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Original Research Article

An observational study of effect of Mullerian anomalies on pregnancy

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ABSTRACT

Background: Mullerian anomalies occur in approximately 3-4% of fertile and infertile women, 5–10% of women with recurrent early pregnancy loss, and up to 25% of women with late first or second-trimester pregnancy loss or preterm delivery. However, due to low prevalence rate and asymptomatic course of the anomalies, Mullerian anomalies remain underdiagnosed and often overlooked as a possible cause of recurrent pregnancy failures, preterm deliveries, IUGR and low birth weight.
Methods: Total of 30 cases of Mullerian anomalies with pregnancy, prior diagnosed or incidental during LSCS, were studied for complications during pregnancy, history of gynecological complaints and rate of diagnosis with routine imaging technique.
Results: Septate uterus was the most common anomaly seen in this study (36.6%).56.6% were diagnosed incidentally during LSCS despite the fact 26.6% of cases had history of 2 or more abortions and 30% had some or other gynecological complaints previously. 10% of pregnancies ended in abortions, 20% had preterm delivery, 36.6% had malpresentations and there was case of rupture uterus (03.3%).
Conclusions: Mullerian anomalies are often asymptomatic or have subtle gynecological symptoms which are often missed by both patient and gynecologists. It is observed that due to the asymptomatic course of Mullerian anomalies, invasive nature of HSG and lack of 1.5 Tesla MRI at many institutes leads to low rate of diagnosis of Mullerian anomalies. Pregnancy with Mullerian anomalies often have preterm delivery, IUGR and malpresentation, so, require proper counselling and close monitoring during antenatal period.

Keywords: Malpresentation, Mullerian anomalies, Obstetrics complications, Preterm labour, Rupture uterus

INTRODUCTION

Normal development of the female reproductive tract involves a series of complex processes characterized by the differentiation, migration, fusion, and subsequent canalization of the Mullerian system.[1] Congenital anomalies of the female reproductive tract may involve the uterus, cervix, fallopian tubes, or vagina arise from defect in development of Mullerian ducts during foetal life. As per the various studies conducted previously, uterine anomalies occur in approximately 3–4% of fertile and infertile women, 5–10% of women with recurrent early pregnancy loss, and up to 25% of women with late first or second-trimester pregnancy loss or preterm delivery.[2,3] However, the true population prevalence of congenital uterine anomalies is difficult to assess partly because there are no universally agreed standardized classification systems and partly because the best diagnostic techniques are invasive and, therefore, rarely applied to low-risk study populations.

Most of the cases of Mullerian anomalies are either asymptomatic or have subtle gynaecological symptoms. But uterine anomalies are associated with diminished

cavity size, insufficient musculature, impaired ability to distend, abnormal myometrial and cervical function, inadequate vascularity, and abnormal endometrial development.[4] Because of these structural limitations, Mullerian anomalies in pregnancy often result abortion, preterm delivery, growth restrictions, malpresentations and ultimately increased rate of caesarean section.

Present study has been undertaken to assess the effects of the various Mullerian anomalies on the outcome of pregnancy in Indian scenario. Even with the advent of superior imaging modalities like 3D ultrasonography, CT scan, MRI etc. Mullerian anomalies remain an incidental diagnosis in majority of cases in India. This may be accounted to the limited resource setup in India and lack of health seeking attitude amongst infertile and reproductively challenged couples.

METHODS

The proposed study "An Observational Study of Effect of Mullerian Anomalies on Pregnancy was conducted in OBGY department at Lokmanya Tilak Municipal Medical College and General Hospital, a Tertiary Care Medical Centre over a period of two years from January 2015 to December 2017.

The proposed study had a sample size of 30 patients. It was a prospective observational study. Ethical approval of the study protocol was obtained from the ethics committee of institute.

Inclusion criteria

- All registered or referred ANC patients with diagnosed Mullerian anomalies. Patients with incidental diagnosis of Mullerian anomalies intraoperatively during LSCS.

Exclusion criteria

- Patients not willing to be included in the study.
- Infertility patients with Mullerian anomalies who have not conceived.
- Patient with severe co morbidities like severe pre-eclampsia, uncontrolled hypertension, gestational diabetes, maternal cardiovascular disease.

All Mullerian anomalies were classified according to American Society of Reproductive Medicine classification of Mullerian anomalies, 1988. As type I anomaly in ASRM classification is uterine aplasia, no cases were included in this study. The obstetrics profile that is age, parity and no. of previous abortions were studied. Duration of infertility, if any, was also assessed for each Mullerian anomalies.

Since, diagnosing Mullerian anomaly is difficult, timing and diagnostic modalities were studied in detail. Mullerian anomalies cases diagnosed on obstetrics ultrasonography, could not be confirmed on MRI as facility of 1.5 Tesla MRI is not available at our institution. Patients were also enquired about the various gynaecological signs and symptoms, if they experienced any, during their adolescence.

Obstetrics complications of Mullerian anomalies like threatened abortion, preterm delivery and malpresentation were studied diligently in details through indoor records and labor records.

Neonatal outcome was evaluated in form of birth weight and NICU/TCU admissions. All women were subjected to USG KUB postpartum to eliminate any associated renal anomalies.

RESULTS

A total of 30 cases of Mullerian anomalies in pregnancy were enrolled in this study to analyse the effects on pregnancy and its outcome. Out of the 30 cases, 4 (13.3%) were unicornuate uterus, 6 (20%) uterus didelphys, 2 (6.6%) uterus bicornuate, 11 (36.6%) were septate uterus and 7 (23.3%) arcuate uterus (Table 1).

Table 1: Different Mullerian anomalies studied in pregnancy.

Type of Mullerian Anomalies		Total no. of cases (n=30)	%
Type II: Unicornuate uterus	A1a: Communicating horn (with endometrial cavity)	00	0
	A1b: Non-communicating horn (with endometrial cavity)	02	06.6
	A2: Horn with no endometrial cavity	00	0
	B: No rudimentary horn	02	06.6
Type III: Uterus didelphys		06	20.0
Type IV: Uterus bicornuate	A: Complete till internal OS	01	03.3
	B: Partial	01	03.3
Type V: Septate uterus	A: Complete till internal OS	01	03.3
	B: Partial	10	33.3
Type VI: Arcuate uterus		07	23.3
Total		30	100

All the cases were categorized according to different age groups and 53.3% (16 cases) belonged to the age group of 20-30 years. 6 (20%) patients were < 20 years of age and 8 (26.6%) were above 30 years (Table 2). In the present study, majority of the cases (56.6%) were either 2nd or 3rd gravida, 6 (20%) were 3rd gravida and above

and 7 (23.3%) were primigravidas (Table 2). 40% of the patients had history of abortions. 4 (13.3%) had history of only 1 abortion and 5 (16.6%) had history of 2 abortions (Table 3).

There were 3 (10%) patients who had history 3 or more abortions. These patients were diagnosed as complete bicornuate uterus (Type IV A), complete septate uterus (Type V A) and partial septate uterus (Type V B).

The patient with complete septate uterus was 5th gravida but had 3 abortions and a preterm delivery resulting in neonatal death. Her present pregnancy also resulted in a preterm breech vaginal delivery at 29 weeks of gestation. Most of the Mullerian anomalies without any cervical or vaginal defect remain asymptomatic, however, often there are subtle gynaecological symptoms.

Most common gynaecological complaint was dysmenorrhea seen in 7 out of 30 cases (23.3%), followed by abnormal uterine bleeding, found in 5 out of 30 cases (16.6%). 2 patients gave history of chronic pelvic pain (6.6%) and endometriosis (6.6%) each (Table 4).

Table 2: Demographic profile of the patients.

Age	Type II: Unicornuate uterus	Type III: Uterus didelphys	Type IV: Uterus bicornuate	Type V: Septate uterus	Type VI: Arcuate	Total (n=30)	%
<20 years	01	01	01	02	01	06	20.0
20-30 years	03	03	00	06	04	16	53.3
>30 years	00	02	01	03	02	08	26.6
Total	04 (13.3%)	06 (20%)	02 (06.6%%)	11 (36.6%)	07 (23.3%)	30	100
Parity wise distribution							
Primi gravida	01	04	01	01	00	07	23.3
2nd-3rd gravida	03	01	00	07	06	17	56.6
>3 gravida	00	01	01	03	01	06	20.0

Table 3: Distribution according to previous pregnancy loss.

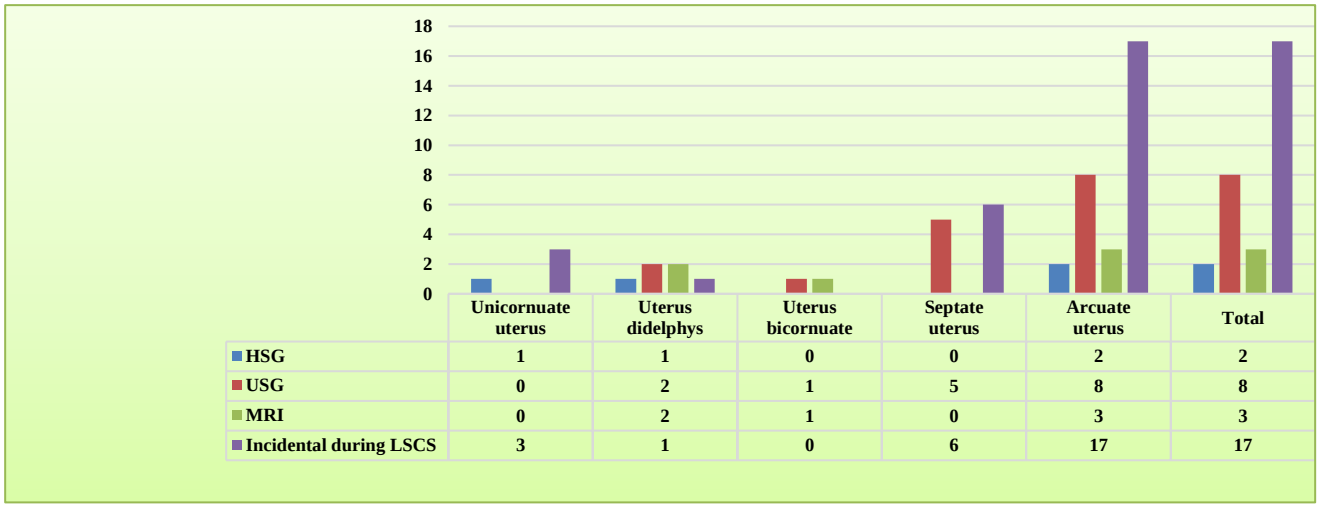
	Type II: Unicornuate uterus	Type III: Uterus didelphys	Type IV: Uterus bicornuate	Type V: Septate uterus	Type VI: Arcuate	Total (n=30)	%
No. of abortions	02	04	01	06	05	18	60.0
1 abortion	01	01	00	01	01	04	13.3
2 abortions	01	01	00	02	01	05	16.6
3 or >3 abortions	00	00	01	02	00	03	10.0
Total	4 (13.3)	6 (20)	2 (06.6)	11 (36.6)	7 (23.3)	30	100

Table 4: History of gynaecological complaints.

Gynaecological symptoms		Type II: Unicornuate uterus	Type III: Uterus didelphys	Type IV: Uterus bicornuate	Type V: Septate uterus	Type VI: arcuate	Total	%
No symptoms		02	03	00	09	07	21/30	70.0
Chronic pelvic pain		00	01	01	00	00	02/30	06.6
Dysmenorrhea		02	01	02	02	00	07/30	23.3
AUB		00	02	02	01	00	05/30	16.6
Endometriosis		00	01	01	00	00	02/30	06.6
Infertility	<5 years	01	02	01	02	00	06/30	20.0
	>5 years	00	01	01	00	00	02/30	06.6

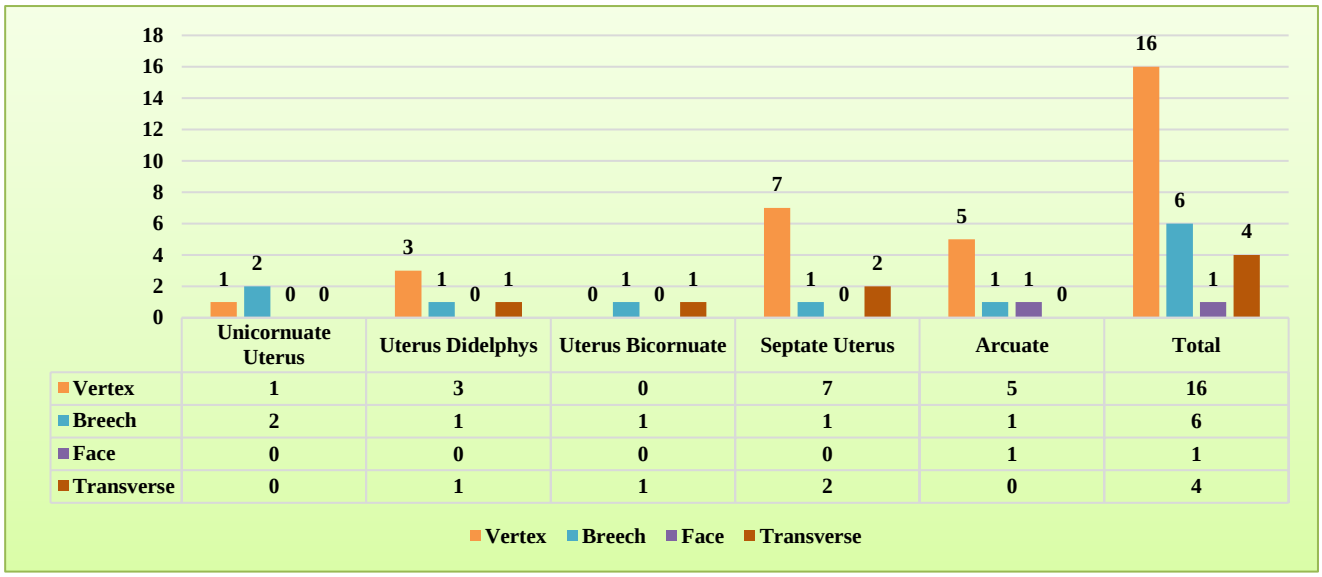
All the patients were enquired if they had any history of infertility (including both primary or secondary infertility) and undergone any kind of evaluation or treatment for infertility. Only 8 (26.6%) patients confirmed that they had history of infertility, out of which 2 (6.6%) had history of infertility of more than 5 years (Table 4). These two cases belonged to category of uterus didelphys (Type III) and partial bicornuate uterus (Type IV B). 56.6% of Mullerian anomalies in this study were

diagnosed incidentally during LSCS. 13 cases (43.4 %) were diagnosed either on HSG, USG or MRI (Figure 1). 8 cases (26.6%) were diagnosed on USG, 6 during pregnancy and 2 prenatally. 3 cases (10%) were diagnosed on MRI.



	Unicornuate uterus	Uterus didelphys	Uterus bicornuate	Septate uterus	Arcuate uterus	Total
HSG	1	1	0	0	2	2
USG	0	2	1	5	8	8
MRI	0	2	1	0	3	3
Incidental during LSCS	3	1	0	6	17	17

Figure 1: Diagnostic modalities.



	Unicornuate Uterus	Uterus Didelphys	Uterus Bicornuate	Septate Uterus	Arcuate	Total
Vertex	1	3	0	7	5	16
Breech	2	1	1	1	1	6
Face	0	0	0	0	1	1
Transverse	0	1	1	2	0	4

Figure 2: Distribution according to the presentation.

All these 3 cases were primigravidas with history of infertility. 2 cases (6.6%) were diagnosed on HSG as a part of their infertility workup.

These cases were unicornuate uterus with no horn (Type II B) and uterus didelphys (Type III). As malpresentation was the most common obstetric complication in this study (Table 5). A detailed analysis various presentation in different category of Mullerian anomalies was done. Vertex was the most common presenting part, seen in 16 out of 30 cases (53.3%). It includes all the positions (Figure 2). There was only 1 case of deep transverse arrest seen in G2P1IUFD1 with partial septate uterus (Type V B). Most common malpresentation encountered was breech, a total of 6 out of 30 cases (20%) followed by Transverse lie (13.3%) and face presentation (03.3%).19 out of 30 (63.3%) patients included in this study underwent LSCS (Table 6). Most common indication for LSCS was malpresentation, seen in 10 out 19 cases (52.6%). 2 out of 19 LSCS (10.5%) were done electively for infertility conception in a diagnosed of Mullerian anomalies. Normal delivery was done only in 7 cases out of the total 30 cases (23.3%). Forceps delivery was seen in a single case (3.3%) of partial septate uterus

(Type V B). Forceps were applied for foetal distress in a 2nd stage of labour. As malpresentation was the most common obstetric complication in this study. A detailed analysis various presentation in different category of Mullerian anomalies was done. Vertex was the most common presenting part, seen in 16 out of 30 cases (53.3%). It includes all the positions (Figure 2).

Table 5: Obstetrics complications.

Obstetrics complications	Type II: Uni cornuate uterus (%)	Type III: Uterus didelphys (%)	Type IV: Uterus bi cornuate	Type V: Septate uterus	Type VI: Arcuate uterus (%)	Total (n=30)	%
Threatened abortion	02/04 (50)	03/06 (50)	00/02 (0)	02/11 (18.1)	00/07 (00.0)	07/30	23.3
Abortion	01/04 (25)	01/06 (16.6)	00/02 (0)	01/11 (09.0)	00/07 (00.0)	03/30	10
Preterm delivery	00/04 (0)	02/06 (33.3)	01/02 (50.0)	02/11 (18.1)	01/07 (14.2)	06/30	20
Malpresentation	02/04 (50)	02/06 (33.3)	02/02 (44.4)	03/11 (27.2)	02/07 (28.5)	11/30	36.6
Rupture	01/04 (25)	00/06 (0.0)	00/09 (0)	00/11 (00)	00/07 (00.0)	01/30	03.3
No complication	00/04 (0)	01/06 (16.6)	00/09 (00.0)	07/11 (63.6)	04/07 (57.1)	12/30	40

Table 6: Mode of delivery.

Mode of delivery	Type II: Uni cornuate uterus	Type III: Uterus didelphys	Type IV: Uterus bicornuate	Type V: Septate uterus	Type VI: Arcuate uterus	Total (n=30)	%
Abortion	01	01	00	01	00	03	10
Normal	00	03	01	03	00	07	23.3
Forceps	00	00	00	01	00	01	03.3
LSCS	03	02	01	06	07	19	63.3
Total	04 (13.3%)	06 (20%)	02 (06.6%)	11 (36.6%)	07 (23.3%)	30	100

There was only 1 case of deep transverse arrest seen in G2P1IUFD1 with partial septate uterus (Type V B). Most common malpresentation encountered was breech, a total of 6 out of 30 cases (20%) followed by Transverse lie (13.3%) and face presentation (03.3%) 19 out of 30 (63.3%) patients included in this study underwent LSCS (Table 6).

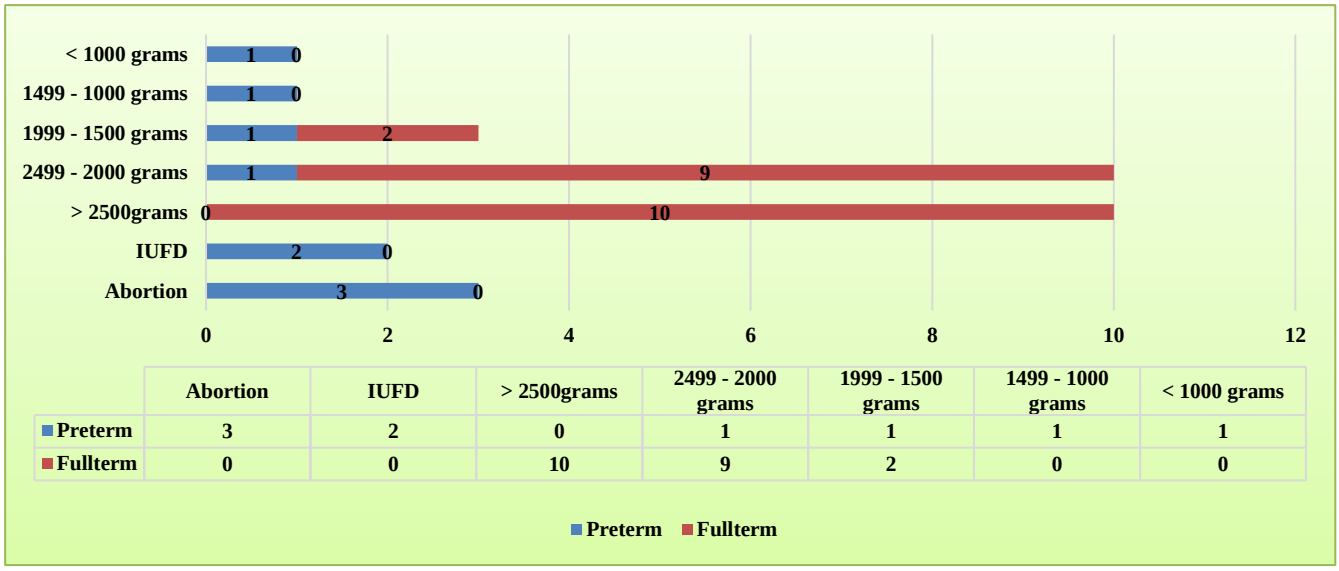


Figure 3: Distribution according to the foetal outcome.

Most common indication for LSCS was malpresentation, seen in 10 out 19 cases (52.6%). 2 out of 19 LSCS (10.5%) were done electively for infertility conception in a diagnosed of Mullerian anomalies. Normal delivery was done only in 7 cases out of the total 30 cases (23.3%). Forceps delivery was seen in a single case (3.3%) of partial septate uterus (Type V B). Forceps were applied for foetal distress in a 2nd stage of labour. Neonatal outcome has been described in terms of foetal weight, term or preterm delivery. There were 2 IUFDs (6.6%) in the study, both were preterm belonging to uterus didelphys (Type III) and complete bicornuate uterus (Type IV A). There were 3 abortions (09.9%). 21 out of 30 deliveries were full term, whereas there were 4 preterm live births (Figure 3). 15 out of 25 live births were low birth weight. Mullerian anomalies are often associated with renal anomalies. So, all the patients were subjected to an USG KUB to look for any renal anomaly. There was no renal anomaly in 73.3 % (22 out of 30 cases) of cases. Unilateral renal atresia was the commonest renal anomaly with the incidence of 13.3% (4 out of 30 cases) followed by ectopic kidney with the incidence of 10% (3 out of 30 cases) (Table 7). There was only one case of horseshoe kidney (3.3%) seen with complete bicornuate uterus (Type IV A).

Table 7: Associated renal anomalies.

Renal anomalies	Type II: Uni cornuate uterus	Type III: Uterus didelphys	Type IV: Uterus bicornuate	Type V: Septate uterus	Type VI: Arcuate uterus	Total (n=30)	%
No Anomaly	03	03	00	10	06	22	73.3
Unilateral renal agenesis	01	02	01	00	00	04	13.3
Horseshoe kidney	00	00	01	00	00	01	03.3
Ectopic kidney	00	01	00	01	01	03	10.0
Total	04 (13.3%)	06 (20%)	02 (06.6%)	11 (36.6%)	07 (23.3%)	30	100

DISCUSSION

In the present study incidence could not be calculated due to limited resources and time. However, a differential incidence has been provided within the sample size of 30 in this study. The most common anomaly encountered in the study was Type VB (10) that is partial septate uterus followed by Arcuate uterus. A metanalysis of 94 studies comprising of 89861 women was published in oxford journal to study the prevalence of congenital uterine anomalies in unselected and high-risk populations.[5] The prevalence of Mullerian anomalies was 5.5% in the low risk population, 8.0% in women with infertility, 13.3% in those with a recurrent pregnancy loss and 24.5% in those with both RPL and infertility. Arcuate uterus is most common in the unselected population (3.9%), and its prevalence is not increased in high-risk groups.[5] In contrast, septate uterus is the most commonly associated with obstetrics complication. Mullerian anomalies are often associated with recurrent miscarriages.[6] In the present study, 40% of patients had history of one or more abortions and 26.6 % cases had two or more abortions. Moreover, 10 % of pregnancies enrolled in this study also ended up as abortions. A metanalysis of 9 studies, published in journal of ultrasound in obstetrics and gynecology, documented that there is increased relative risk by 2.89 time of first trimester abortions in Mullerian anomalies.[7] Subgroup analysis showed that women with either subtype of canalization defect (sub septate or septate) have the maximum risk of first-trimester miscarriage. As present study was not a cohort study, author cannot comment on the relative risk, however, an increased rate of abortion was reported in all the categories of Mullerian anomalies. Subtle Mullerian anomalies are difficult to diagnose. HSG gives a view of the endometrial cavity but does not visualize the fundus and the uterine contour and is invasive. 2D ultrasonography gives a fair idea about the external contour of the uterus but might fail to visualize some lateral fusion defects. Magnetic resonance imaging (MIR) allowed for the avoidance of these issues while offering accuracy, thus becoming the gold standard diagnostic imaging modality.[8] Moreover, only 1.5 Tesla MRI can be used for diagnosing Mullerian anomalies in pregnancy which might be unavailable at some centre. These shortcomings of diagnosing modalities lead to a high rate (56.6%) of incidental diagnosis of Mullerian anomalies in the present study. In a recent study, it was found that 3D ultrasonography has accuracy similar or higher than MRI.[9] Although many women with Mullerian anomalies are asymptomatic, several gynecologic signs and symptoms are associated with specific anomalies. Fedele et al in 2006 found increased menstrual complaints in diagnosed cases of septate uterus10. 30% of patients in the study had gynecological complaints, most common being dysmenorrhea seen in 23.3% cases. Grimbizis et al. published a metanalysis studying 30 research papers on reproductive outcome in patients with Mullerian anomalies. In the present study maximum abortion rate was seen in unicornuate uterus but in the Grimbizis' metanalysis maximum abortion rate was seen in septate uterus.[11] This discrepancy can be attributed to the fact that most of the septate uterus studied in this research was partial in nature. Secondly, the sample size of unicornuate

uterus is too sample to be compared with result of the metanalysis. Preterm delivery rate is 20% in this study as compared to 39.3% preterm delivery rate reported in Hua et al.[12] Most of the research papers on reproductive outcomes in Mullerian anomalies stated that malpresentation was a common and a consistent complication associated with all Mullerian anomalies except arcuate uterus. Malpresentation was seen in 36.7% of cases in the present study. The current study reported a very high rate of caesarean section rate of 63.3% as compared to 34.7% in Hua et al.[12] This high rate can be justified by the fact 56.6% of cases included in this study were diagnosed incidentally during LSCS. Nagarathnamma et al published a paper on pregnancy outcome in uterine anomalies with a sample size of 10. They reported a very high pregnancy rate of 80%.[13] Mullerian anomalies are often associated with renal anomalies owing to embryological association of the urinary and reproductive system due to a close embryological association between them.[14,15] 26.7% cases had renal anomalies in the present study. These renal anomalies are often asymptomatic and may not have any significance in the pregnancy. However, for the complete documentation of the anomaly a detailed ultrasonography of the abdomen should be done to rule out renal agenesis, ectopic kidney, defect in ureteric system, horse shoe kidney etc.

CONCLUSION

The major concern which this study raises is the difficulty to diagnose Mullerian anomalies. It is observed that due to the asymptomatic course of Mullerian anomalies, invasive nature of HSG and lack of 1.5 Tesla MRI at many institutes leads to low rate of diagnosis of Mullerian anomalies. The study establishes that pregnancy with Mullerian anomalies often have preterm delivery, IUGR and malpresentation. These might result in a higher risk of caesarean delivery. Patients with Mullerian anomalies should have a detailed counselling session with senior obstetrician and consultants about all the anticipated maternal and neonatal complications.

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