

# Intracervical lakes as a sonographic marker of placenta accreta spectrum (PAS) in patients with previa and low-lying placenta: A prospective observational study

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**AUTHORS' CONTRIBUTION:** (A) Study Design · (B) Data Collection · (C) Statistical Analysis · (D) Data Interpretation · (E) Manuscript Preparation · (F) Literature Search · (G) No Fund Collection

## SUMMARY

**Objective:** We evaluated the diagnostic accuracy of a new ultrasound sign, "intracervical lakes", in predicting presence and outcome of placenta accreta spectrum (PAS).

**Methods:** An observational study was done on 110 women with placenta previa or low-lying placenta at 36 weeks' gestation, referred to Ain Shams Maternity Hospital between January 2021 and December 2021, with all examined by ultrasound to confirm placental location, presence/absence/degree of invasion, and intracervical lakes sign. All underwent caesarean section and final diagnosis of PAS was made intraoperatively. Specimen was histologically examined.

**Results:** US findings predicted PAS with sensitivity 76.8% and specificity 85.2%, while PAS sign+ intracervical lakes increased specificity to 98.1%, positive predictive value 96.2%, LR+ 24.11% and DOR 42.74, but decreased other characteristics. US findings predicted percreta with sensitivity 95.2% and NPV 98.3%, and intracervical lakes did not markedly decrease sensitivity 90.5% and NPV 97.6%, but markedly increased other diagnostic characteristics with specificity 92.1%.

**Conclusion:** Intracervical lakes may become a marker of deep villus invasion in women with ultrasound-suspected PAS and predict the occurrence of severe maternal morbidity with specificity 98.1%.

**Keywords:** Intracervical lakes; Placenta accreta spectrum (PAS); Placenta previa; Low-lying placenta

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## INTRODUCTION

Placenta previa refers to the presence of placental tissue that extends over the internal cervical OS [1]. Placenta previa and placenta accreta are associated with high maternal and neonatal morbidity and mortality [2].

The rates of placenta previa and accreta have increased and will continue to do so as a result of rising rates of caesarean deliveries, increased maternal age and use of assisted reproductive technology (ART) [3]. The estimated incidence of placenta previa at term is 1 in 200 pregnancies [2].

Placenta accreta occurs when placental trophoblasts invade the endometrium beyond the Nitabuch's layer of decidua basalis, placenta increta occurs when placental trophoblasts invade the myometrium, and placenta percreta occurs when placental trophoblasts invade the serosa [4].

Morbid adherent placenta (MAP) is generally associated with excess blood loss, bladder injuries and hysterectomies. The incidence of MAP has increased significantly over the last 50 years [5].

The three forms of placenta accreta spectrum: placenta accreta, increta and percreta, represent a significant obstetric challenge, at times resulting in life-threatening bleeding and/or peripartum hysterectomy. The increasing rate of cesarean section (CS) deliveries correlates with the rising incidence of MAP [6].

This condition is often diagnosed during CS, upon placental removal, with unfavorable maternal outcome: attempts to remove the placenta can cause severe uterine bleeding. An accurate prenatal diagnosis is required to reduce the risk of maternal/fetal morbidity and mortality [7].

## PATIENTS AND METHODS

**Type of study:** A prospective observational study.

**Study setting:** Ain Shams University Maternity Hospital.

**Study period:** 12 month from January to December 2021.

**Study population:** Women with previa and low-lying placenta.

### Inclusion criteria:

- Age group (20–35 years old)
- BMI between (20–35 kg/m<sup>2</sup>)
- Single, viable, pregnancy ≥ 36 week's gestation
- Previous one or more C.S

### Exclusion criteria:

- Patients with bleeding disorders or on anticoagulant therapy
- Mental illness
- Abruptio placenta.
- Over distended uterus e.g.: Multiple gestations, polyhydramnios, fetal macrosomia (>4.5 kg).
- Rupture of membranes, intra-ammonitic infection and fever during admission (> 38°C).

### Elimination of bias:

- All procedures were done by obstetricians having the same level of surgical skills
- Laboratory samples were done in the same laboratory preoperative and postoperative
- Preoperative ultrasound was performed by the same sonographer

### Ethical considerations

The nature and scope of the clinical study were explained in an understandable way to the patients and an informed consent form, in Arabic language, including all the study procedures, advantages and possible risks and specifying who informed the patient, were provided and the patient signed on it before participation. The study protocol and patient informed consent were reviewed and approved by the Ethics Committee of the Obstetrics and Gynecology Department, Ain Shams University.

### Sample size

Using PASS 11 program for sample size calculation and assuming rate of placenta accreta spectrum =13%, sensitivity and specificity of intracervical lakes =95%, sample size of 110 women can detect this measures with power 92% for sensitivity and 100% for specificity with  $\alpha$ -error 0.05

### Study procedures

All women who met the inclusion criteria underwent full assessment. This assessment was included:

**Detailed history:** Personal (age, duration of marriage), Present (any current medical or surgical diseases and any current medication), Past history (history of any medical disorders), Obstetric history (including Parity, Gestational age, obstetric complications), Contraception history and Menstrual history.

### Clinical examination

#### General examination:

- 1) Assessment of the patients general condition (Chronic fatigue e.g.: in anemic patients)
- 2) Body Mass index (BMI) measured in kg/m<sup>2</sup>
- 3) Color of complexion e.g.: pallor in anemic patients
- 4) Vital data (Pulse, blood pressure, temperature)

**Abdominal examination:** Assessment of fundal level, fetal lie, presentation, liquor volume and previous scar were done.

**Vaginal examination:** Not done.

#### Ultrasound examination:

- 1) Using Samsung H 60 machine, 2D ultrasound was carried out trans-abdominally to assess fetal viability and number, placental location, determined gestational age and fetal anomalies and calculated exact amniotic fluid index (AFI).
- 2) TVUS and placental bed Doppler were done to confirm exact placental site and to assess whether the placenta is morbidly adherent according to RCOG criteria or not which were as follows [8].

#### \*2D greyscale signs:

- Loss of the 'clear zone'
- Abnormal placental lacunae
- Bladder wall interruption
- Myometrial thinning
- Placental bulge
- Focal exophytic mass

#### \*2D colour Doppler signs:

- Utero-vesical hyper-vascularity
- Subplacental hypervasculariry
- Bridging vessels
- Placental lacunae

All patients were evaluated by Ultrasonography examinations using Samsung H 60 machine. That were performed in Ain Shams University Maternity hospital ultrasound unit staff to confirm the gestational age, placental location, criteria for invasion and intracervical lakes sign which is defined as tortuous Anechoic spaces within the cervix which appear hypervascular at color Doppler.

All the patients in the study underwent caesarean section and final diagnosis of MAP was made intraoperative and specimen was sent for pathological examination

## Baseline laboratory investigations

Venous blood sample was withdrawn from all participants to assess:

- Hemoglobin level
- Hematocrit value
- Platelet count
- RH and blood group
- Preparation of 4 units of cross matched PRBCs and 4 units of FFP will be ensured.
- Viral markers (HBs Ag, HCV Ab)
- Coagulation profile (PT, PTT, and INR)

**Pre anesthetic medication:** Antibiotic prophylaxis was given as a single dose of intravenous 1<sup>st</sup> generation cephalosporins (Cefazoline®) 2 gm to be taken 30 to 60 minutes before skin incision and the dose was repeated if the operation lasted for more than 3 hours or blood loss was more than 1500 cc [9].

## Operative technique:

- Patients were placed in dorsal lithotomy position followed by induction of general anaesthesia, urinary catheterization and skin anti-sepsis.
- Skin was incised through a transverse or midline sub umbilical incision followed by opening of anterior abdominal wall in layers then observation for invasion like placenta bulge or invasion of pelvic structures by placental tissue.
- Identification and selective ligation of uterovesical venous plexus were done.
- The bladder dissected downwards.
- A low transverse uterine incision was done in the lower uterine segment followed by delivery of the fetus.
- Bilateral uterine artery ligation while waiting for placental separation.
- If placenta is adherent we proceeded for caesarean hysterectomy.
- In case of partially separated placenta accreta with ensuring bleeding, further action depends on patient's fertility wishes, conservative surgery was done.
- Ensuring adequate hemostasis and counting of towels and gauzes.

- Closure of anterior abdominal wall in layers.
- Subcutaneous tissue closure followed by skin closure using non-absorbable prolene suture No.2/0.

## Postoperative:

- Post-operative venous blood samples of hemoglobin and hematocrit levels were withdrawn from patients after 24 hours to avoid wrong results due to hemodilution by intravenous fluids in the first 24 hours

## Measured variables:

- Diagnostic accuracy of intracervical lakes in detecting the presence and the depth of PAS disorders.
- Explore the accuracy of this sign in predicting the following clinical outcomes:
- Total estimated blood loss
- Antepartum bleeding; post-partum haemorrhage at the time of caesarean section
- Need for Caesarean hysterectomy

**Tab. 1.** shows that: Demographic characteristics of the studied cases in which mean  $\pm$  SD of age  $30.2 \pm 2.6$  (years), BMI  $30.6 \pm 2.6$  (Kg/m<sup>2</sup>), gestational age  $36.7 \pm 0.6$  (weeks) and previous cesarean section median (1<sup>st</sup>- 3<sup>rd</sup> IQ) 3.0 (2.0–4.0).

**Tab. 2.** show that: PAS signs were found in less than half third of the studied cases. Intracervical Lakes was found in less than one quarter of the studied cases, all cases with Intracervical Lakes had positive PAS sign. **Tab. 3.** shows the ultrasound finding in cases with PAS disorder.

**Tab. 4.** shows that: PAS diagnosis finally confirmed about half of the studied cases, while placenta percreta finally confirmed in less than two tenths of the studied cases.

**Tab. 5.** shows that: Antepartum hemorrhage was the most frequent maternal complication; detected in more than half of the studied cases.

**Tab. 6.** shows that: PAS sign in predicting PAS had moderate diagnostic characteristics, PAS sign+ Intracervical Lakes increased specificity, positive predictive value, LR+ and DOR, but decreased other characteristics.

**Tab. 7.** shows that: PAS sign in predicting percreta had high sensitivity & NPV, and moderate other diagnostic characteristics, PAS sign+ Intracervical Lakes not markedly

**Tab. 1.** Demographic characteristics of among the studied cases.

Variables	Mean $\pm$ SD	Range
Age (years)	30.2 $\pm$ 2.6	23.0–35.0
BMI (kg/m <sup>2</sup> )	30.6 $\pm$ 2.6	23.0–34.9
GA (week)	36.7 $\pm$ 0.6	36.0–38.0
-	<b>Median (1<sup>st</sup>-3<sup>rd</sup> IQ)</b>	<b>Range</b>
Previous CS	3.0 (2.0–4.0)	1.0–4.0
Total=110. BMI: Body Mass Index; GA: Gestational Age, IQ: Interquartile		

**Tab. 2.** Ultrasound findings among the studied cases.

Findings		N	%
PAS sign	Positive	51	46.4
	Negative	59	53.6
Intracervical Lakes	Positive	26	23.6
	Negative	84	76.4

**Tab. 3.** Ultrasound finding in cases with PAS disorder.

Number of cases	Loss of the clear zone	Abnormal placental lacunae	Bladder wall interruption	Myometrial thinning	2D color Doppler
28 case	Positive	Positive	Positive	Positive	Positive
15 case	Positive	Positive	Negative	Positive	Negative
8 case	Positive	Positive	Negative	Negative	Negative
59 case	Negative	Negative	Negative	Negative	Negative

**Tab. 4.** Final PAS diagnosis findings among the studied cases.

Final diagnosis	N	%
Any PAS	56	50.9
Placenta percreta	21	19.1

**Tab. 5.** Maternal morbidities among the studied cases.

Morbidities	N	%
Antepartum hemorrhage	61	55.5
Severe intraoperative bleeding	12	10.9
Hysterectomy	22	20.0
Postpartum hemorrhage	17	15.5

**Tab. 6.** Diagnostic characteristics of US findings in predicting PAS.

Characteristics	PAS sign		PAS sign+ Intracervical Lakes	
	Value	95% CI	Value	95% CI
Sensitivity	76.8%	63.6%–87.0%	44.6%	31.3%–58.5%
Specificity	85.2%	72.9%–93.4%	98.1%	90.1%–100.0%
DA	80.9%	72.3%–87.8%	70.9%	61.5%–79.2%
YI	62.0%	47.4%–76.5%	42.8%	29.3%–56.3%
PPV	84.3%	71.4%–93.0%	96.2%	80.4%–99.9%
NPV	78.0%	65.3%–87.7%	63.1%	51.9%–73.4%
LR+	5.18	2.69–9.98	24.11	3.38–171.75
LR-	0.27	0.17–0.44	0.56	0.44–0.72
DOR	19.02	7.18–50.37	42.74	5.52–331.13
Kappa	0.619	0.473–0.765	0.424	0.282–0.565

CI: Confidence Interval; YI: Youden's Index; DA: Diagnostic Accuracy; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR+: Positive Likelihood Ratio; LR: Negative Likelihood Ratio; DOR: Diagnostic Odds Ratio

**Tab. 7.** Diagnostic characteristics of ultrasound findings in predicting percreta.

Characteristics	PAS sign		PAS sign+ Intracervical Lakes	
	Value	95% CI	Value	95% CI
Sensitivity	95.2%	76.2%–99.9%	90.5%	69.6%–98.8%
Specificity	65.2%	54.3%–75.0%	92.1%	84.5%–96.8%
DA	70.9%	61.5%–79.2%	91.8%	85.0%–96.2%
YI	60.4%	47.0%–73.9%	82.6%	68.9%–96.4%
PPV	39.2%	25.8%–53.9%	73.1%	52.2%–88.4%
NPV	98.3%	90.9%–100.0%	97.6%	91.7%–99.7%
LR+	2.73	2.03–3.69	11.50	5.57–23.74
LR-	0.07	0.01–0.50	0.10	0.03–0.39
DOR	37.42	4.79–292.17	111.29	21.40–578.77
Kappa	0.391	0.245–0.536	0.757	0.608–0.907

CI: Confidence Interval; YI: Youden's Index; DA: Diagnostic Accuracy; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR+: Positive Likelihood Ratio; LR: Negative Likelihood Ratio; DOR: Diagnostic Odds Ratio

decreased sensitivity& NPV, but markedly increased other diagnostic characteristics.

**Tab. 8.** shows that: PAS sign had moderate diagnostic

characteristics in predicting antepartum hemorrhage, PAS sign+ Intracervical Lakes increased specificity, positive predictive value, LR+ and DOR, but decreased other characteristics.

**Tab. 9.** shows that: PAS sign had moderate diagnostic characteristics in predicting severe bleeding, PAS sign+ Intracervical Lakes increased specificity, positive predictive value, LR+ and DOR, but decreased other characteristics.

**Tab. 10.** shows that: PAS sign in predicting hysterectomy had high sensitivity & NPV, and moderate other diagnostic characteristics, PAS sign+ Intracervical Lakes not markedly decreased sensitivity& NPV, but markedly increased other diagnostic characteristics.

**Tab. 11.** shows that: PAS sign had low diagnostic characteristics in predicting postpartum hemorrhage, PAS sign+ Intracervical Lakes increased specificity, positive

predictive value, LR+ and DOR, but decreased other characteristics.

## RESULTS AND DISCUSSION

Novel finding of this study introduces a new ultrasound sign, intracervical lakes (ICL), associated with placenta accreta spectrum disorder in women with placenta previa or low-lying placenta, which potentially represents a marker of deep villus invasion.

Presence of ICL seems to be an independent predictor of placenta percreta and its incorporation into ultrasound examination may increase the diagnostic accuracy for

**Tab. 8.** Diagnostic characteristics of ultrasound findings in predicting antepartum hemorrhage.

Characteristics	PAS sign		PAS sign+ Intracervical Lakes	
	Value	95% CI	Value	95% CI
Sensitivity	72.1%	59.2%–82.9%	39.3%	27.1%–52.7%
Specificity	85.7%	72.8%–94.1%	95.9%	86.0%–99.5%
DA	78.2%	69.3%–85.5%	64.5%	54.9%–73.4%
YI	57.8%	42.9%–72.8%	35.3%	21.8%–48.7%
PPV	86.3%	73.7%–94.3%	92.3%	74.9%–99.1%
NPV	71.2%	57.9%–82.2%	56.0%	44.7%–66.8%
LR+	5.05	2.50–10.20	9.64	2.39–38.80
LR-	0.33	0.21–0.49	0.63	0.51–0.78
DOR	15.53	5.85–41.23	15.24	3.38–68.69
Kappa	0.567	0.416–0.718	0.329	0.194–0.465

CI: Confidence Interval; YI: Youden's Index; DA: Diagnostic Accuracy; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR+: Positive Likelihood Ratio; LR: Negative Likelihood Ratio; DOR: Diagnostic Odds Ratio

**Tab. 9.** Diagnostic characteristics of ultrasound findings in predicting severe bleeding.

Characteristics	PAS sign		PAS sign+ Intracervical Lakes	
	Value	95% CI	Value	95% CI
Sensitivity	83.3%	51.6%–97.9%	58.3%	27.7%–84.8%
Specificity	58.2%	47.8%–68.1%	80.6%	71.4%–87.9%
DA	60.9%	51.1%–70.1%	78.2%	69.3%–85.5%
YI	41.5%	18.3%–64.7%	38.9%	10.0%–67.9%
PPV	19.6%	9.8%–33.1%	26.9%	11.6%–47.8%
NPV	96.6%	88.3%–99.6%	94.0%	86.7%–98.0%
LR+	1.99	1.41–2.81	3.01	1.61–5.63
LR-	0.29	0.08–1.03	0.52	0.26–1.02
DOR	6.95	1.45–33.42	5.82	1.66–20.36
Kappa	0.171	0.045–0.297	0.258	0.051–0.465

CI: Confidence Interval; YI: Youden's Index; DA: Diagnostic Accuracy; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR+: Positive Likelihood Ratio; LR: Negative Likelihood Ratio; DOR: Diagnostic Odds Ratio

**Tab. 10.** Diagnostic characteristics of US findings in predicting hysterectomy.

Characteristics	PAS sign		PAS sign+ Intracervical Lakes	
	Value	95% CI	Value	95% CI
Sensitivity	95.5%	77.2%–99.9%	90.9%	70.8%–98.9%
Specificity	65.9%	55.0%–75.7%	93.2%	85.7%–97.5%
DA	71.8%	62.4%–80.0%	92.7%	86.2%–96.8%
YI	61.4%	48.2%–74.5%	84.1%	71.0%–97.2%
PPV	41.2%	27.6%–55.8%	76.9%	56.4%–91.0%
NPV	98.3%	90.9%–100.0%	97.6%	91.7%–99.7%
LR+	2.80	2.07–3.80	13.33	6.09–29.19
LR-	0.07	0.01–0.47	0.10	0.03–0.37
DOR	40.60	5.21–316.62	136.67	25.64–728.39
Kappa	0.411	0.264–0.557	0.787	0.647–0.928

CI: Confidence Interval; YI: Youden's Index; DA: Diagnostic Accuracy; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR+: Positive Likelihood Ratio; LR: Negative Likelihood Ratio; DOR: Diagnostic Odds Ratio

**Tab. 11.** Diagnostic characteristics of US findings in predicting postpartum hemorrhage.

Characteristics	PAS sign		PAS sign+ Intracervical Lakes	
	Value	95% CI	Value	95% CI
Sensitivity	58.8%	32.9%–81.6%	35.3%	14.2%–61.7%
Specificity	55.9%	45.2%–66.2%	78.5%	68.8%–86.3%
DA	56.4%	46.6%–65.8%	71.8%	62.4%–80.0%
YI	14.7%	-10.7%–40.2%	13.8%	-10.4%–38.0%
PPV	19.6%	9.8%–33.1%	23.1%	9.0%–43.6%
NPV	88.1%	77.1%–95.1%	86.9%	77.8%–93.3%
LR+	1.33	0.84–2.11	1.64	0.77–3.48
LR-	0.74	0.41–1.34	0.82	0.57–1.19
DOR	1.81	0.63–5.17	1.99	0.66–6.05
Kappa	0.081	-0.062–0.224	0.113	-0.086–0.313

CI: Confidence Interval; YI: Youden's Index; DA: Diagnostic Accuracy; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR+: Positive Likelihood Ratio; LR: Negative Likelihood Ratio; DOR: Diagnostic Odds Ratio

Cesarean hysterectomy and major postpartum hemorrhage in women with placenta previa or low-lying placenta [10].

The large majority of studies reports the diagnostic performance of different ultrasound signs merely in detecting the presence of PAS disorder, but did not explore whether they could predict the severity of the condition [11]. On these grounds, the introduction of new imaging signs for PAS disorders seems crucial to improve the performance of ultrasound in identifying women affected by the most severe types of these conditions, in order to minimize the risk of adverse outcome.

The purpose of the present study was to evaluate the role of a new ultrasound sign, named intracervical lakes (ICL), in predicting the presence of PAS disorder and delivery outcome in patients with placenta previa or low-lying placenta.

This was a prospective observational study of 110 women with placenta previa or low-lying placenta at  $\geq 36$  week's gestation, which was referred to Ain Shams Maternity Hospital between Januarys 2021 and December 2021.

Only women with delivery outcome were included with Age group (20–35 years old), BMI between (20–35 kg/m<sup>2</sup>), Single, viable, pregnancy  $\geq 36$  weeks gestation, Previous one or more C.S.

Women excluded from this study with bleeding disorders or on anticoagulant therapy, Mental illness, Abruptio placenta, Over distended uterus e.g.: multiple gestation, polyhydramnios, fetal macrosomia (>4.5 kg), Rupture of membranes, intra-ammonitic infection and fever during admission (>38°C).

Using Samsung H 60 machine, 2D ultrasound was carried out trans-abdominally to assess fetal viability and number, placental location, determined gestational age and fetal anomalies and calculated exact amniotic fluid index (AFI).

TVUS and placental bed Doppler were done to confirm exact placental site and to assess whether the placenta is morbidly adherent according to RCOG criteria or not which were as follows [10].

All patients were evaluated by Ultrasonography examinations using Samsung H 60 machine. That were performed in Ain Shams University Maternity hospital ultrasound unit staff to confirm the gestational age, placental location, criteria for invasion and intracervical lakes sign which is defined as tortuous Anechoic spaces within the cervix which appear hypervascular at color Doppler.

All the patients in the study underwent caesarean section and final diagnosis of MAP was made intraoperative.

### The results were as follow:

Demographic characteristics of the studied cases in which mean  $\pm$  SD of age 30.2  $\pm$  2.6 (years), BMI 30.6  $\pm$  2.6 (Kg/m<sup>2</sup>), gestational age 36.7  $\pm$  0.6 (weeks) and previous cesarean section median (1<sup>st</sup>- 3<sup>rd</sup> IQ) 3.0 (2.0–4.0).

PAS signs were found in 51 cases of the studied cases. Intracervical Lakes was found 26 cases of the studied cases, all cases with Intracervical Lakes had positive PAS sign.

PAS diagnosis finally confirmed in 56 of cases with percentage 50.9% of the studied cases, while placenta percreta finally confirmed in 21 cases with percentage of 19.1% the studied cases.

Antepartum hemorrhage was the most frequent maternal complication; detected in 61 cases with percentage of 55.5% of the studied cases.

As regard Diagnostic characteristics of US findings in predicting PAS, PAS had moderate diagnostic characteristics with sensitivity 76.8% and specificity 85.2%, while PAS sign+ Intracervical Lakes increased specificity to 98.1%, positive predictive value 96.2%, LR+ 24.11% and DOR 42.74, but decreased other characteristics.

As regard Diagnostic characteristics of US findings in predicting percreta PAS sign had high sensitivity 95.2% & NPV 98.3%, and moderate other diagnostic characteristics, PAS sign+ intracervical lakes not markedly decreased sensitivity 90.5% & NPV 97.6%, but markedly increased other diagnostic characteristic with specificity 92.1%.

As regard Diagnostic characteristics of US findings in

predicting antepartum hemorrhage PAS sign had moderate diagnostic characteristics in predicting antepartum hemorrhage, with sensitivity 72.1% and specificity 85.7%, while PAS sign+ Intracervical Lakes increased specificity 95.9%, positive predictive value 92.3%, LR+ 9.64 and DOR 15.24, but decreased other characteristics.

As regard Diagnostic characteristics of US findings in predicting severe bleeding PAS sign had moderate diagnostic characteristics in predicting severe bleeding with sensitivity 83.3% and specificity 58.2% while, PAS sign+ Intracervical Lakes increased specificity 80.6%, positive predictive value 26.9%, LR+ 3.1 and DOR 5.82, but decreased other characteristics.

As regard Diagnostic characteristics of US findings in predicting hysterectomy, PAS sign had high sensitivity 95.5% & NPV 98.3%, and moderate other diagnostic characteristics, PAS sign+ Intracervical Lakes not markedly decreased sensitivity 90.9% & NPV 97.6%, but markedly increased other diagnostic characteristics with specificity 93.2%.

As regard Diagnostic characteristics of US findings in predicting postpartum hemorrhage PAS sign had low diagnostic characteristics in predicting postpartum hemorrhage, with sensitivity 58.8% and specificity 55.9% while PAS sign+ Intracervical Lakes increased specificity 78.5%, positive predictive value 23.1%, LR+ 1.64 and DOR 1.99, but decreased other characteristics.

The findings of this study showed that presence of ICL in women with a low-lying placenta or placenta previa is associated independently with major postpartum hemorrhage, Cesarean hysterectomy and placenta percreta.

Presence of both ICL and at least one typical sonographic sign of PAS disorder yielded a higher prediction of these complications compared with presence of typical sonographic signs of PAS disorder alone.

The following study is in agree with our study Di Pasquo E, et al. first published at March [10].

This was a retrospective multicenter study of women with placenta previa or low-lying placenta at  $\geq 26$  weeks' gestation, who were referred to three Italian tertiary units from January 2015 to September 2018. The presence of ICL, defined as tortuous anechoic spaces within the cervix which appeared to be hypervascular on color Doppler, was evaluated on ultrasound images obtained at the time of referral. The primary aim was to explore the diagnostic accuracy of ICL in detecting the presence and depth of PAS disorder. The secondary aim was to explore the accuracy of this sign in predicting total estimated blood loss, antepartum bleeding, major postpartum hemorrhage at the time of Cesarean section and need for Cesarean hysterectomy. The diagnostic accuracy of ICL in combination with typical sonographic signs of PAS disorder was assessed by computing summary estimates of sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios and diagnostic odds ratios (DOR).

A total of 332 women with placenta previa or low-

lying placenta were included in the analysis, with a median maternal age of 33.0 (interquartile range, 29.0–37.0) years. ICL were noted in 15.1% of patients. On logistic regression analysis, the presence of ICL was associated independently with major postpartum hemorrhage (odds ratio (OR), 3.3 (95% CI, 1.6–6.5);  $P < 0.001$ ), Cesarean hysterectomy (OR, 7.0 (95% CI, 2.1–23.9);  $P < 0.001$ ) and placenta percreta (OR, 2.8 (95% CI, 1.3–5.8);  $P \leq 0.01$ ), but not with the presence of any PAS disorder (OR, 1.6 (95% CI, 0.7–3.5);  $P = 0.2$ ). Compared with the group of patients without ultrasound signs of PAS disorder, the presence of at least one typical sonographic sign of PAS disorder in combination with ICL had a DOR of 217.2 (95% CI, 27.7–1703.4;  $P < 0.001$ ) for placenta percreta and of 687.4 (95% CI, 121.4–3893.0;  $P < 0.001$ ) for Cesarean hysterectomy.

No other studies published in the same topic against our results.

## STRENGTHS AND LIMITATIONS

The main strengths of this study was prospective study in, inclusion of consecutive patients, evaluation of different clinical outcomes and assessment of the ultrasound images by expert examiners in the prenatal diagnosis of PAS disorder, and intraoperative observation which was done by expert obstetrician.

Other studies were retrospective assessment of ICL and the lack of evaluation of the intra- and interobserver variability of the explored signs represent the major weaknesses of these studies.

The limitation of the study is Inclusion of only women affected by placenta previa or low-lying placenta represents another limitation of the study. A significant proportion of PAS disorders have been shown to occur in women with no recognizable risk factors for these anomalies.

Other limitation is small number of sample size 110 cases and the outbreak of COVID 19.

In this scenario, the findings from this study are applicable only to women presenting with placenta previa or low-lying placenta.

In this preliminary study, the number and distribution of the ICL were not assessed because our main outcome was to assess the clinical significance of this new sign and to assess its association with the risk of PAS disorder

## CONCLUSION

In the present study, may represent a marker of deep villus invasion in women with suspected PAS disorder on antenatal ultrasound and anticipate the occurrence of severe maternal morbidity with specificity 98.1%.

## RECOMMENDATIONS

Intracervical lakes sign is recommended to be a routine screening test in cases with previa and low lying placenta. Further studies are needed in order to evaluate

the reproducibility of this sign and to elucidate whether its introduction into ultrasound screening of women at risk of

PAS disorder may improve the identification of patients at higher risk of adverse outcome.

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