IVF (in-vitro fertilization), thus requiring enhanced luteal support prior to conception.[22] Interestingly, there has been a discrepancy in women with a sonographically diffuse adenomyosis undergoing IVF/ICSI (in-vitro fertilization/intracytoplasmic sperm injection) with GnRH pretreatment for either short-term (3 months) or long-term (more than 3 months) with Chiang et al.,[22] documenting a higher spontaneous rate of miscarriage with both regimens.[24] However, Mijatovic et al.'s most recent retrospective study showed no adverse outcomes with women who were treated with the same regimen.[22,23] Youm et al.,[25] provided evidence that women undergoing IVF-ET (in-vitro fertilization-embryo transfer) with a myometrial thickness of 2.50cm on transvaginal ultrasound (TVUS), led to a significant decrease in successful implantation, clinical pregnancy, live birth rate, and increased abortion rate.[25] The findings of Youm et al.,[25] were corroborated by Thalluri et al.,[26] who additionally corrected for increased maternal age and duration of infertility.[26]

It was previously demonstrated that women with adenomyosis who conceived using ART were at an increased risk of obstetrical complications, such as placenta previa and placenta abruption.[10] A recent review article states that not a negligible risk of placenta previa and placenta accreta exists in those who become pregnant with adenomyosis.[11] In patients with endometriosis, Exacoustos et al.,[17] has provided evidence that a higher risk of placenta previa and placental abruption exists.[17] Pregnant women with adenomyosis had a high risk of placental abruption and fetal growth restriction compared to those without.[18] Furthermore, a statistically significant higher frequency of placenta previa cases have been reported in those with adenomyosis, as the uterine environment is greatly altered in these patients.[10,13]

Placental pathologies in those with adenomyosis have been examined. A single case report described a 52-year-old woman with adenomyosis who had a live twin delivery after taking GnRH agonist (GnRHa) therapy. This medication decreased uterine size and JZ thickness; however, her delivery was complicated by expansive accretas of both placentas requiring cesarean hysterectomy. Pathology of both placentas demonstrated no decidualized endometrium. Previous molecular studies have offered evidence that genetic variance in the expression of the gonadotropin releasing hormone receptor (GnRH-R) could explain the expansive lack of decidualized endometrium after GnRHa therapy. However, further studies are needed to determine if GnRHa therapy contributes to placental abnormalities (Table 1).[9]

Proposed physiologic mechanisms for adverse obstetrical outcomes

Through disordered anatomic, functional, and immunological mechanisms in the uteri of adenomyotic patients, there is an increased risk of abnormal placentation.[10] Rationale for placental abruption in patients is due to increased incidence of PPROM in adenomyotic patients. Blood flow to the adenomyotic lesions is increased, decreasing blood flow to the placenta, thus decreasing its size. As a result, there is an increase risk placental membranes can rupture preterm, compounding the risk for placental abruption.[10] Further, in adenomyotic affected women, alterations of the JZ leads to vascular resistance, contributing to insufficient deep placental placentation and failure of spinal artery remodeling. In fact, the altered remodeling of the placental vasculature can lead to placental abruption and PEC.[5,12] It has been proposed that the underlying physiology leading to the obstetrical outcomes listed above is the increased inflammatory environment in the uterus due to elevated levels of inflammatory factors such as prostaglandin E2, cyclooxygenase 2, and interleukin 8.[5] These inflammatory markers are thought to trigger endometrial vasoconstriction and stimulation of cervical ripening which serves as the basis for PEC, preterm birth, and PPROM. Because of the functional and structural changes of the uterus over time, uterine function is inherently impaired, increasing risk of a multitude of adverse obstetrical outcomes.

Lastly, AMH serum (anti-Mullerian hormone) levels are a lead predictor of cumulative pregnancy rate (CPR). In patients with adenomyosis and even endometriosis numerous studies have found low AMH levels. Poor ovarian reserve is defined as under 2ng/ml while others define the cutoff of 1 or 0.6 ng/ml. There is a higher CPR when patients have an AMH serum elevation above 2ng/ml, while no benefit was observed after two ICS-IVF (intra-cytoplasmic-in vitro fertilization) cycles with an AMH below this level.[27]

Proposed management strategies to improve obstetrical outcomes

Removal of ectopic endometrial lesions in patients led to improvement in both spontaneous and IVF pregnancy rates, as evidenced by Stepniewska et al.,[28] Though the study examined patients with endometriosis, it should be attempted to be translated in patients with focal adenomyosis where removal of lesions is more feasible.[28] Another study by de Ziegler has provided adequate evidence that removal of focal adenomyotic/endometriotic implants should be an option in patients less than 38 years, with documented good ovarian reserve, and no other indications compromising natural conception such as tubal or semen abnormalities. Interestingly, Costello et al.,[24] provided evidence that ultrasound diagnosed adenomyosis did not significantly affect outcomes in women undergoing IVF/ICSI with no documented differences in clinical outcomes.[24] Ballester et al.,[27] measured the cumulative pregnancy rate (CPR) for patients undergoing IVF/ICSI cycles; however, the CPR in patients with adenomyosis was significantly decreased compared to those without.[29] Barri et al.,[30] showed that the combination of both ICSI-IVF and endoscopic surgery led to a significant higher CPR in patients younger than 35 than individual intervention alone. Surgery should be considered after failure of two ICSI–IVF cycles for patients younger than 35 years with poor ovarian reserve before opting for an oocyte donation program.[30]

Alternatively Berlanda et al. states that women receiving GnRHa pre-treatment reported an improved CPR with a reduced miscarriage rate.[10] As expected, an increased live birth rate was observed after surgical management, which was mentioned previously.[10] There is a multitude of contradictory studies described in this section, and more time needs to be invested into research on the impact that adenomyosis not only has on fertility but also farther along during pregnancy and post-partum.

Discussion

Adenomyosis is a disease that has not been well researched in pre-menopausal women who desire fertility, as it has traditionally been determined upon pathological evaluation of the uterus post-hysterectomy. Traditional signs and symptoms of adenomyosis are characterized by abnormal uterine bleeding, pelvic pain, and dysmenorrhea; however, many women may remain asymptomatic. The relationship between adenomyosis and adverse obstetrical

outcomes is an understudied facet. This literature review consolidates and clarifies specific mechanisms by which adenomyosis leads to adverse obstetrical outcomes in the pre-menopausal population. Further, recent advances in management strategies for pregnancy maintenance in the adenomyotic population are stated. Based on extensive literature review sufficient evidence that adenomyosis contributes to increased risk of ectopic pregnancy, placental abruption, PEC, GDM, LBW, IUGR, PTD, PPROM, spontaneous abortion, fetal malpresentation, C/S, fetal malpresentation, SGA, LBW, and PPH. In fact, the path by which pregnancy was attained also plays a role in adverse obstetrical and neonatal outcomes. For those women with adenomyosis conceiving through ART, this patient had significantly higher rate of PTD and LBW neonates. Likewise, this patients also had increased risk of placenta previa and placental abruption. Plausible explanations for the adverse obstetrical outcomes listed above include disordered anatomic, function, and immunological environment of the uterus. At this time, two management strategies have yielded positive results for improved obstetrical outcomes: GnRHa pre-treatment before conception and removal of adenomyotic lesions.

Essentially, the large gaps in the literature when it comes to the relationship between poor obstetrical outcomes and adenomyosis is a great field of opportunity for further exploration. The main limitation of this article is that research identifying the aforementioned relationship between adenomyosis and adverse obstetrical outcomes is not as thorough as it should be, and major gaps exist when it comes to extensive management strategies to allow for a safe pregnancy.

Strengths of this article is the expansive timeline by which articles were evaluated and use of relevant resources to provide explanations as to the rationales behind observed impact of adenomyosis. This article clearly lists proposed mechanisms by which adenomyosis impacts obstetrical outcomes cohesively; further, relevant outcomes to research are listed in table format. Shortcomings of this review include the overall abysmal amount of research being done to investigate the relationship between adenomyosis and obstetrical outcomes. Over the designated timeline, about 30 papers were included after exclusion criteria is accounted for. Further, there needs to be more baseline research done concerning the pathogenesis and treatment management strategies to improve our outcomes of interest in women with infertility. Ultimately, more research is required to not only further substantiate either approaches listed prior to aid those women struggling with infertility given an adenomyotic uterus, but also elucidate adverse obstetrical outcomes.

Conclusion

As expected adenomyosis does have significant adverse obstetrical outcomes. Adverse obstetrical outcomes described previously have been linked to the altered uterine environment which contribute to abnormal placentation that places expectant mothers at risk for hypertensive disorders of pregnancy, placental pathologies, and poor preterm outcomes (both PPROM and FGR). Specifically, adenomyotic lesions consume an increased amount of blood decreasing placental blood flow. This decreases the placental size and increases risk of early rupture and ultimately both PPROM and placental abruption. Further, alterations of the JZ leads to vascular resistance, contributing to insufficient deep placental placentation and failure of spinal artery remodeling. In fact, the altered remodeling of the placental vasculature leads to placental abruption and PEC. It has also been proposed that the underlying physiology leading to adverse obstetrical outcomes listed above is the increased concentration of inflammatory markers. These markers are thought to trigger endometrial vasoconstriction and stimulation of cervical ripening which serves as the basis for PEC, preterm birth, and PPROM. Thus, adverse obstetrical outcomes observed in women impacted by adenomyosis are multifactorial.

Women with adenomyosis have baseline lower AMH levels, indicative of low ovarian reserve. Therefore, in women with adenomyosis undergoing ART there is a significantly higher preterm birth rate and higher spontaneous abortion rate. There is conflicting data about the use of GnRH pretreatment for either short (less than 3 months) or long term (more than 3 months) for women undergoing IVF in order to achieve pregnancy. However, for those with focal adenomyosis removal of the lesions has led to more successful natural conception. Management strategies to improve obstetrical outcomes in this population continue to remain quite sparse; however GnRHa pretreatment before conception in combination with surgical removal of focal adenomyotic lesions have provided promising results.

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Conflicts of interest

None to disclose.

References

1. Vannuccini S, Tosti C, Carmona F, et al. Pathogenesis of adenomyosis: an update on molecular mechanisms. *Reprod Biomed Online*. 2017;35(5):592–601.
2. García–Solares J, Donnez J, Donnez O, et al. Pathogenesis of uterine adenomyosis: invagination or metaplasia?. *Fertil Steril.* 2018;109(3):371–379.
3. Nirgianakis K, Kalaitzopoulos DR, Schwartz ASK, et al. Fertility, pregnancy and neonatal outcomes of patients with adenomyosis: a systematic review and meta–analysis. *Reprod Biomed Online.* 2021;42(1):185–206.
4. Champaneria R, Abedin P, Daniels J, et al. Ultrasound scan and magnetic resonance imaging for the diagnosis of adenomyosis: systematic review comparing test accuracy. *Acta Obstet Gynecol Scand.* 2010;89(11):1374–1384.
5. Razavi M, Maleki-Hajiagha A, Sepidarkish M, et al. Systematic review and meta-analysis of adverse pregnancy outcomes after uterine adenomyosis. *Int J Gynaecol Obstet.* 2019;145(2):149–157.
6. Muneyyirci–Delale O, Chandrareddy A, Mankame S, et al. Norethindrone acetate in the medical management of adenomyosis. *J Pharm.* 2012;5(10):1120–1127.
7. Gruber TM, Ortlieb L, Henrich W, et al. Deep Infiltrating Endometriosis and Adenomyosis: Implications on Pregnancy and Outcome. *J Clin Med.* 2021;11(1):157.
8. Wendel MP, Magann EF. The impact of adenomyosis on pregnancy and pregnancy outcomes: a review. *Obstet Gynecol Surv.* 2022;77(8):495–500.
9. Agrawala S, Patil J, Campbell S, et. al. A rare case of extensive placenta accreta in twin pregnancy after GnRH agonist treatment of adenomyosis. *Fertil Research Pract.* 2021;7(1):1–6.
10. Berlanda N, Donati, A, Fedele, F, et al. Adenomyosis and Reproduction: a Narrative Review. *Curr Obstet Gynecol Rep.* 2022;11(3):198–224.
11. Harada T, Taniguchi F, Amano H, et al. Adverse obstetrical outcomes for women with endometriosis and adenomyosis: A large cohort of the Japan Environment and Children's Study. *PLoS One.* 2019;14(8):e0220256.

12. Dommisse J, Tiltman AJ. Placental bed biopsies in placental abruption. *Br J Obstet Gynaecol*. 1992;99:651–654.
13. Hashimoto A, Iriyama T, Sayama S, et al. Adenomyosis and adverse perinatal outcomes: increased risk of second trimester miscarriage, preeclampsia, and placental malposition. *J Matern–Fetal Neo M*. 2018;31(3):364–369.
14. Mochimaru A, Aoki S, Oba M S, et al. Adverse pregnancy outcomes associated with adenomyosis with uterine enlargement. *J Obstet Gynaecol.* 2015;41(4):529–533.
15. Shin YJ, Kwak DW, Chung JH, et al. The risk of preterm births among pregnant women with adenomyosis. *J Med Ultrasound.* 2018;37(8):1937–1943.
16. Yamaguchi A, Kyozuka H, Fujimori K, et al. Risk of preterm birth, low birthweight and small-for-gestational-age infants in pregnancies with adenomyosis: A cohort study of the Japan Environment and Children's Study. *Acta Obstet Gynecol Scand.* 2019;98(3):359–364.
17. Exacoustos C, Lauriola I, Lazzeri L, et al. Complications during pregnancy and delivery in women with untreated rectovaginal deep infiltrating endometriosis. *Fertil Steril*. 2016;106(1129–1135):e1121.
18. Hasdemir P, Farasat M, Aydin C, et al. The role of adenomyosis in the pathogenesis of preeclampsia. *Geburtshilfe Frauenheilkd*. 2016;76:882.
19. Juang CM, Chou P, Yen MS, et al. Adenomyosis and risk of preterm delivery. *BJOG*. 2007;114:165–169.
20. Porpora MG, Tomao F, Ticino A, et al. Endometriosis and pregnancy: a single institution experience. *IJERPH.* 2020;17(2):401.
21. Shinohara S, Okuda Y, Hirata S, et al. Adenomyosis as a potential risk factor for adverse pregnancy outcomes: a multicenter case–control study. *Tohuku. J Exp Med.* 2020;251(3):231–239.
22. Chiang CH, Chang MY, Shiau CS, et al. Effect of a sonographically diffusely enlarged uterus without distinct uterine masses on the outcome of in vitro fertilization–embryo transfer. *J Assist Reprod Genet.* 1999;16:369–372.
23. Mijatovic V, Florijn E, Halim N, et al. Adenomyosis has no adverse effects on IVF/ICSI outcomes in women with endometriosis treated with long–term pituitary down–regulation before IVF/ICSI. *Euro J Ob Gynec Reprod.* 2010;151(1):62–65.
24. Costello MF, Lindsay K, McNally G. The effect of adenomyosis on in vitro fertilization and intra–cytoplasmic sperm injection treatment outcome. *Euro J Ob Gynec Reprod.* 2011;158(2):229–234.
25. Youm HS, Choi YS, Han HD. *In vitro* fertilization and embryo transfer outcomes in relation to myometrial thickness. *J Assist Reprod Genet.* 2011; 28:1135–1140.
26. Thalluri V, Tremellen KP. Ultrasound diagnosed adenomyosis has a negative impact on successful implantation following GnRH antagonist IVF treatment. *Hum Reprod.* 2012;27(12):3487–3492.
27. Ballester M, d'Argent EM, Morcel K, et al. Cumulative pregnancy rate after ICSI–IVF in patients with colorectal endometriosis: results of a multicentre study. *Hum Reprod.* 2012;27(4):1043–1049.
28. Stepniewska A,Pomini P, Scioscia M, et al. Fertility and clinical outcome after bowel resection in infertile women with endometriosis. *Reprod Biomed Online.* 2010;20:602–609.
29. De Ziegler D, Borghese B, Chapron C. Endometriosis and infertility: pathophysiology and management. *Lancet.* 2010;3(376):730–738.
30. Barri PN, Coroleu B, Tur R, et al. Endometriosis–associated infertility: surgery and IVF, a comprehensive therapeutic approach. *Reprod Biomed Online.* 2010;21(2):179–185.

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