# **ORIGINAL ARTICLE**

# Comparison of Transvaginal Sonographic Doppler Indices Between Normal Intrauterine and Extrauterine Pregnancies Confirmed by Maternal Serum Beta-HCG in the First Trimester of Pregnancy

TAYEBA ALI<sup>1</sup>, RAHAM BACHA<sup>1</sup>, SAIRA AMIN<sup>1</sup>, SYED MUHAMMAD YOUSAF FAROOQ<sup>1</sup>, MEHREEN FATIMA<sup>1</sup>, IQRA MANZOR<sup>1</sup> <sup>1</sup>University Institute of Radiological Sciences & Medical Imaging Technologies (UIRSMIT), The University of Lahore, Pakistan Corresponding author: Saira Amin, Email: sairaamin073@gmail.com

## ABSTRACT

**Background:** Transvaginal Sonography provides high-resolution images with high reliability and is typically used for the diagnosis of intrauterine pregnancy and ectopic conception. The extra-uterine pregnancy responsible for morbidity and mortality in First Trimester and is 80 percent accounts for maternal death. Doppler ultrasound is a safe and non-invasive technique in the evaluation of uterine artery flow patterns. It can calculate the indices like Resistivity index and Pulsatility index in numerical value. It is also observed that there are changes noted between the uterine artery indices in normal intrauterine and extrauterine pregnancies. However, it is important to compare them in normal intrauterine and extrauterine pregnancies.

**Objective:** To compare the trans-vaginal sonographic Doppler indices of the uterine artery between normal and ectopic pregnancies confirmed by maternal serum Beta-hCG.

**Methodology:** This case-control study was conducted at Shireen Ultrasound Clinic Peshawar, KPK Pakistan. This study enrolled a purposive sample of 80 (40 ectopic & 40 intrauterine) pregnant female patients with age 18 to 45 years. The examination was performed with Toshiba Nemio 20(Xario Prime with TVS Probe frequency range 7-14MHz). The Resistive index, Pulsatility index, mean and standard deviation were calculated for the continuous variables.

**Results:** In normal early pregnancy, the mean RI of the right uterine artery was 0.53±0.10 and the mean RI of the left uterine artery was 0.52±0.07. In the cases of (ectopic pregnancy), the mean RI of the right uterine artery was 0.73±0.08 and the mean RI of the left uterine artery was 0.73±0.08. The p-value of the right and left uterine arteries in normal intrauterine and extrauterine ectopic pregnancies were significant at 0.05 level.

**Conclusion:** The resistivity index of uterine arteries is significantly high in ectopic conceptions than in normal intrauterine pregnancies. But there was no significant change in PI of normal intrauterine and ectopic pregnancies.

Keywords: adnexal mass, ectopic pregnancy, Transvaginal ultrasound, tubal pregnancy.

# INTRODUCTION

The extrauterine ectopic pregnancy responsible for the disease and death ratio in First Trimester is about 80% and accounts for maternal death in the first three months of pregnancy in the US and UK. So, it's a life-threatening condition. Ectopic word is derived from the Greek term Ectopos which means not in place. When the implantation occurs not in the uterine cavity termed ectopic pregnancy. Ectopic pregnancy is classified into two major groups, tubal and non-tubal. 95% of extra-uterine pregnancies are tubal and only 5% are non-tubal. The extra-uterine pregnancies that occur in ovaries, cervix, ischium, and previous CS scar are all non-tubal types. The condition where intrauterine and extra-uterine pregnancies occur simultaneously is described as heterotrophic pregnancy, before the introduction of Sonography, was the serum Beta-hCG<sup>1,2,3</sup>.

A woman with a positive pregnancy test experienced abdominal and cervical tenderness inform the clinician to rule out the ectopic pregnancy. In only 30 percent of patients, the clinical presentations were present but the signs and symptoms were not-specific. Before 1970, more than 80 percent of extra uterine pregnancies were diagnosed after the tubal rupture and 50 percent were presenting with hypovolemic shock <sup>4, 5</sup>.

The very first pregnancy that occurred after in-vitro fertilization was an extra uterine pregnancy<sup>6</sup>. The ratio of scar pregnancy increases with the increasing rate of caesarian section<sup>7</sup>. <sup>8, 9</sup>. The extra-uterine ectopic pregnancies increased with the use of IUCDs in women who become pregnant <sup>10</sup>.

The Beta-hCG test and ultrasound testimg are not exclusive. The diagnosis of an intra - uterine gestational and yolk sac during an ultra-sound is important for the diagnosis of a normal intrauterine pregnancy, which is possible when beta-hCG levels are between 1,500 and 2,500 mlU / mL<sup>11</sup>. Early diagnostic methods that ultrasound is only necessary in condition of high level Beta-hCG and a specific threshold widely recognised the dependence of sonography on the higher level of Beta-hCG to diagnose normal intra-uterine pregnancy<sup>12</sup>. These methods were predicated on the idea that detecting an ectopic pregnancy required demonstrating the absence of an intrauterine pregnancy when one should be present. But in extra-uterine ectopic pregnancies, trans- vaginal ultrasonography can identify free intra- peritoneal fluid or dnexal masses. The sensitivity of these findings is less reliant on level of beta-hCG as compared to the typical intra-uterine pregnancy<sup>13</sup>. In female, who have abdominal pain, positive urine pregnancy tests, and vaginal bleeding, the transvaginal ultrasonography is advised as the initial diagnostic technique<sup>14</sup>.

# MATERIALS AND METHODS

This case-control study was conducted at the Shireen Ultrasound Clinic Peshawar, KPK in Pakistan while recruiting enrolled 80 pregnant women aged 18 to 45 years (40 normal intrauterine and 40 extra-uterine ectopic pregnancies) in the first trimester, from November 2021 to June 2022. The study was approved by the Ethical Review Committee of the University of Lahore. The procedure was briefly explained to the patients. The patients were also briefed about the exposure and the TVS transducer insertion and assured of their privacy. Informed written consent was obtained from all the participants. Transvaginal Sonography was carried out for all the patients during this period to detect vascular changes in the uterine artery in ectopic and normal intrauterine pregnancies. All pathological pregnancies were excluded. Ultrasonography was performed, using Toshiba Nemio 20 (Xario Prime with frequency range 7-14 MHz TVS probe). Patients were positioned in a lithotomy position and a TVS transducer was inserted. During the examination, The AIUM guidelines were followed. The privacy of the patient was prioritized during the sonographic examination. The pelvic study was conducted with real-time Sonography. Uterus was evaluated in the long and short axis view as shown in Figures 1 to 2.

The Following parameters were studied in each case

• Sonographic data regarding the Size and echogenicity of the uterus and endometrial thickness were obtained with Gray Scale

• Normal first-trimester pregnancy parameters were calculated like gestational sac diameter and crown-rump length. (Figure 1)

• The bilateral uterine artery indices like RI and PI were obtained in each case by using Doppler Sonography. (Figures 1 to 2)

Data were evaluated with the help of Statistical Package for the Social Sciences (SPSS) software (SPSS 24, IBM, Armonk, NY, United States of America). The mean, standard deviation, and range are used to describe descriptive data. The RI and PI of the uterine arteries were compared in normal intrauterine and extrauterine ectopic pregnancy.

### RESULTS

In this study, the results indicate that the mean endometrial thickness was low in ectopic pregnancy than in normal pregnancy. Of the 40 women in the ectopic pregnancies, the mean gestational age was 7±1 weeks, and presented with pelvic pain and vaginal bleeding. Of the 40 women in normal pregnancies, the mean gestational age was 6±1 week. There was a significant difference between the uterine artery RI of normal intrauterine and ectopic pregnancies. But the PI of the uterine artery in normal intrauterine artery PI of ectopic pregnancies, detail is given in Table 1.

Table 1: Group Statistics of RI and PI in Right U-A and Left U-A in ectopic and normal early pregnancy

Parameters	Ectopic cases (n=40)		Control group (n=40)		P –value	T-test
	Mean	Std. deviation	Mean	Std. deviation		
Right U-A RI	0.73	0.08	0.53	0.10	0.006	8.04
Right U-A PI	2.79	0.75	2.35	0.71	0.50	0.44
Left U-A RI	0.78	0.07	0.52	0.10	0.00	86.74
Left U-A PI	2.71	0.84	2.39	0.85	0.74	0.11



Figure 1: A 35 years old female patient presenting with 45 days of amenorrhea. (a) A transvaginal longitudinal greyscale image shows an enlarged uterus containing an active CRL (appointed by an arrow) corresponding to a gestational age of 7 weeks. (b) Transvaginal Doppler image shows left uterine artery confirmed by color Doppler and power Doppler shows RI=0.54 and PI=2.37.



Figure 2: Left tubal pregnancy at 6 weeks of gestation. A 36 years old female presented with pelvic pain, vaginal bleeding, and 45 days of amenorrhea and was positive for the urine pregnancy test. (a) The Grey scale image shows normal size uterus with normal endometrium. A gestational sac is seen in the left fallopian tube with no embryonic pole (Appointed by an arrow) (b) Transvaginal Doppler image shows the left uterine artery spectrum obtained by power Doppler shows the indices RI= 0.78 and PI=2.72.

#### DISCUSSION

Our study was designed to compare trans-vaginal sonographic Doppler indices of the uterine artery in normal intrauterine pregnancies and extrauterine ectopic pregnancies confirmed by maternal serum beta-hCG. Based on diagnostic performance and it was a case-control study. Data were evaluated and analyzed statistically by SPSS version 24.0. Entirely comprised patients were queried concerning variables such as size and echogenicity of the uterus, early pregnancy, and ectopic pregnancy were noted by grayscale and uterine artery was obtained with both greyscale and Doppler, the pattern of blood flow, Resistive index (RI), and Pulsatility index (PI) were obtained by pulsed Doppler. Data of 80 patients were included in this study 40 cases of intrauterine pregnancies and 40 cases of extrauterine ectopic pregnancies confirmed by maternal serum beta HCG.

In 2016<sup>15</sup> a study was conducted in Iran which states that the mean value of endometrial thickness was less in ectopic pregnancy than in normal early pregnancy similarly our study also reported thin endometrium in ectopic cases.

In a case-control study Laser JN, their study concluded that extra uterine conception was reported with vaginal bleeding and abdominal pain<sup>16</sup>. Of the patients in the current study diagnosed

with extra-uterine ectopic pregnancies (50%) presented with the above-mentioned symptoms.

Condous Get.AL,<sup>17</sup> in his study concluded that for ectopic pregnancy the most occurring trans-vaginal sign was Blob sign (57%), (13.2%) embryo cardiac activity, and (20%) adnexal masses with 2 heterotopic cases were noticed. Similarly, Saulat Sarfaraz, <sup>18</sup> conducted a study in Lahore, they reported in their study that the most common sign of ectopic pregnancy is the adnexal mass (84%) Similarly in our study the most common sign of ectopic pregnancy was adnexal mass (90%). Thus, the results of our study are comparable with Saulat Sarfaraz study but not with the Condous Get AL study.

A study reported by Jurkovic et al.<sup>19</sup> that the mean RI of the uterine artery in normal early pregnancy was reduced with increasing gestation age However in extra uterine conception these indices remained unchanged with increasing Gestation age.

In a study conducted by Wang et al, <sup>20</sup> in 2010, the mean RI of the uterine artery in pregnant women was  $0.8\pm0.1$  and also  $0.8\pm0.1$  in ectopic cases and  $0.8\pm0.1$  in normal cases. It means that there was no change noted in all the above-mentioned three groups. Güzelet al.<sup>21</sup> published in 2015 in their study that there is no significant difference in mean RI of the uterine artery in pregnant and non-pregnant women similarly Kim et al.<sup>22</sup> in 2015 Found in their study that there is no significant difference in mean RI of the uterine artery in pregnant and non-pregnant and non-pregnant women. From the above-mentioned studies, we found that there is no significant difference in the mean RI of the uterine artery between pregnant and non-pregnant women.

Another study conducted by Kurjack et al.<sup>23</sup> that the mean value of RI in the Right Uterine artery was 0.84±0.06 and in the left uterine artery was 0.86±0.06 in normal early conceptions. In 2015<sup>24</sup> in another study, it was found that the mean Doppler indices of the uterine artery are significantly low in pregnancy cases as compared to non-pregnant women. Ivanovski et al.<sup>25</sup> investigated in their study that the Doppler indices of the uterine artery were significantly high in non-pregnant cases as compared to a pregnant group, therefore results of the above studies supported one another.

In 2016 study reported which is stated as the mean RI of the uterine artery was 0.64±0.058 in extra uterine pregnancy and 0.42±0.059 in normal early pregnancy so that uterine artery RI in ectopic pregnancy was less than normal early pregnancy (p<0.001)<sup>16</sup>. In our study mean value of the RI of the right uterine artery was 0.73± 0.01 and of the left uterine artery was 0.78± 0.14 in an extra uterine ectopic pregnancy (Figure 2). The mean RI of the right uterine artery is 0.53± 0.10 and of the left uterine artery is 0.52±0.07 in normal early pregnancy (Figure 1) therefore the mean RI of the right uterine artery (p<0.005) and left uterine artery (p<0.005) is significantly high in ectopic pregnancy than normal early pregnancy (Table 1). The mean RI of the right and left uterine arterv is a bit higher than the mean RI reported in the above study because of inter-observer and technical variability among the hardware and software of different devices in different centers. The compression of results of different centers could not be the same but the conclusion of our results is supported by the abovementioned studies that the mean RI of the uterine artery in extrauterine ectopic pregnancy is higher than the normal intrauterine pregnancy.

### CONCLUSION

The resistivity index of uterine arteries is significantly high in extrauterine pregnancy than in normal intrauterine pregnancy. But there was no significant change in the PI of normal intrauterine and ectopic pregnancies.

#### REFERENCES

 Lewis G (ed) The Confidential Enquiry into Maternal and Child Health (CEMACH). Saving Mothers' Lives: Reviewing Maternal deaths to make Motherhood safer – 2003–2005. The Seventh Report on Confidential Enquiries into Maternal deaths in the United Kingdom. London: CEMACH, 2008.

- Zane S, Keike B, Kendrick J, Bruce C. Surveillance in a time of changing health care practices: estimating ectopic pregnancy incidence in the United States. Matern Child Health J 2002; 6: 227–36.
- Cantwell R, Clutton-Brock T, Cooper G, Dawson A, Drife J, Garrod D, Harper A, Hulbert D, Lucas S, McClure J, Millward-Sadler H. Saving mothers' lives: reviewing maternal deaths to make motherhood safer: 2006-2008. The eighth report of the confidential inquiries into maternal deaths in the United Kingdom. BJOG: an international journal of obstetrics and gynecology. 2011;118:1-203.
- Nezhat C, Nezhat F, Nezhat C. Nezhat's operative gynecologic laparoscopy and hysteroscopy. Cambridge University Press; 2008 Jul 7.
- Gashi AM, Elshani B, Latifi H, Sopa G, Ismajli J, Sherifi A. Ectopic Pregnancy-An 8-year survey. GinekologiaiPolożnictwo medical project. 2021 Dec 27;16(4):1-4.
- Steptoe PC, Edwards RG. Reimplantation of the human embryo with subsequent tubal pregnancy. Lancet 2006; 1: 880–82.
- Maymon R, Halperin R, Mendlovic S, Schneider D, Herman A. Ectopic pregnancies in a Caesarian scar: a review of the medical approach to an iatrogenic complication. Human Reprod Update 2014; 10: 515–23.
- Shennon AH. Recent developments in obstetrics. Br Med J 2013; 327: 604–8.
- Jurkovic D, Hillaby K, Woelfer B, Lawrence A, Salim R, Elson CJ. Firsttrimester diagnosis and management of pregnancies implanted into the lower uterine segment Caesarean section scar. Ultrasound ObstetGynecol 2013; 21: 220–7.
- Bouyer J, Rachou E, Germain E, Fernandez H, Coste J, Pouly JL, Job-Spira N. Risk factors for extrauterine pregnancy in women using an intrauterine device. FertilSteril 2000; 74: 899–908.
- Goh YI, Bollano E, Einarson TR, Koren G. Prenatal multivitamin supplementation and rates of congenital anomalies: a meta-analysis. Journal of obstetrics and gynaecology Canada. 2006 Aug 1;28(8):680-9.
- Tully HM, Dobyns WB. Infantile hydrocephalus: a review of epidemiology, classification and causes. European journal of medical genetics. 2014 Aug 1;57(8):359-68.
- Pessiglione M, Vinckier F, Bouret S, Daunizeau J, Le Bouc R. Computational approach to motivation deficits in neuro-psychiatric diseases. Brain. 2018 Mar 1;141(3):629-50.
- Berkowitz RL, Romero R, Tortora M, Mayden K, Duncan C, Mahoney MJ, Hobbins JC. The diagnosis of fetal hydrocephalus. American journal of obstetrics and gynecology. 2011 Nov 18;147(6):703-15.
- 15. SalehiMilani, Mahmoud (2020) Comparison of Rlin flow color doppler ultrasound of endometrium between normal pregnancies and ectopic pregnancies in early phase of pregnancy. Post-Doctoral thesis, Faculty of Medicine, Kerman University of Medical Sciences, Kerman, Iran.
- Larsen JV, Solomon MH. Pregnancy in a uterine scar sacculus-an unusual cause of postabortalhaemorrhage. A case report. S Afr Med J 1978;53(4):142–143. PMID: 653492
- Condous G, Okaro E, Khalid A, Lu C, Van Huffel S, Timmerman D, et al. The accuracy of transvaginal ultrasonography for the diagnosis of ectopic pregnancy prior to surgery. Hum Reprod 2005;20:1404-9
- SaulatSarfaraz, Khadija Arif, Abdullah Hussain, Shoaiblftikhar, Muhammad Ikram, AmnaJaved. Value of Transvaginal Sonography in Antenatal Management of Ectopic Pregnancy. Proceedings S.Z.M.C [Internet]. 2022Jul.23 [cited 2022Aug.27];36(3):30-5.
- Jurkovic D, Bourne TH, Jauniaux E, Campbell S, Collins WP. Transvaginal color Doppler study of blood flow in ectopic pregnancies. FertilSteril 1992 Jan;57(1):68-73.
- Wang et al.: Role of endometrial blood flow assessment with color Doppler energy in predicting pregnancy outcome of IVF-ET cycles. Reproductive Biology and Endocrinology 2010 8:122
- Guzel Al, Erkilinc S, Ozer I, Tokmak A, Kurt Sahin A, Ugur M. Are Uterine and Ovarian Artery Doppler Velocimetry Values Good Pregnancy Predictors in Clomiphene Citrate Cycles? Int J FertilSteril. 2015;9. doi:10.22074/ijfs.2015.4207.
- 0.Kim A, Han JE, Yoon TK, Lyu SW, Seok HH, Won HJ. Relationship between endometrial and subendometrial blood flow measured by threedimensional power Doppler ultrasound and pregnancy after intrauterine insemination. FertilSteril. 2010;94:747–52.
- Kurjak A, Crvenkovic G, Salihagic A, Zalud I, Miljan M. The assessment of normal early pregnancy by transvaginal color Doppler ultrasonography. J Clin Ultrasound. 1993 Jan;21(1):3-8.
- Adibi A, Khadem M, Mardanian F, Hovsepian S. Uterine and arcuate arteries blood flow for predicting of ongoing pregnancy in in vitro fertilization. J Res Med Sci. 2015; 20:879
- Ivanovski M, Damcevski N, Radevska B, Doicev G. Assessment of uterine artery and arcuate artery blood flow by transvaginal color Doppler ultrasound on the day of human chorionic gonadotropin administration as predictors of pregnancy in an in vitro fertilization program. AkushGinekol (Sofiia). 2012;51:55–60.