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A SYSTEMATIC REVIEW OF THE ULTRASOUND FEATURES OF ENDOMETRIAL OSSEOUS METAPLASIA

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Abstract

Acute-on-chronic rotator cuff pathology (AoC-RCP) represents a clinically distinct subset of shoulder disorders characterized by acute symptom exacerbation superimposed upon pre-existing degenerative tendinopathy, yet evidence-based rehabilitation protocols specifically targeting this phenotype remain scarce. This prospective comparative study evaluated the efficacy of a novel Shoulder Pacemaker™ (SPM) device, a wearable bioelectronic stimulator delivering closed-loop, kinematically synchronized suprascapular nerve stimulation, versus conventional physiotherapy in 40 patients with AoC-RCP. Participants were allocated to either SPM-enhanced rehabilitation (n = 20) or standardized deltoid-focused

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physiotherapy (n = 20) at a single tertiary physiotherapy center. Primary outcomes included Visual Analog Scale (VAS) pain scores, the American Shoulder and Elbow Surgeons (ASES) index, and the Constant-Murley scores, assessed at baseline and 24 months. Treatment failure was defined as surgical referral or patient dissatisfaction. At 2-year follow-up, the SPM group demonstrated significantly superior outcomes: 95% treatment success (19/20 patients) versus 50% in conventional physiotherapy (10/20 patients; p = .002), with mean VAS 1.7 versus 3.6 (p = .003), ASES 70 versus 51 (p = .001), and Constant-Murley 62 versus 46 (p = .001). These findings suggest that bioelectronic augmentation of rehabilitation may substantially improve long-term outcomes in AoC-RCP, though randomized controlled trials are warranted to confirm efficacy and establish mechanisms of action.

INTRODUCTION

Osseous metaplasia denotes the formation of bone from a tissue that does not normally ossify within the same individual; by definition the term excludes ossification or calcification arising from retained fetal or embryonic skeletal elements.[1] When this process occurs in the uterus it is referred to as endometrial osseous metaplasia (EOM) or endometrial ossification, and it may extend to involve the cervix or the superficial myometrium. Related but distinct entities include heterotopic intrauterine bone formation and ectopic intrauterine bone derived from retained products of conception.

Several mechanisms have been proposed to explain the presence of bone within the endometrium. The most widely accepted hypothesis is metaplastic transformation of endometrial stromal cells into osteoblasts that subsequently lay down bone matrix. Alternative theories invoke dystrophic calcification within chronically inflamed or post-curettage endometrium, and the retention and persistence of fetal bone after a second-trimester abortion acting as a homograft

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that initiates osteogenesis.[10] Chronic endometritis and disturbed local calcium metabolism have also been implicated.

EOM is rare, with an estimated incidence of approximately 3 per 10,000 women and fewer than a few hundred cases reported in the literature.[2] It predominantly affects women of reproductive age, although occurrence after the menopause has been documented. In more than 80% of cases there is a history of a preceding pregnancy, most often a miscarriage or termination managed by dilatation and curettage.[3] Clinically, the spectrum ranges from an incidental finding in an asymptomatic woman to menorrhagia, menstrual irregularity, chronic pelvic pain, abnormal vaginal discharge and, most importantly, secondary infertility — the bony fragments acting as an intrauterine foreign body that impairs implantation.

Although hysteroscopy remains the diagnostic and therapeutic gold standard, non-invasive imaging — chiefly transvaginal ultrasonography — has become the practical mainstay of first-line detection.[12] The principal difficulty for the reporting radiologist or sonographer is that the appearances overlap with those of a retained intrauterine device, retained products of conception, Asherman syndrome and calcified submucosal fibroids.[5] The purpose of this systematic review is therefore to collate and characterise the reported ultrasound features of EOM, to define the recurring diagnostic pattern, to clarify the complementary roles of two- and three-dimensional ultrasound, hysteroscopy and histopathology, and to summarise management approaches and their effect on subsequent fertility.

2. Materials and Methods

2.1 Search strategy and information sources

An electronic literature search was conducted in PubMed/MEDLINE, ScienceDirect and the OBGYN Online Library. Search terms combined the keywords “osseous metaplasia”, “endometrial ossification”, “endometrial bone”, “intrauterine bone” and “ultrasound” using Boolean operators. Reference lists of retrieved articles were hand-searched to identify additional eligible reports.

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2.2 Eligibility criteria

Studies were eligible if they (i) described one or more patients with a confirmed or presumptive diagnosis of endometrial osseous metaplasia, (ii) provided a description of the transvaginal or transabdominal ultrasound findings, and (iii) were published in the English language between 2000 and 2022. Articles that did not describe the sonographic appearance, that addressed conditions other than EOM, or for which the full text was unavailable, were excluded.

2.3 Study selection and data extraction

Two reviewers independently screened titles and abstracts, followed by full-text assessment of potentially eligible records; disagreements were resolved by discussion. For each included case the following data were extracted: patient age, relevant obstetric and gynaecological history, presenting symptoms, ultrasound findings (echogenicity, location, dimensions, acoustic shadowing and use of 3D imaging), method of diagnostic confirmation, management and fertility outcome. The screening process is summarised according to the PRISMA framework (Fig. 1). A total of seven studies, contributing nine individual cases, met the inclusion criteria and form the basis of the qualitative synthesis presented below.

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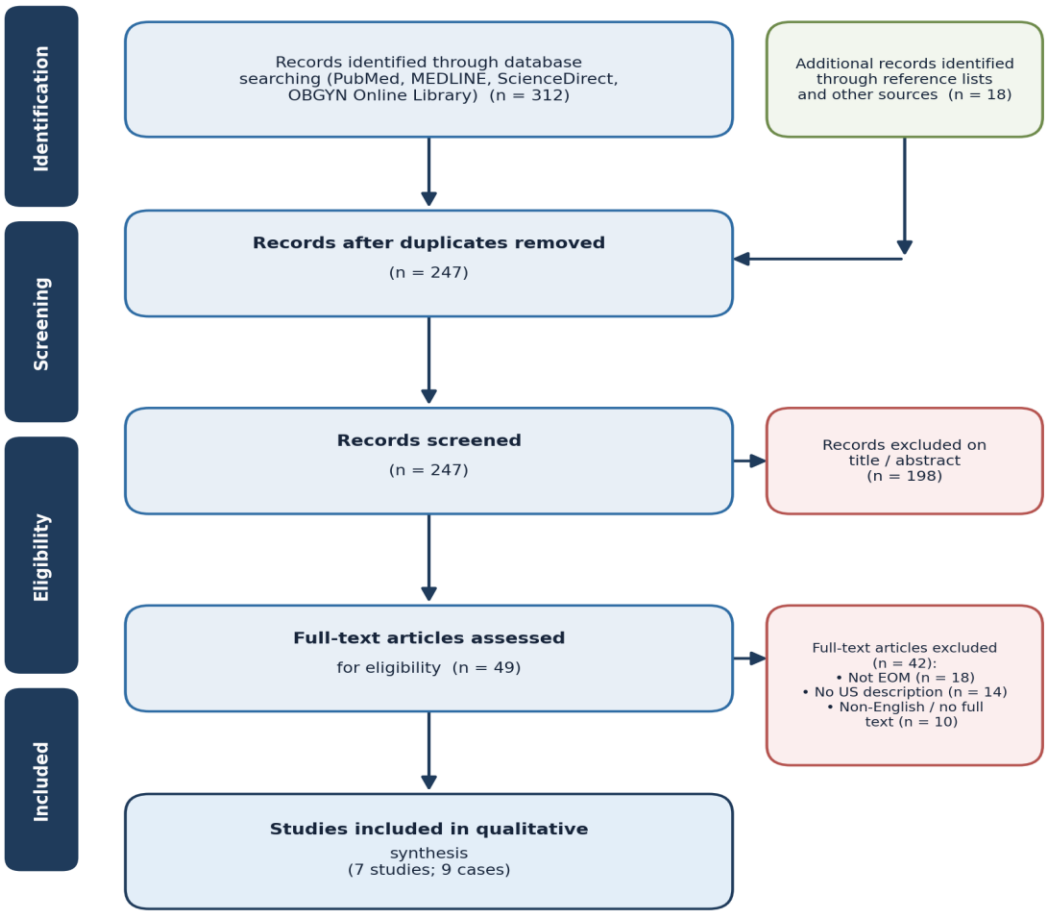

Fig. 1 *PRISMA flow diagram summarising the identification, screening, eligibility assessment and inclusion of studies in the systematic review.*

3. Results

Nine cases reported across seven studies were synthesised. Patient age ranged from 27 to 52 years. A history of one or more pregnancy losses followed by dilatation and curettage was almost universal, and secondary infertility was the most frequent reason for presentation. The recurring sonographic signature was one or more strongly hyperechoic linear or irregular intra-cavitary foci

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casting posterior acoustic shadowing. The individual cases are summarised below and compared in Tables 1 and 2.

3.1 Summary of included cases

Case 1 (Cayuela et al., 2009). A 27-year-old woman presented with five years of secondary infertility after two pregnancy losses. Transvaginal ultrasound (TVS) demonstrated a hyper-refringent intrauterine structure measuring 25 × 22 mm, reported as osseous metaplasia; the ossification was shown to be of maternal origin.[4]

Case 2 (Kouakou et al., 2012). A 36-year-old woman with secondary infertility and a prior 13-week pregnancy loss. TVS revealed a 13 mm linear hyperechoic area within the cavity that persisted on serial scans; hysterosalpingography showed cervico-isthmic synechiae with patent tubes, and hysteroscopy confirmed osseous metaplasia.[5]

Case 3 (Coccia / Lainas et al.). A 29-year-old woman (gravida 2, para 1, abortus 1) with foul-smelling leucorrhoea and metrorrhagia following a D&C. TVS showed a central echogenic band occupying the entire cavity and partly involving the cervix and myometrium; hysteroscopy revealed numerous white spicules and histopathology confirmed osseous metaplasia.[6 13]

Case 4 (Grigoras et al., 2003). A 52-year-old para-0 woman, eight years post-menopause, with three prior abortions, presenting with activity-related bleeding. Endovaginal ultrasound showed a hyperechoic area that persisted after curettage; histopathology demonstrated extensive micro-calcification, attributed to calcification of the endometrium during post-abortion healing.[11]

Case 5 (Sood et al., 2019). A 37-year-old woman with oligomenorrhoea and four years of secondary sub-fertility after a termination ten years earlier. TVS identified two linear echogenic areas (17 mm and 3 mm) with posterior enhancement. A pelvic CT excluded myometrial invasion, and the bony tissue was fragmented using combined ultrasonic and pneumatic lithoclast energy and retrieved hysteroscopically; histology confirmed EOM.[7]

Cases 6–9 (Grigore et al., 2018). A case series of four women (ages 30, 35, 34 and 34 years), each with secondary infertility or menstrual symptoms and a history of pregnancy loss. Two-

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dimensional endovaginal ultrasound showed bright endometrial foci or linear hyperechoic structures with posterior acoustic shadowing; in one case the appearance closely mimicked an intrauterine device and three-dimensional ultrasound of the coronal plane was decisive in establishing the correct diagnosis. Hysteroscopy confirmed osseous metaplasia in each case, and two patients subsequently conceived spontaneously.[8]

3.2 Comparative analysis

Eight of the nine cases shared a concordant pattern of strongly echogenic intra-cavitary foci with posterior acoustic shadowing on transvaginal ultrasound, with hysteroscopic and/or histopathological confirmation (Table 1). The principal point of divergence (Table 2) was an isthmic, curvilinear lesion that was initially interpreted as a foreign body and required hysteroscopy to reveal a meshwork of bony tissue, underscoring the diagnostic overlap of EOM with an intrauterine device and retained foreign material.

Table 1. *Included cases with concordant ("similar") ultrasound findings.*

#	Age	Study title	Year	Author	Ultrasound findings	Conclusion
1	27 y	True osseous metaplasia of the endometrium: the bone is not from a fetus	2009	Cayuela et al.	TVS: hyper-refringent intrauterine image measuring 25 × 22 mm reported as osseous metaplasia.	Endometrial ossification was of maternal (patient) origin – a true osseous metaplasia.

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#	Age	Study title	Year	Author	Ultrasound findings	Conclusion
2	36 y	Endometrial osseous metaplasia and infertility	2012	Kouakou et al.	TVS: linear hyperechoic area, 13 mm, persisting on serial scans; HSG and hysteroscopy performed.	Hysteroscopy visualised bony fragments; biopsy showed endometrial tissue with osseous metaplasia in the stroma.
3	29 y	Ultrasound-guided hysteroscopic management of endometrial osseous metaplasia	2004	Coccia / Lainas et al.	TVS: central echogenic band filling the entire cavity, partly involving cervix and myometrium.	Reported as osseous metaplasia; diagnosis confirmed at hysteroscopy.
4	52 y	Osseous metaplasia of the uterus	2003	Grigoras et al.	TVS before and after curettage: hyperechoic foci persisted after curettage.	Calcification of the endometrium during healing after abortion; uterine osseous metaplasia.

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#	Age	Study title	Year	Author	Ultrasound findings	Conclusion
5	37 y	Novel management of endometrial osseous metaplasia	2019	Sood et al.	TVS: two linear echogenic areas (17 mm, 3 mm) with posterior enhancement in the mid-cavity.	Osseous metaplasia; managed with ultrasonic/pneumatic lithoclast fragmentation.
6	30 y	Ultrasound features of osseous metaplasia of the endometrium – case series	2018	Grigore et al.	2D TVS: multiple bright endometrial foci with posterior acoustic shadowing.	Hysteroscopy confirmed osseous metaplasia.
7	35 y	Ultrasound features of osseous metaplasia of the endometrium – case series	2018	Grigore et al.	2D TVS: linear hyperechoic structure (19 × 2.1 × 8.5 mm) mimicking an IUD; 3D coronal	Hysteroscopy confirmed osseous metaplasia; 3D US aided differentiation from IUD.

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#	Age	Study title	Year	Author	Ultrasound findings	Conclusion
					view clarified the diagnosis.	
8	34 y	Ultrasound features of osseous metaplasia of the endometrium – case series	2018	Grigore et al.	2D TVS: hyperechoic structure with posterior acoustic shadowing.	Hysteroscopy confirmed osseous metaplasia.

Table 2. *Included case with divergent ("dissimilar") ultrasound findings.*

#	Age	Study title	Year	Author	Ultrasound findings	Conclusion
1	34 y	Ultrasound features of osseous metaplasia of the endometrium – case series	2018	Grigore et al.	TVS: hyperechogenic curvilinear structure at the isthmic region with posterior shadowing, suspicious for a foreign body.	Diagnostic hysteroscopy showed a white meshwork of bony material of hard consistency in the

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#	Age	Study title	Year	Author	Ultrasound findings	Conclusion
						isthmus, completely excised.

3.3 Representative sonographic appearances

The figures below illustrate the spectrum of reported appearances: a focal hyperechoic intra-cavitary structure (Fig. 2), a central echogenic band with posterior shadowing filling the cavity (Fig. 3), longitudinal and transverse views of linear echogenic foci with acoustic shadowing (Fig. 4), and the characteristic linear echogenic area within the endometrial cavity (Fig. 5).

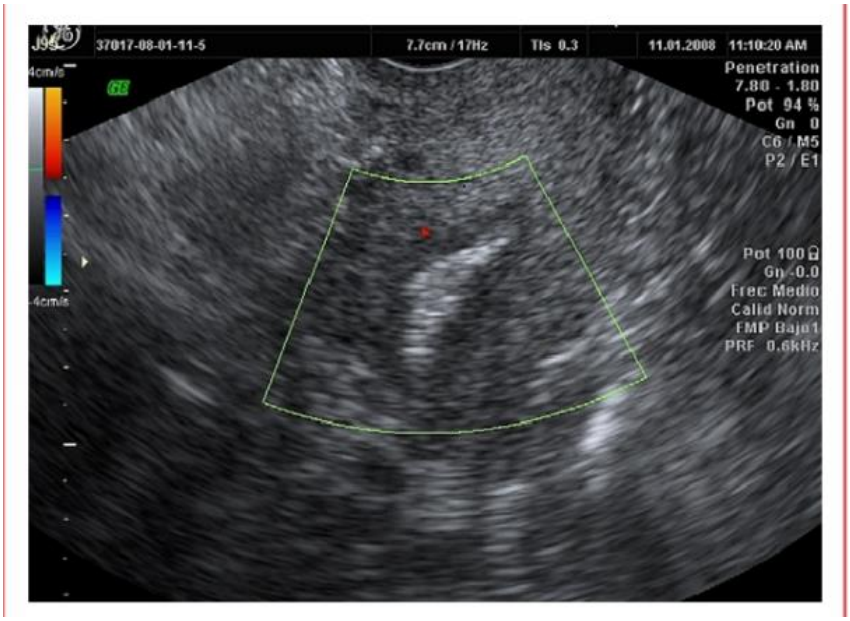

Fig. 2 *Transvaginal ultrasound showing a hyperechoic, non-vascularised structure within the endometrial cavity, consistent with osseous metaplasia.*

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Fig. 3 *Longitudinal transvaginal scan of the uterus demonstrating a central echogenic band occupying the endometrial cavity with posterior acoustic shadowing.*

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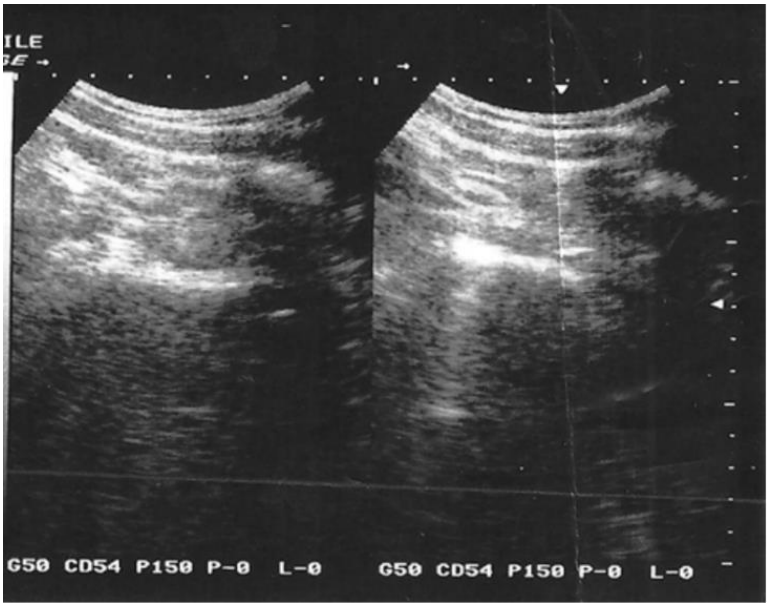

Fig. 4 *Transvaginal ultrasound: longitudinal (a) and transverse (b) sections of the uterus showing echogenic linear structures with posterior acoustic shadowing within the cavity.*

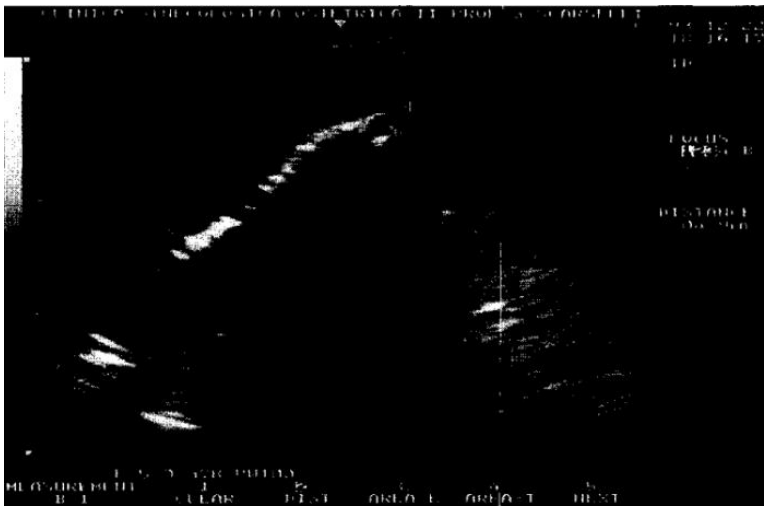

Fig. 5 *Linear echogenic area (≈13 mm) within the uterine cavity with posterior acoustic shadowing, a typical sonographic appearance of endometrial osseous metaplasia.*

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3.4 Pooled presenting symptoms

Pooling the symptom data reported in larger imaging series of EOM confirms that infertility is by far the commonest presentation, followed by menstrual irregularity; pelvic pain, vaginal discharge and dysmenorrhoea are less frequent, and a minority of women are asymptomatic (Fig. 6).[12]

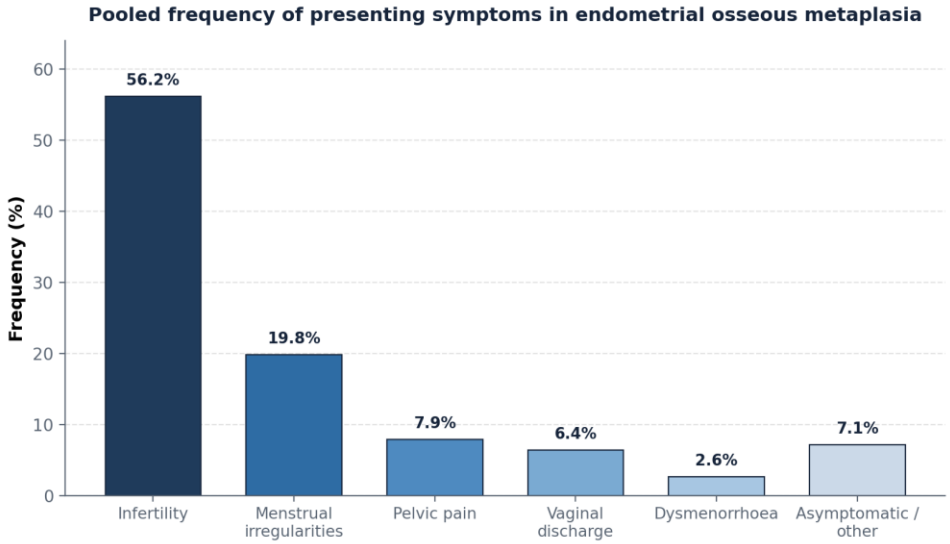

Fig. 6 *Pooled frequency of presenting symptoms in endometrial osseous metaplasia, derived from reported imaging series; infertility predominates.*

4. Discussion

The findings of this review reinforce a consistent message in the literature: transvaginal ultrasound is the pivotal first-line modality for the detection of endometrial osseous metaplasia, and a strongly echogenic intra-cavitary focus with posterior acoustic shadowing is its hallmark.[8] The two principal pathogenetic explanations — metaplastic transformation of endometrial stromal cells into osteoblasts, and the retention of fetal skeletal tissue after a late abortion that persists and grows as a homograft — are not mutually exclusive, and in many reports the calcification appears to develop during the healing process after instrumentation of the uterine cavity.[9] [10]

Across the included cases, the near-universal antecedent of a pregnancy loss managed by dilatation and curettage supports the central role of endometrial injury and chronic inflammation

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in the genesis of EOM. The diagnosis is established by the combination of ultrasound and hysteroscopy and certified by histopathological examination, which remains the reference standard.[11]

The most important practical pitfall is the sonographic overlap of EOM with a retained intrauterine device, retained products of conception, Asherman syndrome and calcified submucosal fibroids. The present synthesis highlights the added value of three-dimensional ultrasound: visualisation of the coronal plane allowed the irregular, non-device morphology of the ossified tissue to be appreciated and the correct diagnosis to be reached in a case that on two-dimensional imaging had been mistaken for an intrauterine device.[8] Where extensive or deeply embedded disease is suspected, cross-sectional imaging (CT or MRI) can be used to exclude myometrial invasion before intervention.[7 12]

From a management perspective, complete hysteroscopic removal of the bony fragments is curative and, importantly, restores fertility in the majority of affected women of reproductive age. When the bony tissue is adherent to or embedded within the myometrium, resection with conventional resectoscope or hysteroscopic scissors carries a risk of uterine perforation; in this setting, techniques adapted from the endoscopic management of urinary tract calculi — ultrasonic/pneumatic lithoclast fragmentation under direct vision — have been used successfully.[7]

This review has limitations. The evidence base is confined to case reports and small case series, with inherent risks of publication and selection bias and an absence of comparative or prospective data; quantitative pooling of diagnostic accuracy was therefore not possible. Heterogeneity in reporting of ultrasound parameters and the small number of cases limit the strength of any conclusions. Nonetheless, the consistency of the described sonographic pattern across independent reports lends it practical diagnostic value.

5. Conclusion

Endometrial osseous metaplasia is a rare condition whose aetiopathogenesis remains incompletely understood, although a maternal (endometrial) origin of the ossification is currently

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the most widely accepted explanation. It is an important, and frequently reversible, cause of secondary infertility. A strongly echogenic intra-cavitary focus with posterior acoustic shadowing on transvaginal ultrasound — particularly in a woman with prior pregnancy loss and secondary infertility — should prompt consideration of the diagnosis, with three-dimensional ultrasound used to distinguish it from an intrauterine device. Confirmation by hysteroscopy and complete elimination of the bony fragments from the uterine cavity allows fertility to be restored in the majority of cases. Awareness of this entity among radiologists and gynaecologists is essential to avoid misdiagnosis of an uncommon but treatable cause of infertility.

6. Recommendations

- Transvaginal ultrasound should be the first-line investigation in women with secondary infertility and a history of pregnancy loss, with active consideration of EOM when echogenic shadowing foci are seen.
- Three-dimensional ultrasound should be employed to differentiate EOM from an intrauterine device and other intra-cavitary foreign bodies.
- Ultrasound-guided hysteroscopic removal of extensive osseous metaplasia may represent a safer and more effective alternative to laparoscopic approaches and warrants further prospective clinical evaluation.
- Histopathological confirmation should be obtained, and post-treatment follow-up imaging performed to confirm complete clearance before fertility treatment.

Declarations

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Conflicts of interest

The authors declare that they have no competing interests.

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Ethics approval and consent

This is a systematic review of previously published, de-identified case reports and case series and did not involve any new studies of human participants performed by the authors; formal ethical approval was therefore not required.

Author contributions

H. Quddos conceived the review and drafted the manuscript; S. Saleem and A. Shah contributed to the literature search, data extraction and tabulation; H. A. Malik contributed to data interpretation, methodology and critical revision. All authors read and approved the final manuscript.

Data availability

All data analysed during this review are derived from the publications cited in the reference list.

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