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RESEARCH ARTICLE

ROLE OF CONTRAST ENHANCED ULTRASOUND (CEUS) IN THE DIAGNOSIS OF GYNECOLOGIC PATHOLOGIES- A CASE SERIES

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Abstract

The aim of this case series is to evaluate the role and illustrate diagnostic superiority of Contrast Enhanced Ultrasound (CEUS) over B-mode and/or Doppler ultrasound in the diagnosis of structural gynaecologic pathologies, unknown pelvic masses, differentiation of Benign and Malignant lesions and correlation with Histopathology. Over the past decade, contrast-enhanced ultrasound (CEUS) has gained immense popularity. This technique is based on the real-time evaluation of microcirculation in selected areas of interest, and further assists in comparison with vascularity pattern of normal tissues. It is relatively easy to use in clinical practice, minimally invasive, relatively less costly and, it improves the detection and characterization of various diseases, reducing the need for additional imaging examinations such as computed tomography (CT) or magnetic resonance imaging (MRI). Literature data on Contrast tuned imaging (CnTI) applications in gynaecological pathologies are relatively few. The development of more sophisticated methods of qualitative as well as quantitative analysis of the time-intensity curves (TIC) could open new perspectives for the application of CnTI-SonoVue in gynecologic diseases. The purpose of this study was to describe the sonographic patterns of SonoVue distribution in the microcirculation in different gynaecologic lesions analysed by the CnTI technology using vascular parameter calculating software.

Introduction:-

Ultrasonography is a widely used diagnostic tool for the preoperative evaluation of gynaecological pathologies. It is simple, safe, repeatable, and cost-effective, typically falling within the low to medium-cost range. In recent years, advancements in technology have significantly improved the ability to visualize intratumoral vascularity through contrast-enhanced sonography. Contrast Tuned Imaging (CnTI) is a novel, contrast-specific technology applied using a transvaginal probe with the second-generation contrast agent, SonoVue, which contains sulphur hexafluoride microbubbles.[1]

Contrast-enhanced ultrasound offers detailed analysis of blood flow in microcirculation and is further enhanced by post-processing software that allows for the calculation of various flow parameters. Malignant lesions typically exhibit higher vascular flow rates compared to benign masses.[2]

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Our case series included 8 patients with various gynaecological conditions. The contrast agent used was SonoVue, supplied by BRACCO. Using post-processing software, we derived several perfusion parameters, including Time-Intensity Curves (TIC) for two regions of interest (normal tissue and pathological tissue), as well as Area Under the Curve (AUC), Time to Peak (TTP), Peak Intensity (PI), and Wash-In Slope (WIS).

Case 1

52-year-old woman with 4-month history of heavy vaginal bleeding. Clinical/gynaecological examination showed bleeding soft polypoid mass at the cervical os per speculum. B mode ultrasound shows a large pedunculated polyp arising from the fundus extending into the cervix with mild vascularity. CEUS imaging depicts early intense hyperenhancement and quick washout suggestive of malignancy. The corresponding TTP, WIS, PI and AUC values for the ROC in the polyp and normal myometrium respectively are 17.4 sec, 12.3 dB/sec, 16.6 dB, 1868.6 dB sec and 34.1 sec, 1.32 dB/sec, 6.3 dB, 345 dB sec **(Figure 1).** Histopathological analysis shows fibroid with sarcomatous changes.

Case 2

56-year-old woman with gradually growing painless lump in the lower abdomen, intermittent bleeding. CA 125 levels are within normal range. On grey scale 5.2 x 4.8 cm sized right adnexal unilocular cystic lesion with few thin septations showing near absent colour flow. CEUS imaging shows no enhancement within the septations. No solid components detected. The corresponding TTP, WIS, PI and AUC values for the ROC in the intralesional septations and surrounding normal adnexal parenchyma respectively are 28.4 sec, 5.3 dB/sec, 5.8 dB, 278 dB sec and 31.1 sec, 7.2 dB/sec, 6.3 dB, 302 dB sec **(Figure 2).** Likely suggestive of benign lesion? serous cystadenoma. Histopathology shows ovarian serous cystadenoma.

Case 3

66-year-old female with historyof known carcinoma endometrium, operated by hysterectomy 12 months ago visits gynaecology clinic with bleeding per vaginum. Clinical examination suggested a hard palpable lesion in the vaginal stump. On B mode ultrasound a solid-cystic hypoechoic round mass along the posterior wall of vaginal stump showing intense vascularity. CEUS imaging shows marked heterogenous hyperenhancement in the early arterial phase suggesting a malignant etiology? vaginal adenocarcinoma? recurrence of previous malignancy. The corresponding TTP, WIS, PI and AUC values for the ROC in the lesion and surrounding normal parenchyma respectively are 16.4 sec, 14.8 dB/sec, 19.5 dB, 1675.6 dB sec and 36.1 sec, 2.56 dB/sec, 8.3 dB, 448 dB sec **(Figure 3).** Histopathology shows endometrial carcinoma recurrence.

Case 4

46-year-old female with complaints of heavy menstrual bleeding. Gynaecological examination shows enlarged palpable uterus. On B mode ultrasound markedly thickened heterogenous circumscribed fundal and posterior uterine wall lesion causing posterior shadowing. Colour doppler shows no significant vascularity. CEUS imaging shows mild heterogenous hyperenhancement without any early washout or peripheral whorled pattern suggesting a benign etiology - focal adenomyoma/fibroid. The corresponding TTP, WIS, PI and AUC values for the ROC in the lesion and surrounding normal myometrium respectively are 26.8 sec, 6.4 dB/sec, 4.7 dB, 328 dB sec and 29.1 sec, 7.4 dB/sec, 5.2 dB, 312 dB sec **(Figure 4).** Histopathology shows uterine adenomyosis.

Case 5

A 72-year-old female with complaints of post-menopausal bleeding. B mode ultrasound atrophied uterus with 9mm thickness heterogenous endometrium with mild increased vascularity on color doppler. CEUS imaging shows heterogenous hyperenhancement with early washout suggesting a malignant etiology. The corresponding TTP, WIS, PI and AUC values for the ROC in the thickened endometrium and surrounding myometrium respectively are 18.8 sec, 12.7 dB/sec,18.64dB, 1688.6 dB sec and 31.1 sec, 2.11 dB/sec, 9.6 dB, 418.7 dB sec **(Figure 5).** Histopathology shows FIGO stage Ib endometrial carcinoma.

Case 6

67-year-old woman with post-menopausal bleeding from 3 months. Clinical/gynaecological examination showed bleeding soft polypoid mass at the cervical os. PAP smear results awaited. B mode ultrasound shows a 3x 2.4 cm round hypoechoic polypoid mass with mild internal vascularity within the cervical canal. CEUS imaging depicts heterogenous hyper enhancing polyp with intense early arterial enhancement suggestive of malignancy. The corresponding TTP, WIS, PI and AUC values for the ROC in the polyp and normal myometrium respectively are

17.2 sec, 13.3 dB/sec, 17.20 dB, 1576.6 dB sec and 28.1 sec, 1.96 dB/sec, 8.65 dB, 328.7 dB sec **(Figure 6).** Histopathological analysis shows malignant endocervical polyp.

Case 7

A 38-year-old woman with intermenstrual bleeding. Clinical/gynaecological examination showed soft red bleeding mass protruding from cervical os. B mode ultrasound reveals well defined hypoechoic 2.8 x2.4 cm mass within the cervical canal showing mild vascularity and predominant soft consistency on sono-elastography. CEUS imaging shows very mild enhancement and slow washing out-? benign cervical polyp. The corresponding TTP, WIS, PI and AUC values for the ROC in the polyp and normal myometrium respectively are 16.2 sec, 5.3 dB/sec, 3.6 dB, 245 dB sec and 13.6 sec, 7.9 dB/sec, 6.8 dB, 634 dB sec **(Figure 7).** Histopathological analysis shows cervical fibroid with hyaline degeneration.

Case 8

46-year-old woman with abnormal uterine bleeding. CA 125 level is increased (526 units/ml). On grey scale 5.6 x 5.1 cm sized hypoechoic solid cystic left adnexal lesion with moderate vascularity on doppler study. CEUS imaging shows heterogenous hyperenhancement of the solid component of the lesion with increased peak enhancement values. The corresponding TTP, WIS, PI and AUC values for the ROC in the lesion core and surrounding normal adnexal parenchyma respectively are 11.9 sec, 15.7 dB/sec, 18.2 dB, 1572.0 dB sec and 21.4 sec, 3.96 dB/sec, 8.64 dB, 365.5 dB sec, likely suggestive of malignant adnexal lesion **(Figure 8).** Histopathology shows left ovarian endometroid carcinoma.

Discussion:-

Contrast-enhanced ultrasonography has become a valuable tool in oncology, with numerous potential clinical applications. The use of contrast agents enables direct visualization of tumor neovascularity, which often appears as clusters of vessels with varying calibers. Modern contrast agents consist of microbubbles that are injected intravenously.[3,4] These microbubbles, being much smaller than red blood cells and vastly different from the acoustic properties of living tissues, produce intense hyper echogenicity when circulating in the body. These enhanced echo signals effectively highlight perfusion and blood flow rates within pathological areas.[5] Furthermore, microbubbles are safely eliminated from the body within minutes, making contrast agents suitable for patients with renal or liver failure, as well as those with cardiac morbidities.[6]

Ultrasonography remains a well-established and reliable diagnostic tool for evaluating pelvic masses, providing detailed insights into lesion characteristics, correlating with lab tests, and guiding surgical decisions for gynaecologists. Recent advancements in ultrasound equipment and contrast media have significantly expanded the scope of gynaecological diagnoses. Contrast agents, which contain microparticles, allow for enhanced visualization of microcirculation within various pathological masses, providing a level of vascular detail that surpasses that of traditional colour Doppler ultrasound.

Contrast Tuned Imaging (CnTI) is an advanced, contrast-specific technology that uses the second-generation contrast agent, SonoVue, containing sulphur hexafluoride microbubbles. This imaging technique can be applied with different probes during the scan. In gynaecological oncology, contrast-enhanced ultrasonography offers significant advantages, particularly in the early detection and preoperative assessment of ovarian cancer. [7,8] Combined morphological and vascular imaging improves diagnostic accuracy. CEUS is also helpful in differentiating fibroids from adenomyomas, characterizing endometrial pathologies (including malignancies and their extent of invasion), assessing unknown adnexal masses, confirming ovarian torsion, distinguishing between retained products of conception, clots, and arteriovenous malformations, testing tubal patency in infertility cases, and diagnosing vaginal fistulas.

In our series, CEUS results showed strong correlation with lab parameters such as CA125 in the diagnosis of ovarian neoplasms. Malignant lesions displayed early arterial enhancement followed by rapid wash-out.

Conclusion:-

CEUS offers a detailed assessment of both lesion morphology and vascularization in gynaecological pathologies. The specific enhancement patterns and blood flow parameters it provides are crucial for accurate characterization,

guiding treatment decisions, and helping to differentiate benign conditions from invasive malignancies. The diagnostic accuracy of contrast-enhanced ultrasound surpasses that of B-mode and/or colour Doppler sonography.

Compared to other imaging modalities such as CT/MRI with contrast agents or molecular radionuclide imaging, microbubble-enhanced ultrasonography is safer as it does not involve radiation, and the contrast agents used are completely harmless to the body. Additionally, CEUS is relatively cost-effective and can be safely used in patients with renal failure or those with allergies to iodine-based contrast agents.

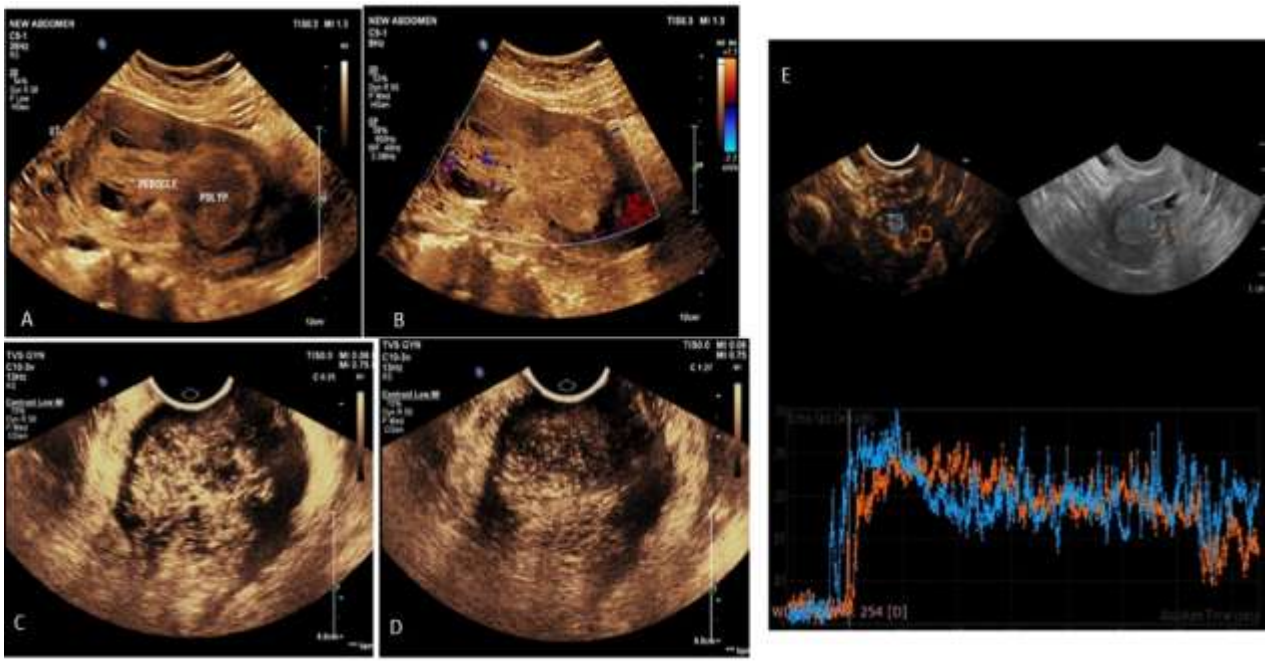

Figure 1:-B mode (A) and color doppler (B) images of the fundal polyp showing early arterial enhancement (C) and quick washout (D). TIC curves (E) blue ROI in the polyp and red ROI in the normal myometrium.

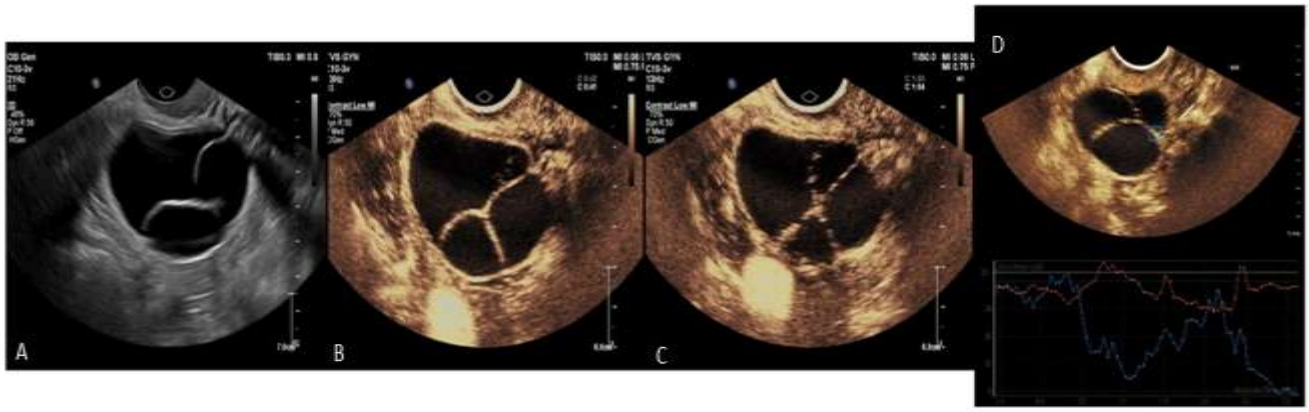

Figure 2:-B mode (A) image of the adnexal lesion showing no arterial enhancement (B) and no washout (C). TIC curves (D) blue ROI in the septa within lesion and red ROI in the normal adnexa.

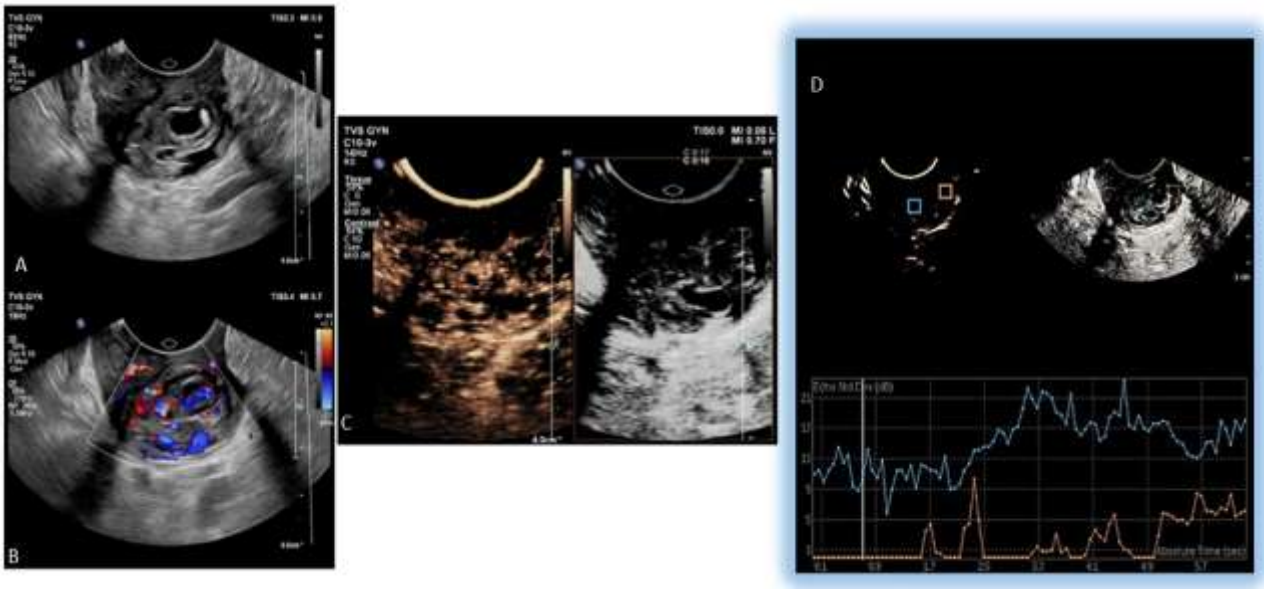

Figure3:-B mode (A) and color doppler (B) images of the vaginal stump lesion showing marked arterial enhancement (C). TIC curves (D) blue ROI in the lesion and red ROI in the normal surrounding parenchyma.

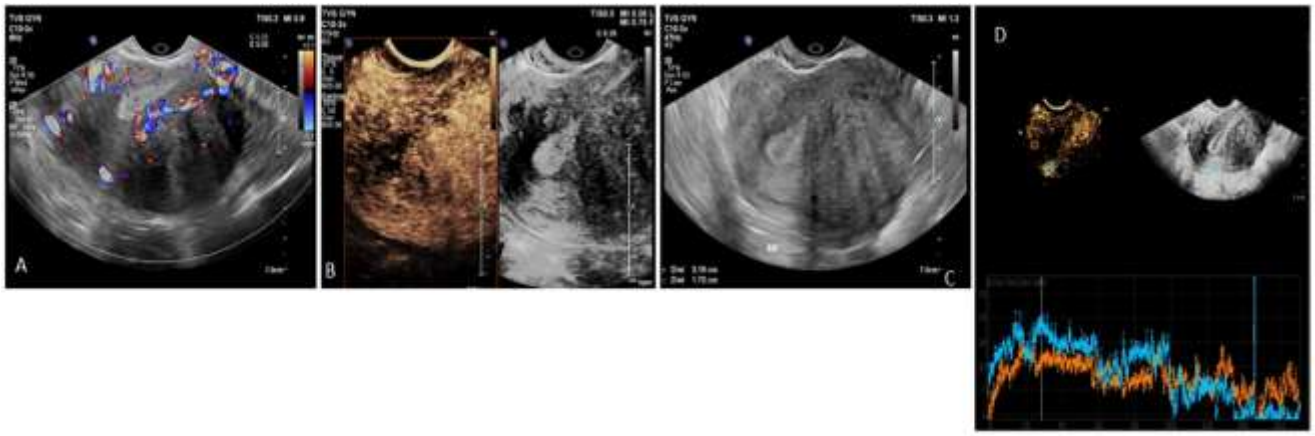

Figure 4:-B mode (C) and color doppler (A) images of the posterior uterine lesion showing mild heterogenous enhancement with posterior shadowing (C). TIC curves (D) blue ROI in the lesion and red ROI in the normal surrounding parenchyma.

Figure5:-B mode (A) and color doppler (B) images of the thickened endometrium showing marked arterial enhancement and quick washout (C). TIC curves (D) red ROI in the lesion and blue ROI in the normal myometrium

Figure6:-B mode (A) image of the thickened cervical walls showing marked arterial enhancement (B) and prompt wash out (C). TIC curves (D) red ROI in the cervical lesion and blue ROI in the normal surrounding myometrium

Figure7:-B mode and elastography (A) images of the cervical fibroid showing mild arterial enhancement (B) and slow late phase washing out (C). TIC curves (D) blue ROI in the lesion and red ROI in the normal surrounding parenchyma.

Figure8:-B mode and color doppler (A) image of the adnexal lesion showing marked arterial enhancement (B) and immediate subsequent washout (C). TIC curves (D) blue ROI in the lesion and red ROI in the normal surrounding parenchyma.

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