Role of Office Hysteroscopy in Evaluation of Cases with Unexplained Recurrent Embryonic Pregnancy Loss

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Abstract: Objective: to evaluate the value of Role of office hysteroscopy in evaluation of cases with unexplained recurrent embryonic pregnancy loss **Design:** prospective case control study **Setting:** university hospital. **Patients:** one hundred and Fifty patients with early recurrent pregnancy loss recruited from the attendees of Gynecology Outpatient Clinic and office hysteroscopy clinic. **Interventions:** All women were subjected to hysterosalpingography (HSG) and hysteroscopy with a follow up for the pregnancy outcome of who have uterine abnormalities. **Results:** Hysteroscopy revealed 65 uterine abnormalities out of 150 patients in the form of 51 acquired uterine anomalies which include (15 fibroid, 6 polyp, 13 adhesion 10 infection, 7 mixed) and 14 congenital anomalies (8 subseptate, 4 unicornate, 2 bicornate).While HSG revealed 51uterine anomalies out of 150 patients in the form of 32 acquired uterine anomalies (11 Adhesions and 21 filling defect) and 19 congenital anomalies (7 subseptate, 8 bicornate, 4 unicornate). **Conclusion:** Office Hysteroscopy is an easier, safer and better tolerated for patients with recurrent pregnancy loss, is an excellent diagnostic tool can be used as preliminary test for screening of uterine anomalies and prepare them for operative hysteroscopy, must be done for every patient with unexplained early recurrent pregnancy loss.

[AmeerAbdallah. **Role of Office Hysteroscopy in Evaluation of Cases with Unexplained Recurrent Embryonic Pregnancy Loss.** *J Am Sci* 2013; 9(12):221-228]. (ISSN: 1545-1003). http://www.jofamericanscience.org. 27

Key words*:* embryonic loss, TVUS, HSG& hysteroscopy

1. Introduction

Recurrent pregnancy loss (RPL) is a problem that often places couples under a great deal of emotional distress and poses physicians with a formidable challenge. Although spontaneous abortion occurs in approximately 15% of clinically diagnosed pregnancies of reproductive aged women, RPL occurs in approximately 1 to 2% of this same population (Kutteh, 2002). Anatomic uterine defects have been identified as a cause of RPL, can be grouped into congenital (disorders of the Müllerian tract) or acquired anomalies consisting of adhesions, cervical incompetence, polyps, and uterine leiomyomas. Although some anomalies may have little to no impact on pregnancy outcome, others may cause recurrent pregnancy loss, intrauterine growth retardation (IUGR), preterm labor, malpresentation, and dystocia (Salim *et al.,* 2003). Hysterosalpingography is still a useful screening test for the evaluation of the uterine cavity. If a hysterogram demonstrates intrauterine abnormalities, hysteroscopy should be considered to make a definite diagnosis and treatment. Both procedures should be complementary to each other (Preutthipanand Linasmita, 2003).Women with uterine anomalies have poorer reproductive outcomes and lower pregnancy rates with all conceptions whether spontaneous or induced with assisted reproductive techniques ART compared with women with normal uteri (Lin, 2004). Congenital anomalies and acquired diseases of the uterus may negatively impact on the complex processes of embryo implantation. Hysteroscopic surgery to correct uterine septa, intrauterine synechiae, and myomas that distort the uterine cavity may benefit women with infertility or recurrent pregnancy loss. The effect of endometrial polyps on fertility is uncertain, but their removal, once identified, is justifiable. Complex congenital anomalies such as unicornuate uterus and uterus didelphys may negatively affect fertility and pregnancy outcome, and surgical treatment may benefit select patients (Taylor and Gomel, 2008).

2. Methodology

This prospective case control study was conducted at the Department of Obstetrics & Gynecology, EL- Minia University Hospital; it included **150** patients with early recurrent pregnancy loss recruited from the attendees of Gynecology Outpatient Clinic and office hysteroscopy clinic. It was carried out from the 1st of October 2007 to the 1st of October 2008 on those complaining of early recurrent pregnancy loss, the study was explained to all patients & all patients consented to participate in the study. Inclusion criteria include Patients in the reproductive age complaining of recurrent embryonic early pregnancy loss (two or more) including patient with 1st trimester abortion with documented embryonic pregnancy loss, Negative TORCH IgM investigations & negative for antiphospholipid syndrome. Exclusion criteria include major maternal illness, Contraindication of office hysteroscopy procedure include Known or suspected pregnancy,

Coagulation disorders or on oral anticoagulant therapy, Hypothyroidism or hyperthyroidism, Liver diseases, evidence of PID& Any cervical abnormality. All patients will be counseled about the technique, safety, possible complications and outcome of the procedure. Oral consent was been obtained for all cases. All patients will be subjected thorough history taking, General examination, Gynecological examination: Including vaginal examination, bimanual examination, speculum examination and per-rectal examination for assessment of size and direction of the uterus and examination of the adnexa for any abnormalities and any cervical pathology. Routine investigations: were done for all patients including pregnancy test (if there is a history of amenorrhea), Complete urine analysis, Complete blood picture, Random blood sugar assay, Renal and liver function tests, Thyroid function test, Antiphospholipid & TORCH IgM. Transvaginal Ultrasonography (TVUS): Transvaginal ultrasonography was done using 7.5 Mhz endovaginal probe fitted to Toshiba Model (SSA-340) ultrasonography machine. All scans were done post menstrual. The patients were instructed to evacuate the bladder before the procedure. The probe was covered with a thin layer of gel and loaded in a disposable glove and inserted slowly into the vagina. The vaginal cavity, cervix, bladder and then the uterus were identified; a slow movement of the probe from side to side, and then pointing posteriorly is made. Once the uterus has been located, its position (anteverted or retroverted) and its size are noted. Retroversion of the uterus may be physiological. The uterus was evaluated initially in the sagittal plane. The uterine cavity was completely imaged from the ectocervix to the fund us of the uterus. After complete sagittal evaluation was made, the transducer was rotated ninety degrees perpendicular to the sagittal plane to evaluate the uterus through its coronal image. Again, the uterine cavity was completely assessed from the external os to the endocervical canal into the endometrial cavity till the fundus and from the cornu to the other one. Measurements was then taken. The size of the uterus was measured in the longitudinal and anteroposterior diameters. The measurements of the endometrium were taken at its thickest part in the longitudinal plane and included both endometrial layers. If an intracavitry abnormality such as a polyp or submucosalmyoma was present, it was included in the measurement. Specific observations were made to ascertain the normality of the endometrium, myometrium and endometrial-myometrial interface. Similar observations were made for the cervix and endocervical canal. Scanning for both adnexa was done to detect any pathology that could have been missed during clinical examination. The endometrium and uterine cavity were considered normal if TVUS showed a hyperechoic line in the middle of the uterus with a homogenous endometrial lining and distinct margins to the myometrium (Laing *et al.,* 2001).All other findings such as deformities of the endometrial lining, absence of the central hyperechoic line, and the appearance of any structure with or without well-defined margins or variable echogenicity, were considered abnormal. An endometrial polyp was defined as a smooth marginated, echogenic mass of variable size and shape with a fairly homogenous texture; it emerges from the endometrium and does not disrupt the myometrial-endometrial interface. A submucosal myoma was defined as a solid round structure of mixed echogenicity originating from the myometrium disrupting the inner circular muscle layer and protruding to the uterine cavity (Blumenfeld and Turner, 1996). Hysterosalpingography (HSG): was performed in within one or two days in the radiology department using water soluble contrast medium as urogrffin under fluoroscopic monitoring by another examiner not aware by the results of office hysteroscopy.

Office Hysteroscopy:Instrument:

Office Hysteroscopy (Verscope of Johnson and Johnson) angle of vision 0 and diameter 2.7. The telescope was attached to the light source by a fiber optic cold light cable of high intensity and to the head of endo-camera, while the outer sheath is connected to the manual infusion pump that allowed distension of the uterus with fluid medium Glycine. The procedure was monitored by Autoclavable 3CCD camera head (Olympus OTV-SP1, digital processor) attached to the eyepiece and the image was displayed on a color monitor recorded and saved directly on laptop computer. Timing of Procedure: Although it is not always possible to schedule an office procedure at the best time in the menstrual cycle, ideally the best time to perform hysteroscopic evaluation is just after the conclusion of the menstrual cycle during the early proliferative phase (Serden, 2000). In our study the procedure was done just post menstrual. Priming the cevix: If the patient was scheduled for the procedure, they will give 400 mcgm Misopristol (Misotac®) vaginally 4 hours prior to procedure. Distention medium: Distention of the cavity with Glycine, the pressure was adjusted by using graded pressure bag. Analgesia: Dilatation of cervix and isthmus to insert the hysteroscope is of no need, as all this was abolished by using office hysteroscopy. In order to maintain patient comfort during the procedure, the patient was instructed to take a nonsteroidal analgesic (1 Ketolak ampoule) approximately 1 hour before the procedure and was requested not to eat a large meal preoperatively. Technique: The patient was asked to evacuate bladder voluntarily, then patient was put in the lithotomy position with the buttocks projecting

slightly beyond the edge of the table to facilitate the tilting of the hysteroscope in cases of acute uterine anteversion. The area around the vulva, vagina and the cervix were carefully cleansed using gauze soaked in a non foaming antiseptic solution, the hysteroscope was introduced through the external cervical os and then was introduced through the cervical canal under vision or with the application of the camera before the introduction. The idea was to follow up the fluid flow to delineate the direction of the cervical canal as introducing the hysteroscope blindly can lead to the production of a false passage, uterine perforation or scrapping of the endometrial surface that result in intracavitary bleeding that can obscure the view. After the hysteroscope had been introduced in the uterine cavity, a panoramic overview of the uterine cavity was the first step in the procedure to exclude uterine malformations or deformed cavity. Then both tubal ostia were visualized and then the anterior, posterior and both lateral walls were examined. If there was an intrauterine pathology detected, the shape, the size and the site of it was estimated. As regard the shape of the lesion, it was possible to denote if the pathological structure is a myoma or polyp. This was done by observing the surface, if it was smooth or irregular and if there was surface necrotic tissues, bleeding surface or dilated vessels on the surface. In Submucous fibroid appears as a hemispherical protrusion bulging into the cavity, smooth, regular, firm and covered with atrophic endometrium with its surface traversed by blood vessels (Cooper and Brady, 1999). As regard the size of the lesion, it was estimated by comparing the mass to the whole uterine cavity. The site of the lesion was easily denoted by moving the optic around the side wall of the mass to detect the point of origin and the pedicle of pedunculated masses. Follow up of the patient after the procedure.

3. Results:

Seventy percent of the study groups were regularly menstruating while 30 % showed irregularities in the form of oligomenorrhea 6%, hypomenorrhea 6.6%, menorhheagia 12% and menometorrhagia 9.3. Regarding the parity, the majority of cases were nullipara or with low fertility 96.6% also all of cases showed at least two abortions. The primary abortion percentage was 4.7, the secondary was 32.1 and the tertiary abortion was of 13.2%. Hysterosalpingography was compared to hysteroscopy which was taken as standard technique and the result was statistically analyzed. Hysteroscopy revealed 65 uterine abnormalities out of 150 patients in the form of 51 acquired uterine anomalies which include (15 fibroid, 6 polyp, 13 adhesion 10 infection, 7 mixed) and 14 congenital anomalies (8 subseptate, 4 unicornate, 2 bicornate). While HSG revealed 51uterine anomalies out of 150 patients in the form of 32 acquired uterine anomalies (11 Adhesions and 21 filling defect) and 19 congenital anomalies (7 subseptate, 8 bicornate, 4 unicornate). The pregnancy outcomes were compared between acquired group before and after ttt and the result was a high significant decrease in percentage of 1st trimester abortion and also in the preterm labor after treatment, while there was no significant difference in full term labor and living child percentage. Also pregnancy outcomes were compared between congenital group before and after treatment and the result was a high significant decrease in percentage of 1st trimester abortion and also in the full term labor after treatment, while there is no significant difference in preterm labor and living child percentage. Comparison between hysterscopic finding in recurrent abortion with 2 versus 3 or more consecutive abortion in which there is no significant difference both in acquired and congenital anomalies. Hysteroscopic findings of the study group presented as 56.7% normal finding, 43.3 % was abnormal. Details of hysteroscopic finding of the study group: for acquired anomalies: submucousmyoma 10 %, polyps 4 %, adhesion 8.7 %, infection 6.7 % and 4.6 % for mixed acquired anomalies. For congenital anomalies: subeptate uterus 5.3 %, unicornate 2.6, and 1.3 for bicornate.

Comparison between HSG and Hysteroscopy Findings In The Study Group

Table (1): Shows comparison between HSG and Hysteroscopy finding in the study grouping which there is no significance difference between HSG and Hysteroscopy both in normal and abnormal findings.

Finding	HSG		Hysteroscopy		*P* value
	N	%	N	%	
Normal	99	66	85	56.6	**.12**
Abnormal	51	34	65	43.4	**0.94**
Unicornate	4	2.66%	4	2.66%	
Bicornate	8	5.3%	2	1.3%	
Subseptate	7	4.66	8	5.3%	
Intrauterine adhesion	11	7.3%	13	8.66%	
Filling defect(polyps and fibroids)	**21**	**14%**	**25**	**16.6%**	

P-Value: Insignificant

Sensitivity and specificity of HSG compared to the hysteroscopy in cases of adhesions and polyps/submucusmyoma it was less sensitive (86.2 %, 86.6%) respectively and sensitive as hysteroscopy in cases of uterine malformation).

Details of pregnancy outcome during follow up of study group, 61.9% non pregnant, 38.1% pregnant. Out of 51 pregnant cases 21 cases succeeded to take baby home (37.2%, 23.5% PTL, 39.2% full term pregnancy.

Table (2): Comparison between of the pregnancy outcome in patients with positive hysteroscopic finding.

Pregnancy outcome	Acquired Group		Congenital group		***p***
	No	%	No	%	
First trimester abortion	16	33.3	3	25	**0.84**
P T L	10	20.8	2	16.7	**0.94**
FTL	16	33.3	4	33.4	**0.73**
Living child	**16**	**33.3**	**5**	**41.6**	**0.84**

***P*-value:** Insignificant

Table (3): There is a high significant difference regarding 1st trimester abortion and FTL.

Pregnancy outcome	Congenital Group N= 12				***P***
	Before treatment		After treatment		
	No	%	No	%	
First trimester abortion	12	100	3	25	**<0.0001***
P T L	2	16.7	2	16.7	**0.61**
FTL	0	0	4	33.4	**0.018***
Living child	**1**	**8.3**	**5**	**41.6**	**0.31**

***P* value:** Significant

Table (4): Comparison between pregnancy outcomes in acquired group before and after treatment.

Pregnancy outcome	**Acquired N= 48**				***P***
	Before treatment		After treatment		
	No	%	No	%	
First trimester abortion	48	100	16	33.3	**<0.0001***
P T L	22	45.8	10	20.8	**0.017**
FTL	8	16.7	16	33.3	**0.099**
Living child	**13**	**27**	**16**	**33.3**	**0.66**

***P* value:** Significant

Comparison between pregnancy outcomes in acquired group before and after tratment in which there is a high significant decrease in percentage of 1st trimester abortion and also in the preterm labor while there is no significant difference in full term labor and living child percentage.

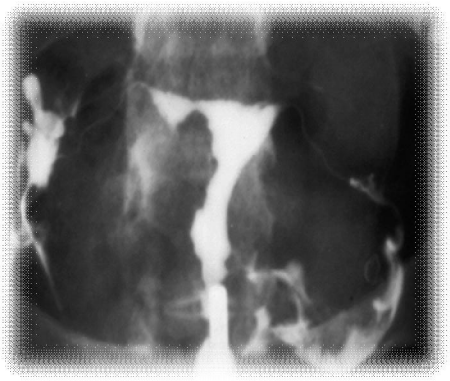

Figure 1:HSG showing filling defect due to synechiae

Figure 2:HSG showing multiple filling defect

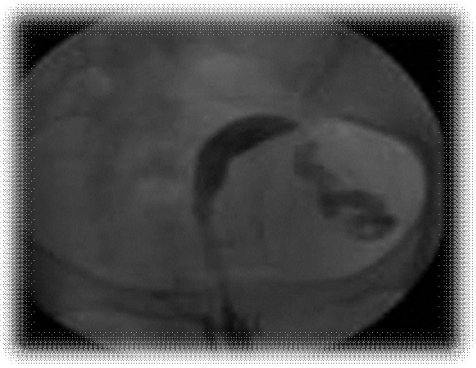

Figure 3:HSG showing unicornate uterus

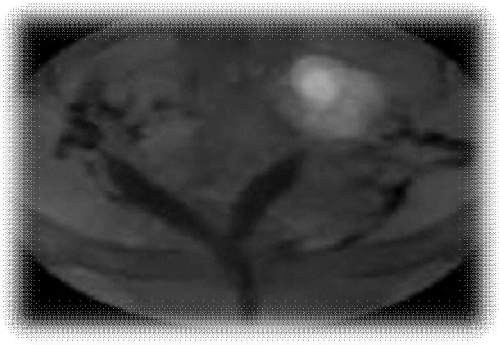

Figure 4:HSG showing bicornate uterus

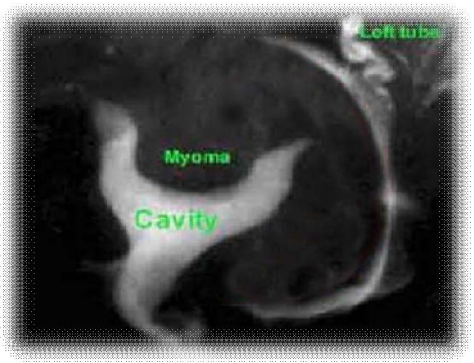

Figure 5: HSG showing submucus fibroid

Figure 6: Hysteroscopic appearance of normal endometrium

Figure 7: Hysteroscopic appearance of Asharman syndrome

Figure 8: Hysteroscopic resection of the fibroid bands

Figure 9: Hysteroscopic appearance of bicornuate uterus

Figure 10: Hysteroscopic appearance of unicornuate uterus

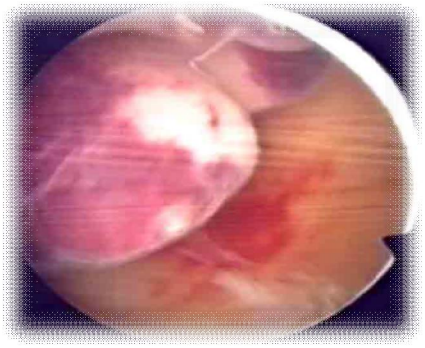

Figure 11: Hysteroscopic appearance of endometrial polyp

4. Discussion

In the present study the percentage of uterine both acquired and congenital uterine anomalies by using hysteroscope among early recurrent miscarriages is 43.3.This percentage is in agreement with Guimaraes Filho *et al.* (2006b), who stated that a sample of 60 patients with recurrent miscarriages was analyzed and it could be observed that (58.3%) had normal examinations, (38.3%) had altered examinations, and (3.3%) of cases, there was failure of the method. However, the percentage is far away from Salim *et al.*(2003) according to medical literature the prevalence of uterine anomalies among patients with RPL varies from 15 to 27%.The percentage of the congenital anomalies of the study group was 9.3 and this is in agreement with Propst and Hill 3rd (2000) who stated that In women with three or more consecutive spontaneous abortions who underwent hysterosalpingography or hysteroscopic examination of their uteri, Mullerian anomalies have been found in 8 to 10%. However Byrne *et al.* (2000) stated that the true incidence of congenital uterine anomalies in the general population and among women with RPL is not known accurately. Although incidences of 0.16 to 10% have been reported, the overall data suggest an incidence of 1% in the general population and 3% in women with RPL and poor reproductive outcomes. By using the HSG in detection of uterine anomalies among the study group the percentage was decreased to 34%, so the hysteroscope is superior to HSG but there was no significant diagnostic difference. This is in agreement with Preutthipanand Linasmita (2003) who stated that Hysterosalpingography is still a useful screening test for the evaluation of the uterine cavity. If a hysterogram demonstrates intrauterine abnormalities, hysteroscopy should be considered to make a definite diagnosis and treatment. Both procedures should be complementary to each other. But in disagreement with Razie*et al.*(1994) who examined the prevalence of structural uterine pathology by hysterosalpingogram (HSG) and hysteroscopy in106 women with RM Their findings included: HSG, abnormal findings 56.3%, uterine septum 17.9% and filling defects and/or uterine wall irregularity 38.7% ; hysteroscopy abnormal findings 46.3, uterine septum 21.7%, intrauterine adhesions 23.6% and endometrial polyp 1%. Comparing the sensitivity and specificity of HSG to the hysteroscope, HSG was less sensitive (86.6%&86.2%) regarding adhesions and polyps/submucusmyoma respectively. but less specific regarding the uterine malformation (94.4). This is in agreement with Guimarães*et al.*(2006) (a) who states that comparing the HSG to the hysteroscope,general sensitivity of the HSG was 75.0% and specificity was 97%. In this study, we compare between hysterscopic finding in recurrent abortion with 2 versus 3 or more consecutive abortion and the result is no significant difference both in acquired and congenital anomalieswhich was 92.6 versus 75.8and 7.4 versus 24.2 respectively, this is in agreement with Weiss *et al.*(2005) who stated that hysteroscopy was performed on 165 women referred for recurrent pregnancy loss: 67 after two and 98 after three or more consecutive miscarriages. The rate of uterine anomalies did not differ significantly and was 32 versus 28% respectively. About the percentage of the of each subcategory of the uterine anomalies in this study, belonging to acquired anomalies from the most common to the less common was: for submucousmyoma (10%), adhesion was 8.7%,infection was 6.7%, polyps was 4.0% and eventually 4.6% for mixed acquired anomalies. Belonging to congenital anomalies (9.3%) from the most common to the less common septate uterus was 5.3%, unicornate was 2.6%, and 1.3% for bicornate. This subcategory percentage can be compared with Dendrinos *et al.* (2008) who stated that from forty eight women with recurrent pregnancy loss, twenty-five women (52%) had a normal hysteroscopy. The remaining (48%) presented SUAs: (19%) had intrauterine adhesions, (8%) had submucousmyomas and (4%) had polyps, (17%) had congenital structural uterine anomalies (10.4%) of septate uterus and

(6.3%) of bicornuate uterus). Also the percentage can be compared with Ventolini *et al.*(2004) in his study of twenty three women with RPL, (60.9%) had a normal hysteroscopy (with biopsies). (39.1 %) had SUD: (21.8%) had intrauterine adhesions, (8.7%) had a septated uterus, (4.3%) had submucosal myoma, and (4.3%) had multiple factors.These differences in percentage of subcategories of uterine anomalies between this study and others may be due to the differences in the number of RPL cases in studygroups. In this study pregnancy outcomes were compared between acquired group before and after ttt and the result was a high significant decrease in percentage of 1st trimester abortion and also in the preterm labor after treatment, *p* value (0.0001&.017) respectively, while there was no significant difference in full term labour and living child percentage. Also pregnancy outcomes were compared between congenital group before and after treatment and the result was a high significant decrease in percentage of 1st trimester abortion and also a high significant increase in the full term labor after treatment, *P* value (0.0001& 0.018) while there is no significant difference in preterm labour and living child percentage. This is in agreement Dendrinos *et al.* (2008) who stated that from forty eight women with recurrent pregnancy loss Patients with abnormal hysteroscopy underwent appropriate therapy, when applicable. (78%) achieved a successful pregnancy, and (22%) had another miscarriage Also in agreement with Zlopasa *et al.* (2007) who stated that uterine anomalies were associated with higher rates of spontaneous abortion, preterm delivery, intrauterine growth retardation, breech presentation, and cesarean delivery ($P<0.001$). Compared with their previous pregnancies, the abortion rates were lower and delivery rates were higher in women who conceived following hysteroscopicmetroplasty ($P<0.001$). In this study pregnancy outcomes during follow up of 60 cases in acquires and congenital anomalies were compared and the result was no significant difference in the pregnancy outcome between acquired and congenital groups. In Conclusion, Hysteroscopy is an excellent diagnostic tool, high sensitive and specific in comparison with HSG which is less sensitive and less specific. The pregnancy outcomes were compared between acquired group before and after ttt and the result was a high significant decrease in percentage of 1st trimester abortion and also in the preterm labor after ttt, while there was no significant difference in full term labor and living child percentage. Also pregnancy outcomes were compared between congenital group before and after ttt and the result was a high significant decrease in percentage of 1st trimester abortion and also in the full term labor after ttt, while there is no significant difference in preterm labor and living child percentage. With increased training and experience with hysteroscopy gynecologists will find that hysteroscopy will be a simple and accurate technique for investigation of intra uterine pathology for cases of recurrent pregnancy loss cases and so appropriate ttt will be done and the pregnancy outcome for those patients will increase.

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11/8/2013