Original Research Article

Multifetal pregnancy reduction: Experience of past 25 years

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Abstract

Background: Objective: To analyze and share experience of performing multifetal pregnancy reduction (MFPR) over past 25 years with emphasis on technique, fetal loss rate, complications. **Methodology:** A retrospective analysis of the prospectively collected data of 975 patients with high-order pregnancies due to assisted reproduction were subjected to MFPR through ultrasound guided either transvaginal and transabdominal technique using KCl before 14wks weeks of gestation from January 1995 to December 2020 and compared. **Results:** out of total 975 MFPR patients, transabdominal approach was followed in 805 (82.56%) cases and for the remaining 170(17.43%) patient's, transvaginal route multifetal reduction techniques were performed. In 655(67.17%) cases triplets were successfully reduced and 251(25.74%) cases with twins' pregnancy were reduced to singletons. In 62(6.35%) quadruplet, 5(0.51%) quintuplet and 2 (0.2%) sextuplet multifetal reduction was successfully carried out respectively. Total 33 (3.28%) pregnancies were lost as a result of procedure. There were 18 (2.24%) cases of fetal loss observed with transabdominal procedure, while 14 (8.24) cases of fetal loss were observed with transvaginal procedure which is significantly higher ($P<0.05$). Complete loss of pregnancy was lowest with twins and increased with higher order multifetal pregnancy ($P<0.05$). Adverse Psychological impact (10.87%), premature delivery (3.28) and vaginal bleeding were the most prominent complications of the procedure. **Conclusion:** MFPR is a widely used technique for reduction of fetuses in multiple gestations for improvement in maternal outcome and survival of remaining fetuses and fetus. Significantly lower incidence of pregnancy loss and complications was observed with transabdominal process as compare to transvaginal route.

Key words: Multifetal gestation, MFPR, transabdominal route, transvaginal route, complications of MFPR

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INTRODUCTION

Increasing prevalence of couples with infertility and wide spread use of assisted reproduction technologies in last few decades has drastically increased the number of multifetal pregnancies. IUI and IVF are frequently used techniques for assisted reproduction which requires use of ovarian stimulatory hormones, contributing to increase in multifetal pregnancies.[1,2] According to US data of CDC report, the triplet and higher-order multiple birth rate (triplet/+) was 87.7 per 100,000 births for 2019, a 6% decline from 2017 (93.0) and down 55% from the 1998 peak (193.5). The triplet/+ birth rate (number of triplets, quadruplets, and quintuplets and other higher-order multiples per 100,000 births), rose more than 400% from 1980 to 1998.[3] Indian data regarding multifetal pregnancies has not been well reported but trend is increasing. This increase in the incidence of multifetal pregnancies is of much concern, as it also increases the morbidity and mortality of both the mother and fetuses. Greater the number of fetuses, greater the maternal and perinatal risk.[4,5] Complications pertaining to fetus may range from complete pregnancy loss and premature birth

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with short term sequelae such as respiratory and gastrointestinal complications, and long-term neurological impairment.[6] Maternal complications include hyperemesis, gestational diabetes mellitus, preeclampsia and postpartum hemorrhage, which if severe may be life-threatening to the mother and have a secondary impact on fetal outcome also.[7] Furthermore, the economic, psychosocial and social impact of multiple births on the patient and family is also huge affecting their quality of life to a great extent.[8-10] Therefore, it is necessary to opt for fetal reduction whenever feasible. In selective termination, (one or more) anomalous fetuses in a multifetal pregnancy are terminated while in multifetal pregnancy reduction (MFPR) the number of fetuses in gestation are reduced in order "to improve the chances of healthy survival in the remaining conceptuses and to reduce the hazards to the mother".[11] Apart from optimization of outcome, fetal reduction may be conducted for social reasons based on the patient's request. The 2006 International Federation of Gynecologists and Obstetricians (FIGO) Committee Report also suggests MFPR as ethical approach in order to save life and wellbeing of mother and fetuses.[12] Data related to MFPR is scares from India. Prevention of higher-order multifetal pregnancies is essential and requires careful monitoring of infertility therapies. The positive effect of MFPR on perinatal outcome is uncontroversial for triplets and higher-order pregnancies. Advances in perinatal medicine have substantially reduced mortality in premature triplet deliveries but NICU expenses are unusually very high for patients of developing country like India, and this should be taken into account when considering the potential benefit of MFPR. In this study, we report our experience of performing reduction in multifetal pregnancies over past 25 years with emphasis on technique, fetal loss rate, complications and why it is used in twins gestation etc.

METHODOLOGY

This was a retrospective analysis of the prospectively collected data from January 1995 to December 2020 from women coming with high-order multiple gestations for embryo reduction at the Dr. B I PATEL'S Gynob Sonoscan center, Ahmedabad.

Study population: Total 975 couples were included for the analysis coming for MFPR from our center. Mothers who refuse to give consent were excluded. All the patients were counseled to reduce the number of fetuses to two and in some it was advised to reduce the fetus to one as per the health of mother and fetus (multiple scars on uterus and high BMI or for family planning purpose), family socioeconomic and psychological condition of the patients.

Procedure: fetal reduction was done as an outpatient procedure IV general anesthesia using short Pentothal or local anesthesia for pregnancies between 12-14 weeks of gestation (55-85mm CRL). Routine sonography was done to evaluate nasal bone, neural tube defects and general anatomy survey in all selected patients for MFPR. Few patients came at 15-18 weeks of gestation for selective feticide in case of other twin is having anomalies as detection of anomalies was late due to lack of facilities in rural areas of India. In cases of Rh negative patients with their husband Rh positive, post procedural anti D given as per the standard treatment protocol. Before procedure, we have taken care of proper selection of fetus which is to be reduced. Procedure Approach was either using transvaginal sonography (TVS) or transabdominal sonography (TAS).

1. In Trans abdominal (TAS) Procedure, patient requires 4 hours stay in hospital. It is being done under local or general anesthesia (LA/ GA). Painting and draping for abdominal was done as like routine. Accuracy achieved because of the high resolution trans abdominal sonography guidance which is a free hand technique, rarely one can use a needle guide with software also. Before targeting the fetus for reduction mapping by 3D TUI of total uterus (Tomographic ultrasound imaging) done and under guidance of sonography continuous visualization of needle is possible. However, fetus is a moving object many a time instead of entry in the heart we may land up into a different part of fetal body to. (Like Thorax, abdomen, cranium, neck) avoid multiple needle entry as chance of abortion increased. Because of the continuous needle visualization complication can be prevented or it can be easily make out.
2. In TVS approach: it was being done under software guide with needle attachment so if movement of fetus is not there it will be convenient but if the fetus moves, we may land up into other parts of fetal body. For vaginal procedure we prepared vagina with 10% povidone iodine and was then thoroughly rinsed with sterile saline solution and drying to remove any traces of povidone iodine. Transvaginal ultrasound was used.

Selection of needle: Smallest bore, length of needle depends upon depth of target but we routinely use spinal needle of 23 gauze. Needle should be able to reflect sound wave so it remains visible throughout the procedure. Tip visualization is important to ensure hitting of target. Needle should be having sharp pointed end to minimizes the pain and risk of injury (should always use disposable). Disposable needle and stellate which gives a well recognizable echo-reflection, are used for the procedure so smoothly that only local anesthesia is sufficient.

Site of instillation: Site of instillation was directly in heart, in thorax and sub thorax region (95% cases) or fetal abdomen and intra cranial or other parts if fetus moves. Many a times when fetus remains in vertical position with head in up position; so, we tried to instill in cranium and got a very good response).

Method of MFPR: Different methods for MFPR is like; Intra-cardiac or intrathoracic KCl, Cardiac puncture with air embolization, Intra-cardiac puncture - no KCl - till asystole, exsanguination - aspiration of blood from heart of fetus till asystole is achieved. Aspiration of embryo (7-9wks) by under guidance of trans abdominal sonography, Cervical dilation and aspiration of gestational sac with large bore needle etc. We used injection KCl (2 ml of 2 mEq/ml) method for MFPR. In some of cases where reduction done after 16-18wks selective feticide for anomalies fetus. In those conditions we use Low Molecular Weight Heparin (LMWH) daily to patient, as dead tissue mass was higher; to prevent the effect of micro embolization to other remaining fetuses.

Post-procedure care: The patients were given prophylactic antibiotics 1 g of IV cefotaxime before the procedure and were discharged after 3 hours with antibiotics and uterine relaxants like is oxsuprine. Follow-up ultrasound examination was done 1 week after the procedure. All patients received routine antenatal care and follow-up of the pregnancy except for those who traveled to other cities of India.

Outcome measures: The number of procedures by transabdominal and transvaginal route and pregnancy loss was analyzed and compared with number of higher order pregnancy and number of fetuses. Reason for selection for route of procedure, site of instillation and time to cease the cardiac activity was also recorded and compared. Complications of the MFPR were also analyzed.

Statistical analysis: Data is analyzed using Microsoft excel 2013. Data is presented as actual frequencies, percentage, mean and standard deviation. For comparison of fetus loss by transabdominal and transvaginal route, chi-square test was used and p value less than 0.05 was considered significant.

RESULTS

Total 975 patients reported to our center from January 1995 to December 2020 with multiple pregnancy requiring MFPR. Fetal reduction was performed on total 975 cases out of which, transabdominal multifetal reduction approach was followed in 805 (82.56%) cases and for the remaining 170 (17.43%) patient's, transvaginal multifetal reduction techniques was employed. Based on number of fetuses, total 655 (67.17%) cases with triplets were found to be the major category of patients who were successfully subjected to multifetal reduction followed by 251 (25.74%) cases with twins' pregnancy. Successful attempt of multifetal reduction was carried out with 62 (6.35%) quadruplet, 5 (0.51%) quintuplet and 2 (0.2%) sextuplet cases respectively. (Table 1). All the pregnancies were either a result of intrauterine insemination or in vitro-fertilization. Major criteria for selecting the vaginal approach were higher BMI, multiple scars over abdomen, multiple myoma or lower lying fetus is anomalous in twins in this study. Table 2 showed the fetal loss after the procedure. Overall, out of total 975 pregnancies, 33 (3.28%) were lost as a result of procedure. There were 18 (2.24%) cases of fetal loss observed with transabdominal procedure, while 14 (8.24) cases of fetal loss were observed with transvaginal procedure. Pregnancy loss rate is significantly higher with transvaginal route ($P<0.05$). Higher incidence of total pregnancy loss, severe preterm birth and long term morbidity was found in women with triplets and higher number of fetus transferred during artificial gestation. The magnitude of risk depends on the number of fetus implanted ($P<0.05$) and their chronicity which has been assessed in present study population and quoted in Table 2. Monitoring of duration of cessation of cardiac activity post injecting lethal dose of KCl at different sites revealed that injection in chambers of fetal heart and fetal cranium leads to immediate fetal cardiac arrest within 5 to 10 seconds, while injection in fetal thorax (10-25 seconds), diaphragm (20-40 seconds) and abdomen (50-120 seconds) takes more time for cessation of cardiac activity as shown in table 3. All the patients were assessed for the complications related to the procedure and analysis is shown in table 4. Serious adverse complications pertaining to the procedure employed for multifetal reduction was found to be less than 10%. Adverse Psychological impact (10.87%), premature delivery (3.28) and vaginal bleeding were the most prominent risk associated with first trimester multifetal reduction. Incidence of procedure related problems like infection and in monochromic pregnancy (MCDA) total five pregnancy were 2 continue for full-term but 2 were having loss after 1 moth and while in one it was complete loss within 2-3 days. (We usually never council for fetal reduction in MCDA.)

Table 1: Total number of cases for Fetal reduction included in the study (n=975)

Fetus numbers	Total no. of cases (n=975)	Trans-abdominal (n=805)	Transvaginal (n=170)	Method for conception (IUI or IVF)
Triplet	655	575	80	IUI – 101 IVF - 554
Quadruplet	62	50	12	IUI – 9 IVF - 53
Quintuplet	5	1	4	IUI – 2 IVF – 3
Sextuplet	2	0	2	IUI – 2 IVF – 0
Twins (Selective fetal reduction in twins)	251	179	72	IUI – 51 IVF - 200

Table 2: Pregnancy loss rate and its comparison with number of fetuses in the study

No. of fetus	Total loss (n=33)	Total Loss in transabdominal route (n=805)	Loss by transvaginal route for MFPR (n=170)
≥6	1	0	1 **
5	1	0	1
4	2	0	1
3	28	18	10
2 (twins)	1	0	1
Total	**33 (3.28)**	**18 (2.24)**	**14 (8.24)***

*P<0.05; suggesting significantly higher pregnancy loss by transvaginal route for MFR.
**FCP-fetal cardiac pulsation disappear after few days of the procedure

Table 3: Cessation of cardiac activity in comparison to Site of instillation

Site of instillation	Time for cardiac activity cessation (in seconds)
Direct in heart	Range(5-11 seconds)
Direct in thorax	Range(10-25 seconds)
Supra diaphragmatic	Range(20-40 seconds)
Intra-abdomen	Range(50-120 seconds)
intracranial	Range(5-10 seconds)

Table 4: Complication of the procedure: (n=975)

Complications	No of patients (%)
Infections	3 (0.31)
Bleeding	20 (2.05)
Damage to the nearby gestation sac	1 (0.1)
Technical failure	1 (0.1)
Abortion/Premature labor/ leaking	32 (3.28) [30 (before 32 weeks);2 (after 32 weeks)]
Psychological impact	106 (10.87)
Monochorionic placentation and its problems (MCDA- 5 (3 live normal 2 both FCP loss)	5 (0.51)

*MCDA- monochromic diamniotic, FCP- Fetal cardiac pulsation

DISCUSSION

Over past one decade there has been a dramatic increase in multiple gestations due to assisted reproductive technologies. Multifetal pregnancy prominently in case of presence of more than two fetus increases the incidence of perinatal and obstetric mortality including maternal mortality.[13,14] Multifetal pregnancy with triplets demonstrate a fetal mortality rate of 5-25% with 15% of newborns fail to survive the infancy duration.[15] Multifetal pregnancy reduction led to improved outcomes related to reduction in mortality rates and successful birth were observed and is steadily increasing during last decade.[16-18] Singletons were associated with lower rate of morbidity and longer gestation periods with minimum risk of premature births and early miscarriage.[19] MFPR is most commonly performed using transabdominal approach. Transvaginal ultrasound guided multifetal reduction technique is used during 8th to 11th week of gestation by puncturing the fetal heart area and injecting potassium chloride (KCl) solution and simultaneously observing the fetal sacs and monitoring the cardiac activity. Selection of transvaginal multifetal reduction techniques is followed

for reduction of fetus with closer proximity to vaginal probe early in trimester of gestation. The double needle method has lower risk of uterine contraction but is commonly associated with infection and maternal intravascular coagulopathy with high serum alpha-fetoprotein.[20] Trans abdominal techniques are the most preferred, skillful and safe techniques performed within 9-14 weeks of gestational period employing NaCl/KCl injection near the fetal heart accompanied with amniotic fluid aspiration.[21] Compared to transabdominal technique, transvaginal technique is associated with a higher risk of miscarriage due to injection of NaCl solution into the fetal thorax resulting into limb reduction or anencephaly.[22,23] The relative loss of pregnancy was higher in transvaginal approach compared to trans-abdominal approach in this study which was consistent with previously reported studies by Ilan E. Timor-Tritsch *et al.*[24] Our data suggest that MFPR has been considerably successful on many patients with transabdominal technique, with reduced pregnancy loss and premature deliveries. Overall assessment of pregnancy loss suggest that triplets and higher order fetal gestations were more prone to have fetal loss compared to twins and singletons. This may be attributed to decomposition of placental tissues and fetal tissues which was found to be consistent with results noted in previous studies.[25] MFPR procedure needs intense care to avoid miscarriage which is the major complication after embryo reduction. On comparison of time for cessation of cardiac activity for different site of instillation of KCl solution, it was observed that direct injection of KCl in heart and intra-cranial injection consumes minimum duration for cessation of cardiac activity followed by intra-thoracic and supra and sub diaphragmatic injection. We also found that intra-abdominal injection consumes maximum duration for cessation of cardiac activity prolonging the duration of the surgical process and increasing the incidence of technical difficulties during the surgery. These duration of cessation of cardiac activity were similar to previously reported studies by Lambet *et al.*[26] The benefits of embryo reduction far outweigh the risks associated with the procedure, however few complications are associated with all techniques of fetal reduction. As multifetal pregnancy reduction is emotionally difficult for most of the couples, its psychological impact was found to be the most common complication among patients undergoing fetal reduction procedure. Majority of females suffer from multiple depressive disorders followed by depression and severe psychiatric symptoms which was also observed in our study.[27] This stress can be easily managed by proper counselling of the patients. In our study, rate of abortion was found to be 3.8%. It was also observed that less than 5 percent of women suffered from premature delivery or abortion and bleeding during the surgical process, indicating higher rate of success of transabdominal approach in multifetal reduction.[27] proper use of technique in experienced hands can reduce the chances of abortions. Infectious complications like ammonites can be prevented by talking proper aseptic precautions. This study has highlighted the huge data related to MFPR for last 25 years. Its techniques and complications are also analyzed. Some limitation of the study is that it is having data from the single center only. More prospective comparative studies should be carried out on this issue.

CONCLUSION

MFPR through transabdominal approach significantly reduces the risks of pregnancy loss as compared to transvaginal route. Fetal loss is directly proportional to the number of fetuses. Still, transabdominal MFPR significantly reduces the risk of pregnancy loss in triplets and higher-order pregnancies to a greater extent with minimal complications. Still there a room for assessment of possible risk and success rate associated with transabdominal approach of multifetal reduction.

Ethical considerations: multi-fetal pregnancy reduction (MFPR) is an ethically acceptable procedure aimed to increase survival and well-being of the remaining fetuses from higher-order multifetal gestations. This study was approved by the ethics committee and written informed consent was obtained from all the patients included in the study. All couples were counselled about the risks and benefit of the procedure, technique and assured about the feasibility of the procedure and confidentiality of their record. They were given chance to clarify all the questions they have regarding procedure before giving consent.

Consent to Participate: All the participants were explained clearly about the nature and purpose of the study in the language they understood and written informed consent was obtained from them. All the participants were ensured that their identity will not be revealed at any stage of the study.

Availability of Data and Material: The detailed data can be obtained from corresponding author if required.

Competing Interest: The authors have no competing interest to declare.

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Author's Contribution: Dr. B. I Patel has designed the concept of the study and literature review. Dr. Nisha Patel and Dr. Saumil Patel has contributed in data collection and data analysis. Dr. Vipali Trivedi has contributed in treatment of patients and manuscript writing.

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