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# The diagnostic accuracy of ultrasound in the prediction of placenta accreta spectrum (PAS)

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## Abstract

**Objective:** To evaluate the ability of each sonographic parameter in the prediction of PAS and to correlate this ultrasound assessment to operative judgement of an experienced accreta team and to histopathology of the specimen in cases who were indicated for hysterectomy.

**Materials and Methods:** A total of 60 patients diagnosed as having placenta previa with high possibility of placenta accreta, PAS was diagnosed by the presence of at least one of the following features in color Doppler scan: diffuse or focal lacunar flow, sonolucent vascular lakes and hypervascularity of the utero-vesical interface with bridging vessels connecting the placenta to the bladder. The sonographic provisional diagnosis of accreta was documented. An experienced accrete team who were blinded for the ultrasound result made an intraoperative judgment and classified the case to either (mostly accreta) or mostly (non accreta). Histopathological examination was done to assess the presence of placental invasion & to confirm the diagnosis of placenta accreta for the specimens who required hysterectomy by a pathologist who were also blinded for the ultrasound diagnosis,

**Results:** Placental invasion was found in 35(58.3%) by ultrasound examination of placenta previa cases. Intraoperatively, 36 (60%) patients were assessed to have morbidly adherent placenta (MAP). By histopathological examination 16 cases (45.7 %) were confirmed as placenta accreta and 19 cases (54.3 %) were confirmed as placenta increta .Out of the different ultrasound parameters abnormal lacunae was found to have the highest sensitivity, specificity, PPV, NPV and accuracy in its relation to both intraoperative assessment and histopathological analysis.

**Conclusion:** prenatal ultrasound is the best screening tool for PAS and presence of abnormal lacunae and loss of retro-placental clear zone are accurate predictors for the operative findings and histopathological diagnosis.

**Keywords:** Placenta accreta, ultrasonography, Diagnosis, operative findings.

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## **Introduction**

Over the last decade, abnormal placentation (accreta, increta and percreta) has emerged as one of the obstetric catastrophes (1). Placenta accreta is classified according to the depth of myometrial invasion with the risk of hemorrhage and maternal morbidities directly related to the depth of myometrial invasion (2,3).

Uterine surgical procedures were claimed as the predisposing-factors for placenta accreta, yet repeated cesarean section and placenta previa remains the major contributing risk factor for the development of placenta accreta spectrum (PAS) (3,4).

Early diagnosis of abnormal placentation allows proper counselling of the patients and improves the maternal and fetal outcomes by allowing multidisciplinary management and optimizing the timing and the preparation for cesarean delivery (5, 6).

Ultrasonography remains the primary golden method for diagnosis of PAS while Doppler is the first line tool for diagnosis of myometrial invasion (5,7,8). Multiple ultrasound variables have been used to diagnose abnormal placentation, these markers included myometrial thinning <1 mm, presence of irregular vascular spaces (i.e., placental lacunae), loss of the normal retroplacental hypoechoic area, thinning and irregularity of the uterine-bladder interface together with the vessels bridging between bladder and myometrium detected by color Doppler (9-13).

The current study aimed to evaluate the accuracy of different ultrasound parameters (separately) in the diagnosis of PAS and their correlation with operative judgement and histopathological diagnosis.

## **Material and methods**

The current study was a prospective cohort one conducted in Kasr El-Ainy hospital

(The obstetrics & Gynecology department - Faculty of medicine - Cairo University) in the duration between December 2017 and January 2021. 60 pregnant women (aged from 20 to 40 years) with singleton living healthy fetus diagnosed as having placenta previa with high possibility of placenta accreta (claimed by level 2 ultrasound), and candidate for repeated elective cesarean section (CS) or elective cesarean hysterectomy (if the diagnosis of placenta accreta is confirmed intra-operatively) were included. Inclusion criteria included: gestational age more than 28 weeks (confirmed by a reliable date for the last menstrual period and/or 1st trimester ultrasound scan) and one or more previous cesarean delivery. Women who had chronic or pregnancy induced diseases or any emergency or unplanned delivery were excluded. Women who became hemodynamically unstable or requested conservative management for accreta (if possible) were also excluded. The study was approved by the hospital ethical committee and was registered at ClinicalTrials.gov (registration No.: NCT03286998).

Informed consents were obtained from all patients after explanation of the aim of the study & discussing the potential hazards. For all participants, full history was obtained followed by complete physical examination & routine obstetric ultrasound (to confirm the presence of placenta previa i.e., placental tissue covers the internal cervical os or within 2 cm from it). Later on, the placentae were reexamined in systematic manner by gray-scale & color Doppler ultrasound via transabdominal and/or transvaginal approach using Volusion Pro-V ultrasonography machine (GE Healthcare Austria GmbH, Seoul, Korea) and the possibility of concomitant placenta accreta was checked. All ultrasound exams were done by an expert single sonographer. The placenta was scanned with adequate bladder volume to visualize the bladder- uterine serosal interface correctly & the angle of insonation was kept

as low as possible. The presence of one or more of the following features in grey scale ultrasound was considered as indicative of PAS: presence of abnormal placental lacunae, complete loss of retroplacental sonolucent zone, myometrial thinning, disruption of the uterine serosa-bladder interface, presence of mass invading the urinary bladder. Similarly, PAS was diagnosed by the presence of at least one of the following features in color Doppler scan: diffuse or focal lacunar flow, sonolucent vascular lakes, hypervascularity of the utero-vesical interface with bridging vessels connecting the placenta to the bladder. The grey scale and Doppler ultrasound finding were defined according to FIGO consensus guidelines on PAS (14). The presence or absence of the studied sonographic parameter (namely; loss of clear zone, abnormal lacunae, myometrial thinning, bladder wall interruption, placental bulge, uterovesical hyper vascularity, bridging vessels and placental lacunae feeder vessels) for each patient were recorded. The sonographic provisional diagnosis of accreta (i.e., focal, total, accreta, increta or percreta) with the concomitant invasion of adjacent structures (e.g., the urinary bladder) was documented (Figure 1).

Routine preoperative labs were obtained 48 hours before the elective termination of pregnancy (whether by elective CS or elective cesarean hysterectomy) which were done multidisciplinary team (accreta team) consisted of senior staff obstetricians, urology team and general surgery team. Intra-operatively, following the bladder downward displacement and exposure of the lower uterine segment just before the uterine incision, a quick evaluation was done by the accreta team (if placenta invade the outer uterine wall, placenta is bulging or bridging vessels were present) to decide whether the placenta was accreta or not (operative judgement) and accordingly they are classified into "MOSTLY ACCRETA" or "MOSTLY NOT ACCRETA". Following

the delivery of the fetus and cord clamping, if placenta was not separated for 5 minutes in spite the use of ecbolics, the accreta team proceeded to caesarean hysterectomy (Figure 2). The operative judgement (Mostly accreta or mostly not accreta), operative procedure, operative findings (as regard the invasion of adjacent structures) and all operative steps were documented. For hysterectomy specimens, histopathological examination was done to assess the presence of placental invasion & to confirm the diagnosis of placenta accreta (Figure 3). According to the pathological examinations, the specimens were classified into accreta & non-accreta. Both the accreta team and the pathologist were blinded to the ultrasound report. Each of the following eight sonographic parameters (Loss of clear zone, abnormal lacunae, myometrial thinning, bladder wall interruption, placental bulge, uterovesical hyper vascularity, bridging vessels, placental lacunae feeder vessels) was correlated to the operative judgement of the accreta team & the histopathological reports.

Primary outcome measured the ability of each sonographic parameter (the above-mentioned) in the prediction of PAS while the secondary outcome measured their correlation to operative judgement of experienced accreta team.

### **Statistical analysis of the collected data**

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 24. Data was summarized using mean and standard deviation in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Standard diagnostic indices including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic efficacy were calculated as described by Galen (15). Comparisons

between groups were done using unpaired t test (16). For comparing categorical data, Chi square ( $\chi^2$ ) test was performed. Exact test was used instead when the expected frequency is less than 5 (17). P value less than 0.05 was considered as statistically significant.

A priori sample size calculation using Fisher's exact test predetermining the alpha error to be 0.05 and the power to be 0.95 showed a required sample size to be 56 generated by G\*power 3.1 statistical package.

Assuming a dropout rate of 20% (N=11) we decided to recruit 67 candidates.

## **Results**

Sixty pregnant women diagnosed as having placenta previa with high possibility of being placenta accreta were finally included in this prospective study. 35 patients (58.3%) were diagnosed as having accreta (confirmed by histopathological examination that denotes myometrial invasion) [accreta cases] while 25 cases (41.7%) were diagnosed as placenta previa without invasion (either when the placenta separated after fetal delivery or when pathological examination of the specimen denied any myometrial invasion) [not accreta cases]. Flow of patients were summarized in figure 4 and participants' demographic features and pregnancy characteristics were summarized in table 1.

### **Parameters of ultrasound in correlation to intraoperative judgement:**

Intraoperatively and before uterine incision, the accreta team classified 36 patients as MOSTLY ACCRETA while the remaining 24 were classified as MOSTLY NOT ACCRETA (figure 4). Our results showed a significant correlation between loss of clear zone (n=29, 80.6%), presence of placental lacunae (n=31, 86.1%), myometrial thinning, (n=27, 75%), bladder wall interruption (n=28, 77.8%), uteroplacental hyper vascularity (n=29, 80.6%) and the operative judgement of

accreta team (Table 2). Based on such results, presence of abnormal lacunae in ultrasound had the highest sensitivity and accuracy (86 & 92%, respectively) in predicting the operative judgement followed by the loss of clear zone (81 & 85%, respectively) (Table 3).

### **Parameters of ultrasound in correlation with histopathological findings:**

Following the delivery of the fetus, 42 placentae were not separated for 15 minutes in spite the use of ecbolics, the accreta team proceeded to caesarean hysterectomy. Out of 42 specimens, histopathological examination confirmed placenta invasion in 35 specimens [16 cases (45.7 %) were confirmed as placenta accreta and 19 cases (54.3 %) were confirmed as placenta increta] (figure 4).

Our results showed only statistically significant correlation between loss of and clear zone (n=29, 82.9%), presence of abnormal lacunae (n=32, 91.4%) with the histopathological examination (Table 4). Based on such results, presence of abnormal lacunae in ultrasound had the highest sensitivity and accuracy (91 & 93%, respectively) in predicting the histopathology of accreta followed by the loss of clear zone (83 & 83%, respectively) (Table 5).

According to these data abnormal lacunae was found to have the highest sensitivity, specificity and accuracy in its relation to both intraoperative judgement and histopathological analysis of accreta.

## **Discussion**

Placenta accreta spectrum is multifactorial disorders in which the placental trophoblastic tissue abnormally adheres and invades the myometrium and uterine serosa. It has been associated with severe adverse maternal outcomes including severe life-threatening bleeding, massive blood transfusion, injury to adjacent structures, prolonged ICU admissions and death. The definitive diagnosis

is made by the pathological examination of hysterectomy specimens; however, early prenatal diagnosis of PAS is crucial step that allows the multidisciplinary planned management to be tailored for each case which in turns helps to reduce maternal/fetal morbidity and mortality. Ultrasonography is highly sensitive and specific primary tool in the diagnosis of placenta accreta especially those performed by skilled sonographer. Several ultrasound parameters have been reviewed as regard their diagnostic accuracy to predict PAS in order to obtain a universal definition and to standardize the sonographic evaluation of such conditions.

In the current study we tested the diagnostic value of eight sonographic parameters (i.e., loss of clear zone, abnormal lacunae, myometrial thinning, bladder wall interruption, placental bulge, uterovesical hyper vascularity, bridging vessels and placental lacunae feeder vessels) when applied individually as predictor for PAS in correlation to both the intraoperative assessment and histopathological analysis. Our results demonstrated that presence of abnormal lacunae had the highest sensitivity, specificity and accuracy in correlation to both intraoperative judgement (86%, 87.5% and 92%, respectively) and histopathological analysis of accreta (91%, 100% and 93%, respectively) followed by the loss of clear zone.

This agrees with several studies that found a strong relationship between presence of abnormal lacunar spaces and placental invasion and considering it a reliable ultrasound sign (9,10,14,18-21). Comstock and his colleagues (22) reported that presence of placental lacunae in 3rd trimester ultrasound scan is the most reliable diagnostic sign (sensitivity was 93% and PPV was 93%) for the diagnosis of accreta among women with previous caesarean delivery. Similarly, Boroomand and his colleagues (20), reported that the sole presence of abnormal lacunae had a predicting power of 96 to 100% for

PAS. Also, D'Antonio and his colleagues (21) in their review stated that among 13 studies, that tested the diagnostic performance of placental lacunae, a pooled sensitivity and specificity of 77 and 95% respectively were demonstrated in the diagnosis of placenta accreta.

The lack of decidua basalis (loss of the retroplacental clear zone in ultrasound) and trophoblastic invasion into the myometrium are constant and early findings in all variants of PAS. Our results demonstrated a significant correlation between loss of clear zone in ultrasound when corelated with intraoperative judgement (sensitivity, specificity and accuracy were 81%, 87.5% and 85%, respectively) as well as with histopathological examination (sensitivity, specificity and accuracy were 83%, 86 % and 83%, respectively). Our results were in accordance with those demonstrated by Cali and his coworkers (23) who reported that the absence of the retroplacental clear zone was the most effective sonographic measure for detection of PAS with certain limitation as the lower uterine segment appears as a very thin line in late third trimesteric ultrasounds making the evaluation of the interface between the myometrium and the placenta a challenging process. The same was reported by D'Antonio and his colleagues (21) who reported a pooled sensitivity and specificity of 66 and 96% respectively.

The presence of bladder wall abnormality (i.e., focal interruption, uterovesical hypervascularity OR exophytic mass) is a reliable ultrasound finding that rules in the diagnosis of accreta (21). Our study demonstrated significant correlation between bladder wall interruption and uterovesical hyper vascularity with only the intraoperative judgement of placental invasion (no significant correlation with histopathological diagnosis). The sensitivity, specificity and accuracy of bladder interruption in predicting the operative findings were 78%, 71% and 77% respectively, while

the sensitivity, specificity and accuracy of uterovesical hyper vascularity were 81%, 79% and 73% respectively. Our results were in agreement with Cali and his colleagues (23) and D'Antonio and his colleagues (21) who reported a pooled sensitivity of 50% and specificity of 99.7 for abnormalities of uterus–bladder interface in the diagnosis of placenta accreta. The same reported by Boroomand and his coworkers (20) who introduced a highly predictive ultrasound model for PAS included abnormal lacunae, bladder wall interruption and uterovesical vascularity.

Our finding also showed that myometrial thinning (less than 1mm) had sensitivity of 75% and accuracy of 69% in the prediction of PAS. This was in accordance with Twickler and his coworkers (9). On the other hand, our results demonstrated that the presence of placental bulge, bridging vessels or placental lacunae feeder vessels had low predictivity for PAS sensitivity was 57, 57 and 51% respectively and accuracy was 55,

50 and 50%, respectively). This agrees with Comstock (22) who stated that placental bulge wasn't sensitive sign.

To the best of our knowledge, the current study is the 1st one that assessed the relation between different ultrasound markers (solely) in relation to operative findings and judgement. Add to the strengths, the operative team and the pathologist were blinded to the ultrasound findings and all ultrasounds were done by single expert sonographer. Yet, we faced some limitations such as the small sample size and the ultrasound findings are not correlated to the degree of placenta invasion (accreta, increta or percreta) which in turn may classify the severity of the condition and adjust the plan of management.

In conclusion, prenatal ultrasound is the best screening tool for PAS and presence of abnormal lacunae and loss of retroplacental clear zone are accurate predictors for the operative findings and histopathological diagnosis.

**Table 1: Demographic profile, gestational age, estimated blood loss and number of cesarean sections.**

	Accreta Cases (n=35)		Not accreta Cases (n=25)		P value
	Mean	SD	Mean	SD	
Age (in years)	31.20	4.89	32.44	5.22	0.350
Parity	2.91	1.07	3.32	1.18	0.170
BMI (kg/m <sup>2</sup> )	29.59	5.64	25.39	3.15	0.002
GA at termination (in weeks)	35.83	2.33	35.92	2.27	0.880
Estimated blood loss (in ml)	2642.86	824.37	2056.00	1065.79	0.019
No. of CS	2.60	1.01	2.92	1.15	0.258

**BMI: body mass index / GA: gestational age / CS: caesarean section**

**Table 2: Parameters of ultrasound in correlation to operative judgement.**

Ultrasound Parameter	Operative Judgement		P- value
	Mostly Accreta (n=36)	Mostly not Accreta (n=24)	
Loss of clear zone	Yes 29 No 7	Yes 3 No 21	> 0.001
Abnormal lacunae	Yes 31 No 5	Yes 3 No 21	> 0.001
Myometrial thinning	Yes 27 No 8	Yes 9 No 16	0.003
Bladder wall interruption	Yes 28 No 8	Yes 7 No 17	0.001
Placental bulge	Yes 21 No 15	Yes 9 No 15	0.190
Uterovesical hyper vascularity	Yes 29 No 7	Yes 5 No 19	> 0.001
Bridging vessels	Yes 21 No 15	Yes 10 No 14	0.315
Placental lacunae feeder vessels	Yes 19 No 17	Yes 11 No 13	0.793

**Table 3: Sensitivity, specificity, PPV, NPV of different ultrasound parameters in relation to operative judgment**

	Sensitivity	Specificity	PPV	NPV	Accuracy
Loss of clear zone (%)	80.6	87.5	90.6	78.6	85
Abnormal lacunae (%)	86.1	87.5	94.1	88.4	91.7
Myometrial thinning (%)	75	66.7	74.2	64	70
Bladder wall interruption (%)	77.8	70.8	80	72	76.7
Placental bulge (%)	58.3	62.5	66.7	50	58.3
Uterovesical hyper vascularity (%)	80.6	79.2	82.3	30	73
Bridging vessels (%)	58.3	58.3	64.5	48.2	56.7
Placental lacunae feeder vessels (%)	52.8	54.2	60	43.3	51.7

**PPV: positive predictive value / NPV: negative predictive value**

**Table 4: Parameters of ultrasound in correlation to histopathological diagnosis**

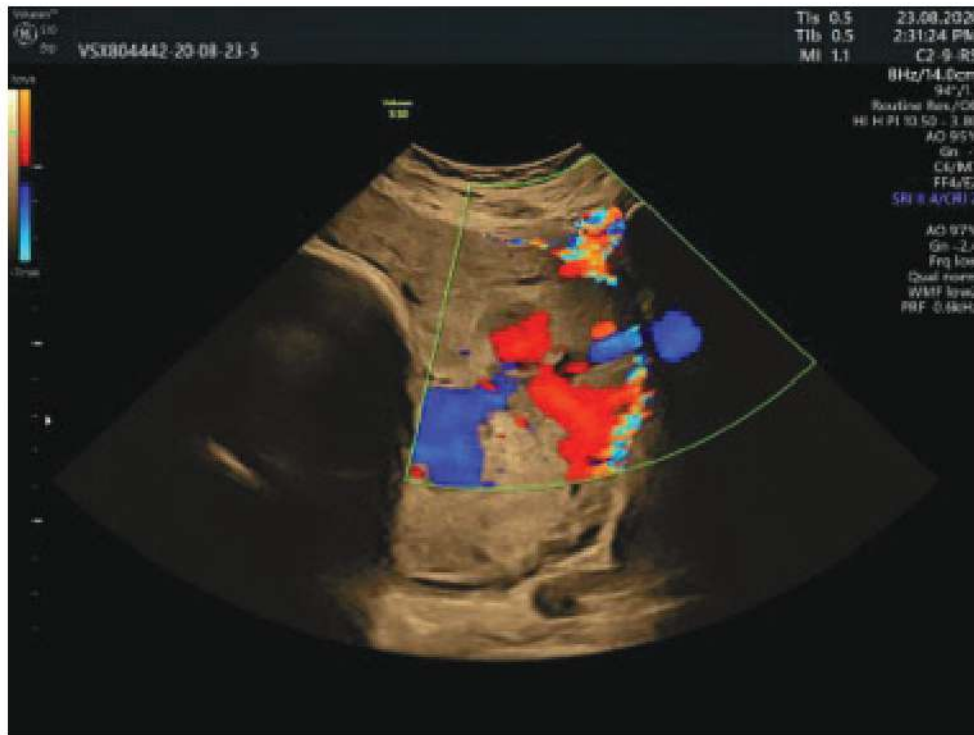
Ultrasound parameter	Histopathological diagnosis				P- value
	Accreta specimens (n=35)		Non-accreta specimens (n=7)		
Loss of clear zone	Yes	29	Yes	1	<0.001
	No	6	No	6	
Abnormal lacunae	Yes	32	Yes	0	<0.001
	No	3	No	7	
Myometrial thinning	Yes	26	Yes	4	0.359
	No	9	No	3	
Bladder wall interruption	Yes	28	Yes	4	0.195
	No	7	No	3	
Placental bulge	Yes	20	Yes	4	1.00
	No	15	No	3	
Uterovesical hypervascularity	Yes	28	Yes	4	0.195
	No	7	No	3	
Bridging vessels	Yes	20	Yes	6	0.222
	No	15	No	1	
Placental lacunae feeder vessels	Yes	18	Yes	4	1.00
	No	17	No	3	

**Table 5: Sensitivity, specificity, PPV, NPV of different ultrasound parameters in relation to histopathological diagnosis.**

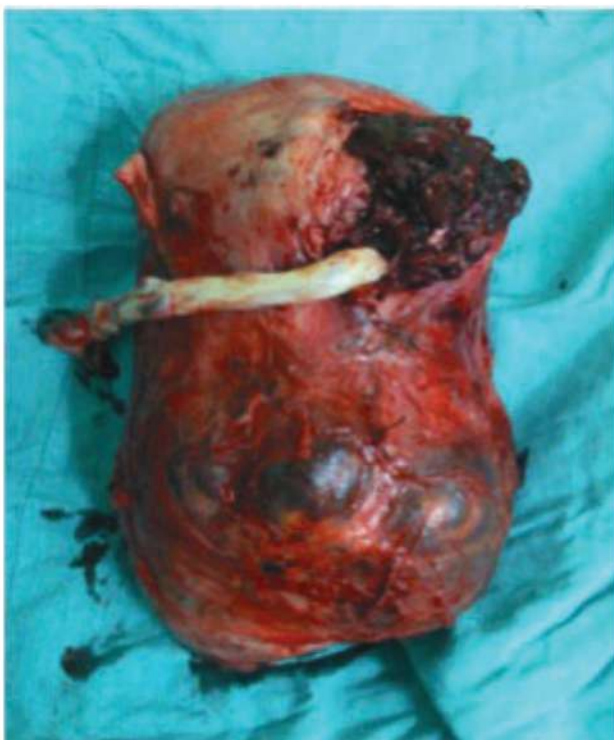
	Sensitivity	Specificity	PPV	NPV	Accuracy
Loss of clear zone (%)	82.9	85.7	96.7	50	83.3
Abnormal lacunae (%)	91.4	100	100	70	92.9
Myometrial thinning (%)	74.3	42.9	86.7	25	69
Bladder wall interruption (%)	80	42.9	87.5	30	73.8
Placental bulge (%)	57.1	42.9	83.3	16.7	54.8
Uterovesical hyper vascularity (%)	80	42.9	87.5	30	73.8
Bridging vessels (%)	57.1	14.3	76.9	6.3	50
Placental lacunae feeder vessels (%)	51.4	42.9	81.8	15	50

**PPV: positive predictive value / NPV: negative predictive value**

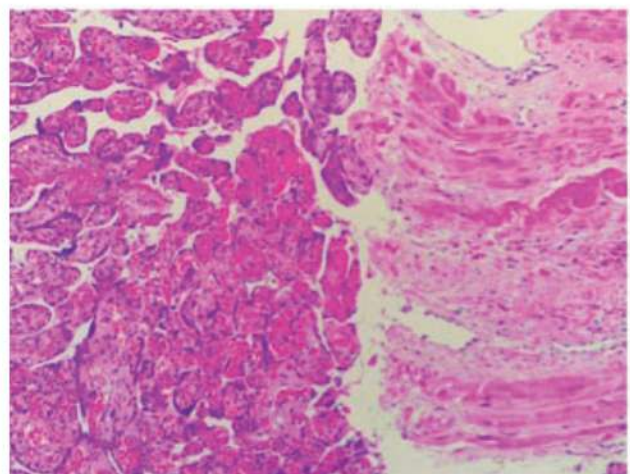




**Figure (1):** Ultrasound a case of placenta accreta with thinned out myometrium and striking vesico-placental vascularity with bridging vessels.



**Figure (2):** CS hysterectomy specimen (The case of placenta accreta with the ultrasound in fig 1).



**Figure (3):** Histopathology of the specimen in Figure 2, showing trans-myometrial invasion by small sized chorionic villi showing increased vascularity, focal fibrin deposition and evident trophoblastic knots (third trimesteric villi) with absent normal decidual plate (original magnification x100.H&E stain).

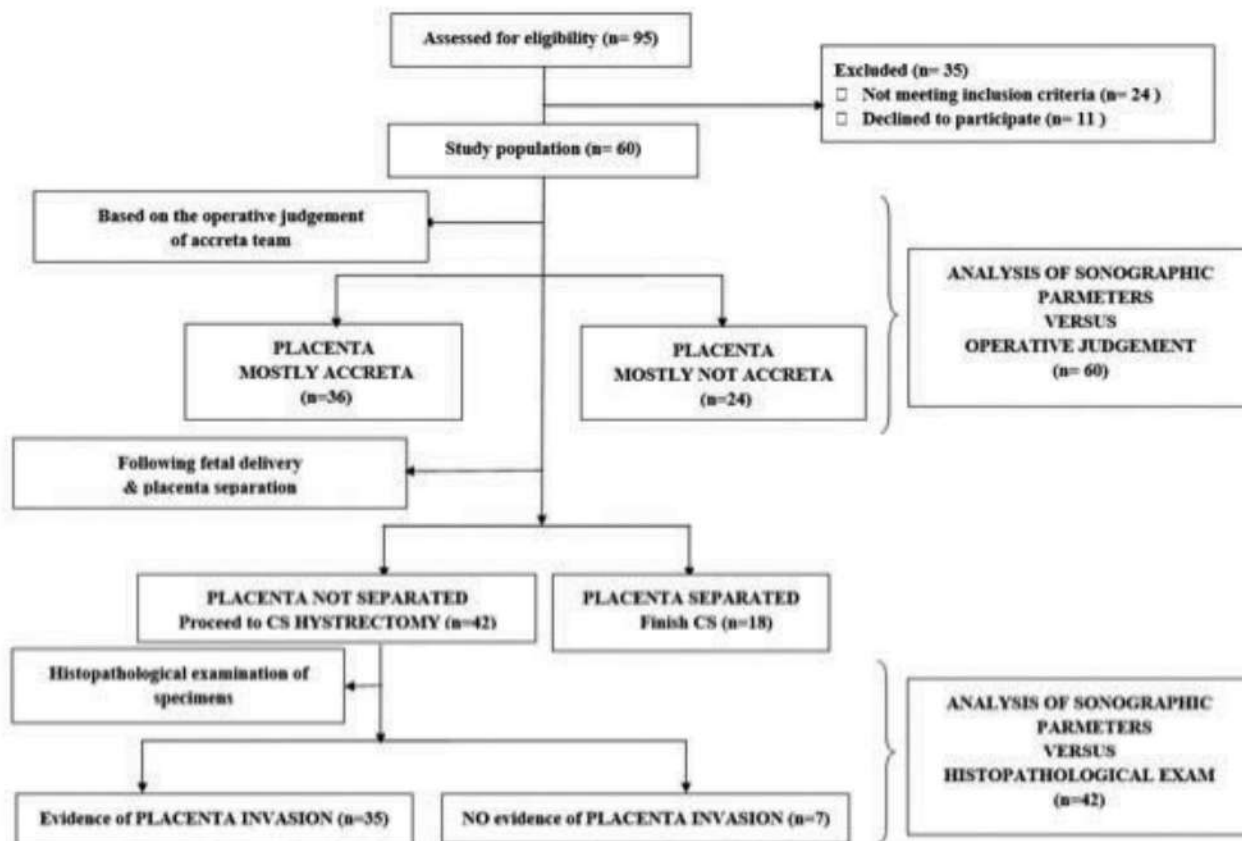


Figure 4: Flow of patients.

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