Three-Dimensional Sonohysterography Compared With Vaginoscopic Hysteroscopy for Evaluation of the Uterine Cavity in Patients with Recurrent Implantation Failure in *In Vitro* Fertilization Cycles

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Abstract: Study Objective: To estimate the degree of agreement between 3-dimensional sonohysterography (3D-SHG) and vaginoscopic hysteroscopy (VH) in detection of uterine cavity abnormalities in patients with recurrent implantation failure in vitro fertilization cycles. **Design:** Comparative observational cross-sectional study. **Setting:** Private assisted-conception unit. **Patients:** Seventy five patients with a history of at least 2 previous implantation failures despite transfer of good quality embryos in assisted-conception cycles. **Interventions:** 3D-SHG was followed by VH. The Cohen k for interrater agreement was calculated for the level of agreement between the 2 diagnostic procedures. Patients were asked to rate their degree of discomfort or pain during both procedures using a visual analog scale. Measurements and Main Results: There was a substantial degree of concordance between the visual analog scale pain scores also showed that 3D-SHG was better tolerated than VH. **Conclusion:** Our results show that there is a substantial degree of concordance between 3D-SHG and VH in diagnosing uterine cavity anomalies. We also found that 3D-SHG took significantly less time and induced less patient discomfort than didVH. We recommend that 3D-SHG should be the method of first choice for outpatient evaluation of the uterine cavity.

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Keywords: Three dimensional ultrasound, Sonohysterography, Vaginoscopic hysteroscopy, Recurrent implantation failure, in vitro fertilization.

Introduction

Although the treatment of infertility using assisted reproductive techniques has yielded improved results since its inception, implantation failure remains one of the major factors limiting IVF treatment, according to ESHRE data on ART outcomes across Europe in 2009, only 32% of fresh embryo transfer resulted in clinical pregnancies (**Ferraretti et al., 2013**).

Implantation requires a precise crosstalk between the embryo and the endometrium, and the exact mechanism remains largely unknown. Even with the introduction of preimplantation genetic screening (PGS) and replacement of chromosomally normal embryos. data from ESHRE PGD consortium 2009/2010 reported recurrent implantation failure rates 23.9% **(Moutou et al.,2014).**

Implantation is aprocess where by embryo attaches itself to the luminal surface of the endometrium and invasion into the deep layer of endometrium to become embeeded in to the deeper layer, traditionally, implantation has been considered as a process involving only the embryo and the endometrium, but recent studies show that cumulus cell competency may also contribute to the process **(Benkhalifa et al., 2012).**

Recurrent implantation Failure is a clinical entity which refers to situation when implantation has repeatedly failed to reach a stage of recognizable by transvaginal ultrasonography (**Das et al., 2012**).

Recurrent implantation failure refers to failure to achieve aclinical pregnancy after transfer of at least four good-quality embryos in aminimum of three fresh or frozen cycles in awoman under the age of 40 years **(Coughlan et al., 2013**). Hystroscopy is one of the most important investigation in cases of recurrent implantation failure **(Coughlan et al., 2013).**

It allows reliable visual assement of the uterine cavity and cervical canal **(Coughlan et al., 2013**).

Current evidences suggests that the incidence of abnormal hystroscopic findings in women with recurrent implantation faliures varies between 25 and 50% **(Makrakis and pantos, 2010)**.

The diagnostic modalities that are commonly employed to evaluate the regularity and shape of the uterine cavity include a convenentional 2-D and 3-D transvaginal scan, saline infusion sonohystrography (SIS), hystrosalpinigiogram (HSG) and hystroscopy. while the transvaginal scan is generally performed to screen for uterine pathologies, and submucous fibroids being missed, recent studies have reported poor senstivity and positive predictive value rates of transvaginalsonography in the detection of polypoid lesions (**Bingolet al., 2011**).

SIS is aminimally invasive cost effective and acceptable diagnostic modality (**Hajishaiha et al., 2011**).

This study was a prospective comparative cross sectional study study. it was performed from May 2015 to December 2016 at a private assisted conception. The study protocol had been approved by the internal ethics committee and all enrolled patients will be given a written informed consent.

Inclusion criteria:

Patients had been included in the study if they had a history of at least 3 previous IVF failures despite transfer of good quality embryos, thus fulfilling the criteria for recurrent implantation failure, and if the previous failed IVF cycles were conducted at our unit, to ensure the presence of complete data for the quality and number of the transferred embryos in the previous cycles.

Exclusion criteria:

Patients had been excluded if a uterine cavity abnormality was noted at a previous hysteroscopichysterosalpingographic, or ultrasound examination.

Sample size:

In the present study, sample size was calculated based on sensitivity of 3D sonohysterography in diagnosing IU lesions in cases with recurrent implantation failure. As previously published, the maximum reported sensitivity was 95% while the minimum was 40% **(Sherif, M. et al., 2012).** According to these assumptions, the calculated sample size was 75 cases with recurrent implantation failure. Alpha error was set on 0.05 and the power was adjusted at 80%. Calculations were done using **Flahault et al., (2005)** equation**.**

Methodology:

All patients had done a3D sonohystrography first, then hysteroscopy and finding during the two procedures had been recorded.

Timing of 3D- SHG: was done at day 3 post menstruation.

Timing of hysteroscopy: will be done at the first week post menstrual after 3D-SHG.

After performing the two procedures all findings showing the sensitivity of the two modalities of interventions was recorded for each patient separately.

3D-SHG Technique:

Patients were placed in the lithotomy position, and a lubricated Cuscoe speculum was inserted to visualize the cervix, which was cleaned using a swab moistened with povidone– iodine 10% (Betadine; Nile Pharmaceuticals & Chemical Industries, Cairo, Egypt) moistened swab. A soft embryo transfer catheter (Cook Sydney IVF Embryo Transfer Catheter; Cook Medical Europe, Ltd., Limerick, Ireland) was then passed through the cervix into the uterine cavity. This catheter system consists of a double-lumen catheter set. The guiding (outer) catheter is 19 cm long, has a polycarbonate hub, and a bulb tip, and the distal end is angled and is 6.6F in diameter, and is inserted until resistance by the internal os is felt. The transfer (inner) catheter is 23 cm long, with a 2.8F tip, and can easily be passed through the internal os into the uterine cavity. We chose this catheter because it can be easily inserted in most cases without the need to grasp the cervix, and causes minimal patient discomfort. If the catheter could not be inserted easily, the cervix was grasped using a tenaculum to straighten the angle between the cervix and body of the uterus. The speculum was then removed, and a 4-to 9-MHz multi-frequency transvaginal probe (Accuvix XQ, Medison Co., Ltd., Seoul, Korea; Voluson 730 Pro, GE Healthcare, Piscataway, NJ) was inserted into the vagina. The uterine cavity was visualized in the longitudinal plane, and the position of the catheter in the uterine cavity was confirmed. The catheter was then gently withdrawn to a level just above the internal os. A 20-mL syringe filled with sterile saline solution was then attached to the catheter, and 5 to 20 mL saline solution was instilled to distend the uterine cavity. The 3-dimensional volume box was then applied, covering the entire uterus, and a 3-dimensional volume was generated by the automatic sweep of the mechanical transducer. The acquired volume was the shape of a truncated cone, with a depth of 4.5 to 9 cm and a vertical angle of 90 degrees. The volume was stored digitally, and analyzed off-line using the multi-planar view. With this technique, it was possible to examine the uterine cavity in 3 orthogonal planes.

VH Technique:

The procedure was performed using a rigid 3.6-mm diagnostic continuous-flow office hysteroscope with a 2.0-mm rod lens (Bettocchi Hysteroscope; Karl Storz GmbH & Co. KG, Tuttlingen, Germany). Aseptic technique was observed throughout the procedure. Neither analgesia nor local anesthesia was administered to any patient, and the cervix was not dilated. The technique averts the need to introducea speculum and a tenaculum. The vagina, being a potential cavity, was distended by introducing normal saline solution through the hysteroscope, which was placed in the lower vagina. The anatomy was then followed with gentle movements of the instrument toward the cervix and cervical canal and then through the internal cervical os into the endometrial cavity. Infusion pressure was elevated using a pneumatic cuff under manometric control at a pressure of 80 to 120 mm Hg. If the vaginoscopic approach was unsuccessful, conventional office hysteroscopy was performed with cervical exposure using a Cuscoe speculum and tenaculum to straighten the cervical angle and facilitate cervical passage of the hysteroscope. A high-intensity cold light source and fiberoptic cable was used to illuminate the uterine cavity. The procedure was monitored using a single chip video camera, and the image was displayed on a monitor visible to the operator.

Statistical methods:

IBM SPSS statistics (V. 25.0, IBM Corp., USA, 2017-2018) was used for data analysis. Date were expressed as Mean±SD for quantitative parametric measures in addition to median and percentiles for quantitative non-parametric measures and both number and percentage for categorized data.

The following tests were done:

1. Chi-square test to study the association between each 2 variables or comparison between 2 independent groups as regards the categorized data.
2. Comparison between 2 proportions as regards univariant categorized data using Z test.

The probability of error at 0.05 was considered sig., while at 0.01 and 0.001 are highly sig.

Diagnostic validity test: It includes:

a. The diagnostic sensitivity: It is the percentage of diseased cases truly diagnosed (TP) among total diseased cases (TP+FN).

b. The diagnostic specificity: It is the percentage of non-diseased truly excluded by the test (TN) among total non-diseased cases (TN+FP); The predictive value for a +ve test: It is the percentage of cases truly diagnosed among total positive cases; The predictive value for a -ve test: It is the percentage of cases truly negative among total negative cases; The efficacy or the diagnostic accuracy of the test: It is the percentage of cases truly diseased plus truly non-diseased among total cases.

Diagnostic Validity Test:

Sp.%	=	100
Sn.%	=	100
P-ve%	=	100
P+ve%	=	100
Eff.%	=	100

The ability to discriminate the positive finding (Sensitivity %); the ability to discriminate negative findings (Specificity %); the ability to discriminate true negative findings among all negative results (Predictive value of negative test %); the ability to discriminate true positive test among all positive results (Predictive value of positive test) and the ability to discriminate true results (both Positive and Negative) among all cases (Efficacy %) are equal 100%.

All studied items can be sorted regards to their agreement with the reference technique (Hystro) according to their Cohen Kappa Agreement according to the following table.

Table (1): The *K* value can be interpreted as follows **(Altman, 1991)**:

Value of *K*	**Strength of agreement**
< 0.20	Poor
0.21 - 0.40	Fair
0.41 - 0.60	Moderate
0.61 - 0.80	Good
0.81 - 1.00	Very good

Table (2): Shows the mean age and the mean body mass index (BMI) of patients involved in the study.

Descriptive Statistics:					
	n	Min.	Max.	Mean	SD
Age	75	28	32	30.4	3.57
BMI	75	27	35	32.52	3.89

Table (3): Shows the incidence of primary (1ry) and secondry (2ry) infertility between patients involved in the study.

			Total
Type of Infertility	**1ry**	Count	69
		%	92%
	2ry	Count	6
		%	8%
Total		Count	75
		%	100.0%

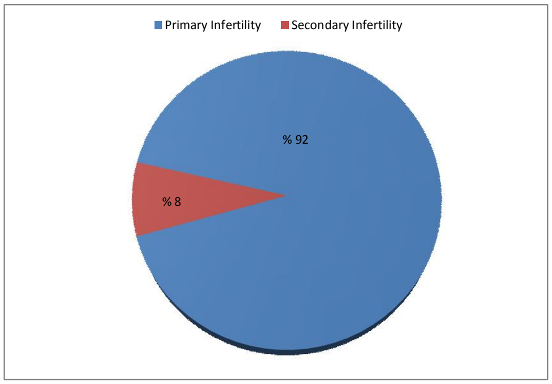

Figure (1): Shows the incidence of primary (1ry) and secondry (2ry) infertility between patients involved in the study.

Hysteroscopy

Table (4): Describing intrauterine lesions detected by hysteroscopy.

		Frequency	Percent
Valid	ARCUATE UTERUS	2	2.7
	Intra uterine adhesions	6	7.9
	No	44	58.7
	Polyp	10	13.3
	Polypoid endometrium	5	6.6
	Submucous fibroid	4	5.3
	UTERINE SEPTUM	4	5.3
	Total	**75**	**100.0**

3D-SHG

Table (5): Describing intrauterine lesions detected by 3D-SHG.

		Frequency	Percent
Valid	ARCUATE UTERUS	3	4.0
	Intra uterine adhesions	2	2.7
	No	49	65.3
	Polyp	9	12.0
	Polypoid endometrium	4	5.3
	Submucous fibroid	4	5.3
	UTERINE SEPTUM	4	5.3
	Total	**75**	**100.0**

Z test for comparison between 2 proportions

Table (6): Ability of both modalities in diagnosis of intrauterine lesions.

No	Hystro	75	58.67	44			
	3D	75	65.33	49	0.841079	>0.05	NS

No significant difference between the two modalities in diagnosis of intrauterine lesions.

Table (7): Ability of both modalities in diagnosis of arcuate uterus.

		Total	%	n	Z	P	Sig.
Arcuate Uterus	Hystro	75	2.67	2			
	3D	75	4.00	3	0.454859	>0.05	NS

No significant difference between the two modalities in diagnosis of arcuate uterus.

Table (8): Ability of both modalities in diagnosis of intrauterine adhesions.

Intra-uterine adhesions	Hystro	75	8.00	6			
	3D	75	2.67	2	1.45	>0.05	NS

No significant difference between the two modalities in diagnosis of intrauterine adhesions.

Table (9): Ability of both modalities in diagnosis of polyps.

Polyp	Hystro	75	13.33	10			
	3D	75	12.00	9	0.24549	>0.05	NS

No significant difference between the two modalities in diagnosis of intrauterine polyps.

Table (10): Ability of both modalities in diagnosis of polypoid endometrium.

Polypoid Endometrium	Hystro	75	6.67	5			
	3D	75	5.33	4	0.343807	>0.05	NS

No significant difference between the two modalities in diagnosis of intrauterine polypoid Endometrium.

Table (11): Ability of both modalities in diagnosis of submucous fibroid.

Submucous fibroid	Hystro	75	5.33	4			
	3D	75	5.33	4	0	>0.05	NS

No significant difference between the two modalities in diagnosis of intrauterine submucous fibroid.

Table (12): Ability of both modalities in diagnosis of intrauterine septum.

Uterine septum	Hystro	75	5.33	4			
	3D	75	5.33	4	0	>0.05	NS

No significant difference between the two modalities in diagnosis of intrauterine septum.

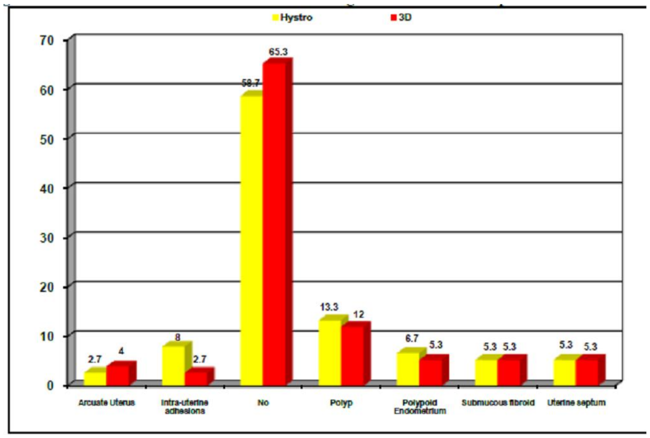

Figure (2): Describing intrauterine lesions detected by hysteroscopy and 3D SHG.

Table (13): Ability of two modalities to diagnose submucous fibroid.

Crosstab

			3D	Hystro	Total
Hystrosubmucous fibroid	**Neg**	**Count**	71	71	142
		%	94.7%	94.7%	94.7%
	Pos	**Count**	4	4	8
		%	5.3%	5.3%	5.3%
Total		**Count**	75	75	150
		%	100.0%	100.0%	100.0%

Table (14): Difference between the two modalities in diagnosis of submucous fibroid.

Chi-Square Tests

	Value	P
Pearson Chi-Square	0.000^{a}	1.000

Non-significant difference between the 2 techniques as regards frequency of positivity of submucous fibroid (p>0.05).

Table (15): Ability of two modalities to diagnose polyps.

Crosstab

			3D	Hystro	Total
Hystro polyp	**Neg**	**Count**	66	65	131
		%	88.0%	86.7%	87.3%
	Pos	**Count**	9	10	19
		%	12.0%	13.3%	12.7%
Total		**Count**	75	75	150
		%	100.0%	100.0%	100.0%

Table (16): Difference between the two modalities in diagnosis of polyps.

Chi-Square Tests

	Value	P
Pearson Chi-Square	$.060^a$	.806

Non-significant difference between the 2 techniques as regards frequency of positivity of uterine polyps (p>0.05).

Table (17): Ability of two modalities to diagnose intrauterine adhesions.

Crosstab

			3D	Hystro	Total
Hystro IUA	**Neg**	**Count**	73	69	142
		%	97.3%	92.0%	94.7%
	Pos	**Count**	2	6	8
		%	2.7%	8.0%	5.3%
Total		**Count**	75	75	150
		%	100.0%	100.0%	100.0%

Table (18): Difference between the two modalities in diagnosis of intrauterine adhesions.

Chi-Square Tests

	Value	P
Pearson Chi-Square	2.113^a	.146

Non-significant difference between the 2 techniques as regards frequency of positivity of intrauterine adhesions (p>0.05).

Table (19): Ability of two modalities to diagnose arcuate uterus.

Crosstab

			3D	Hystro	Total
HystroArcuate	**Neg**	**Count**	72	73	145
		%	96.0%	97.3%	96.7%
	Pos	**Count**	3	2	5
		%	4.0%	2.7%	3.3%
Total		**Count**	75	75	150
		%	100.0%	100.0%	100.0%

Table (20): Difference between the two modalities in diagnosis of arcuate uterus.

Chi-Square Tests

	Value	P
Pearson Chi-Square	$.207^a$	.649

Non-significant difference between the 2 techniques as regards frequency of positivity of arcuate uterus (p>0.05).

Table (21): Ability of two modalities to diagnoseuterine septum.

Crosstab

			3D	Hystro	Total
Hystro septum	**Neg**	**Count**	71	71	142
		%	94.7%	94.7%	94.7%
	Pos	**Count**	4	4	8
		%	5.3%	5.3%	5.3%
Total		**Count**	75	75	150
		%	100.0%	100.0%	100.0%

Table (22): Difference between the two modalities in diagnosis of uterine septum.

Chi-Square Tests

	Value	P
Pearson Chi-Square	$.000^a$	1.000

Non-significant difference between the 2 techniques as regards frequency of positivity of uterine septum (p>0.05).

Table (23): Ability of two modalities to diagnose polypoid endometrium.

Crosstab

			3D	Hystro	Total
Hystropolypoid endometrium	**Neg**	**Count**	71	70	141
		%	94.7%	93.3%	94.0%
	Pos	**Count**	4	5	9
		%	5.3%	6.7%	6.0%
Total		**Count**	75	75	150
		%	100.0%	100.0%	100.0%

Table (24): Difference between the two modalities in diagnosis of polypoid endometrium.

Chi-Square Tests

	Value	P
Pearson Chi-Square	.118^{a}	.731

Non-significant difference between the 2 techniques as regards frequency of positivity of polypoid endometrium (p>0.05).

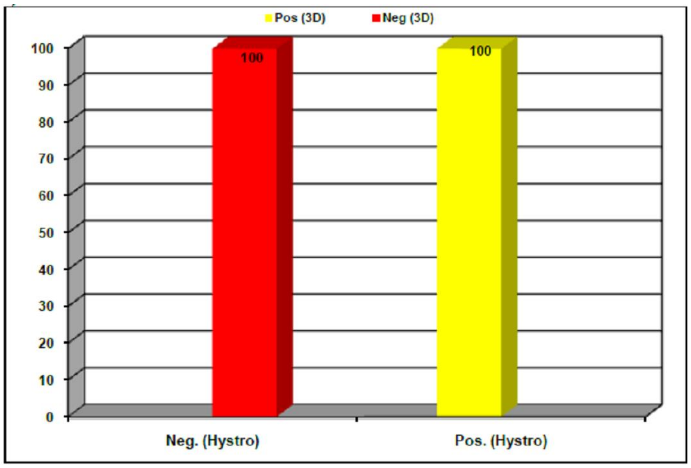

Figure (3): Sensitivity and specificity of both modalities.

Table (25): Degree of correlation between the two modalities in diagnosing the submucous fibroid.

Crosstab

			3D	Hystro	Total
3D submucous fibroid	**Neg**	**Count**	71	0	71
		%	100.0%	0.0%	94.7%
	Pos	**Count**	0	4	4
		%	0.0%	100.0%	5.3%
Total		**Count**	71	4	75
		%	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	P
Pearson Chi-Square	75.000^{a}	.000

Highly significant correlation between the 2 techniques as regards frequency of positivity of submucous fibroid (p<0.001).

Table (26): Degree of agreement between the two modalities in diagnosing submucous fibroid.

Symmetric Measures

		Value	P
Measure of Agreement	Kappa	1.000	.000

Very good agreement between the two modalities in diagnosis of submucous fibroid (k value between 0.81-1.00).

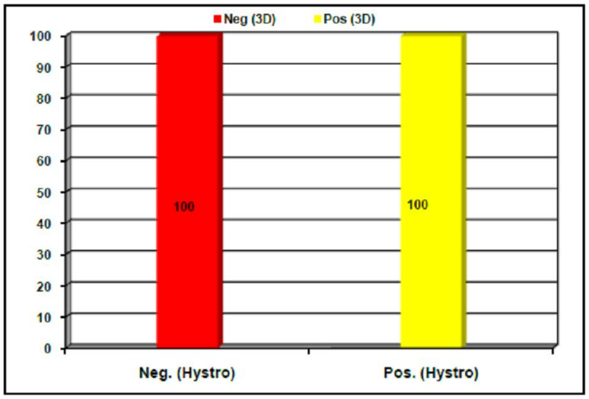

Figure (4): Shows the degree of the agreement between the two modalities as regard submucous fibroid diagnosis.

Table (27): Degree of correlation between the two modalities in diagnosing the endometrial polyps.

			Hystro polyp		**Total**
			Neg	**Pos**	
3D Polyp	**Neg**	**Count**	65	1	66
		%	100.0%	10.0%	88.0%
	Pos	**Count**	0	9	9
		%	0.0%	90.0%	12.0%
Total		**Count**	65	10	75
		%	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	**P**
Pearson Chi-Square	66.477^{a}	.000

Highly significant correlation between the 2 techniques as regards frequency of positivity of polyps.

Table (28): Shows the degree of the agreement between the two modalities as regard endometrial polyps.

Symmetric Measures

		Value	**P**
Measure of Agreement	Kappa	.940	.000

Very good agreement between the two modalities in diagnosis of endometrial polyp (k value between 0.81-1.00).

Diagnostic Validity Test:

Sp.% = 100
Sn.% = 90
P-ve% = 98.5
P+ve% = 100
Eff.% = 98.7

Table (28): Degree of correlation between the two modalities in diagnosing the intrauterine adhesions

Crosstab

			Hystro IUA		**Total**
			Neg	**Pos**	
3D IUA	**Neg**	**Count**	69	4	73
		%	100.0%	66.7%	97.3%
	Pos	**Count**	0	2	2
		%	0.0%	33.3%	2.7%
Total		**Count**	69	6	75
		%	100.0%	100.0%	100.00%

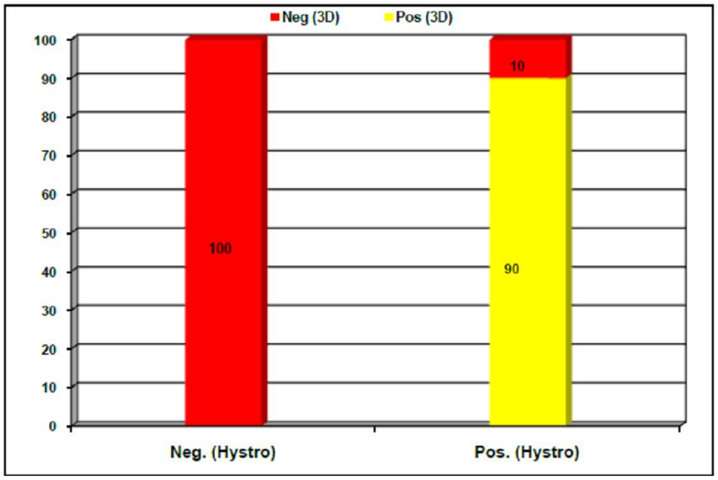

Figure (5): Shows degree of agreement between the two modalities as regards endometrial polyps.

Chi-Square Tests

	Value	**P**
Pearson Chi-Square	23.630[a]	.000

Highly significant correlation between the 2 techniques as regards frequency of positivity of intrautertine adhesions.

Table (29): Degree of agreement between the two modalities in diagnosis of intrauterine adhesions.

Symmetric Measures

		Value	**P**
Measure of Agreement	Kappa	.479	.000

Moderate agreement between the two modalities in diagnosis of intrauterine adhesions (k value between 0.4-.60).

Diagnostic Validity Test:

Sp.% = 100
Sn.% = 33.3
P-ve% = 94.5
P+ve% = 100
Eff.% = 94.7

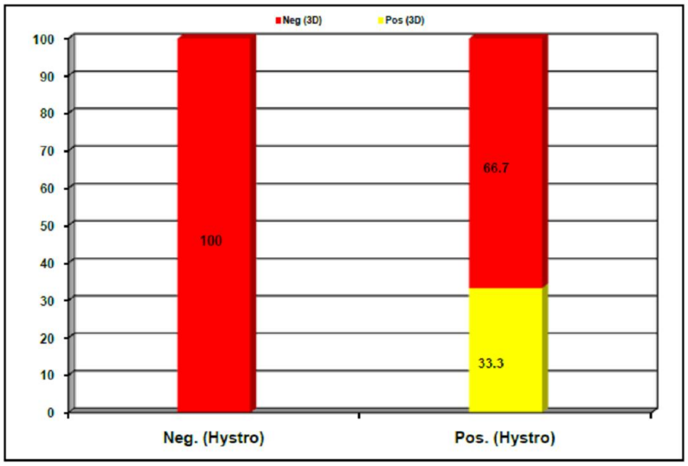

Figure (6): Shows degree of agreement between the two modalities as regards intrauterine adhesions.

Table (30): Degree of correlation between the two modalities in diagnosing the arcuate uterus.

Crosstab

			HystroArcuate		**Total**
			Neg	**Pos**	
3D Arcuate	**Neg**	**Count**	72	0	72
		%	98.6%	0.0%	96.0%
	Pos	**Count**	1	2	3
		%	1.4%	100.0%	4.0%
Total		**Count**	73	2	75
		%	100.0%	100.0%	100.00%

Chi-Square Tests

	Value	**P**
Pearson Chi-Square	49.315^a	.000

Highly significant correlation between the 2 techniques as regards frequency of positivity of arcute uterus.

Table (31): Degree of agreement between the two modalities in diagnosis of arcuate uterus.

Symmetric Measures

		Value	**P**
Measure of Agreement	Kappa	.793	.000

Good agreement between the two modalities in diagnosis of arcuate uterus (k value between 0.6-.80).

Diagnostic Validity Test:

Sp.% = 98.6
Sn.% = 100
P-ve% = 100
P+ve% = 66.7
Eff.% = 98.7

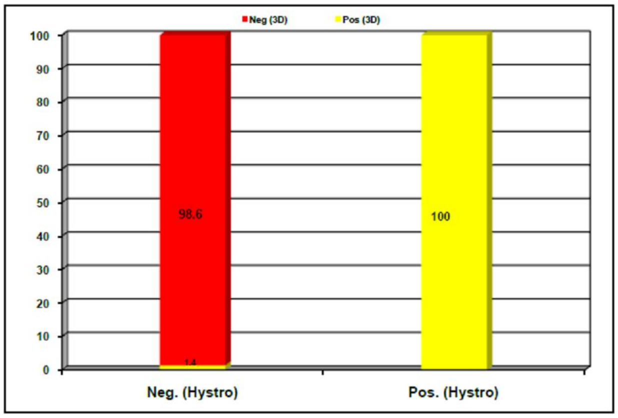

Figure (7): Shows degree of agreement between the two modalities as regard the arcuate uterus.

Table (32): Degree of correlation between the two modalities in diagnosing the uterine septum.

Crosstab

			Hystro septum		**Total**
			Neg	**Pos**	
3D septum	**Neg**	**Count**	71	0	71
		%	100.0%	0.0%	94.7%
	Pos	**Count**	0	4	4
		%	0.0%	100.0%	5.3%
Total		**Count**	71	4	75
		%	100.0%	100.0%	100.00%

Chi-Square Tests

	Value	P
Pearson Chi-Square	75.000^{a}	.000

Highly significant correlation between the 2 techniques as regards frequency of positivity of uterine sptum.

Table (33): Degree of agreement between the two modalities in diagnosis of septum.

Symmetric Measures

		Value	P
Measure of Agreement	Kappa	1.000	.000

Very good agreement between the two modalities in diagnosis of septum (k value between 0.81-1.00).

Diagnostic Validity Test:

Sp.% = 100
Sn.% = 100
P-ve% = 100
P+ve% = 100
Eff.% = 100

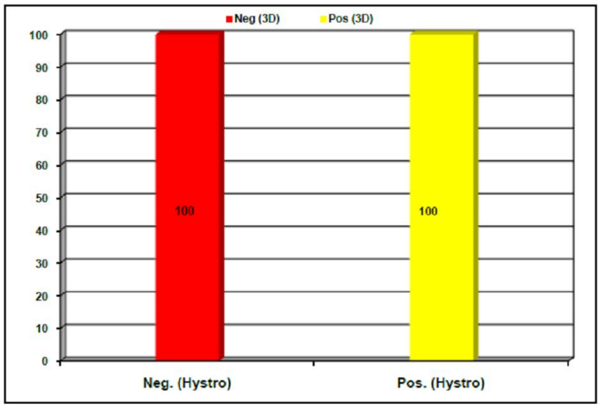

Figure (8): Shows the degree of the agreement between the two modalities as regard uterine septum diagnosis.

Table (34): Degree of correlation between the two modalities in diagnosing the polypoid endometrium.

Crosstab

			Hystropolypoid endometrium		**Total**
			Neg	**Pos**	
3D polypoid endometrium	**Neg**	**Count**	70	1	71
		%	100.0%	20.0%	94.7%
	Pos	**Count**	0	4	4
		%	0.0%	80.0%	5.3%
Total		**Count**	70	5	75
		%	100.0%	100.0%	100.00%

Chi-Square Tests

	Value	P
Pearson Chi-Square	59.155^{a}	.000

Highly significant correlation between the 2 techniques as regards frequency of positivity of polypoid endometrium.

Table (35): Degree of agreement between the two modalities in diagnosis of polypoid endometrium.

Symmetric Measures

		Value	P
Measure of Agreement	Kappa	.882	.000

Very good agreement between the two modalities in diagnosis of polypoid endometrium (k value between 0.81-1.00).

Diagnostic Validity Test:

Sp.% = 100
Sn.% = 80
P-ve% = 98.6
P+ve% = 100
Eff.% = 98.7

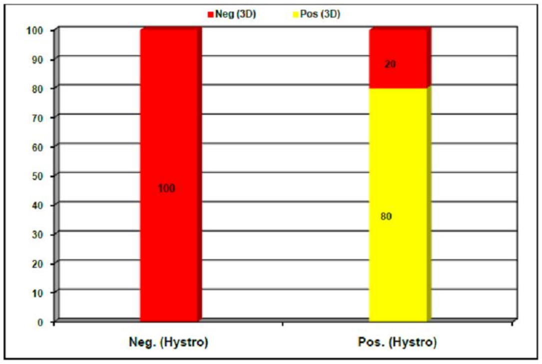

Figure (9): Shows degree of agreement between the two modalities as regard polypoid endometrium diagnosis.

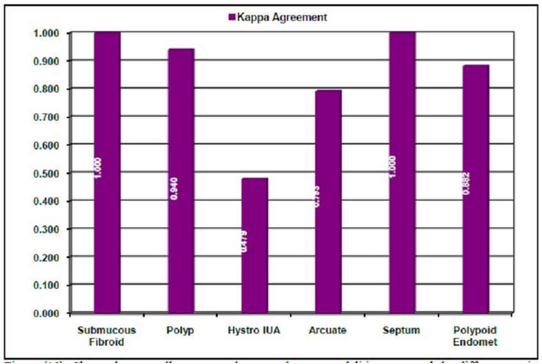

Figure (10): Shows the overall agreement between the two modalities as regard the different uterine lesions diagnosis.

Table (36): Different VAS scores reported by the patients during the two procedures.

			Grps		**Total**
			3D	**Hystro**	
VAS	**1.00**	**Count**	23	0	23
		%	30.7%	0.0%	15.3%
	2.00	**Count**	24	0	24
		%	32.0%	0.0%	16.0%
	3.00	**Count**	28	37	65
		%	37.3%	49.3%	43.3%
	4.00	**Count**	0	3	3
		%	0.0%	4.0%	2.0%
	5.00	**Count**	0	35	35
		%	0.0%	46.7%	23.3%
Total		**Count**	75	75	150
		%	100.0%	100.0%	100.0%

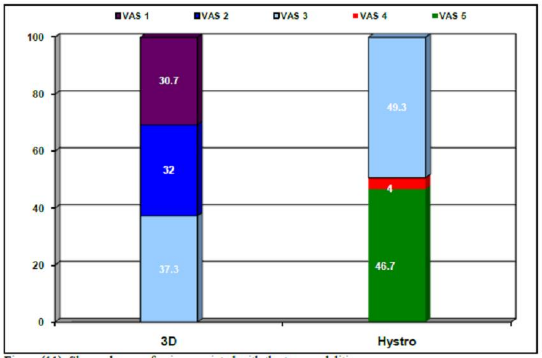

Figure (11): Shows degree of pain associated with the two modalities.

Table (37): Degree of difference between the two modalities regarding the VAS score.

Chi-Square Tests

	Value	**P**
Pearson Chi-Square	86.246^{a}	.000

Highly significant difference between the two modalities regarding the VAS score.

Among those 3D (total=75); 30.7 score 1; 32.0 score 2 and 37.3 score 3; while among those hystro (total= 75); 49.3% score 3; 4.0 score 4 and 46.7 score 5 i.e.; both technique are different regarding VAS; being hystro characterized by higher score than those 3d (p<0.001).

Table (38): Shows collected findings in the study.

Item	TP	FN	TN	FP	Sensitivity	Specificity	(+)ve PV	(-)ve PV	Accuracy
Submucousmyoma	4	0	71	0	100.00	100.00	100.00	100.00	100.00
Polyp	9	1	65	0	90.00	100.00	100.00	98.48	98.67
IUA	2	4	69	0	33.33	100.00	100.00	94.52	94.67
Arcuate uterus	2	0	72	1	100.00	98.63	66.67	100.00	98.67
Septum	4	0	71	0	100.00	100.00	100.00	100.00	100.00
Polypoid endometrium	4	1	70	0	80.00	100.00	100.00	98.59	98.67
All lesions	25	6	43	1	80.65	97.73	96.15	87.76	90.67

4. Discussion

The present study examined the agreement between 3-D SHG and VH in patients with recurrent in vitro fertilization implantation failure. The current study shows that, overall, there is a substantial degree of concordance between the 2 outpatient procedures and the over all sensitivity in detecting uterine lesions via 3D sonohyystrography in relation to hysteroscopy was 80.65% and overall accuracy was 90.67%.

In the current study, it was found that 41.3% of study patients had abnormalities in the endometrial cavity that could be contributing factors in the patient's history of repeated implantation failure. The current study is not in agreement with different results obtained by other research workers as intrauterine pathologies revealed in about 50% of women with RIF in **Bozdag G. et al., (2008)**. Higher incidence was also reported by **Arefi et al., (2008)** who reported abnormalities in 59.5% of their patients. In **Reda et al., (2017)** detected intrauterine abnormalities in 26.6% of patients which is not in agreement with the current study. In the current study, it is found that 3D-SHG took significantly less time and induced less patient discomfort than did VH and this was in agreement with what was reported by **Graziano et al., (2013).**

The current study results is not in agreement with those reached by other investigators who compared the role of 3D-SHG and hysteroscopy in evaluation of the uterine cavity **(De Kroon CD. et al., 2004; Makris N. et al., 2007; Sylvestre C. et al., 2003).** In one such study, **Sylvestre et al., (2003)** found that, compared with hysteroscopy, 3D-SHG had a sensitivity of 100% and a positive predictive value of 92% in diagnosing intrauterine lesions. SIS was also demonstrated to be as accurate as hysteroscopy in detecting intrauterine abnormalities **(Bingol B. et al., 2011).**

In **Reda et al., (2017)**, the overall accuracy of SIS in detecting intrauterine abnormalities was significantly less than hysteroscopy although analysis of the accuracy in detecting a specific pathology separately showed a nonsignificant difference between both procedures.

These finding is in agreemenet with **Qazizadeh et al., (2006)** who reported that SIS is significantly less accurate than hysteroscopy in detecting intrauterine lesions and stated that small lesions may be unnoticed with SIS. In **Minzhi et al., (2015),** among the 334 cases of women with RIF in the HS group, a total of 124 women had intrauterine abnormalities, with an overall abnormality rate of 37.13%. In 2010, **Karayalcin et al.,** reported that 22.9% of 2500 preoperative IVF women that underwent HS examination had uterine abnormalities, while only 11% of first IVF women with normal TVS had intrauterine abnormalities. The current study is also in agreement with the systematic review done by **S. Seshadri et al., (2014)**; which demonstrated that SIS has a high degree of diagnostic accuracy in the detection of all types of intrauterine abnormalities with a sensitivity and specificity of 88 and 94%.

Based on the findings of hysteroscopy in the present study, results showed abnormal findings in (31) of the (75) examined patients (41.3%), including endometrial polyps in (10), polypoid endometrium in (5), intrauterine adhesions in (6), septate uterus in (4), arcuate uterus in (2), and submucousmyomas in (4). These findings are in a quite agreement with those of previous studies that examined the endometrial cavity in patients both before undergoing an IVF-ET cycle **(Fatemi HM., et al., 2010; Hinckley MD., et al., 2004)** and after repeated implantation failure **(Demirol A., et al., 2004; Golan A., et al., 1992; Oliveira et al., 2003; Minzhi et al., 2015; Reda et al., 2017).**

In the present study, 3D-SHG and hysteroscopy showed the greatest Agreement in diagnosing submucousmyomas 100% sensitivity of both with accuracy 100% and the (k= 1.000), this was in agreement with the study by **Salim et al., (2005)**, who compared 3D-SHG and hysteroscopy for classification of submucousmyomas. Also this results in agreement with **Shiva et al., (2018)**, who compared the sensitivity of the 2D transvaginalsonography and hysteroscopy in diagnosing the intra uterine lesions in the cases of recurrent implantation faliure.

The current study is in agreement with **Chayanis et al., (2016)** which compared the ability of 3-D ultrasound to detect intrauterine abnormalities in comparison with hystrscopy. Their results showed good overall agreement between the 2 diagnostic methods agreement 100% with accuracy 100% in relation to submucousmyoma diagnosis.

In the present study, there was a 90% degree of agreement between 3D-SHG and VH in diagnosing endometrial polyps (k=0.940) as the over all cases detectected by hysteroscopy was 10 cases while 9 cases were detected by 3d – SHG. The present study is not in agreement with **Chayanis et al., (2016) and Fang et al., (2013)** as the current study shows that ultrasound is more sensitive in detection of endometrial polyp mor than in **Chayanis et al., (2016)** in which ultrasound showed a sensitivity of 61% and also more than **Fang et al., (2013)**; which showed a sensitivity of 64%. Also, it is in a quite agreement with **Elsherbiny et al., (2015)** and **Shiva et al., (2018)** which showed asenstivity of 99.2% and 80% sensitivity for detection of the endometrial polyp respectively.

For polypoidal endometrium, agreement was noted in 80% of cases (k=0.882) between the two used modalities which a very good agreement, total number of polypoid endometrium was 5 on hysteroscopy and 4 in 3D-SHG. This result is not in agreement with **Negm et al., (2012)** which showed substantial degree of agreement between the two modalities (k=0.62). The current study is also not in agreement with **Shiva et al., (2018)** as regarding diagnosis of polypoid endometrium as the Kappa coefficient was 0.42 (k=0.42) and this agreement level is moderate.

In the present study, the ability of 3D-SHG to demonstrate the coronal plane of the uterus facilitated accurate detection and classification of mullerian anomalies, according to **(ESHRE-ESGE consensus 2013)**.

There was 100% agreement between 3D-SHG and VH in diagnosing septate uterus (Defined as absent or incomplete resorption of the uterovaginal septum) with (k=1.000). The current study is in agreement with **Chayanis et al., (2016)** and **Elsherbiny et al., (2015)** in which (k=1.00). the current study is not in agreemenet with **Shiva et al., (2018)** which shows a moderate agreement between the two modalities in regard the diagnosis of septate uterus (k=0.45). However, in diagnosis of the arcuate uteri, 3 cases was detected at 3D-SHG (Defined as a mild indentation at the level of the fundus from near complete resorption of the uterovaginal septum), 2 were considered abnormal at hystroscopy, resulting in good agreement between 3D-SHG and VH (k=0.793). the current study is not in agreement with **Negm et al., (2012)** which showed poor agreement as (k=0.33) and also the current study is not in agreement with **Shiva et al., (2018)**, which shows a fair agreement (k=0.27) between the two modalities regarding the diagnosis of arcuate uterus.

It is evident from the current study that both 3D-SHG and hystroscopy are valuable diagnostic tools that may complement one another in evaluation of the uterine cavity, in particular in poorly understood conditions such as recurrent implantation failure, because both diagnostic methods have advantages and drawbacks.

While 3D-SHG seems to enable accurate diagnosis of mullerian anomalies, which would otherwise require combined laparoscopy and hysteroscopy, it was less sensitive in enabling diagnosis of intrauterine adhesions, missing 4 of 6 cases diagnosed at hysteroscopy with a moderate agreement (k=0.479) and an accuracy of 33.3% sensitivity, the current study is not in agreement with **Elshebiny et al., (2015)** which showed a sensitivity of 97.2% which is much higher than that in the current study. The current study also is in agreement with **Negm et al., (2012)** which showed a moderate agreement between the two modalities as (k=0.5). The current study is not in agreement with **Shiva et al., (2018)** which showed a poor agreement between the two modalities as regard the diagnosis of intrauterine adhesions (k=0.16).

Regarding the discomfort and pain sensation both technique are different regarding VAS; being hystro characterized by higher score than those with 3D ($p<0.001$) and one explanation for the perceived pain difference between the 2 procedures may be the higher intrauterine pressure generated during vaginoscopic hysteroscopy, in which the infusion pressure ranged between 80 and 120 mm Hg. However, 3D-SHG required instillation of only a small amount of saline solution inside the uterine cavity.

Thus generating significantly less intrauterine pressure. The current study is in agreement with **Negm et al., (2012)** whisch shows less pain score recorded by the patients during 3D-SHG.

In the present study, 3D-SHG demonstrated good overall agreement with vaginoscopic hysteroscopy. It also took less time and was associated with less patient discomfort than hysteroscopy. We thus recommend that 3D-SHG should be the method of first choice for outpatient evaluation of the uterine cavity.

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