

Frequency of Congenital Anatomical Uterine Abnormalities in a Group of Infertile Women in Mosul city

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Abstract

Background: Congenital Müllerian defects are a fascinating clinical problem encountered by obstetricians and from a therapeutic point of view, it is interesting to know the prevalence of the different types of uterine anomalies. The incidence of the anatomical uterine anomalies in the infertile women population was found to range between 1-26.2 %; however the exact incidence of congenital uterine anomalies in women with ^{reproductive} failure remains unclear, largely due to methodological bias.

Objectives: The aims of this study are to estimate the incidence of congenital uterine anomalies in women with infertility, to determine the frequencies of different subtypes of these anomalies in infertile women and to compare the contribution of these anomalies with acquired one.

Setting: Infertility unit in Al-Batool Maternity Teaching Hospital/ in Mosul city in Northern Iraq.

Methods: This was a retrospective study that was conducted over a period of 4 months started from 1st January 2008 to April 30th 2008. The data were collected from the medical reports of women referred to the infertility unit over the period of 1998-2008 for infertility problems. All of them had undergone laparoscopic assessment beside hysterosalpingography. They were classified into 3 groups: Group 1: included women who were presented with primary infertility (n=1070), group 2: included 512 women presented with secondary infertility, and, group 3: which included 10 women, presented with primary infertility and primary amenorrhea. The uterine malformations were grouped in accordance with the American Fertility Society classification (AFS).

Results: Ninety one (5.68%) out of 1601 infertile women had got congenital anatomical uterine anomalies. According to AFS classification uterine agenesis /dysgenesis was reported in 54(3.37%) out of 1601 infertile women, while septate uterus identified in 13 (0.81%) out of 1601 infertile women. On the other hand the laparoscopic reports of 12 (0.74%) out of 1601 infertile women revealed the presence of bicornuate uterus, while unicornuate type was identified in 3 (0.18%) out of 1601 infertile women. Four (0.24%) out of 1601 infertile women had got didelphic uterus, while more than one class was revealed in the reports of 5(0.31%) out of 1601 infertile women. Agenesis /dysgenesis represent highest frequency among Müllerian anomalies in infertile women in 54 out of 91(59.34%), while septate class was being the second to the Agenesis /dysgenesis and was shown in 13 out of 91(14.29%) women. The ratio of septate /bicornuate uterus in this study was 1:1. On the other hand, 176(10.99%) out of 1601 infertile women had got acquired anatomical uterine anomalies.

Conclusion: The overall incidence of congenital anatomical uterine anomalies in infertile women attending the infertility unit in Mosul city was 5.68%. Highest frequency among Müllerian anomalies in infertile women was in Agenesis /dysgenesis; while septate class was the second frequent one. The frequencies of acquired anatomical (uterine and tubal) anomalies were significantly higher than that of congenital anomalies ($P<0.05$). Further studies will be recommended to define the actual incidence of uterine anomalies in fertile and infertile women beside the determination of reproductive performance of these anomalies.

Keywords: Infertility, congenital uterine anomalies, Müllerian anomalies.

Introduction

Uterine malformations consist of a group of miscellaneous congenital anomalies of the female genital system. They are the result of four major disturbances in the development, formation or the fusion of the Müllerian or paramesonephric ducts during fetal life ^[1].

The major disturbances in the development of the Müllerian ducts include failure of one or more Müllerian ducts to develop (agenesis or unicornuate uterus without rudimentary horn), failure of the ducts to canalize (unicornuate uterus with rudimentary horn without proper cavities),

failure or abnormal fusion of the ducts (uterus didelphys, bicornuate uterus), and failure of reabsorption of the midline uterine septum (septate uterus and arcuate uterus) ^[2].

Uterine malformations are classified according to the degree of failure of normal development into six major types based on AFS classification ⁽²⁾. These include Müllerian agenesis or hypoplasia (Class I), Unicornuate uterus (Class II), Didelphys uterus Class III, Bicornuate uterus (Class IV), Septate uterus (Class V), and Arcuate uterus (Class VI), Figure (1).

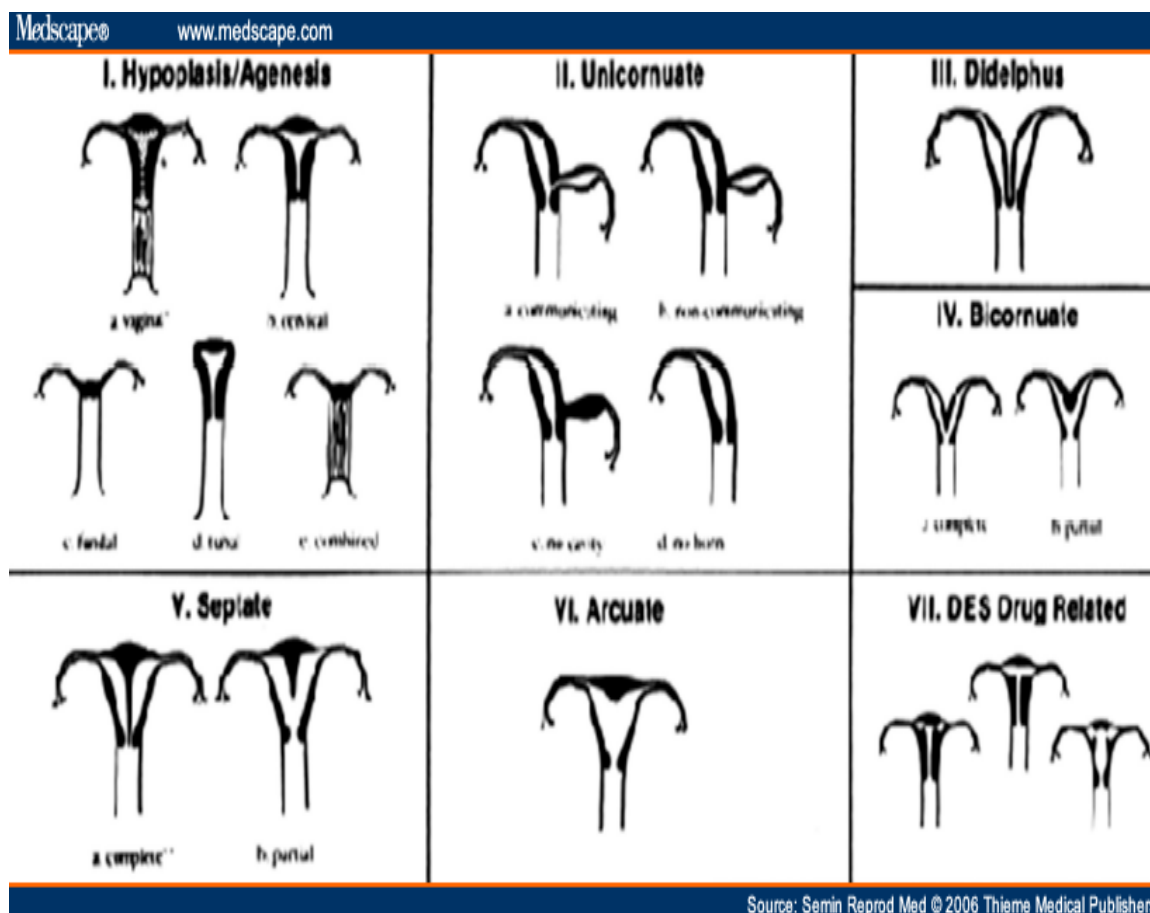


Figure (1). The American Fertility Society classification (AFS) of Müllerian malformations.

Buttram and Gibbons^[3] in 1979 grouped the anatomic uterine anomalies according to their clinical morphology. This was later modified in 1988 by the American Fertility Society (currently known as the American Society for Reproductive Medicine) which is now the most commonly accepted means of characterizing Müllerian tract defects^[4].

The true incidence of uterine anomalies in the general and in the infertile population is not accurately known^[5]. The discrepancy between reports is due to the inaccuracy of the diagnostic methods employed and the lack hitherto of a uniform system of classification, in addition many of these defects are asymptomatic and therefore remain undiagnosed^[6]. However the introduction of the vaginal probes in the conventional gynaecological screening has improved the diagnosis of such malformations even before a woman attempts to become pregnant^[6]. In addition, new ambulatory endoscopic surgical methods have been developed for the diagnosis of congenital Müllerian anomalies^[7]. With the general widespread use of transvaginal ultrasound and hysterosalpingogram (HSG) in reproductive age women, increased detection of uterine anomalies in the general population can be expected, especially in the infertile and recurrent miscarriage subgroups. Following detection of uterine anomalies by

ultrasound and HSG, the availability of magnetic resonance imaging (MRI) and three-dimensional ultrasound (3D US) should increase the accurate diagnosis of these anomalies as diagnostic criteria are applied more consistently^[5, 7,8,9].

The incidence of the anatomical uterine malformations in the general population was found to range between 0.5-8.0%^[1,6,7], while the incidence of the anatomical uterine anomalies in the infertile women population was found to range between 1-26.2 % , however the incidence in recurrent pregnancy loss was found to range between 5.0-25.4 %^[1,2,7,10].

Congenital uterine anomalies have been found to be linked to a wide spectrum of clinical implications like infertility, recurrent pregnancy loss, preterm labor and other obstetric complications whereas in others, these uterine malformations remain asymptomatic^[6,11]. Women with uterine anomalies such as unicornate, bicornate, didelphys and septate uteruses have shown to have a high of primary infertility (failure to conceive) or more often as an increase rate of early pregnancy loss (impaired implantation and early development)^[6, 12,13]. Later in pregnancy, unsuspected uterine malformations may be presented as impaired intrauterine fetal growth (due to abnormal placentation), or abnormal fetal positioning related to mechanical factors in the

shape of the uterine cavity. However, labor, delivery, and third stage problems may occur due to in-coordinate uterine muscular activity^[12].

This study aims to establish the actual incidence of the congenital anatomical malformations of a group of infertile women undergone diagnostic laparoscopy during the years 1998-2008, and to determine the frequencies of different types of these malformations. In addition it also aims to determine the contribution of congenital uterine anatomic factors to the infertility compared to the acquired uterine anomalies.

Materials & Methods

This is a retrospective study that was carried out in Al-Batool Maternity Teaching Hospital in Western Mosul over a period of 4 months started from 1st January 2008 to April 30th 2008. The data were collected from the medical reports of women who were referred to the Infertility Unit by their consultant or from the out patient clinic or from the consultative clinic due to infertility problems over the period of 10 years extending between 1998-2008.

The women were classified into 3 groups: Group 1: included women who were presented with primary infertility (n=1070), Group 2: which included 521 women presented with secondary infertility, and Group 3: which included 10 women who were presented with primary infertility and oligomenorrhea/amenorrhea. The uterine malformations were grouped according to the American Fertility Society (1988) classification, which divides the anomalies into classes with similar clinical features, therapeutic options and prognoses^[4]. Each women included in this study had a report of hystrosalpingography (HSG) followed by diagnostic laparoscopy in order to ascertain the correct morphology of the uterus (investigating both the uterine cavity and the external uterine contour).

Laparoscopic assessment was carried out in the Infertility Unit /Al-Batool Maternity Teaching Hospital enabling the direct visualization of the peritoneal cavity, ovaries, outside of the tubes and the uterus^[14]. A database file was set up using Microsoft Excel for Windows to facilitate data entry and retrieval. Statistical analysis was performed using SPSS for Windows. The proportions of congenital and acquired uterine anomalies were compared using the Pearson χ^2 test, statistical significance were considered at $P < 0.05$ ^[15].

Results

This study analyzed medical reports of 1601 women who were referred to the infertility unit in Al-Batool Maternity Teaching hospital during the period from 1998 to 2008. The results are shown according to grouping of subjects where they were classified according to their complaints into 3 groups:

Group 1 includes 1070 women, who aged between 13 to 45 years (mean 28.11 ± 4.85 years). They were presented as cases of primary infertility for a period ranged between 1 and 20 years (mean 5.34 ± 2.95 years). The laparoscopic examination revealed normal uterus in 816 (76.2%), while 254 (23.8 %) women showed different anatomical uterine abnormalities whether congenital, acquired or both.

Sixty four (5.98%) women had got different congenital anatomical uterine abnormalities including 5(0.46 %) women with tubal agenesis, and two (0.18%) women with unilateral tubal dysgenesis (with absent other tube). Small or infantile uterus (dysgenesis) was reported in 18 (1.68%) women, two (0.18%) women with small uterus plus tubal dysgenesis.

Small uterus with tubal cyst and cervical dysgenesis were reported in 1 case (0.09%), while small uterus and tubal cyst with vaginal dysgenesis were reported in 1(0.09%), however, only one (0.09%) case had got small uterus with cyst of morgagni. On the other hand, vaginal dysgenesis with tubal agenesis was reported in 4(0.37 %), while cervical dysgenesis plus tubal cyst was reported in 1(0.09 %) woman.

Bicornuate uterus was shown in 9(0.84 %) women as shown in Figure (2), while bicornuate uterus and rudimentary horns was reported in 1(0.09 %) case. On the other hand, a case of two rudimentary uterus that do not meet in the center reported in 1(0.09 %) case. Didelphys uterus was revealed in three (0.28%) cases, while septate uterus identified in 3(0.28 %) women. On the other hand longitudinal vaginal septum reported in 4(0.37 %).

Only one case (0.09 %) of unicornuate uterus, however, another case (0.09 %) of unicornuate uterus was reported in association with rudimentary horn. Unicornuate uterus plus rudimentary horn and with no cavity was reported in one (0.09 %) case.

A case of double cervix with septate vagina was reported in 1(0.09 %) case only with another (0.09 %) case that showed both bicornuate uterus and septate uterus together. On the other hand a case of rudimentary horn with tubal agenesis was shown in 1(0.09 %) case.

Didelphys uterus in association with vaginal dysgenesis and tubal dysgenesis were reported in 1(0.09 %) case, and didelphys uterus and rudimentary horn was shown in one (0.09 %) case as well.

Retroverted uterus identified in 68 (6.35%) women, from these cases one (0.09 %) case of retroverted uterus with small uterus was reported while retroverted uterus and vaginal dysgenesis identified in 1(0.09 %) case.

Different acquired uterine anomalies were noticed in 116 (10.8%) women in group 1

.However, congenital and acquired anatomical uterine anomalies were noticed as together in 6(0.6%) women in group one including two (0.18 %) cases with dysgenesis and uterine fibroid, while dysgenesis and retroverted uterus with endometriosis were shown in 2(0.18%).On the other hand one (0.09%) case of unicornuate uterus and endometieriosis was reported and another one (0.09%) case of unicornuate uterus with endometriosis and uterine fibroid was also identified.

Normal Fallopian tubes identified in 762 (71.2%) women in group (1).However, the reports of 308(28.78%) indicated the presence of tubal abnormalities that included 17(1.58%) women with anatomical congenital abnormalities, 289(18.05%) women with acquired anomalies

And two (0.12%) women with both acquired and congenital abnormalities (including unilateral agenesis tube with a blocked other tube in 1(0.9%) case ,and another one (0.9%) case of unilateral tubal agenesis tube with another dilated tube .

Group 2 included 521 women with secondary infertility. Their ages range between 18 to 45 years (mean =29.23year $\pm$ 5.1) .The mean of duration was 5.19 $\pm$ 2.35 (range 2 years to 17 years).

The laparoscopic examination revealed normal uterus in 409 (78.5%) women while 112(21.5%) showed different uterine abnormalities. Eighteen (3.54%) women had got congenital anatomical uterine abnormalities including 2(0.38%) women with unilateral tubal agenesis. In addition, unilateral tubal dysgenesis was identified in 3 (0.57%) cases .On the other hand vaginal dysgenesis was noticed in 3(0.57%), where 2 cases of them were accompanied with

unilateral tubal agenesis. Cervical dysgenesis was noticed in 3(0.57%) cases and cervical dysgenesis plus cyst of morgagni were identified in one case of them. One (0.19%) woman had got bicornuate uterus while the reports of 4(0.76%) women revealed the presence of vaginal septum. The laparoscopic reports of 2 (0.38%) women showed the presence of septate uterus and septate vagina. Retroverted uterus was identified in 34(6.6%) women.

Different acquired anatomical uterine abnormalities were noticed in 60(11.7%) women in group 2.

Concerning tubal abnormalities, 335 (64.3%) women in group 2 had their laparoscopic findings indicated the absence of tubal abnormalities, while 186(36.30%) women showed different tubal abnormalities including 9(1.75%) with congenital ones, and 177(34.50%) with different acquired ones. On the other hand, unilateral tubal agenesis with the dilated other tube was identified in 1(0.2%) case.

Group 3: included 10 women, their ages ranged between 18 to 20 years (mean =19.6 year $\pm$ 0.6). The duration of their complaints ranged between 1 to 14 years (mean =3 year $\pm$ 3.91).

One (10.0%) woman had got normal uterus, while 9 (90.0 %) women showed different congenital anatomical uterine abnormalities. Five (50.0 %) exhibited combined Müllerian agenesis as shown in Figure (3), while uterine agenesis was seen in 1(10.0 %) woman. On the other hand the laparoscopic reports of one (10.0%) woman revealed agenesis in the uterus and tubes. However, agenesis of the uterus and the cervix in association with vaginal dysgenesis was seen in 1(10.0 %) case.



Figure 2. A laparoscopic view of bicornuate uterus in a 29 year old woman with primary infertility.

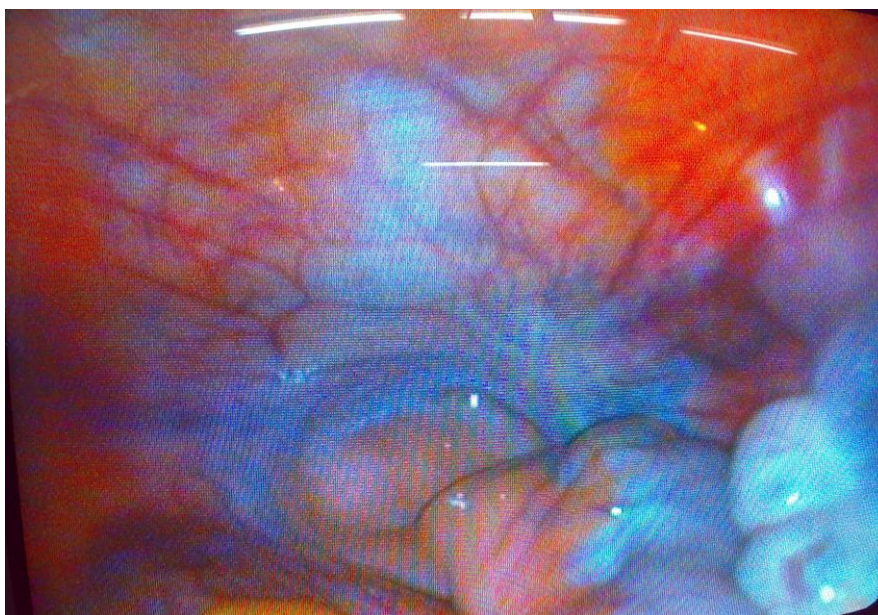


Figure 3. A laparoscopic view of combined Müllerian agenesis in a 17 year old woman with primary infertility and primary amenorrhea.

One (10.0%) case had got didelphys uterus. The laparoscopic findings of eight (80.0%) women in group 3 indicated the presence of normal tubes, while congenital absent tubes were shown in 2(20.0%) cases.

The frequencies of the different identified congenital, acquired and mixed anatomical uterine anomalies of the three study groups are shown in **Table (s) 1, 2, and 3** respectively.

Table1. The frequencies of different identified subtypes of congenital anatomical uterine abnormalities according to AFS classification in the three study groups.

Groups Uterine findings	Primary infertility N =1070		Secondary infertility N=521		Primary Infertility & amenorrhea N=10		Total N=1601	
	No	%	No	%	No	%	No	%
Agenesis /dysgenesis	35	3.27	11	2.11	8	80	54	3.37
Septate Uterus	7	0.65	6	1.15	0	0.0	13	0.81
Bicornuate Uterus	1	1.02	1	0.19	0	0.0	12	0.74
Unicornuate Uterus	3	0.28	0	0.0	0	0.0	3	0.18
Didelphys Uterus	3	0.28	0	0.0	1	10	4	0.24
More than One subtype	5	0.46	0	0.0	0	0.0	5	0.31
Total	64	5.98	18	3.45	6	90	91	5.68

Table 2. The frequencies of different acquired uterine anomalies in the three study groups.

Groups Uterine Abnormalities	Primary Infertility N= 1070	Secondary Infertility N= 521	Primary Infertility & Primary Amenorrhea N= 10	Total N= 1601
Endometriosis	42 (3.9%)	21 (4.1%)	0 (0.0%)	63
Fibroid	69 (6.4%)	32 (6.2%)	0 (0.0%)	101
More than One subtype	5 (0.4%)	7 (1.3%)	0 (0.0%)	12
Total	116(10.8%)	60(11.7%)	0(0.0%)	176

Table (4) shows the frequencies of the different identified acquired tubal abnormalities in the three study groups.

Ninety- one (5.68%) out of 1601 women who represent the whole study sample had got congenital anatomical uterine anomalies, which is significantly lower than that of acquired ones which was identified in 176(10.99%)out of 1601,P value<0.05(**Table 3**).

This study indicated that agenesis /dysgenesis represents the most frequent subtype among the Müllerian anomalies identified in the studied infertile women (54 out of 91(57.95%)), while septate class was the second frequent (13out of

91(14.77%)).On the other hand bicornuate class was present in 12(13.63%)) out of 91 women. The septate /bicornuate ratio was 1:1.

The unicornuate class was identified in 3 out of 91(3.40%) women. Four cases out of 91(4.54%) had got didelphic uterus, while "more than one class "was revealed in 5out of 91(5.68%)

Concerning the retroverted uterus 68 out of 1601 (4.24%)women had got retroverted uterus and presented with primary infertility, while 34(2.12%)out of 1601women with retroverted uterus and presented with secondary infertility, and the over all frequency of retroverted uterus was 102 out of 1601(6.37%) women .

Table 3. The frequencies of combined congenital and acquired uterine abnormalities in the 3 study groups.

Groups Uterine Findings	Primary infertility N =1070	Secondary infertility N=521	Primary infertility& amenorrhea N=10	Total N= 1601
Absent abnormalities	816 (50.96%)	409 (25.5%)	1 (0.06%)	1226 (76.57%)
Acquired abnormalities	116 (7.24%)	60 (3.74%)	0 (00.00%)	176 (10.99%)
Mixed abnormalities	6 (0.37%)	0 (00.00%)	0 (00.00%)	6 (0.37%)
Congenital abnormalities	64 (3.99%)	18 (1.12%)	9 (0.56%)	91 (5.68%)
Total	1070 (66.83%)	521 (32.5%)	10 (0.62%)	N=1601 (100.00%)
P- value	<0.05	<0.05	NS	<0.05

* P- value> 0.05 is not significant. Comparisons made using χ^2 test.

Table 4. The frequencies of different identified acquired tubal abnormalities in the three study groups.

Groups Tubal Abnormalities	Primary infertility N =1070	Secondary infertility N=521	Primary infertility& amenorrhea N=10	Total N= 1601
Dilated Tubes	45 (4.2%)	19 (3.7%)	0 (0.0%)	64
Blocked Tubes	149 (13.9%)	102 (19.9%)	0 (0.0%)	251
Tuberculosis	4 (0.37%)	2 (0.39%)	0 (0.0%)	6
Inflamed Tubes	29 (2.7%)	26 (5.0%)	0 (0.0%)	55
More than 1 abnormality	62 (5.7%)	28 (5.4%)	0 (0.0%)	90
Total	289 (18.0%)	177 (34.5%)	0 (0.0%)	466

Discussion

Congenital Müllerian defects are a fascinating clinical problem encountered by obstetricians. Many studies confirmed a strong association between congenital uterine anomalies and adverse reproductive outcomes^[16, 17, 18].The true incidence in the general population is hard to determine for two main reasons: most data are

derived from studies of patients presented with reproductive problems, and because accurate diagnosis and complete assessment of the uterine morphology has not always been performed^[1].

The frequency of the congenital anatomical uterine anomalies encountered in the infertile women enrolled in the current study was 5.49% which is similar to the figures revealed by other

studies^[1, 6]. Saravelos *et al* in 2008 reported that the prevalence of congenital anatomical uterine anomalies in a group of infertile women was 7.3% using laparoscopy and hysteroscopy^[13]. On the other hand, the overall frequency of retroverted uterus among the whole study sample was 6.37% ,in primary infertility was 4,24%, while in cases of secondary infertility was 2.12%. These frequencies are consistent with those of Ismail in 2007, who reported the presence of relationship between retroverted uterus and infertility^[12].

Raga *et al* in 1996, reported that 26.2% of a group of infertile women had got one or more Müllerian defects^[19]. Another study done by Acien in 1997 reported a frequency of Müllerian defects equals to 16.0% in again a group of infertile women^[7]. In fact, both figures are higher than that in this study. This difference may be due to the small sample size of patients that the current study has analyzed their data. On the other hand; the other studies used transvaginal ultrasound and three dimensional ultrasound rather than laparoscopy and HSG for the diagnosis of anomalies.

According to AFS classification; the frequency of class I (agenesis / dysgenesis) was 3.37% , septate uterus was 0.81% ,bicornuate uterus 0.74% ,unicornuate 0.18% ,didelphic uterus 0.31%,more than one subtypes 0.24% as already shown in Table 1. These frequencies are similar to that of Raga *et. al* in 1997^[6], who reported that the highest incidence encountered among different subtypes of uterine defect , excluding agenesis/ dysgenesis was that of septate type ,this picture is of clinical interest because of the fact that the septate type can be easily managed by therapeutic hysteroscopy^[6,20].

Agenesis/ dysgenesis represented the most frequent anomaly among Müllerian anomalies found in a group of 91 infertile women that this work revealed their possession of congenital uterine anomalies (59.34%). The uterine agenesis was shown in eight cases out of the total 91 cases (8.79%). This finding is similar to that of Vercillini *et al* in 1999^[12]. The higher figures by this study compared to that by Acien in 1996 may be due to the fact that most patients in western societies are more often seen in paediatric and endocrine clinics because of primary amenorrhea^[1, 22], in addition to the difference in the diagnostic methods^[19,20], socioeconomic status , racial factors or exposure to environmental factors possibly due to war conditions in Iraq

Among the 91 women with different congenital uterine anomalies ,bicornuate uterus was revealed in 12 (13.18%), this is similar to that of other study^[21], and unicornuate in 3 cases(3.2%), which is similar to that of Raga *et al* and Kovacicic *et al* , Martínez Reveles *et al*^[6,23,24].

Didelphic uterus was revealed in (5.49%) of those congenital uterine anomalies ,which is similar to that of other studies^[6,23,24], however , a study used the HSG only as a diagnostic method revealed that the frequency of didelphic uterus among total uterine anomalies was 0.8 % which is lower than that in this study^[23]. Those low figures , may be due to the fact that the diagnosis of Müllerian anomalies was based on incomplete analysis of the uterine morphology ,so the majority of cases with double uterus were misdiagnosed by HSG and classified as bicornuate^[1]. Having more than subtypes in 4 out of 91(4.39%) , however only few authors enlightened the presence of more than one class in one patient , and that was limited to presenting them in the form of case report^[25,26,27].

The ratio of septate /bicornuate uterus in this study was 1:1, which is similar to that of Raga *et al* who considered that infertile women had an increased incidence of bicornuate uteri^[6]. Estimates of the frequency of Müllerian duct anomalies vary widely owing to different patient populations, use of non - standardized classification systems, and differences in diagnostic data acquisition.

Although AFS classification system serves as a framework for description of anomalies, communication among physicians and comparison of therapeutic modalities, there is often a confusion about appropriate reporting of certain anomalies, particularly those with features of more than one class^[28]. Many of the anomalies are initially diagnosed when hystrosalpingography and ultrasonography are applied; however, further imaging is often required for definitive diagnosis and elaboration of secondary findings^[29,30].

At this time, magnetic resonance imaging is the study of choice because of its high accuracy and detailed elaboration of uterovaginal anatomy^[31]. Laparoscopy and hysteroscopy are reserved for women in whom interventional therapy is likely to be undertaken^[28].

Accurate diagnosis should be based on the estimation of the uterine serosal surface.

Thus, a combination of laparoscopy and hysteroscopy seems to be used to be necessary for the precise classification of uterine malformations and of course the best surgical treatment improving the fertility rates^[32,33]. Although almost most previous studies investigated women with history of recurrent pregnancy loss^[1,6,19,34], or infertility (as in the case of this study) , The difference in the rates uterine anomalies encountered by these studies compared to those in the reports of those studied women at low risk of having an anomalous uterus almost certainly reflect differences in study design^[6,8]. Comparisons between different studies are hampered not only by the differences in study populations, but also by differences in diagnostic

methods and criteria used to differentiate between various types of uterine anomalies^[8,35,36]. In respect to acquired anatomical uterine and tubal anomalies, this study revealed higher figures compared to those of congenital ones ($P<0.05$). This agrees with that of a study done by Marcus *et al* which maintained that infertility is generally caused by non congenital factors^[6,37].

It was concluded that the overall incidence of congenital anatomical uterine anomalies in infertile women attending the infertility unit in Mosul city was 5.68%. Highest frequency among Müllerian anomalies in infertile women was in Agenesis /dysgenesis, while septate class was the second one.

The frequencies of acquired anatomical (uterine and tubal) anomalies are significantly higher than that of congenital anomalies ($P<0.05$).

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