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ORIGINAL PAPERS

Fetal Growth Restriction in Patients with Adenomyosis. Incidence and Mechanism

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Abstract

Reports on adenomyosis in pregnancy are few and include a small number of patients. Currently, ultrasound is the first-line imaging diagnostic tool, with a sensitivity of about 84%. Controversies exist regarding the relation of adenomyosis with infertility and pregnancy complications. We analyzed the intrauterine growth restriction (IUGR) cases for a period of one year aiming to determine if adenomyosis impacts negatively the pregnancy outcome. The preterm birth rate in our study population was 20%. From the preterm birth subgroup, the greatest percentage was attributed to late prematurity. The incidence of adenomyosis in this group of pregnancies complicated with IUGR was about 9%. According to our results, there is a higher incidence of preterm birth in cases complicated with fetal growth restriction, as reported by other much larger studies. At this point, there is no established associated risk or method to prevent unfavorable outcomes related to the impact of adenomyosis on pregnancy.

Keywords: adenomyosis, fetal growth restriction, preterm birth.

Rezumat

Rapoartele privind adenomioza în timpul sarcinii sunt puține și includ un număr mic de paciente. În prezent, ecografia este instrumentul de diagnostic imagistic de primă linie, cu o sensibilitate de aproximativ 84%. Există controverse cu privire la relația adenomiozei cu infertilitatea și complicații in sarcina. Am analizat cazurile de restricție de creștere intrauterine (RCIU) pentru o perioadă de un an pentru a determina dacă adenomioza are un impact negativ asupra prognosticului sarcinii. Rata nașterii premature în populația de studiu a fost de 20%. Din subgrupul de nașteri premature, cel mai mare procent a fost atribuit prematurității tardive. Incidența adenomiozei în acest grup de sarcini complicate cu RCIU a fost de aproximativ 9%. Conform rezultatelor noastre, există o incidență mai mare a nașterii premature în cazurile complicate cu restricția creșterii fetale, așa cum au raportat alte studii mult mai mari. În acest moment, nu există un risc asociat sau metode stabilite pentru a preveni un rezultat nefavorabil legat de impactul adenomiozei asupra sarcinii.

Cuvinte cheie: adenomioză, restricție de creștere fetală, naștere prematură.

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INTRODUCTION

Adenomyosis is a benign gynecological condition defined by the presence of stroma and endometrial glands within the myometrium resulting in a hypertrophic uterine musculature, abnormal uterine bleeding and dysmenorrhea[1]. There are tree theories suggested for adenomyosis pathogenesis; first is endo-myometrial invagination of the endometrium, followed by the de novo pathogenesis from mullerian remnants and last, microtrauma of the junction zone[2]. Recently, the role of local hyperestrogenism and hyperperistalsis of the uterine wall are thought to be the mechanisms implicated in infertility in patients with adenomyosis[3]. The incidence reported in specialties studies range from 9 to 62%, the variability is due mainly to the different diagnostic criteria used and number of histologic sections examined. Reports on adenomyosis in pregnancy are few and include a small number of patients as adenomyosis is a pathology developed between 40 and 50 years, but there are studies that report a mean age of 26 years with an imaging diagnosis[4]. The incidence of adenomyosis based on hysterectomy specimens is reported to be about 25%[5]. Currently, ultrasound is the first-line imaging diagnostic tool, with a sensitivity of about 84 % based on the following findings[6]:

1. Globular uterus
2. Myometrial asymmetry (Figure 1)
3. Fan shadows
4. Myometrial cystic areas (Figure 2)
5. Echogenic islets
6. Intramyometrial heterogeneous echogenicity lesions (adenomyomas)
7. Increased focal myometrial vascularization (Figure 2)
8. Altered endo-myometrial junction, thickened > 8 mm, irregular, interrupted seen on 3D evaluation

Controversies exists regarding the relation of adenomyosis with infertility and pregnancies complications. The direct mechanisms which negatively impacts fertility is not completely understood and several theories are described. Altered uterotubal transport and distortion of the uterine cavity can cause a downstream effect and impaired endometrial metabolism. It is important to mention that adenomyosis can be diagnosed only in pre-conception and, until now, large cohort studies showed a positive relation of this pathology with placental abruption, increased risk of placenta accreta and fetal growth restriction[7].

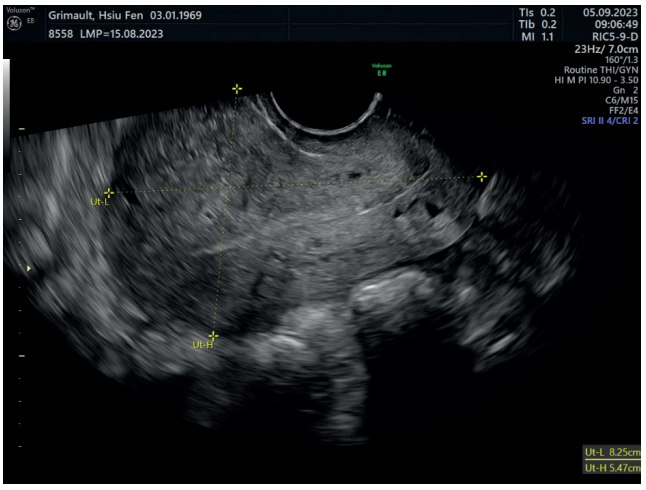

Figure 1. Myometrial asymmetry

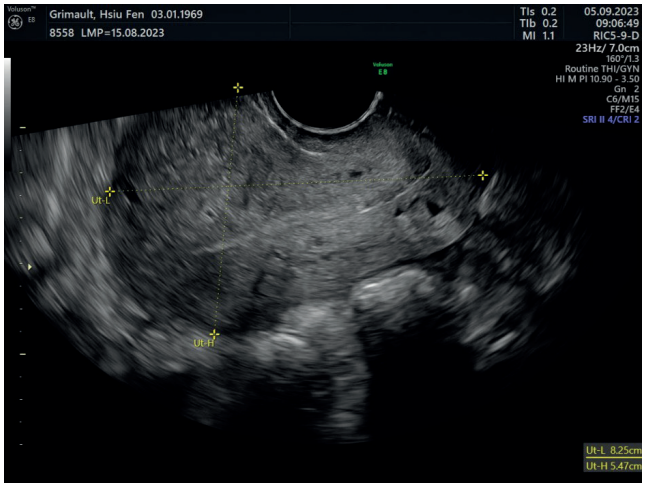

Figure 2. Hyperechogenic islets and hyperintense vascularization

Diffuse adenomyosis in pregnancy acquires a non-specific ultrasound appearance. During the first trimester, diffuse adenomyosis can cause a mass effect on the gestational sac, especially if the whole posterior or anterior uterine wall is affected trough an abnormal decidual reaction of the heterogeneous myometrium (Figure 3). In the second and third trimester, if the placenta underlies the adenomyosis site, the interface between both structures is not well defined and can lead to a misdiagnosis of abnormally adherent placenta.

Intrauterine growth restriction reproduces chronic fetal distress mainly due to placental dysfunction resulted from defective placentation leading to hypoperfusion and oxidative stress. In context of adenomyosis, the abnormal placentation results if the placental insertion is close or on the adenomyotic myometrium with subsequent poor placental vascularization and reduced utero-placental vascular flow[8].

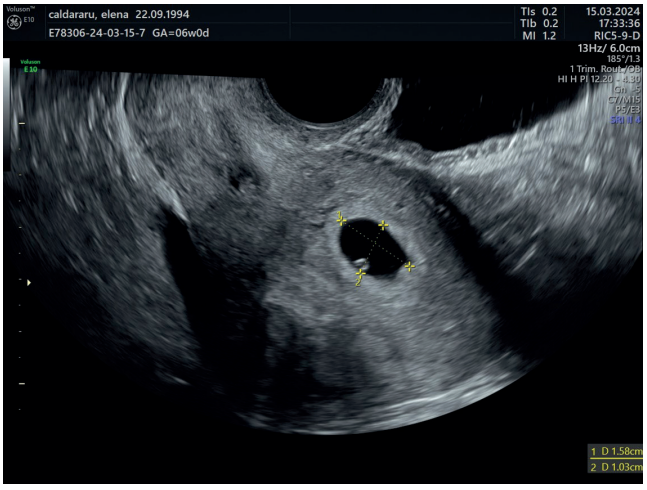

Figure 3. Posterior wall focal adenomyosis appearance in the first trimester of pregnancy

The diagnosis of fetal growth restriction is the key component in the management of these cases and the main factor in reducing the associated perinatal morbidity and mortality.

AIM

We analyzed the fetal growth restriction cases for a period of one year aiming to determine if adenomyosis impacts negatively the pregnancy outcome and if there is a significant association with intrauterine fetal growth restriction.

MATERIAL AND METHOD

This was a prospective study on 54 cases diagnosed antenatally with intrauterine growth restriction (IUGR). The prognosis of these cases was analyzed with focus on the gestational age at birth and neonatal outcome. Also, the assessment of cases diagnosed preconceptionally with adenomyosis was made, comparatively.

RESULTS

The mean age of the pregnant women included in the study was 28 years with a minimum value of 16 years and a maximum of 40 (Figure 4).

Preterm birth rate in our study population was 20%. From the preterm birth subgroup, the greatest percentage was attributed to late prematurity (Figure 5).

Early neonatal adaptation, reflected by the Apgar score at 1 minute, was very good in about 50% of our cases and good in 37% (Figure 6). The mean hospitalization days was 13 with the longest period of 85

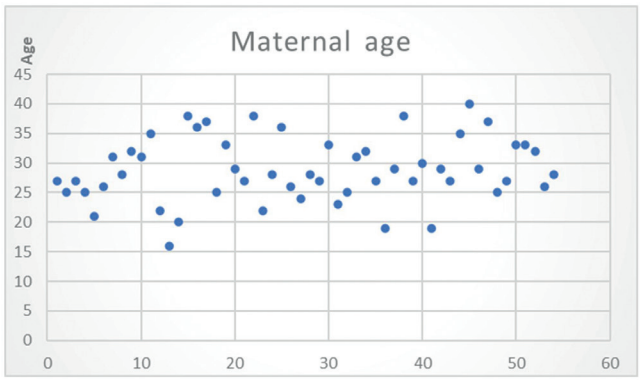

Figure 4. Age distribution in the study group

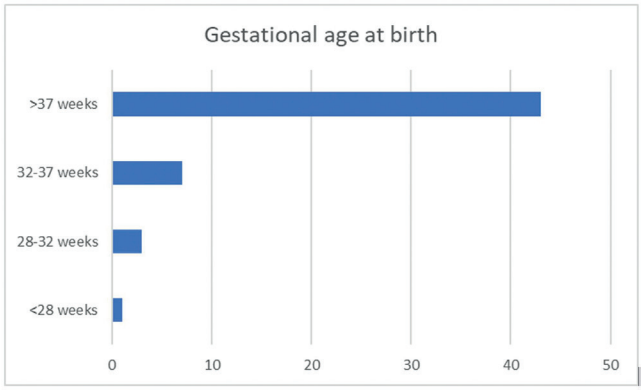

Figure 5. Distribution by gestational age at birth

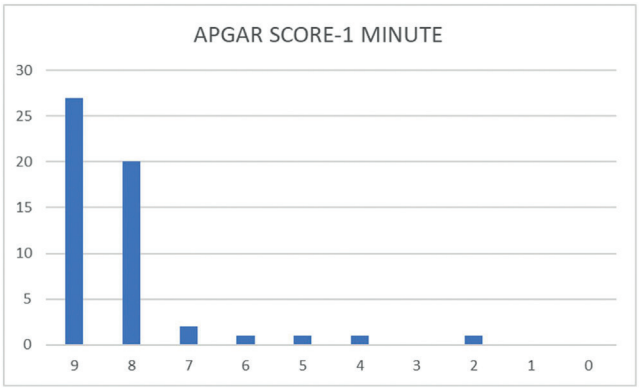

Figure 6. Early neonatal score objectified by Apgar score at 1 minute

days. From our case only one case of neonatal death was registered.

The incidence of adenomyosis in this group of pregnancies complicated with IUGR was about 9%, respectively 5 cases.

DISCUSSIONS

According to our results, there is a higher incidence of preterm birth in cases complicated with fetal growth restriction, as reported by other much larger studies[8].

In IUGR cases the main goal is to adapt the monitoring to the particular case and identify the fetuses that have the highest risk of stillbirth and, implicitly, need to be managed through early delivery. Thus, we could not differentiate in the subgroup of preterm births those of iatrogenic prematurity. There is not a clear indication for caesarean birth in IUGR cases. Furthermore, in the context of an unfavorable Bishop score and reversed flow of the uterine artery, birth trough caesarean section is recommended, as these fetuses may not tolerate the labor as the uterine contraction will add a significant hypoxic stress in an already existing fetal hypoxemia[9].

Adenomyosis is relatively new pathology and evidences regarding the impact of this condition on pregnancy outcome rely on small studies and mainly retrospective. At this point there is not an established associated risk or methods to prevent un unfavorable outcome related to the impact of adenomyosis on pregnancy. Yamaguchi et al published in 2019 a study focused on the impact of adenomyosis on pregnancy outcome including a significant number of over 100 000 pregnancies[10]. According to the published results, adenomyosis was significant related with IUGR, more specific, birth weight < 1500 grams. This was a prospective study in which is speculated that the main factor implied is the inflammation status specific to endometriosis.

As regards the pathogenic mechanism responsible for IUGR in adenomyosis, the assumption is that impaired placentation with subsequent placental insufficiency is the result of a thickened and disrupted junctional zone and abnormal myometrium leading to deep placentation and diverting blood flow from the placenta[11,12]. In about 50% of cases, adenomyosis co-exists with uterine fibroids, endometriosis in 11% and endometrial polyps in 7%, so it is very hard to attribute an abnormal fertility status to a single condition.

On this note, IUGR is thought to be multifactorial, so the limitation of the majority of studies published, including ours, is not excluding any other pathology or possible risk factor.

CONCLUSION

In summary, adenomyosis is a benign pathology with increasing incidence among pregnant women as the childbearing age has an upward trend in the last decades and a higher diagnosis rate trough better imaging technique. A preconceptionally diagnosis of adenomyosis is crucial for adequate management and conciliation regarding the possible complications. Until now, there is sufficient evidence that show a positive relation between adenomyosis and adverse pregnancy outcome. Preterm birth and IUGR are complications associated with significant perinatal morbidity and mortality and have a higher incidence in pregnant women with adenomyosis. There is a need for more prospective studies on this matter, as both mentioned above pathologies are multifactorial and the specific impact of adenomyosis alone has not yet been determined.

The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.
Conflicts of interest: There are no conflicts of interest regarding this article.

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