

## **Relation between Fetal Renal Artery Doppler Indices and Non-PROM Oligohydramnios in Third Trimester of Pregnancy**

### **Abstract**

**Background:** Amniotic fluid is the liquid which surround the fetus after the first few weeks of gestation. Amniotic fluid is derived mostly from the fetus and has many functions that are essential for normal growth and development. The aim of this work is to study the relation between fetal renal artery flow velocity waveforms and amniotic fluid volume in normal pregnancies and those complicated by oligohydramnios.

**Methods:** This prospective observational study was carried out on 40 pregnant women (10) of them were with normal amount of amniotic fluid (group I), while (30) of them suffered from oligohydramnios (group II). By using color doppler ultrasound imaging, the fetal renal circulation can be assessed. Intermittent assessment of renal artery flow velocity waveforms during the early stages of pregnancy may help in predicting changes in amniotic fluid dynamics.

**Results:** There was a non-significant difference between cases with normal amount of amniotic fluid and cases with oligohydramnios in Gestational age, Maternal age, fetal femur length, bi parietal diameter, abdominal circumference and Fetal weight. There were increased values of fetal renal artery Resistance index (RI) and Pulsatility index (PI) in cases of oligohydramnios than cases with normal amount of amniotic fluid. There was no correlation between Peak systolic velocity (PSV) and Amniotic fluid index (AFI). There was a significant difference in End diastolic velocity (EDV) between cases with normal amount of

amniotic fluid and cases with oligohydramnios. Also, there was a significant difference in Systolic diastolic ratio (S/D) and Amniotic fluid index (AFI) between cases with normal amount of amniotic fluid and cases with oligohydramnios.

**Conclusions:** There is a relation between renal artery flow velocity waveforms and oligohydramnios using Pulsed wave Doppler Ultrasonography. There are higher values of renal artery Resistance index and Pulsatility index in cases of oligohydramnios more than cases with normal amount of amniotic fluid.

**Keywords:** Fetal Renal Artery, Doppler Indices, Non-PROM Oligohydramnios, Third Trimester, Pregnancy.

## Introduction:

In the third trimester of pregnancy amniotic fluid volume is an indicator of fetal well-being and is an important measurement during antenatal fetal testing. Amniotic fluid volume has been described as oligohydramnios if Amniotic fluid index (AFI) is less than 5 . However, the definition of normal amniotic fluid has previously been made according to each gestational age<sup>(1-3)</sup>.

Moore and Cayle published some normative data for amniotic fluid index throughout pregnancy and noted that the mean amniotic fluid index changes weekly<sup>(4)</sup>. Causes of oligohydramnios include :Fetal urinary tract anomalies as renal agenesis, polycystic kidneys, or urinary obstructive lesions, Premature rupture of membranes and chronic leakage of the amniotic fluid, Placental insufficiency as seen in pregnancy-induced hypertension, maternal diabetes, and Maternal use of prostaglandin synthase inhibitors or angiotensin-converting enzyme inhibitors<sup>(5)</sup>.

A decreased amniotic fluid volume is thought to be a factor in the increased incidence of complications during labor, an approximately twofold increased risk of cesarean sections for non-reassuring fetal heart rate patterns, and adverse perinatal outcome<sup>(6, 7)</sup>.

There are several potential mechanisms by which changes in the kidney can cause oligohydramnios in pregnancies. One is fetal hypovolemia and hemoconcentration due to changes in the placental fetal fluid balance, as proposed by Rightmire and Campbell<sup>(8)</sup>.

**Bar-Hava et al.** considered oligohydramnios to be the result of excessive tubular reabsorption of urine due to above-normal sensitivity to vasopressin in prolonged pregnancies. Another possibility is the decrease in fetal urine production as a consequence of increased intrarenal vascular resistance, which can be measured using Doppler velocimetry and by using ultrasound imaging. assessment of renal artery flow velocity waveforms during pregnancy may help in determining the cause of changes in amniotic fluid dynamics<sup>(9-11)</sup>.

Normal renal artery resistance index in third trimester is  $0.98 \pm 0.04$ , normal renal artery pulsatility index is  $2.57 \pm 0.47$ . **Yoshimura et al.** reported that renal artery pulsatility index (PI) values were higher in pregnant women with oligohydramnios. Another study evaluated the renal artery Doppler indices in fetuses with oligohydramnios and reported that PI and RI values were higher than in the those with normal amount of amniotic fluid<sup>(12, 13)</sup>.

The aim of this work is to study the relation between fetal renal artery flow velocity waveforms and amniotic fluid volume in normal pregnancies and those complicated by oligohydramnios.

### **Patients and Methods:**

This is a case control study that was carried out on (40) pregnant ladies, (10) of them were with normal amount of amniotic fluid (group I), while (30) of them suffered from oligohydramnios (group II). All pregnant women enrolled in the study were selected from those attending the outpatient clinics in the Radiodiagnosis and Medical Imaging Department in Tanta University hospital and the Radiodiagnosis Department of El-Menshawy General Hospital in Tanta. Informed consent was obtained from pregnant women according to policy of Tanta University hospitals that necessitates no harmful procedure was performed or used for any patient. An approval of the study was taken from the Ethics Committee of Tanta University Hospitals. This study was conducted from January 2018 to October 2020.

Pregnant women with single fetus at third trimester with normal amount of amniotic fluid and pregnant women with single fetus at third trimester with a decreased amount of amniotic fluid (Non-PROM oligohydramnios) were included.

Pregnant women at third trimester with PROM, pregnant women with multiple pregnancies and cases of oligohydramnios caused by maternal disease as diabetes and hypertension were excluded.

**All included patients were subjected to the following:**

- Full history taking and Ultrasound examination using ultrasound machines equipped with 3.5 -5 MHz convex transducers.

**All measurements were done by one author to evaluate:** Fetal biometric measurements were obtained (biparietal diameter, femur length, abdominal circumference and fetal weight). Doppler study of renal arteries were obtained Resistance index (RI), Pulsatility index (PI), End diastolic velocity (EDV), Peak systolic velocity (PSV) and systolic / diastolic (S/D) ratio. Amniotic fluid volume were evaluated in four quadrants (AFI).

All data which were tabulated, statistically analyzed and compared between the two groups.

**Risks and ethical considerations:** An informed consent was taken from all participants in this research after full explanation of the benefits and risks of the procedure.

Pregnant ladies in this study were divided into 2 groups : Group I: with normal amount of amniotic fluid and group II : with oligohydramnios.

**Steps of performance and technique used:**

Fetal anomaly scan was performed to exclude major fetal anomalies and multiple pregnancy. Fetal biometric measurements were obtained placental location and structure and the amniotic fluid volume were evaluated in four quadrants. After detailed ultrasonography of the fetus. Renal artery Doppler values were evaluated for all fetuses Pulsatility index (PI) resistance index (RI), End diastolic velocity (EDV), Peak systolic velocity (PSV) and systolic / diastolic (S/D) ratio were recorded and the amniotic fluid volume was evaluated. Pulsed wave Doppler sonographic studies were performed on the participants with a 3.5-MHz convex transducer. The wall filter was set at the lowest available setting (50–75 Hz) to preserve the end-diastolic component of the waveform. The angle between the ultrasound beam and the direction of blood flow was maintained below 30°. All recordings were obtained in the absence of fetal breathing and fetal movements. An average of three

consecutive Doppler velocity waveforms was used for analysis. For evaluating renal artery blood flow, an axial image of the fetal abdomen was obtained at the level of the fetal kidneys. Using color flow Doppler, the renal arteries were evaluated at the level of their origin from the abdominal aorta. The Doppler gate was placed within the lumen in a straight segment of the vessel.

A minimum of three consecutive waveforms were used to calculate the PI and RI.

Amniotic fluid index (AFI): with the patient supine, the ultrasound transducer was applied to the maternal abdomen and was positioned perpendicular to the floor. The abdomen was divided into 4 quadrants, and the deepest pocket of amniotic fluid not containing umbilical cord was measured in centimeters in each. The sum of all 4 quadrants is the AFI.

#### **Statistical analysis:**

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t- test. Qualitative variables were presented as frequency and percentage (%) and were analysed utilizing the Chi-square test or Fisher's exact test when appropriate. Linear Correlation Coefficient [r] and Probability (P-value) were also calculated. A two tailed P value < 0.05 was considered statistically significant.

#### **Results:**

There was non-significant difference between group I and group II according to AGA (P. value 0.665), Maternal age (P. value 0.799) and Fetal weight (P. value 0.253).

**Table 1: Showing demographic data of group I,II**

Demographic data		Group I	Group II	T. test	P. value
AGA (weeks)	Range	32 – 39	30 – 38	0.437	0.665
	Mean $\pm$ SD	36.00 $\pm$ 2.75	35.60 $\pm$ 2.43		
Maternal age (years)	Range	20 – 36	21 – 36	0.799	0.429
	Mean $\pm$ SD	27.90 $\pm$ 4.70	29.13 $\pm$ 4.07		
EFW(grams)	Range	1834 – 3804	1510 – 3543	0.253	0.801
	Mean $\pm$ SD	2907.80 $\pm$ 732.01	2849.47 $\pm$ 595.41		

AGA: Average gestational age, EFW: estimated fetal weight

There was non-significant difference between group I and group II according to estimated fetal weight (P. value = 0.801). There was non-significant difference between group I and group II according to Bi parietal diameter (P. value = 0.465). There was non-significant difference between group I and group II according to femur length (P. value = 0.726). The Mean  $\pm$  SD for AC in group I is (36.20  $\pm$  2.82 weeks) and in group II is (35.67  $\pm$  2.70 weeks) with non-significant difference (P. value = 0.595).

**Table 2: Comparison between group I and group II according to estimated fetal weight, BPD, FL and AC.**

<b>EFW</b>	<b>Group I</b>	<b>Group II</b>
<b>Range (grams)</b>	1834 – 3804	1510 – 3543
<b>Mean <math>\pm</math> SD (grams)</b>	2907.80 $\pm$ 732.01	2849.47 $\pm$ 595.41
<b>T. test</b>	0.253	
<b>P. value</b>	0.801	
<b>BPD</b>	<b>Group I</b>	<b>Group II</b>
<b>Range (weeks)</b>	32 – 39	30 – 38
<b>Mean <math>\pm</math> SD (weeks)</b>	36.00 $\pm$ 2.54	35.33 $\pm$ 2.45
<b>T. test</b>	0.738	
<b>P. value</b>	0.465	
<b>FL</b>	<b>Group I</b>	<b>Group II</b>
<b>Range (weeks)</b>	32 – 39	30 – 38
<b>Mean <math>\pm</math> SD (weeks)</b>	36.00 $\pm$ 2.75	35.67 $\pm$ 2.54
<b>T. test</b>	0.353	
<b>P. value</b>	0.726	
<b>AC</b>	<b>Group I</b>	<b>Group II</b>
<b>Range (weeks)</b>	32 – 40	29 – 39
<b>Mean <math>\pm</math> SD (weeks)</b>	36.20 $\pm$ 2.82	35.67 $\pm$ 2.70
<b>T. test</b>	0.536	
<b>P. value</b>	0.595	

BPD:Bi parietal diameter, SD:standard deviation, FL:femur length, AC: abdominal circumference.

There was significant difference between group I and group II according to RI (P. value = 0.001). The mean  $\pm$  SD for PI in group I was (1.47  $\pm$  0.16) While in group II was (2.44  $\pm$  0.49) with significant difference (P. value = 0.001). There was non-significant difference between group I and group II according to PSV (P. value= 0.556).



**Table 3: Comparison between group I and group II according to RI, PI and PSV of the main fetal renal artery and**

<b>RI</b>	<b>Group I</b>	<b>Group II</b>
<b>Range</b>	0.71 – 0.83	0.76 – 1.19
<b>Mean ± SD</b>	0.77 ± 0.03	0.96 ± 0.16
<b>T. test</b>	3.687	
<b>P. value</b>	0.001*	
<b>PI</b>	<b>Group I</b>	<b>Group II</b>
<b>Range</b>	1.16 – 1.8	1.54 – 3.28
<b>Mean ± SD</b>	1.47 ± 0.16	2.44 ± 0.49
<b>T. test</b>	6.058	
<b>P. value</b>	<b>0.001*</b>	
<b>PSV</b>	<b>Group I</b>	<b>Group II</b>
<b>Range (cm/s)</b>	16.8 – 71.24	25 – 97.04
<b>Mean ± SD (cm/s)</b>	54.88 ± 15.17	59.20 ± 21.19
<b>T. test</b>	0.595	
<b>P. value</b>	0.556	

\*: significant as P value < 0.05, RI: resistance Index, PI: Pulsatility index, PSV: Peak systolic velocity

This table shows no correlation between Peak systolic velocity and AFI.

**Table 4: Showing correlation between systolic velocity and amniotic fluid index.**

	AFI	
	r	P
PSV	- 0.254	0.155

AFI: Amniotic fluid index

EDV ranged in group I (4.1 – 16.51 cm/s) and in group II (3.7 – 16.51cm/s), Mean  $\pm$  SD in group I ( $12.41 \pm 3.38$  cm/s) and in group II ( $8.87 \pm 3.03$  cm/s) with significant difference (P. value 0.004). The mean  $\pm$  SD for S/D in group I was ( $4.44 \pm 0.71$ ) and in group II was ( $6.86 \pm 1.95$ ) with significant difference (P. value = 0.001). The AFI ranged in group I was (8 – 14) and in group II was (2 – 4), Mean  $\pm$  SD in group I was ( $10.80 \pm 2.25$ ) and in group II was ( $2.93 \pm 0.78$ ) with significant difference (P. value = 0.001).

**Table 5: Comparison between group I and group II according to EDV, S/D of the main fetal renal artery and AFI.**

<b>EDV</b>	<b>Group I</b>	<b>Group II</b>
<b>Range (cm/s)</b>	4.1 – 16.51	3.7 – 16.51
<b>Mean <math>\pm</math> SD (cm/s)</b>	12.41 $\pm$ 3.38	8.87 $\pm$ 3.03
<b>T. test</b>	3.111	
<b>P. value</b>	<b>0.004*</b>	
<b>S/D</b>	<b>Group I</b>	<b>Group II</b>
<b>Range</b>	3.44 – 5.88	4.19 – 11.47
<b>Mean <math>\pm</math> SD</b>	4.44 $\pm$ 0.71	6.86 $\pm$ 1.95
<b>T. test</b>	3.814	
<b>P. value</b>	<b>0.001*</b>	
<b>AFI</b>	<b>Group I</b>	<b>Group II</b>
<b>Range</b>	8 – 14	2 – 4
<b>Mean <math>\pm</math> SD</b>	10.80 $\pm$ 2.25	2.93 $\pm$ 0.78
<b>T. test</b>	16.670	
<b>P. value</b>	<b>0.001*</b>	

\*: significant as P value < 0.05, EDV:End Diastolic velocity, S/D: Systolic diastolic ratio

## Discussion

Any amniotic fluid abnormalities such as oligohydramnios is the leading cause of fetal morbidity and mortality. So that the amniotic fluid index can predicts the function of the fetal kidneys and allows evaluation of fetal circulation. That is why, it is very important to evaluate the renal artery flow intermittently in order to predict changes of amniotic fluid dynamics from the early stages of gestation<sup>(14)</sup>.

In the current study the fetal bi parietal diameter ranged from (30-39) weeks , there was non-significant difference of bi parietal diameter between cases with normal amount of amniotic fluid and cases with oligohydramnios (p value = 0.465)

These results were in agreement with the study of<sup>(11)</sup>who performed his study on 110 pregnant women, divided them into 3 groups , group I with oligohydramnios , group II with

polyhydramnios and group III with normal amount of amniotic fluid, showed non-significant difference in bi parietal diameter between groups (p value = 0.4).

In the current study the fetal femur length ranged from (30-39 weeks) with non-significant difference in femur length between cases with normal amount of amniotic fluid and cases with oligohydramnios with (p value = 0.726)

These results were in agreement with the study of<sup>(11)</sup> who performed his study on 110 pregnant women divided them into 3 groups , group I with oligohydramnios , group II with polyhydramnios and group III with normal amount of amniotic fluid, showed non-significant difference in femur length between groups ( p value = 0.2).

In this current study the abdominal circumference ranged from (29-40) weeks there was non-significant difference in abdominal circumference between cases with normal amount of amniotic fluid and cases with oligohydramnios (p value = 0.595).

These results were in agreement with the study of<sup>(11)</sup> who performed his study on 110 pregnant women, divided them into 3 groups , group I with oligohydramnios , group II with polyhydramnios and group III with normal amount of amniotic fluid, showed non-significant difference in abdominal circumference (p value = 0.3).

In this current study fetal renal artery resistance index of cases with normal amount of amniotic fluid ranged from (0.71 -0.83) and fetal renal artery resistive index in cases with oligohydramnios ranged from (0.76-1.19) ,showing higher values of fetal renal artery Doppler resistance index in cases of oligohydramnios more than cases with normal amount of amniotic fluid and also showing significant difference in renal artery resistive index between both groups ( p value = 0.01).

These results were in agreement with results of<sup>(15)</sup> on 147 study cases , with fetal renal artery resistance index range ( $0.8843 \pm 0.11$ ) and showed that renal artery Resistance index was the only significant predictor of oligohydramnios with (p value > 0.05)

These results were in agreement with results of<sup>(11)</sup> who performed his study on 110 pregnant women, with significant difference in fetal renal artery resistance index between groups (p value = 0.01)

Also these results were in agreement with results of<sup>(16)</sup> who performed a study on a 84 pregnant ladies and divided them into 2 groups according to amniotic fluid volume, showed a significant relationship (p value = 0.024)

In this current study fetal renal artery pulsatility index of cases with normal amount of amniotic fluid ranged from (1.16-1.8) ,fetal renal artery pulsatility index in cases with oligohydramnios ranged from(1.54-3.28) ,showing higher values of fetal renal artery Doppler pulsatility index in cases of oligohydramnios more than cases with normal amount of amniotic fluid and also showing significant difference in renal artery pulsatility index between both groups (p value = 0.01).

These results were in agreement with results of<sup>(11)</sup> who performed a study on 110 pregnant women, with higher values of fetal renal artery pulsatility index in cases with oligohydramnios than cases with normal amount of amniotic fluid and a significant difference in fetal renal artery pulsatility index between groups (p value = 0.00)

Our results were not in agreement with results of<sup>(16)</sup> who performed a study on a 84 pregnant ladies and divided them into 2 groups according to amniotic fluid volume, who showed non-significant difference in pulsatility index of renal artery between both groups (p value = 0.430)

In this current study the range of peak systolic velocities in cases with normal amount of amniotic fluid is (16.8-71.24) cm/s, the range of peak systolic velocities in cases with

oligohydramnios is (25-97.04), with non-significant difference in peak systolic velocity between both groups and a non-significant correlation between SV (systolic velocity) and amniotic fluid index.

These results were with agreement with the study of<sup>(17)</sup> who did a study on 66 women and showed non-significant correlation between SV and AFI.

In current study EDV (end diastolic velocity) range in cases with normal amount of amniotic fluid was (4.1-16.51) cm/s and in cases with oligohydramnios (3.7-16.51), with significant difference between both groups (p value = 0.004)

In the current study S/D of the main fetal renal artery in cases with normal amount of amniotic fluid ranged from (3.44-5.88) and in cases with oligohydramnios ranged from (4.19-11.47), showing a significant relationship between S/D of the main fetal renal artery and amount of amniotic fluid with (p value = 0.001)

These result were not in agreement with results of<sup>(11)</sup> who performed their study on 110 pregnant women, and divided them into 3 groups according to amniotic fluid amount and showed non-significant difference in S/D ratio of the main fetal renal artery between groups (p value = 0.9)

In this current study amniotic fluid index AFI ranged from (8-14) in cases with normal amount of amniotic fluid and ranged from (2-4) in cases with oligohydramnios and showed a significant difference between both groups (p value = 0.001)

These results were in agreement with results of<sup>(16)</sup> who performed a study on a 84 pregnant ladies and showed a significant difference of AFI between cases with normal amount of amniotic fluid and cases of oligohydramnios (p value = 0.025)

## **Conclusions:**

There is a relation between renal artery flow velocity waveforms and oligohydramnios using Pulsed wave Doppler Ultrasonography. There are higher values of renal artery Resistance

index and Pulsatility index in cases of oligohydramnios more than cases with normal amount of amniotic fluid.

#### COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

#### References

1. **Magann EF, Chauhan SP, Sanderson M, McKelvey S, Dahlke JD and Morrison JC.** Amniotic fluid volume in normal pregnancy: comparison of two different normative datasets. J Obstet Gynaecol Res. 2012;38(2):364-70.
2. **Dasari P, Niveditta G and Raghavan S.** The maximal vertical pocket and amniotic fluid index in predicting fetal distress in prolonged pregnancy. Int J Gynaecol Obstet. 2007;96(2):89-93.
3. **Dildy GA, 3rd, Lira N, Moise KJ, Jr., Riddle GD and Deter RL.** Amniotic fluid volume assessment: comparison of ultrasonographic estimates versus direct measurements with a dye-dilution technique in human pregnancy. Am J Obstet Gynecol. 1992;167(4 Pt 1):986-94.
4. **Moore TR and Cayle JE.** The amniotic fluid index in normal human pregnancy. Am J Obstet Gynecol. 1990;162(5):1168-73.
5. **Harper L, Waubant A, Vignes J, Amat S, Dobremez E, Lefevre Y, et al.** Can quantity of amniotic fluid reliably predict postnatal renal function in boys with posterior urethral valves: a decision curve analysis. Prenat Diagn. 2017;37(9):931-4.
6. **Rossi AC and Prefumo F.** Perinatal outcomes of isolated oligohydramnios at term and post-term pregnancy: a systematic review of literature with meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2013;169(2):149-54.

7. **Guin G, Puneekar S, Lele A and Khare S.** A prospective clinical study of feto-maternal outcome in pregnancies with abnormal liquor volume. *J Obstet Gynaecol India.* 2011;61(6):652-5.
8. **Veille JC, Penry M and Mueller-Heubach E.** Fetal renal pulsed Doppler waveform in prolonged pregnancies. *Am J Obstet Gynecol.* 1993;169(4):882-4.
9. **Ek S, Andersson A, Johansson A and Kublicas M.** Oligohydramnios in uncomplicated pregnancies beyond 40 completed weeks. A prospective, randomised, pilot study on maternal and neonatal outcomes. *Fetal Diagn Ther.* 2005;20(3):182-5.
10. **Bar-Hava I, Divon MY, Sardo M and Barnhard Y.** Is oligohydramnios in postterm pregnancy associated with redistribution of fetal blood flow? *Am J Obstet Gynecol.* 1995;173(2):519-22.
11. **Akin I, Uysal A, Uysal F, Oztekin O, Sancı M, Güngör AC, et al.** Applicability of fetal renal artery Doppler values in determining pregnancy outcome and type of delivery in idiopathic oligohydramnios and polyhydramnios pregnancies. *Gineköl Pol.* 2013;84(11):950-4.
12. **Yoshimura S, Masuzaki H, Gotoh H and Ishimaru T.** Fetal redistribution of blood flow and amniotic fluid volume in growth-retarded fetuses. *Early Hum Dev.* 1997;47(3):297-304.
13. **Selam B, Koksai R and Ozcan T.** Fetal arterial and venous Doppler parameters in the interpretation of oligohydramnios in postterm pregnancies. *Ultrasound Obstet Gynecol.* 2000;15(5):403-6.
14. **Moore KL.** Clinically Oriented Anatomy. 3rd ed. Philadelphia: Williams and Wilkins; 1992.



15. **Oz AU, Holub B, Mendilcioglu I, Mari G and Bahado-Singh RO.** Renal artery Doppler investigation of the etiology of oligohydramnios in postterm pregnancy. *Obstet Gynecol.* 2002;100(4):715-8.
16. **Özkan MB, Özkan E, Emiroglu B and Özkaya E.** Doppler study of the fetal renal artery in oligohydramnios with post-term pregnancy. *J Med Ultrasound.* 2014;22(1):18-21.
17. **Figueira CO, Surita FG, Dertkigil MS, Pereira SL, Bennini Jr JR, Morais SS, et al.** Longitudinal reference intervals for Doppler velocimetric parameters of the fetal renal artery correlated with amniotic fluid index among low-risk pregnancies. *Int J Gynaecol Obstet.* 2015;131(1):45-8.