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Original Research Article

Descriptive Clinical Analysis of Congenital Müllerian Anomalies and Associated Maternal and Foetal Outcomes in a Tertiary Care Centre: Indian Scenario

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Abstract:

Background and Objectives: Mullerian anomalies are malformations of the female genital tract. This research study was undertaken to evaluate the magnitude of congenital Mullerian anomalies in women & to analyze maternal and foetal outcomes of mullerian anomalies.

Methodology: In this study, 48512 females who were trying to conceive or had already conceived, attending the Obstetrics and Gynaecology department of Sultania Zanana Hospital and Gandhi medical college, Bhopal were enrolled for the observational study. A general examination was performed on all participants. USG and/or hysterosalpingography and MRI findings were recorded and the patients were followed until delivery for obstetric outcomes.

Results: In this observational study of 48512 female participants, 53 had Mullerian anomalies. Institutional deliveries were 16317 during the period of the study out of which 45 patients had anomalies that were compatible with pregnancy. Septate and arcuate uteri were the most prevalent anomalies seen in the current investigation.

Conclusions: The study found that pregnancies with Müllerian anomalies are associated with adverse pregnancy outcomes like recurrent abortions, IUFD (Intrauterine Fetal Demise) and malpresentations and close monitoring is required. Therefore, carefully planned studies are required to evaluate these associations more precisely.

Keywords: Müllerian anomalies,Recurrent abortions, IUFD (Intrauterine Fetal Demise) and Malpresentations, AMH (Anti Mullerian hormone)

Introduction

Congenital Mullerian anomalies are malformations of the female genital tract which result from the abnormal formation or resorption of Mullerian ducts during foetal development. The differentiation, migration, fusion, and subsequent canalization of the Müllerian system are characteristics of a series of intricate processes required for the normal development of the female reproductive system. However, errors in organogenesis cause these anomalies [1,2]. The urogenital system largely develops from the Mullerian ducts and without AMH (Anti Mullerian hormone) in females, the ducts develop into the uterus, fallopian tubes, cervix, and upper 1/3rd part of the vagina. The disruption in any signalling molecule or genes such as EMX2, HOAZA13, PAX2, and LIM1 can lead to mullerian duct anomalies [3].

The major spectrum of anomalies associated with Mullerian duct formation can be grouped as Agenesis; Anomalies due to defects of lateral fusion; Anomalies due to fusion between Mullerian ducts and urogenital sinus [4,5]. According to the type and degree of failure of normal development of the female genital tract, anomalies can be classified as: a) Hypoplasia: which may involve the vagina, cervix, or fundus; b) Unicornuate: when the associated horn is present; c) Didelphys: Complete or partial duplication of the Vagina, cervix, and uterus; d) Complete or partial bicornuate uterus; e) Complete or partial septate uterus f) Arcuate: a small septate indentation is present at the fundus; g) DES-related abnormalities: A T-shaped uterine cavity with or without a horn is present [6]. Females who have congenital abnormalities in the structure of their uterus often experience less favorable outcomes in terms of reproduction and are more likely to face complications during both pregnancy and childbirth [7,8]

Congenital Mullerian anomalies in the uterus, cervix, vagina, and fallopian tubes cause gynecological and obstetric complications. Data shows that these abnormalities affect 4% of women

and the prevalence of congenital uterine malformation lies from 5% to 25% [9]. Congenital uterine anomalies also have the potential to impact reproductive performance, leading to complications during pregnancy. Study by Min et al. indicated that individuals with canalization defects within the uterus exhibit the most compromised reproductive outcomes during the initial stages of pregnancy [10]

The major effect of congenital Mullerian anomalies can be seen in the reproductive potential of patients and almost all of them are associated with uterine abnormalities. Such anomalies cause primary or secondary infertility, ectopic pregnancies, recurrent pregnancy loss, foetal mortality, etc [3,11]. Mullerian anomalies have various spectrum of manifestations such as complete Mullerian agenesis results in an inability to conceive. The arcuate uterus is a mild concave indentation into the uterine cavity. However, it is currently challenging to estimate the true prevalence of Mullerian anomalies as various diagnostic techniques are being used for the classification [5].

Recently, three-dimensional (3D) ultrasound is being employed for diagnosis but classically, (2D) ultrasound, hysterectomy, and laparoscopy commonly done to detect Mullerian abnormalities. Transvaginal sonography and hysterosalpingography have improved the detection rates of uterine defects [12, 13].

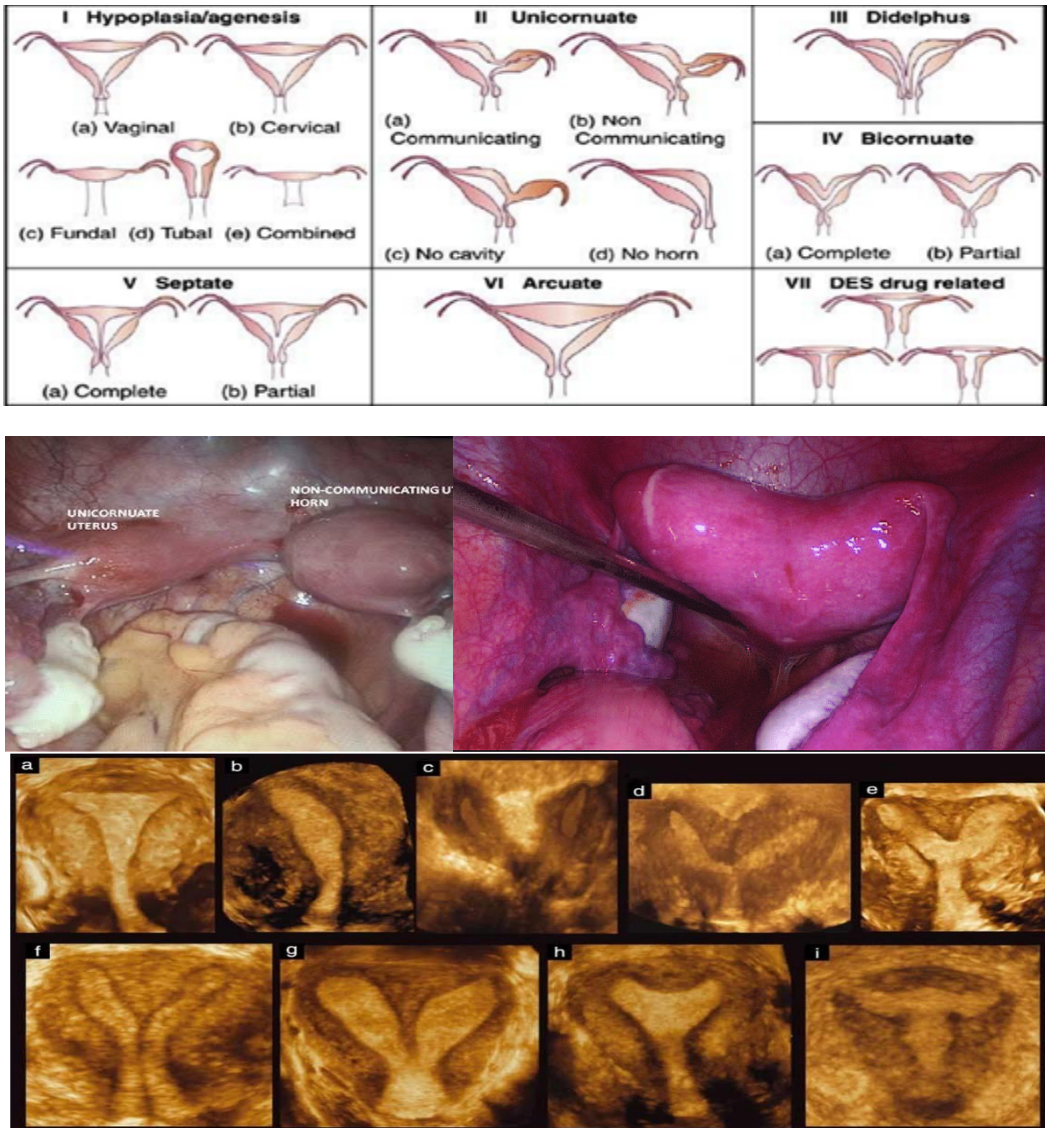

Figure 1: 1.1). American Fertility Society classification of uterine malformations 1.2) represents an image showing various Müllerian anomalies as visualized by 3D USG, 1.3) represents a Laparoscopic view of the unicornuate uterus; and 1.4) Laparoscopic view of the bicornuate uterus [14].

In India, due to limited resources and a low rate of health-seeking behaviour, Mullerian abnormalities remain undetected and are often detected incidentally during Caesarean operation as some minor defects associated with these abnormalities cause no problem in delivery. Hence the major perspective behind conducting this study is to determine the magnitude of congenital Mullerian

anomalies and ascertain the maternal-fetal outcomes in pregnant women with untreated reproductive tract anomalies in a tertiary care centre [15, 6].

Materials & Methods

This study was conducted in the Department of Obstetrics and Gynaecology, Sultania Zanana Hospital and Gandhi Medical College, Bhopal for the period of 17 months I.e., January 2020 to August 2021. Written informed consent was obtained after intimating the patients with the nature and purpose of the study from each patient. Before commencing the study permission from the institutional ethics committee, and university clearance was obtained.

Participants: Patients with congenital Mullerian anomalies attending the Department of Obstetrics and Gynaecology, Gandhi Medical College, and Sultania Zanana Hospital, Bhopal. Patients without congenital Mullerian anomalies, those with congenital Mullerian anomalies who visited for gynecological causes, and patients who were not willing to give informed consent for the study were excluded. All patients were included in the study according to the inclusion and exclusion criteria until the sample size was met.

Tools for assessment: Initially, a pretested questionnaire was employed for the data collection which contained information related to patients such as general demographic details, obstetric history, menstrual history, general examination, investigation details like MRI, Hysterosalpingogram and USG parameters. Patients were followed up with regards to the maternal and foetal outcomes.

Intervention: Study participants who visited the hospital between January 2020 to August 2021 were screened and enrolled after obtaining informed written consent. All details of obstetric history, menstrual history, gestational age, and presentation at the time of delivery and intrapartum details were noted.

Major obstetric outcomes that were studied include: a) Pregnancy outcomes: Live birth, stillbirth, IUFD, and abortion. b) Reproductive outcomes: Difficulty or failure to conceive, preterm labor, PROM, or an uneventful live birth. c) Maternal outcome: Morbidity in the form of rupture uterus, PPH, hysterectomy, and mortality. d) Foetal outcome: Prematurity, low birth weight, APGAR score, NICU admission, morbidity, and mortality.

Final analysis was performed after the collection of data which was entered simultaneously in the Statistical Package for Social Sciences (SPSS) version 23 and coded appropriately. The goals and objectives were taken into consideration when analyzing the data. To enumerate the sample's characteristics in terms of frequency and percentage, descriptive statistics were computed therefore, graphs and charts were prepared accordingly.

Table 1: Distribution of types of Müllerian anomalies and their subtypes

Type of Müllerian Anomaly	Frequency	Percentage
A) Unicornuate	5	9.5%
Type II: Unicornuate Uterus A1a Communicating Horn	1	1.9%
Type II: Unicornuate Uterus A1b Non- Communicating Horn	2	3.8%
Type II: No Rudimentary Horn	2	3.8%
B) Bicornuate	12	22.6%
Type IV B: Bicornuate Uterus Partial	12	22.6%
C) Septate	17	32.1%
Type V A: Septate Uterus Complete	3	5.7%
Type V B: Septate Uterus Partial	14	26.4%
D) Arcuate	17	32.1%
E) Didelphys	2	3.8%
Type III: Uterine Didelphys	2	3.8%
Total	53	100%

Distribution of patients was done according to various criteria and frequency of patients at various age groups where observed and it was found out that the majority (60.4%) of study participants were in the age group of 26-30 years. Where the majority of the participants i.e., 29 out of 53 were from rural residents. Out of 53 participants, 36 participants were unbooked and 32.1% were booked.

The participants were divided based on the site of placental attachment which represents the majority of people having anterior attachment i.e., 18 out of 51 (35.3%) however, only 3.9% showed previa attachment as represented in Table 2 The distribution of patients according to presentation and lie that is reported where 51.1% i.e., 23 participants showed breech presentation, and oblique lie was shown in only 2% of study participants.

Table 2: Distribution of patients according to site of placental attachment

Site of Placenta Attachment	Frequency	Percentage
Fundal	13	25.5%
Anterior	18	35.3%
Posterior	9	17.6%
Previa	2	3.9%
Low Lying	9	17.6%
Total	51	100.0%

In the current study majority of the participants were multigravida i.e., 58.5%. only 9.4% were grand multi gravida and 32.1% were primigravida. From the total of 53 participants, 31 out of 53 (58.5%) had a history of abortions. 34% had a history of one abortion and 20.8% had a history of two abortions rest had a history of three abortions. Table 3 section 3a represents the data for the type of Mullerian anomaly associated with history of abortion. It is evident that all congenital Mullerian anomalies are associated with abortions, with maximum incidents seen with septate uterus. Patients with a history of 3 or more abortions had a septate uterus. History of 1 or 2 abortions was associated with all other Mullerian anomalies.

In this study, the malpresentations are commonly observed in bicornuate, didelphys, and arcuate uterus. All the study participants with uterus didelphys had a breech presentation. Only 2 of the study participants had transverse lie, out of which one had a unicornuate uterus and one had a septate uterus as shown in 3b of Table 3.

Distribution of patients according to gestational age at delivery showed that 21 out of 45 (46.7%) participants had preterm delivery and 6 of them had post-term delivery. Association of mullerian duct anomaly with gestational age as depicted in section 3c of table 3 showed that preterm pregnancies were mostly associated with bicornuate uterus i.e., 42.9% followed by arcuate uterus (23.8%) and 50% of post-term pregnancies showed septate uterus rest 50% showed arcuate uterus.

Table 3: Type of mullerian anomaly associated with various factors.

Type of mullerian anomaly associated with	Type of Müllerian Anomaly						
3a. History of Abortion		1		2		3	
		Count	**N %**	**Count**	**N %**	**Count**	**N %**
	Unicornuate	3	16.7%	2	18.2%	0	0.0%
	Bicornuate	4	22.2%	2	18.2%	0	0.0%
	Septate	5	27.8%	3	27.3%	2	100.0%
	Arcuate	4	22.2%	4	36.4%	0	0.0%
	Didelphys	2	11.1%	0	0.0%	0	0.0%
3b. Presentation/Lie		**Breech**		**Cephalic**		**Transverse Lie**	
		Count	**N %**	**Count**	**N %**	**Count**	**N %**
	Unicornuate	0	0.0%	2	10.5%	1	50.0%
	Bicornuate	7	30.4%	5	26.3%	0	0.0%
	Septate	5	21.7%	6	31.6%	1	50.0%
	Arcuate	9	39.1%	6	31.6%	0	0.0%
	Didelphys	2	8.7%	0	0.0%	0	0.0%
3c. Gestational age at Delivery		**Preterm**		**Term**		**Post Term**	
		Count	**N %**	**Count**	**N %**	**Count**	**N %**
	Unicornuate	3	14.3%	0	0.0%	0	0.0%
	Bicornuate	9	42.9%	3	16.7%	0	0.0%
	Septate	2	9.5%	8	44.4%	3	50.0%
	Arcuate	5	23.8%	7	38.9%	3	50.0%
	Didelyphs	2	9.5%	0	0.0%	0	0.0%
3d. Mode of delivery		**Spontaneous vaginal delivery**		**Induced vaginal delivery**		**LSCS**	
		Count	**N %**	**Count**	**N %**	**Count**	**N %**
	Unicornuate	2	14.3%	0	0.0%	1	3.6%
	Bicornuate	4	28.6%	1	33.3%	7	25.0%
	Septate	4	28.6%	1	33.3%	8	28.6%

	Arcuate	4	28.6%	1	33.3%	10	35.7%
	Didelyphs	0	0.0%	0	0.0%	2	7.1%
3e. Foetal complications		**Low Birth weight**		**NICU admission**		**Depressed APGAR score**	
		Count	**N**	**count**	**N%**	**Count**	**N%**
	Unicornuate	3	14%	2	22%	0	0%
	Bicornuate	8	36%	5	56%	5	83%
	Septate	3	14%	1	11%	0	0%
	Arcuate	6	27%	1	11%	1	17%
	Didelphys	2	9%	0	0%	0	0%

According to the distribution of patients based on the mode of delivery, it was found that 28 out of 45 had LSCS hence it occurred as the most common mode of delivery whereas induced vaginal delivery was the rarest (section 3d, Table 3). In compliance with the data on mode of delivery out of 28 patients who underwent LSCS, 10 had an arcuate uterus and 8 had a septate uterus as represented in table 3 section 3d. In the study for pregnancy outcomes 81.1% had a live birth and 11.2 % had an abortion and it was most commonly seen in septate uterus i.e., 83% percent as represented in section 4a of Table 4.

Table 4: continued Table 3

Type of mullerian anomaly associated with	**Type of Müllerian Anomaly**							
4a. Pregnancy Outcome		**Live Birth**		**IUFD**		**Abortion**		**Ectopic pregnancy**	
		Count	**N %**	**Count**	**N %**	**Count**	**N %**	**Count**	**N %**
	Unicornuate	3	7%	0	0%	0	0%	1	50%
	Bicornuate	11	26%	1	50%	0	0%	0	0%
	Septate	13	30%	0	0%	5	83%	1	50%
	Arcuate	14	33%	1	50%	1	17%	0	0%
	Didelphys	2	5%	0	0%	0	0%	0	0%
4b. maternal complications		**Abruption**		**PPROM**		**PPH**		**Ruptured ectopic**	
		Count	**N %**	**Count**	**N %**	**Count**	**N %**	**Count**	**N %**
	Unicornuate	0	0%	2	18%	0	0%	1	50%
	Bicornuate	1	50%	4	36%	3	75%	0	0%
	Septate	0	0%	1	9%	0	0%	1	50%
	Arcuate	0	0%	3	27%	0	0%	0	0%
	Didelphys	1	50%	1	9%	1	25%	0	0%

PPH, PPROM, abruption and ruptured ectopic pregnancy were the maternal complications studied and it was observed that in the present study there were 2 cases of abruption and they were seen with bicornuate and uterus didelphys. PPROM was most commonly associated with bicornuate and arcuate uterus. PPH was observed in 4 cases, 3 were of bicornuate uterus and one was of uterus didelphys. Rupture of rudimentary horn with an ectopic pregnancy was seen in one case with unicornuate uterus and fallopian tube rupture was seen in one case of septate uterus with a tubal ectopic pregnancy which is depicted in the table 4 section 4b.

Association of foetal complications with mullerian duct anomalies showed that low birth weight which was seen in 22 out of 45 neonates was commonly associated with bicornuate uterus i.e., 36% followed by arcuate uterus (27%). 2.2% of the neonates showed an APGAR score between 0-3 which is a severely depressed APGAR score and is associated with bicornuate (83%) and arcuate uterus (17%). However, NICU admission was associated most commonly with the bicornuate uterus (56%) followed by unicornuate uterus (22%) as shown in section 3e of Table 3. Table 5 represent data that successful pregnancy was most commonly seen with an arcuate uterus (32.6%).

Table 5: Association of success rate of pregnancy and type of Müllerian duct anomalies

Type of Müllerian Anomaly	Pregnancy wastage		Successful pregnancy		Total
	Count	Row N %	Count	Row N %	
Unicornuate	2	20.0%	3	7.0%	5
Bicornuate	1	10.0%	11	25.6%	12
Septate	5	50.0%	13	30.2%	17
Arcuate	2	20.0%	14	32.6%	17
Didelphys	0	0.0%	2	4.7%	2
Total	10			43	53

Results

A hospital-based prospective observational study where total of 48512 obstetric cases were reported out of which 53 were diagnosed with congenital mullerian anomalies, who presented at Sultania Zanana Hospital Bhopal during the study period. However, only 16327 cases were available for institutional deliveries and reported number with CMA was 45 with viable pregnancy i.e. (Prevalance: 0.27%).

According to Table 1 among the different types of anomalies in the study, septate uterus and arcuate uterus were the most common type of anomaly with the occurrence frequency percentage of 32.1% each. While didelphys uterus was the rarest with 3.8%. The percentage of patients having a subtype of Mullerian anomaly where 9.5% had unicornuate uterus, 32.1% had arcuate uterus and 32.1% had separate uterus with rarest i.e., 1.9% having Unicornuate uterus A1a with a communicating horn.

Statistical Analysis:

The collected data was summarized by using frequency, percentage, mean & S.D. To compare the qualitative outcome measures Chi-square test or Fisher's exact test was used. To compare the quantitative outcome measures independent t test was used. If data was not following normal distribution, Mann Whitney U test was used. SPSS version 22 software was used to analyse the collected data. p value of <0.05 was considered to be statistically significant.

Discussion

Out of the entire cohort of 48,512 patients who attended the hospital either for conceiving or after conception, a total of 53 individuals were identified with Müllerian anomalies. Consequently, the observed prevalence of Müllerian anomalies within this cohort was determined to be 0.10%. During the study period, a total of 16,317 patients presented at the hospital for institutional delivery. Among them, 45 patients were diagnosed with anomalies that were consistent with pregnancy-related Müllerian duct anomalies. This results in an institutional prevalence rate of Müllerian duct anomalies of 0.27%. In the present study, the most common anomaly observed was the septate and arcuate uterus whereas the uterus didelphys was the rarest.

The majority of the study participants were in the age group of 26-30 years and the majority were unregistered and from rural areas (54.7%). It could be due to the fact that the desire for pregnancy is higher during this age group and lower awareness among rural residents complies with Mullerian anomalies. Generally, mullerian anomalies are frequently overlooked by both patients and gynaecologists but as it leads to premature delivery and abnormal foetal representation hence it requires close monitoring throughout prenatal phase [16].

Only 9.4% of the studied participants were found to be grand multi-para and the majority of them were multigravida. The data on the abortion history indicates that Mullerian anomalies are often associated with recurrent miscarriages. In the present study, 58.5% of the study participants had a history of abortions, the majority of them had one previous abortion followed by those who had a previous history of two abortions and 2 participants had a history of 3 or more abortions and a maximum number of abortions were seen in the septate uterus. This can be attributable to the partial form of the majority of the septate uteri investigated in this study.

46.7% of the study participants had preterm delivery and were most commonly associated with bicornuate followed by arcuate uterus. Malpresentation has been described as a frequent and consistent complication associated with all Müllerian anomalies in the majority of research studies. In this study majority (51.1%) of the participants had breech presentation.

Most of the participants had live births as per the data shown in this study. Abortion occurred in 11.3% of the study participants, 3.8% of study participants had IUFD and 3.8% of the participants had an ectopic pregnancy. However, Abortion was most commonly seen with a septate uterus and ectopic pregnancy was seen with a unicornuate uterus. Maternal complications were present in 17 out of 53 participants. Only 3.9% of the study participants had abruption and it was found that abruption was most associated with bicornuate uterus and uterus didelphys. Foetal complications were present in 26 out of 53 i.e., 57.8% of the study participants. The mean birth weight for this study was found to be 2407±587 grams and most of the

study participants had normal birth weight (>2500 grams) while 48.9% had low birth weight (<2500 grams). Successful pregnancy was seen in 43 out of 53 study participants which was most seen in the case of arcuate uterus. [17]

Some significant variation was observed in this study in comparison to the previously reported studies which is probably due to the difference in selection criteria, different diagnostic approaches, and insufficient evaluation of uterine morphology.

Conclusion

The study found that whereas pregnancies with Müllerian abnormalities are linked to abortions, those without them can result in preterm birth, IUFD, malpresentation, and a higher likelihood of Caesarean delivery. Reproductive tract abnormalities continue to be an incidental diagnosis in most cases in India, mainly because infertile women do not seek medical attention and there are not enough resources available. This has led to unforeseen effects for both the mother and the neonate. Close monitoring is required since pregnancy with Müllerian abnormalities poses a high risk of problems for both the mother and the foetus.

Since these procedures are now widely accessible, patients with Müllerian abnormalities should undergo a thorough assessment by USG, HSG, lapro- hysteroscopy, and MRI. This study highlights the potential clinical importance of Müllerian defects for female fertility. Therefore, to more precisely assess these correlations, well-designed prospective studies are needed. However, the major limitation of this study is its small sample size due to which the results of this findings can only be applied to settings that are similar to this study. Additionally, in the absence of a control group, it is impossible to draw a direct correlation between Müllerian malformations and poor pregnancy outcomes. However, considering data paucity in our country, our study is unique and a potential basis for further subject exploration by future researchers.

Declarations:

Funding: None **Availability of data and material**: Department of Obstetrics and Gynaecology, Gandhi Medical College, Bhopal **Code availability**: Not applicable **Consent to participate**: Consent taken **Ethical Consideration**: There are no ethical conflicts related to this study. **Consent for publication**: Consent taken

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