

## Role of imaging in Female Infertility

Pushpa Ranjan<sup>1</sup> and Rajeev Ranjan<sup>2</sup>

<sup>1</sup>Department of Radiology, IGIMS, Patna, India. <sup>2</sup>Department of Surgery, NMCH, Sasaram, India  
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**Abstract** Imaging plays key role in diagnostic evaluation of female infertility. Infertility has many causes – tubal and peritubal disorders, uterine disorders including mullerian duct anomalies, ovarian disorders, and cervical disorders. There is increase in incidence of female infertility in association with that there is increase in demand for female imaging modalities. Although HSG is gold standard investigation but USG is first line investigation for female infertility.

Sonosalpingography differentiate among uterine synechiae, endometrial polyps and submucosal leiomyomas. Pelvic MRI is very sensitive for detection of endometriosis. It is also used for detection of adenomyosis, leiomyomas, mullerian duct anomalies. Cervical stenosis is referred as failure or difficulty in cervical cannulation in HSG. Ovarian disorders are usually diagnosed by USG. Multimodality imaging approach with appropriate selection of imaging modality is necessary to know exact cause of infertility because it direct subsequent management of infertility.

**Keywords:-** infertility, hysterosalpingography, ultrasonography, magnetic rasonance imaging.

### Introduction

Infertility is defined as failure to conceive a desired pregnancy after 12 months of unprotected intercourse. It is of two types – primary and secondary infertility. Primary infertility in which a couple never have a child. Secondary infertility is failure to achieve a child following a previous pregnancy. Approximately 10% of couple are infertile. Male and female are equally affected. Potential causes of infertility are numerous and they can be categorized as –

Tubal causes – Infection, obstruction.

**Uterine Causes** – Congenital anomalies,

infections, uterine synechiae, focal lesions, intrauterine scar.

**Ovarian causes** – Follicular and ovulation abnormalities includes pituitary adenoma, polycystic ovarian syndrome, premature ovarian failure, gonadal dysgenesis and endometriosis.

**Cervical causes-** Cervical stenosis caused by Infection, trauma.

### Imaging modalities of infertility

**Ultrasonography (USG) (mainlytransvaginal)** it is first line investigation for infertility and can be coupled with colourDoppler, 3D, 4D. It is easily available, low cost and radiation free. Limitations are subjective variations, limited field of view, obesity, gaseous abdomen, small ovaries, fallopian tube and broad ligament are not properly visualised.

Address for correspondence and reprint requests to:

<sup>1</sup>Department of Radiology, IGIMS, Patna, India. Email:

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Submitted: 5 june 2016 Accepted: 2 october 2016 Published:

USG plays important role in interventional procedure. It guides oocyst retrieval, embryo transfer in in-vitro fertilization procedure, drainage of pelvic collection, cyst and abscess.

**Sonosalpingography (sono - USG):-** It is airless, sterile, saline infusion through soft plastic catheter into cervix with simultaneous endovaginal US. It confirms tubal patency and allows excellent visualization of endometrial cavity and its lining. It differentiates among endometrial polyps, submucosal leiomyomas and intrauterine adhesions.

**Hysterosalpingography:-**It is radiological procedure used to demonstrate uterine and fallopian tube lumen using contrast medium. It is valuable technique in evaluation of female infertility because it provides tubal patency. It involves ionising radiation. Despite development of other diagnostic modalities such as MRI, hysteroscopy, laparoscopy, it remains main examination for fallopian tube patency in developing countries [3]. Uterine filling defect and contour abnormalities may be discovered at HSG but typically require further characterization with pelvic USG, pelvic MRI.

**Selective Salpingography and fallopian tube recanalization:-** Tubal blockage is diagnosed and recanalized non-surgically. This procedure doesn't require incision. Fallopian tube is directly opacified by injecting contrast media through catheter placed in tubal ostium under fluoroscope guidance. If fallopian tube obstruction found, a 3-F catheter over 0.015-inch guide wire is directly advanced through obstruction via cornual catheter and obstruction is recanalized (16).

**MRI:** - It provides excellent soft tissue characterisation of pelvic structure. It detect

lesions like adenomyosis, endometriosis, leiomyomas, tubal disease, mullarian duct anomalies, ovarian pathology.[3]It also detect extra-pelvic causes involved in infertility like pituitary adenoma. MRI predicts the outcome of conservative treatment of adenomyosis, leiomyomas and endometriosis and help in better selection of treatment plan.

Recently, MRI based HSG has been introduced and is superior to USG for studying tube. MRI has potential to replace HSG and laparoscopy in diagnosis of abnormalities of female genital tract [3]. Due to limited availability, and high cost MRI based HSG not become popular.

Sub-centimetric uterine lesions are not detected in MRI. It is contraindicated in patient with pacemaker, cochlear implant.

#### **Causes of infertility:-**

**Fallopian Tube Abnormalities:** - It is most common cause of female infertility, accounting for 30 - 40 % of cases [1]. Hysterosalpingography, provides optimal depiction of FT, allowing detection of tubal patency, occlusion, irregularity and peritubal disease.

Appropriate steps in imaging evaluation of fallopian tube abnormalities are given below:-

Occlusion of FT occurs at any site of long course of tube. Differential diagnosis of tubal occlusion includes tubal spasm, infection, and prior surgery. When tubal occlusion is in the proximal or interstitial part of FT at HSG, tubal spasm should be suspected [1].

When occlusion occurs at ampulla of FT, hydrosalpinx seen, a condition most commonly caused by pelvic inflammatory disease. At hysterosalpingography, tube

appears dilated, tortuous, fluid filled, with absence of intraperitoneal spillage of contrast (Fig. 1).

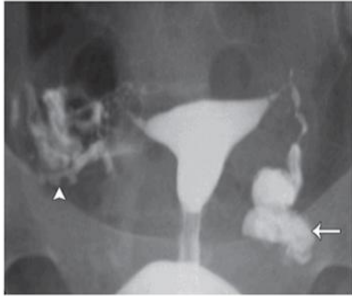


Fig.1 left hydrosalpinx. HSG show dilated left fallopian tube with absence of intraperitoneal spillage of contrast material. Right fallopian is patent with normal spillage of contrast material

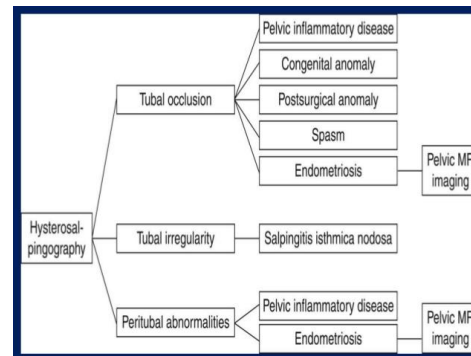
Pelvic inflammatory disease may lead to peritubal adhesion, is one of the common causes of infertility and manifest as pelvic collection and tubo-ovarian mass. (Fig. 2).

**Uterine Adhesion:** - Infertility secondary to uterine adhesion is known as Asherman syndrome. Uterine adhesion must be differentiated from normal uterine fold which also appear as longitudinal filling defect when uterine cavity is not fully distended. Sonosalpingography has greater sensitivity than HSG in diagnosing uterine adhesion which show echogenic bands that traverse the endometrial cavity.

**Uterine Cause:** - Endometrial polyp

Even sub-centimetric endometrial polyp and submucosal leiomyoma contribute to infertility by interfering with embryo transfer and implantation. Sonosalpingography show endometrial lesions that are not visible with pelvic ultrasound and it differentiate endometrial polyp from submucosal leiomyoma (Fig 3). Endometrial polyp typically appears as echogenic intracavitary mass. It allows accurate assessment of its number, location

and provides subsequent guidance for hysteroscopic biopsy and excision [1].



Submucosal leiomyomas appear as hypoechoic masses that distort normal endometrium .

**Adenomyosis :-** is not a common cause of infertility. The frequency of symptomatic adenomyosis peaks between 33 – 50 years is most often found in parous women. Nulliparous women sometimes affected and experience infertility. Exact cause of infertility in patient with adenomyosis is not known. Adenomyosis may be associated with infertility due to impaired uterine contractility which is necessary for directed sperm transport through uterus (6). It reduced uterine and endometrial reception in enlarged uterus [1]. Both TVS and MRI allow accurate, non-invasive diagnosis of adenomyosis. The relevant diagnostic US findings are:-

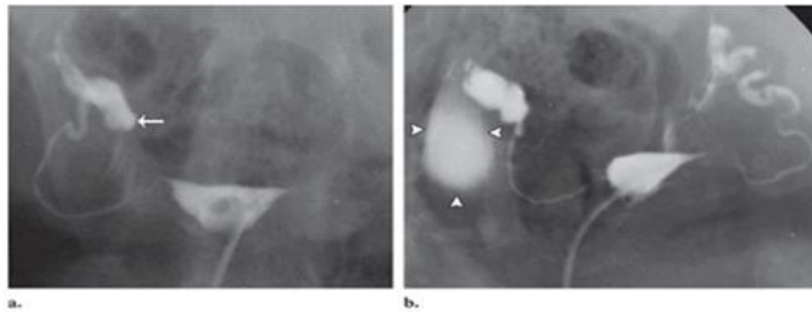
- (a) The thickening and asymmetry of anterior and posterior uterine mass.
- (b) A poorly defined area of decreased or increased echogenicity, heterogenous echotexture, or myometrial cyst [8].

MR imaging criteria include:-

- (a) Myometrial wall of low signal intensity with indistinct margins on both T1 and T2W images.

(b) Diffuse or focal widening of junctional zone thickness on T2W images. A junctional zone thickness of 12mm or more optimize the accuracy of MR imaging for this diagnosis.

or heterogenous in echotexture which may have hyperechoic calcification. Leiomyomas may demonstrate acoustic attenuation or shadowing without a discrete mass making it impossible to estimate size [15]. Colour Doppler reveals peripheral vascularity of mild to moderate resistance,



**Fig. 2** Right peritubal adhesion due to previous pelvic inflammatory infection. (a)early (b)late HSG show normal filling of contrast in right fallopian tube and a rounded collection of leaked contrast material adjacent to ampullary portion of right fallopian tube. The collection is due to peritubal adhesion. Left fallopian tube is normal and patent.

(c) Punctuate high signal intensity, which corresponds to ectopic endometrium, are often demonstrated on T2W images [4], (Fig.4).

**Leiomyomas (Fibroids):-** Infertility may result when leiomyomas are numerous or have submucosal location that interferes with embryo transfer and implantation. Patient with multiple leiomyoma are at increased risk for early spontaneous fetal loss. If leiomyoma located near uterine cornua, it obstructs ipsilateral fallopian tube and causes absence of fallopian tube opacification[1].

On USG leiomyomas have variable appearance. Uterus may be enlarged. Localised leiomyoma appears as well defined, hypoechoic (fig.5a)

differentiate it from adenomyoma which reveal moderate central and peripheral vascularity [2].

Transvaginal US is as effective as MRI for detection but MR imaging outperforms transvaginal US in preoperative evaluation of location, numbers and size of fibroid. Sonohysterography demonstrate relationship between endometrium and submucosal fibroid and serve as important adjunct to TVS. On MRI it appears as sharply marginated mass that typically has lower signal intensity than myometrium on T2W [Fig.5 b]. MRI is highly accurate modality for differentiation of leiomyoma from adenomyosis in case of enlarged uterus; accuracy is 99% [4].

**Mullerian Duct Anomalies:-** If other causes of infertility are excluded, uterine anomalies may be suggested as cause of infertility.

Mutliplanar MRI is diagnostic. Millerian Duct

includes the duplication of uterine cavity,

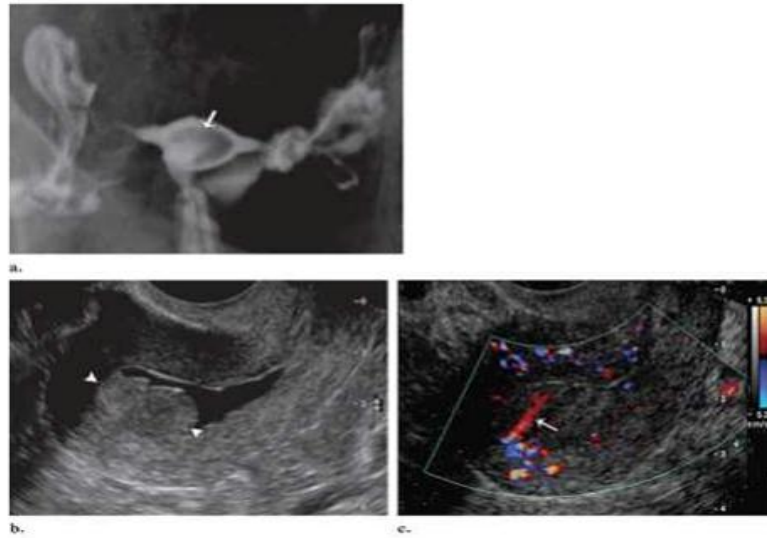


Fig.3 uterine polyp (a)spot radiograph in early filling phase show well defined intrauterine filling defect.(b) sonosalpingography show posterior endometrial fundal polyp. (c)TVS with doppler show central feeding vessel.

Anomalies are classified according to American Society of Reproductive Medicine System [2], [fig'6]

Class I :- Segmental agenesis or variable degree of uterovaginal hypoplasia:

The anomaly can be detected because of amonorrhoea, before HSG performed.

Class II: - Unicornuate uterus:

That represents partial or complete hyperplasia of one of mullerian duct. In rare cases of degeneration of the masonephric duct, the uterine cavity appears monocular when imaged, placed right or left of midline. The unicornuate uterus contacts only the coordinate fallopian tube.

Class III :- Diadelphys uterus:

This is rare abnormality that results from complete nonfusion of mullarian duct and

cervix and vagina. Rarely this uterus has a single vagina.

Class IV: - Bicornuate uterus:

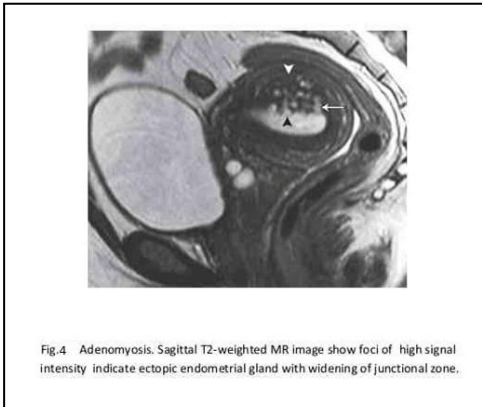
It demonstrates incomplete fusion of superior segment of uterovaginal canal. The uterine cavity is divided into two, each half has a narrow length, shape and stand apart from each other. MRI confirm the presence of bicornuate uterus by showing intercornual distance of  $> 4$  cm and concavity of fundal contour or an external fundal cleft  $> 1$  cm..

Class V:- Septate uterus:

. It represent partial or complete failure of resorption of the uterovaginal septum after failure of mullarian duct. MR imaging help to differentiate a septate uterus from bicornuate uterus by depicting a normal convex, flat or minimally concave ( $< 1$  cm



deep) external fundal contour with septate uterus. MR imaging readily demonstrate composition and extent of septum.



#### Class VI: Arcuate uterus:

Near complete resorption of uterovaginal septum resulting in shallow, smooth, broad based impression on uterine cavity which may be depicted in HSG, US and MRI.

#### Class VII or DES (diethylbestrol) induced-Exposure to this synthetic estrogen

antenatally can result in a T-shaped, hypoplastic, and constricted uterus.

**Endometrioma:-** It is found in 25–50% of infertile women and 30-35% of women with endometriosis are infertile [4]. The condition almost exclusively affects women during reproductive age. This condition mostly involve ovary but secondarily involve other pelvic organs [10]. Laparoscopy is mainstay for diagnosis, staging and treatment of endometriosis. Imaging modality for endometriosis include Pelvic US, MRI. Endometriosis may take in the form of small implant or cyst that change in size and appearance during menstrual cycle and may initiate inflammatory response leading to fibrosis and adhesion [12]. Endometriotic cyst referred as endometrioma, result from repeated haemorrhage within implant. USG has low sensitivity for detection of focal

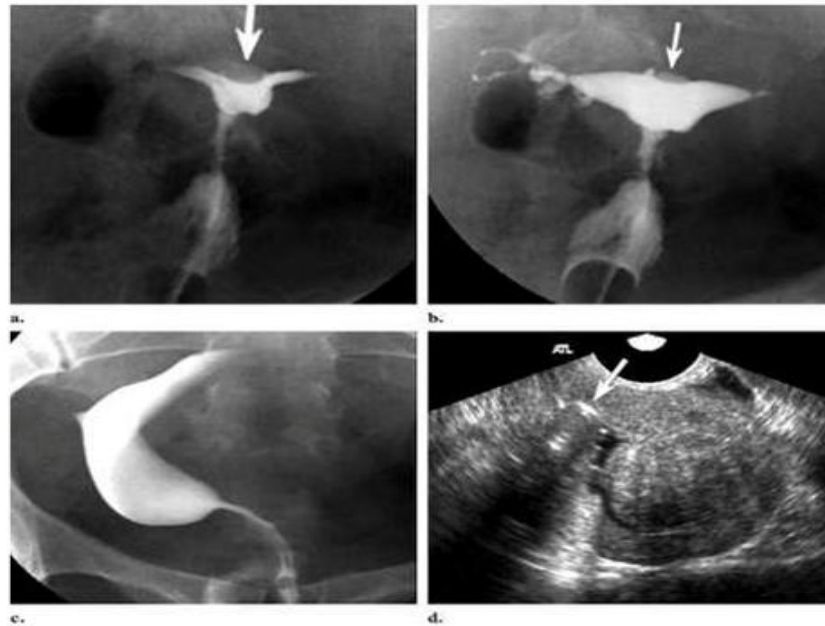
implants. Endometrioma located in ovary show well defined unilocular or multilocular, predominantly cystic lesion containing homogeneous low level internal echoes. It may appear fluid-fluid level. Small linear echogenic foci may be present in the wall of cyst [15] [fig.7].

MRI is more sensitive for detection of endometrioma which show (a) adnexal cyst of high signal intensity on both T1W and T2W image. (b) High signal intensity on T1w image and low signal intensity on T2w image. Dense concentration of cyclic haemorrhage and high viscosity of contents in endometrioma causes T2 shortening and produces shadowing. Fat suppressed T2W image are very useful for detecting peritoneal implants. Tube may be involve in the form of hydrosalpinx or with peritubal adhesion while uterine involvement as adenomyosis. Adhesion is seen on MRI as hypointense strands within adjacent fat, obscuring adjacent interface. A posteriorly displaced uterus, kissing ovaries, elevated posterior fornix, angulated small bowel loop, hydro/haematosalpinx and multilocular fluid collections are indirect indicator of pelvic adhesion [2].

**Ovarian Abnormalities:-** disorder affecting ovulation account for 30 to 40% of cases of female infertility [4]. Ovarian causes of infertility include primary ovarian cause and secondary ovarian cause. Primary ovarian cause includes nonfunctional ovaries, premature ovarian failure and absence of ovaries (gonadal dysgenesis). These conditions are usually diagnosed on the basis of clinical and biochemical findings. Secondary ovarian cause includes polycystic ovarian disease, endometrioma and ovarian cancer. Imaging is more valuable for diagnosing secondary ovarian cause. Pelvic USG is usually performed for initial evaluation of ovaries.

**Polycystic ovarian Syndrome:** - It is one of the most common causes of female

most sensitive and specific sign but the finding is subjective. Only one ovary



**Fig.5** Submucosal fibroid. Spot radiograph show (a) well defined intrauterine filling defect at fundus in early filling stage of HSG. (b) less apparent fibroid when uterus is more distended. (c) large fibroid distorting uterine cavity. (d) sonosalpingogram show saline outline the submucosal fibroid

infertility, accounting upto 8% of women [14]. Diagnosis of polycystic ovarian syndrome is based on hormonal imbalance and laboratory findings. Patients with this syndrome often demonstrate abnormal ratio of LH and FSH. Clinical manifestation includes hirsutism, anovulation and infertility [4]. **2003 joint ESHRE/ASRM meeting in Rotterdam consensus criteria** required at least two of the following three conditions to be present for diagnosis of PCOS (a) oligo- or anovulation (b) clinical and biochemical hyperandrogenism (c) polycystic ovaries [13].

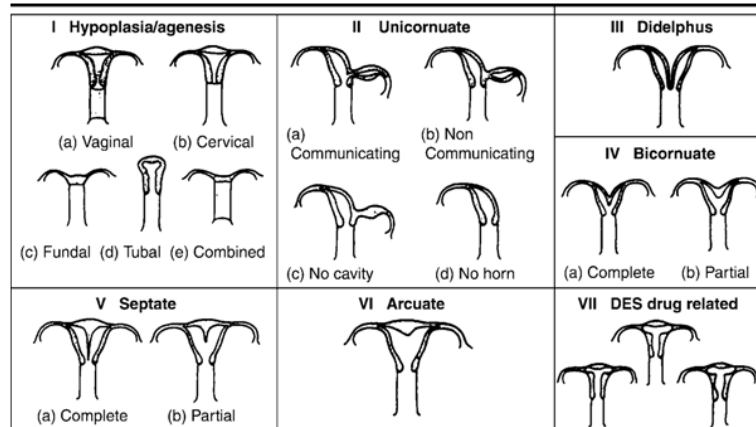
USG criteria for polycystic ovaries are present when (a) one or both ovary demonstrate 12 or more follicles measuring 2-8 mm in diameter (Fig. 8 a ) (b) ovarian volume exceeds 10mm (c) increased echogenicity of the ovarian stroma is the

meeting either of these criteria is sufficient [13]. According to American College of radiology Appropriateness criteria, pelvic MR imaging is generally recommended in case in which TVS and transabdominal US does not offer adequate visualization. In MRI, ovaries in patients with PCOS demonstrate low signal intensity central stroma surrounded by small peripheral cyst hyperintense on T2W. (Fig 8b)

**Pituitary Adenoma:-** Hyperprolactinemia can be cause of infertility and associated with diminished gonadotropin secretion, secondary amenorrhoea and galactorrhoea. Patient should be examined first for drug induced hyperprolactinoma before any infertility work up is initiated. For example antidepressant, cimetidine, dopamine antagonist, reserpine, verapamil etc. are known to interfere with prolactin secretion.

MRI is modality of choice for depicting pituitary adenoma.(Fig 9(a) (b) Microadenoma (<10mm) is usually hypointense to normal pituitary gland on T1W image. Convexity of pituitary contour and deviation of stalk is indirect sign of

and infertility due to inability of sperm to enter the upper genital tract. Cervical factor may be serious hindrance to assisted infertility technique including embryo transfer and intrauterine insemination.



pituitary adenoma. Dynamic postcontrast MRI show strong enhancement of normal pituitary gland and its stalk in early phase of dynamic imaging whereas relatively weak enhancement seen in microadenoma. Macroadenoma (>1mm) may compress or invade surrounding structure including optic chiasma, cavernous sinus and bony sella[4].

At HSG cervical stenosis may appear as narrowing of endocervical canal (normal diameter 0.5 to 3.0 cm) or it may manifest as complete obliteration of cervical os, preventing insertion of HSG catheter. Masses such as cervical polyps, fibroids and neoplasm also cause narrowing of cervical canal [1].

**Cervical Abnormalities:** - cervical factor infertility imply inadequate quality or volume of cervical mucus, a condition that account for approximately 10% of cases of female infertility. Patient with this condition suggested postcoital test that doesn't involve imaging.

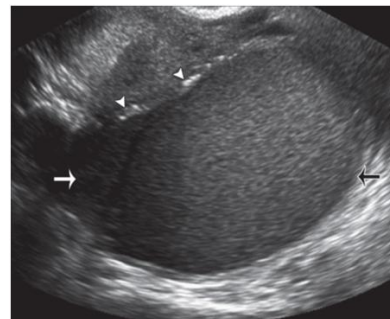


Fig. 7 Endometrioma. Sagittal transvaginal US image obtained in a woman with a history of endometriosis shows an ovarian mass with multiple fine internal echoes (arrows) and several hyperechoic mural foci (arrowheads).

**Cervical Stenosis:** - clinically defined as cervical narrowing that prevents insertion of 2-5mm wide dilator. This condition may be congenital or acquired secondary to infection or trauma.

**Conclusion:**

Infertility has multifactorial causes like tubal, uterine, ovarian, and cervical. A systematic

Consequences of cervical stenosis include obstruction of menstrual outflow with resulting amenorrhoea, dysmenorrhoea,



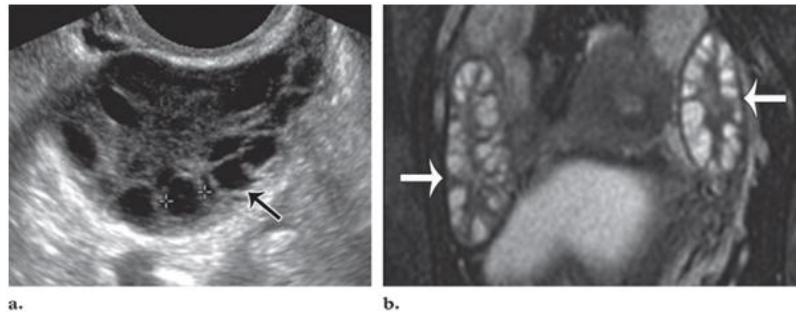


Fig.8 Polycystic ovary syndrome. (a) Transvaginal US of the ovary shows multiple peripheral subcentimetric follicles (arrow). (b) Coronal T2-weighted MR image of same patient shows bilateral ovarian enlargement with multiple peripheral follicles (arrows).

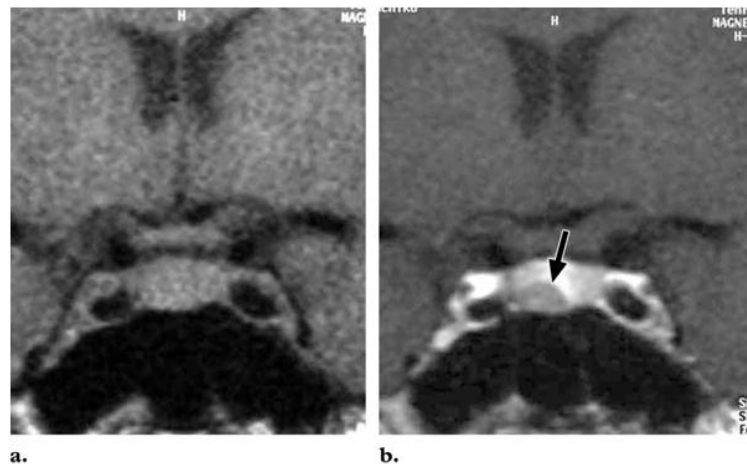


Fig.9 Pituitary microadenoma. (a) Coronal T1-weighted image shows a pituitary gland that is not enlarged. (b) Coronal T1-weighted image obtained after intravenous bolus injection of contrast material shows a mass with decreased enhancement (arrow) in the pituitary gland.

approach of diagnosis is pelvic USG followed by HSG, pelvic MRI. . Multimodality approach may be needed to know the cause of infertility. Selection of appropriate imaging modality is essential because it guides subsequent management. MRI used in case of complex manifestation and when USG findings are normal and equivocal. MRI may be serve as adjunct to diagnostic laparoscopy and HSG in patient with tubal and peritubal diseases. A normal HSG finding in case of infertility suggest extrauterine cause.

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