Uterine and ovarian blood flow in infertile and fertile women :A doppler study.

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مقدمة:
إثنتان و ستون إمرأة تم أختيارها لهذه الدراسة ، واحدة و ثلاثون منهن عقيمات تتراوح أعمارهن بين (١٦ – ٣٩) سنة ، و واحدة و ثلاثون منهن نساء غير عقيمات(أُعتُبرن مجموعة الضبط) . كلتا المجموعتين أُخضعتا لقياس متغيرات جريان الدم للرحم و المبيض بإستعمال جهاز الدوبلر عبر المهبلي . الفحص أُجري خلال الفترة بين اليوم الثاني و اليوم الخامس من الدورة الحيضية للنساء، و خلال نفس الفترة من الدورة الحيضية تم قياس معدل الهرمونات التناسلية الأنثوية في الدم. النتائج أظهرت وجود تأثير معنوي للمبيض المُتعدد الحويصلات على جريان الدم المبيضي و لكن ليس له تأثير معنوي على جريان الدم في عضلات الرحم . و بشكل عام وَجدت الدراسة أن جريان الدم المبيضي عند النساء العقيمات أكثر . كذلك وجدت الدراسة إن جريان الدم في بطانة الرحم أقل عند النساء العقيمات من النساء الغير عقيمات. لم تُثبت الدراسة وجود علاقة بين العمر أو الوزن و بين جريان الدم في الرحم و المبيض.

Abstract

Sixty two women have been recruited in the study , thirty one of them are infertile women whose ages range from 16-39 years , and thirty one are fertile women (regarded as control group) ,their age range from 16-39 years.Both groups are subjected to transvaginal Doppler ultrasound for measurement of blood flow indices : Peak systolic velocity PSV (V1) , Minimal diastolic velocity MDV (V2) and Resistive index (RI) of both ovaries and uterine myometrium and endometrium . This examination is done during the period which extends between day 2-5 of menstrual cycle . Measurement of serum concentration of follicular stimulating hormone FSH , lutenizing hormone LH,estrogen and progesterone is done in the same day of the cycle .

The study reveals that there is a significant effect of polycystic ovarian syndrome on ovarian blood flow but not on uterine myometrial blood flow and in general the results show that ovarian blood flow indices V1 and V2 are significantly higher in infertile patient especially those with polycystic ovarian syndrome than in normal fertile women , but no significant effect was there on RI of ovarian blood flow .The results have shown that endometrial blood flow is significantly lower in infertile women with polycystic ovary than in infertile women with non polycystic ovary.

Introduction:

Infertility affects about 14% of couples and is a medical concern for 2.7 million women of reproductive age in U.S.(1) . Although there has been no change in the prevalence of fertility problems more couples seek help than did previously. The causes of fertility problems include disorder of ovulation , sperm and fallopian tubes , although no identifiable cause is found in one third of couples trying for baby . In 39% of couples a problem will be found in both partners .Fertility treatment may be medical , surgical or involve assisted conception where by the egg and sperm are brought into close proximity to facilitate fertilization. Approximately 50% of couples will conceive

after receiving advice and simple treatment , but the reminder require more complex assisted conception technique , and 4% of couples will remain childless . The chance of conception over the first 6 months of unprotected intercourse is approximately 60% . At the end of first year 85% of couples will have conceived. (2). Regulation of ovarian and uterine blood flow is an important aspect of reproductive physiology . Studying the haemodynamic changes in the uterine and ovarian vessels can be of help in diagnosis of some cases of infertility . Deficient blood flow may be a factor in unexplained infertility (3). Transvaginal color Doppler offers a closer look at blood flow within the reproductive organs(4).

Blood Supply of the ovary: Arterial supply to the ovary is from the ovarian artery which arises from aorta. The ovarian vein drain into inferior vena cava on right side and left renal vein on the left side . Lymph vessels follow ovarian artery and drain into para aortic lymph nodes . Vessels and nerves enter the hilus of the ovary via mesovarium .

Blood Supply of the uterus: The arterial supply of the uterus is from the uterine artery which is a branch of internal iliac artery (5) .

Infertility: It is defined as failure to conceive within one year of unprotected regular sexual intercourse (2). It is called primary when it occurs without any previous pregnancy ,and called secondary when it follows a previous conception (3). Conception requires juxtaposition of male and female gametes at optimal stage of maturation followed by transportation of coceptus to the uterine cavity where the endometrium support its continuous development and implantation.

Relationship between utero-ovarian blood flow, female sex hormones and infertility: It has been suggested that the availability of an adequate vascular supply to provide an endocrine and paracrine signals may play a key role in the regulation of follicular growth (6) . Deficient ovarian and uterine blood flow may be a factor in unexplained infertility. Undetectable basal stromal blood flow in at least one ovary is related to low ovarian reserve in infertile women . It seems that undetectable basal stromal blood flow is not solely a technical issue but rather linked to the pathophysiology of ovarian aging (7) .Mean ovarian stromal peak systolic blood flow velocity was significantly correlated with follicular response and may be a new indicator for predicting ovarian responsiveness in assisted fertility programs. Peak systolic blood flow velocity is significantly lower in poor response group (8) . The age of female is positively correlated with serum FSH concentration. Also antral follicular count is positively correlated with total ovarian blood flow. Patient with tubal surgery have reduced ovarian stromal Doppler indices (9) .Female with tubal ligation or hysterectomy tend to go through menopause several years earlier than the average , likely due to decreased blood flow to the ovaries (10) . Increased ovarian stromal blood flow has been considered to be a new parameter to assist in ultrasonic diagnosis of polycystic ovarian syndrome . In polycystic ovaries the total antral follicular count is positively correlated with serum LH concentration (11)

Materials and Method:

Thirty one infertile volunteers women were selected from infertility center in Al-Zahraa and Al-Sadder teaching hospitals and from private gynecologist clinics during the period between January and April 2008 . The age of these women ranges from 16-39 year , their BMI range from 20-29 kg/m² , complaining primary or secondary infertility . The duration of infertility ranges from 1-20 years .

Also thirty one fertile volunteers women are subjected to the same investigations .The age range of fertile women is 16-39 years. In day 2-5 of the menstrual cycle of the women transvaginal Doppler ultrasound is done ; detection of ovarian stromal blood

flow and uterine endometrial and myometrial stromal blood flow . The parameters of blood flow measured include : peak systolic velocity (PSV) (V1) , minimal diastolic velocity (MDV) (V2) and resistive index (RI). Resistive index is measured according to the following equation :

RI=(PSV(cm/sec)_ MDV(cm/sec))/PSV(cm/sec) (12).

Also during the same day of the cycle measurement of serum concentration of FSH, LH, estrogen and progesterone .

Results:

Fig.1.Comparison of V1 of utero ovarian blood flow between infertile and fertile women: There is significant increment in V1 of right ovary and left ovary in infertile group, while V1 of myometrium and endometrium not significantly differ in the two groups ,also there is no significant difference in V1 between right and left ovaries, as in figure 1

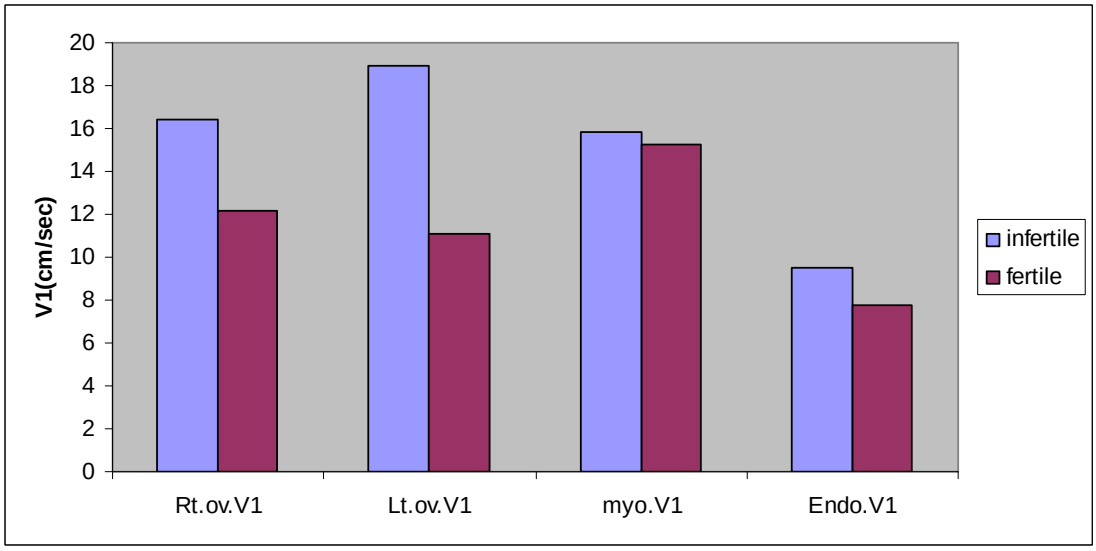

Fig.1

Comparison of V2 of utero ovarian blood flow between infertile and fertile women : There is significant increment in V2 of right ovary and left ovary in infertile women ,while V2 of myometrium and endometrium not significantly differ in the two groups ,also there is no significant differences in V2 between right and left ovaries , as in figure 2

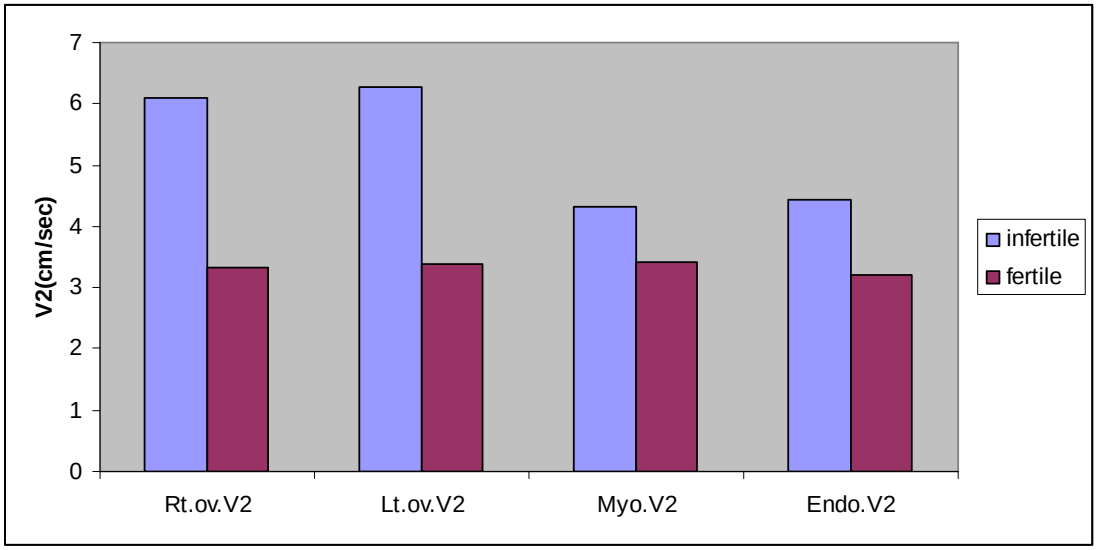

Fig.2

Comparison of RI of utero ovarian blood flow between infertile and fertile women : There is no significant difference in RI of right ovary , left ovary , myometrium and endometrium between infertile and fertile women , as in figure 3.

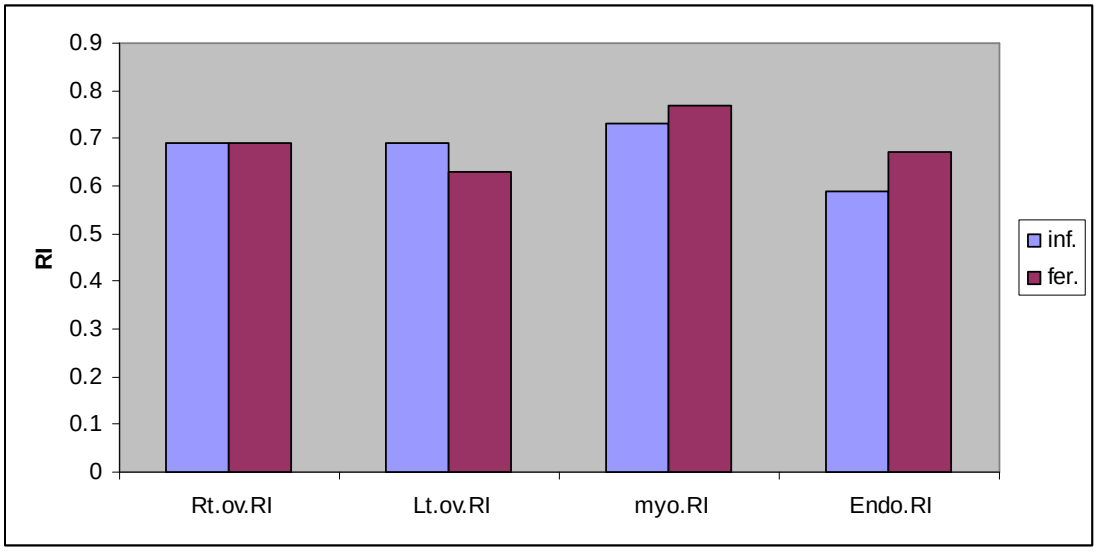

Fig.3.

Comparison of V1 of utero ovarian blood flow between infertile women with polycystic ovary and infertile with non polycystic ovary:

There is significant increment in V1 of right and left ovaries of infertile women with polycystic ovary . Also there is significant increment in ovarian V1 in infertile women with pos in comparison to fertile women with pos.V1 of myometrium is not significantly differs in infertile with polycystic ovary and in infertile with non polycystic ovary , while V1 of endometrium is significantly lower in infertile women with polycystic ovary , as in figure 4.

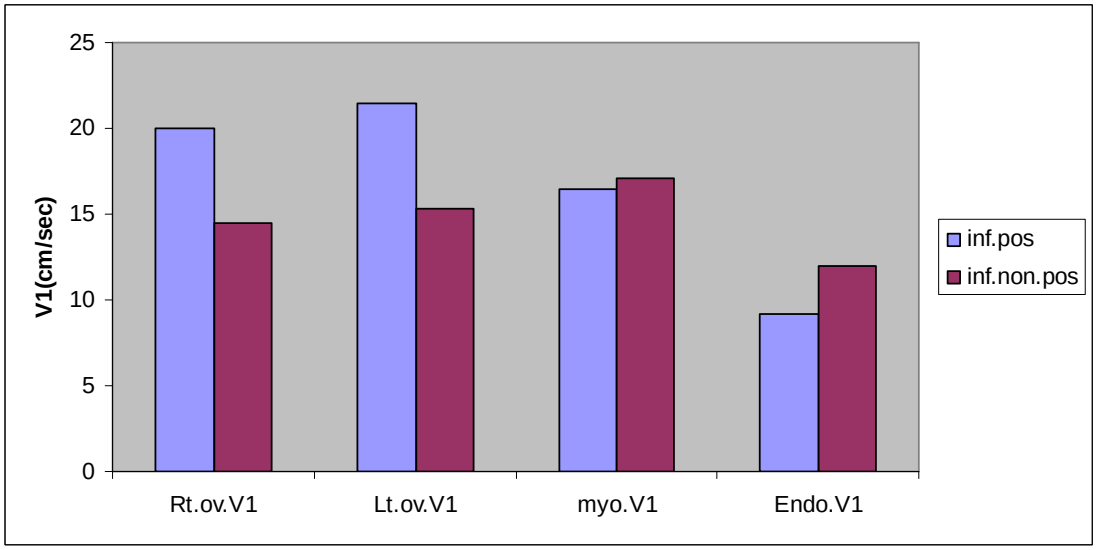

Fig.4

Comparison of V2 of utero ovarian blood flow between infertile with polycystic ovary and infertile with non polycystic ovary:

There is significant increment in V2 of right and left ovary in infertile women with polycystic ovary. Also there is significant increment in ovarian V2 in infertile women with pos in comparison to fertile women with pos.V2 of myometrium not significantly differs between the two groups , while V2 of the endometrium is significantly lower in infertile women with polycystic ovary , as in figure 5.

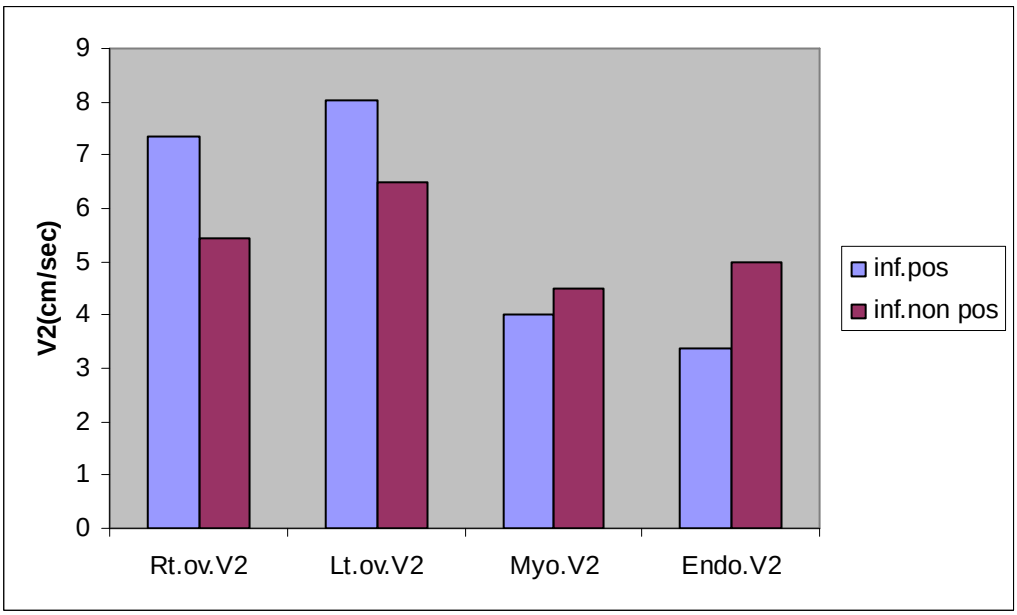

Fig.5

Hormonal investigation:

Comparison of FSH, LH , estrogen and progesterone concentration between infertile and fertile women , as in table 1.

Fertility state	LH Mean ± SD mlu/ml	FSH Mean ± SD mlu/ml	Estrogen Mean ± SD pg/ml	Progesterone Mean ± SD Ng/ml
Infertile n=31	6.75 ± 2.16	6.91 ± 1.61	54.52 ± 18.00	1.47 ± 0.77
Fertile n=31	4.45 ± 2.13	7.12 ± 2.46	61.83 ± 21.48	1.04 ± 0.23

Discussion:

Statistical analysis of the results of utero ovarian blood flow in both infertile and fertile women shows that Doppler indices V1 and V2 are significantly higher in infertile than fertile women , V2 are significantly higher in infertile than fertile women , this finding agrees with the results of the research of Ng et al.,(2005) who found that utero ovarian flow indices are higher in infertile women , this could be due to the effect of high LH . The results have not revealed significant difference in V1 and V2 between right and left ovaries .The results have not revealed significant differences in RI between infertile and fertile women while Battaglia (1995) found that RI of ovarian blood flow is higher in women with primary infertility .The results have not revealed significant differences in myometrial and endometrial blood flow indices this probably due to that the study is done during menstrual phase of the cycle and during this period the estrogen hormone that affect the uterus is in its lower level in both infertile and fertile women so that no significant changes in the endometrium or myometrium has been occur. Statistical analysis of the results of utero ovarian blood flow indices in polycystic and non polycystic infertile and fertile women reveal that ovarian blood flow indices V1and V2 are both significantly higher in infertile women with polycystic ovaries than in infertile with non polycystic ovaries. This finding goes with the results of other researchers who found that significantly greater flow indices in infertile patient with polycystic ovaries than in infertile women with normal ovaries (14) .Also results reveals that there is no significant difference in ovarian RI between infertile women with polycystic ovary and infertile with non polycystic ovary , while other researches found that RI of ovarian blood flow of infertile women with polycystic ovaries is significantly lower than in women with non polycystic ovaries (15) . Also the results of myometrial flow indices did not reveal significant difference between infertile with polycystic ovaries and infertile with non polycystic ovaries . This goes with the result of the research of Isaksson (2000) who found that infertile women with polycystic ovaries have no significant difference in uterine artery haemodynamics comparing to women with non polycystic ovaries .The results show that V1 and V2 of endometrial blood flow are significantly lower in infertile patient with polycystic ovary than in infertile women with non polycystic ovaries .This may be due to effect of high LH that

cause negative feed back effect on estrogen secretion that leads to inhibition of endometrial growth . Some researches found no significant difference in blood flow indices between fertile women and infertile women with polycystic ovaries when Doppler ultrasound done during day 8-16 of the menstrual cycle , where 35% of patient with polycystic ovaries has dominant follicles which would reduce ovarian stromal blood flow in comparison to polycystic ovarian stromal blood flow , while the results of this study revealed significant increment in ovarian blood flow in infertile women with polycystic ovaries in comparison to fertile women with polycystic ovaries. (17). Kupsic and Kurjak (2002)found that polycystic ovarian syndrome not bear an inherent disturbance in blood flow of uterine and ovarian arteries , which would explain the response of polycystic ovaries to stimulation with gonadotropins . In addition ; Ng et al.,(11) found that increased ovarian stromal blood flow in women with polycystic ovary may lead to greater delivery of gonadotropin to the granulosa cells of the developing follicle , therefore we should incorporate assessment of ovarian stromal blood flow in the management of polycystic ovarian patients undergoing ovulation induction or ovarian stimulation in order to reduce the associated risk of ovarian hyperstimulation syndrome. The results show that LH concentration in infertile women is higher than its concentration in fertile women , but this increment not reach level of significance ,the elevation of LH in infertile group could be due to the cases of polycystic ovarian syndrome where LH secretion is increased .Also the study reveals that FSH concentration is lower in infertile than in fertile women but not reach level of significance . Younis et al.,(2007) found that patient with low FSH have no significant difference in ovarian blood flow indices , this proves the previous research works which found that found that no correlation between serum concentration of FSH and LH and flow indices of ovarian stromal vessels , while Zaidi et al.,(1998)prove that the changes in peak systolic velocity of ovarian vessels correlated significantly with the changes in serum FSH , LH and progesterone .In this study estrogen level is lower in infertile than fertile women but does not reach a significant level , this goes with the results of the research of Kupsic and Kurjak (2002) who found that blood flow in the uterus and ovary is related inversely to estrogen level .Results reveal that LH is significantly higher in infertile women with polycystic ovaries than in infertile with non polycystic ovaries , this goes with the results of Ng et al., (2005) who found that there is characteristic elevation in LH in infertile women with polycystic ovarian syndrome . Elevation of LH concentration may be the cause of increased ovarian stromal blood flow in polycystic ovarian syndrome through the action of prostaglandins (16) . Prostaglandin E2 and I 2 are potent vasodilators which markedly increase local blood flow .Linear increase in capillary cross sectional area of theca interna was observed after LH surge in spontaneous cycle , and the increments in the capillary area was attributed to the vasodilatation rather than increase numbers of vessels (10). Also the results show that FSH secretion is significantly lower in infertile women with polycystic ovaries than in infertile with non polycystic ovaries , this goes with the results of the research of Ng et al,.(2005) who found that FSH is lower in infertile women with polycystic ovarian syndrome .the results did not reveals significant effect of age on utero ovarian blood flow , while other studies proved that ovarian stromal blood flow was significantly reduced in women older than 40 years (6). Ng et al (2004) has found that the decline in fertility with aging is likely due to continuous reduction in the number of primordial follicles . The difference between this study and other studies could be due to that women recruited in this study are not older than 40 years. Also the results did not show any significant effect of BMI on utero ovarian blood flow , this goes with some studies that found no significant difference of utero ovarian blood flow

between normal and overweight patients (8) , while other researches found that ovarian stromal blood flow indices is positively correlated with the BMI (Ng et al., 2004) and found that ovarian stromal blood flow is higher in normal than overweight infertile patients (18) .

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