Cohort Study

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Trans-abdominal fetal reduction in higher order multiple pregnancies: a pioneer cohort retrospective study in Nepal

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Objective: To share the initial experience of trans-abdominal multifetal pregnancy reduction (MFPR) in Nepal.
Method: The procedure was performed in 108 patients in a private hospital over a period of 3 years. Under ultrasound guidance, intracardiac injection of 0.2–3.0 ml of 15% w/v (2 mEq/ml) potassium chloride (KCl) was administered via trans-abdominal route.
Results: A total of 108 fetal reduction procedures were carried out at the seventh to fifteenth weeks of gestation, a maximum of 44 (40.7%) of which were done at the ninth to tenth weeks of gestation. A total of 123 fetuses were reduced. Out of total 108 multifetal pregnancies, 96 (88.8%) were due to in-vitro fertilization (IVF). Eighty-five pregnancies (78.7%) underwent reduction from triplet to twin. The second-time reduction was needed in five cases. Two attempts (in the same sitting) were required in three cases. The inadvertent demise of the second fetus was noted in three cases of dichorionic tri-amniotic triplet pregnancy.
Conclusion: Ultrasound-guided trans-abdominal fetal reduction performed between the seventh and twelfth weeks of gestation is safe and effective.

Keywords: in-vitro fertilization (IVF), multifetal pregnancy reduction (MFPR), potassium chloride (KCl), trans-abdominal ultrasound-guided fetal reduction

Introduction

Assisted reproductive technology and stimulated conception have led to an increase in the prevalence of high-order multifetal pregnancies (MFPs) in recent times[1,2]. Two to four embryos are often transferred after in-vitro fertilization (IVF) to increase pregnancy rates[3]. MFPs are associated with high maternal and fetal complications[4,5]. Fetal mortality and morbidity are due to complications of prematurity[6,7]. Prevalence of pregnancy-induced hypertension, pre-eclampsia, eclampsia, antepartum hemorrhage, post-partum hemorrhage, gestational diabetes and difficult deliveries are more in mothers with MFP[8,9]. Embryo/Fetal reduction in high-order MFPs helps in the prolongation of gestation[10]. Studies have shown multifetal pregnancy reduction (MFPR) to be a secondary prevention of the risks associated with MFP[11]. Trans-abdominal intracardiac injection of KCl is a simple, safe and effective technique for MFPR[12]. We are among the first few centers in the country doing MFPR. In this study, we are sharing our initial experience of the procedure.

HIGHLIGHTS

- Trans-abdominal ultrasound-guided embryo/fetal reduction performed between the seventh and twelfth weeks of gestation is safe and effective.
- Intracardiac injection of potassium chloride (KCl) in monochorionic twins should be avoided, and an alternative method for fetal reduction is advised.
- The law regarding fetal reduction should be formulated in the country at the earliest.

Materials and methods

A retrospective cohort study was done in a total of 108 cases of MFP referred from the obstetrics and gynecology department of our hospital, different other hospitals and IVF centers across the country. They underwent ultrasound-guided trans-abdominal embryo/fetal reduction procedure between February 2018 to April 2023 in our department. Ethical clearance for the study was secured from the institutional review committee. Patient consent requirements were waived by the institutional review committee, given the retrospective nature of the study. The procedures were done by the principal author with experience of 14 years in the field of fetal imaging. A detailed review of the medical condition of the patients was done first. After that, an ultrasound evaluation was carried out by the principal author to assess the number of embryos/fetuses, gestational age by CRL, the well-being of the

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Figure 1. Pre-reduction color doppler ultrasound images of a 9-week trichorionic tri-amniotic triplet pregnancy. The number of fetuses, gestational age by CRL, the well-being of the fetuses, chorionicity/amniocity, placental localization and feasibility of trans-abdominal needle puncture are evaluated. Blue and red color in all three fetal thoraces indicate fetal cardiac activity. CRL, crown rump length.

embryos/fetuses, chorionicity/amniocity, placental localization and feasibility of trans-abdominal needle puncture (Fig. 1). The couple was counseled in detail about the potential risks of the technique and informed written consent was obtained before the procedure. The patient was admitted to the hospital a few hours before the procedure and discharged the very next day if no complications occurred.

The procedure was carried out in an operation theater under general anesthesia (1% Propofol) with the patient in the supine position. LOGIQ E10 ultrasound machine of GE Healthcare with 4C-RS convex probe (bandwidth 2–5.5 MHz) was used for the procedure. Trans-abdominal ultrasound assessment was done before the anesthesia to confirm the viability of fetuses and plan needle insertion. All standard aseptic precautions were taken like cleaning the ultrasound probe and abdominal wall with 5% betadine and draping. Under real-time ultrasound guidance, a 22G spinal needle was advanced to the embryonal/fetal heart after puncturing the abdominal wall, anterior uterine wall, and gestational sac (Fig. 2). Easily accessible sac, which most of the time was the upper, and anterior sac was entered. The gestational sac near the cervix was avoided. When possible, an embryo with a small size was chosen. Care was taken not to traverse the needle through the placenta and other gestational sacs, which were not planned for reduction. After puncturing the heart, potassium chloride (KCl) 15% w/v (2 mEq/ml) was injected at 0.2 ml incremental dose until the cardiac activity was arrested. The cessation of cardiac activity was rechecked 5 min after the procedure (Fig. 3). The patient was observed in the maternity ward for 1 day with the use of tocolytics and a single dose of injection progesterone. Embryonal/fetal demise was confirmed the next day before discharging the patient. A new needle was used each time an insertion was made through the abdominal wall. However, if the location of the sacs permitted, the additional sacs were penetrated with the same needle without reinserting it through the abdominal wall. The patients were discharged after 24 hours if the absence of fetal cardiac activity in the reduced fetus was confirmed (Figs. 4A, B), the viability of the remaining fetuses ensured and no other complications were seen. Oral tocolytic was continued for one week to avoid uterine contraction. The patient was followed up with an obstetric ultrasound 1 week later in every case. All patients underwent routine antenatal follow-ups subsequently.

The research was retrospectively registered on clinicaltrial.gov. All the patients' data including name, age, period of gestation, modes of conception, total number of fetuses, number of fetuses reduced, amount of KCl required for each reduction were entered

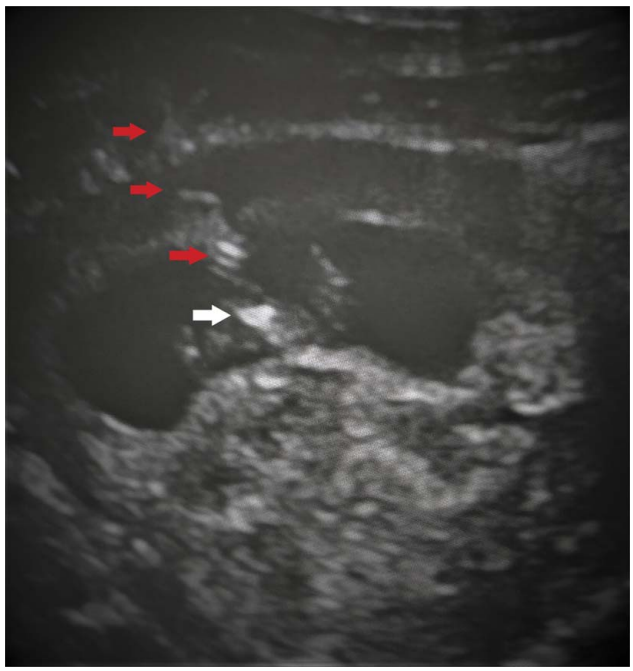

Figure 2. Gray scale two-dimensional ultrasound image of the 22G spinal needle coursing through the abdominal wall, anterior uterine wall, and gestational sac (red arrows). Tip of the needle is seen in the fetal heart (white arrow). The fetus in right antero-superior sac was chosen for reduction due to technical ease. After injection of 0.8 ml of potassium chloride, the fetal heart stopped beating.

Figure 3. Post-reduction color doppler ultrasound image of the 9-week trichorionic tri-amniotic triplet pregnancy (picture taken at recheck ultrasound done after 5 minutes of absence of cardiac activity). Blue and red colors are seen in two fetal thoraces indicating presence of fetal cardiac activity. Absence of color in thorax of fetus in right antero-superior sac indicates absence of fetal cardiac activity and hence successful reduction. The pregnancy can now be labeled as dichorionic diamniotic twin pregnancy.

in Microsoft excel 2019 version by the principal author and rechecked by the coauthors. The results in form of percentage and mean were calculated in Microsoft excel 2019. The work has been reported in line with STROCCS criteria[13]. Tables and diagrams were made in Microsoft Word.

Results

Out of the total of 108 procedures, 1 (0.93%) was performed between seventh and eighth weeks of gestation, 13 (12.03%) between eighth and ninth weeks of gestation, 44 (40.7%) between ninth and tenth weeks of gestation, 30 (27.7%) between tenth and eleventh weeks of gestation, 15 (13.9%) between eleventh and twelfth weeks of gestation, 2 (1.85%) between thirteenth and fourteenth weeks of gestation and 1(0.93%) each at fourteenth to fifteenth and fifteenth to sixteenth week of gestation. MFPR was carried out between seventh to twelfth weeks of gestation in all but five cases, which were done at thirteenth, fourteenth, and fifteenth weeks of gestation. 4 out of 5 of these cases had congenital malformation in one of the fetuses, and selective reduction of the malformed fetus was done. The remaining one was attempted at the fifteenth week because of failed reduction at the eleventh week of gestation. 96 (88.8%) pregnancies were conceived from IVF, 9 (8.3%) spontaneously, and 3 (2.7%) from intrauterine semen injection.

Of 108 MFP, 89 had triplets, 10 quadruplets, and 9 twins. 85 (78.7%) reductions were from triplet to twins, 9 (8.3%) each from quadruplet to twin and twin to a singleton pregnancy, 4 (3.7%) from triplet to singleton pregnancy, and the remaining 1 (0.93%) from quadruplet to singleton pregnancy.

The average time required for the embryo reduction was 10 minutes per sac in early gestation (6th–9th weeks), increasing to 15 minutes per sac for late procedures. This was due to increased mobility and fetal size leading to different levels of difficulties in these patients. The average amount of 15% w/v (2 mEq/ml) KCl required for reduction was 0.75 ml. A minimum of 0.2–3.0 ml was required (Table 1). All reduction procedures were successfully performed in a single session except for five cases (4.6%) where a second reduction was needed. Two attempts in the same session were required in three cases(2.7%). In two of those cases, the heartbeat stopped and reappeared within five minutes; in the remaining one case, 0.4 ml KCl was inadequate to stop the heartbeat, and additional KCl had to be administered a second time. In rest of the two cases, heartbeat was seen in the fetus in the evaluation done the next day. Due to logistic reasons, the reduction was reattempted at fifteenth week of gestation, which became successful. The inadvertent demise of a second fetus sharing the same placenta was seen in three dichorionic triamniotic triplet pregnancies. In the rest of the 2 dichorionic triamniotic triplet pregnancies, intracardiac KCl injection was given to the fetus not sharing the same placent with the other fetus, and no such complication was seen. The fetal loss rate is 0.92%. There was no pregnancy loss. Subchorionic hematoma developed in one case (0.93%), which was resolved in subsequent follow-up.

Congenital anomalies in the form of sacrococcygeal teratoma was seen in one case and anencephaly in two cases and omphalocele and anencephaly combined in one case. The selective reduction of fetus with sacrococcygeal teratoma was done in fifteenth week of gestation. Two twins with anencephaly were reduced in thirteenth and fourteenth week of gestation. The remaining one twin with both anencephaly and omphalocele was reduced in thirteenth week of gestation. No immediate complication was seen in these patients.

Only four patients could be followed till delivery since other patients were referred from other hospitals or IVF centers around the country. Of those pregnancies, three cases (5.4%) did not end well. In one case, there was the death of one twin due to birth asphyxia; in another case, there was the expulsion of one twin at the eighteenth week of gestation, and the cerclage procedure of the cervix was carried out to preserve the next twin. Premature delivery and demise of both twins due to respiratory distress and hypoxic-ischemic encephalopathy at 26 weeks of gestation were seen in the remaining case.

The aim of fetal reduction is not only to prolong pregnancy in MFP but also to selectively terminate fetuses with a congenital malformation[14]. Out of the total of 9 reduced twin pregnancies, 4 had a severe congenital malformation in one of the twins. One twin pregnancy was reduced to singleton pregnancy since the mother had undergone surgery for atrial septal defect closure. Some people might question the ethical aspect of MFPR but it is done with good intentions to prolong pregnancy[15–17].

Complications associated with the procedure such as maternal pain and anxiety, as discussed with the procedure in other studies, were not much of concern in our study as all cases were done under IV anesthesia (propofol).

Discussion

Despite attempts to limit the number of embryos transferred, MFP after IVF is a norm rather than an exception[18]. It should be considered for any pregnancy with three or more fetuses, as there is good evidence that it improves the outcome for survivors[6]. Proper couple counseling about the risks and benefits of the

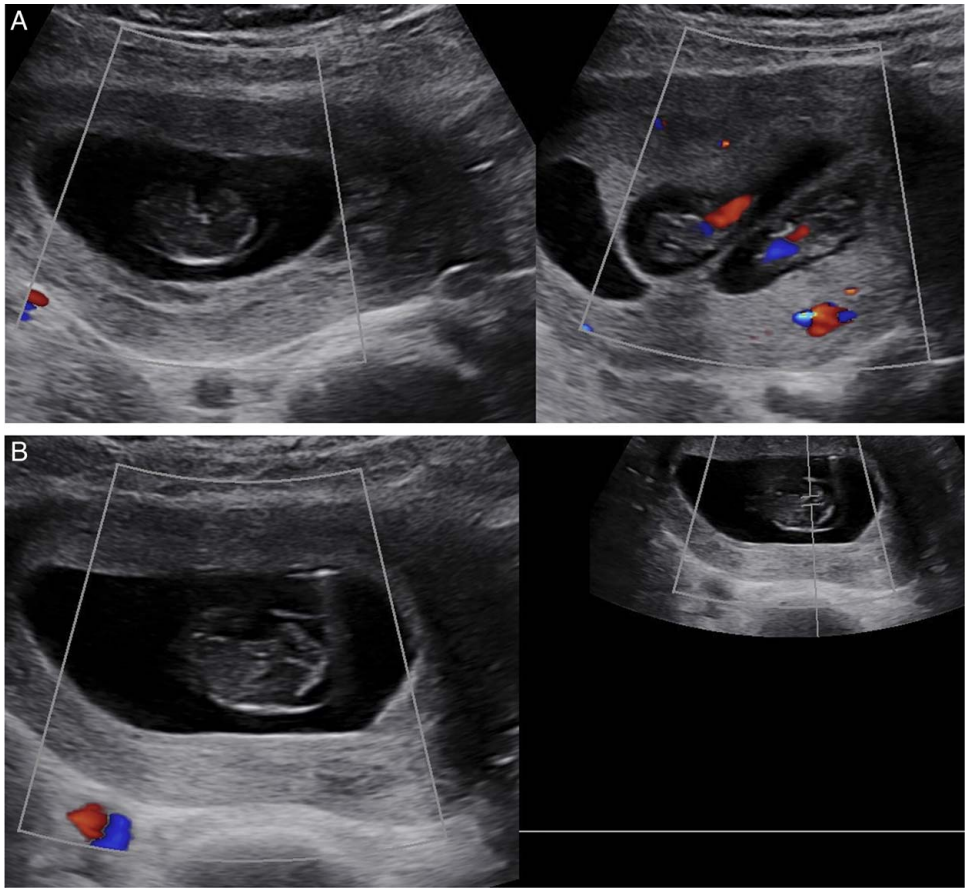

Figure 4. (A) Ultrasonography was repeated the next day before discharging the patient. There is absence of red/ blue color in fetal thorax in color doppler ultrasound image of the reduced fetus (image in left side). (B) Absence of fetal cardiac activity in the reduced fetus was confirmed by the pulse wave doppler. Mild edema is seen in the reduced fetus.

procedure is of vital importance since it is an invasive procedure and an emotionally challenging decision for the couple[19]. The couple undergoes stress, fear, anger, and guilt, which should be tackled properly[20,21].

Among various techniques used for MFPR, transvaginal aspiration, transcervical aspiration, ultrasound-guided transvaginal, and trans-abdominal intracardiac injection of KCl have been widely discussed in the literature[22,23]. Few other techniques like bipolar coagulation, Intrafetal laser have also been tried, but they are not readily available. Trans-abdominal ultrasound-guided intracardiac KCl injection is an easy and effective technique for MFPR. We have used this technique for MFPR. Between the trans-abdominal and transvaginal approaches, different studies have shown the superiority of one over the other regarding safety in terms of pregnancy loss rate. In a study by Timor-Tritsch *et al.*[24] the pregnancy loss rate in the trans-abdominal approach is lower than in the transvaginal approach. Evans *et al.*[25] have concluded that the transvaginal approach is safe in early pregnancy, whereas the trans-abdominal approach is safe in late pregnancy.

Table 1

Amount of 15% w/v (2 mEq/mL) KCl required for reduction.

Amount of 15% w/v (2 mEq/mL) KCl required	Total number of fetuses
> 0–0.5 ml	48
> 0.5–1.0 ml	65
> 1.0–1.5 ml	4
> 1.5–2.0 ml	5
> 2.0 ml	1

KCl, potassium chloride.

We carried out a single intra-thoracic puncture technique for injecting KCl through the trans-abdominal route. The selection of the fetuses to be reduced is based on the technical ease with which the procedure can be performed. In the trans-abdominal approach, it is easier to reduce fetuses located anteriorly in the middle or upper part of the uterine cavity. In case of reduction of the fetus above the cervix, there is an increased risk of infection and uterine irritability that might lead to the loss of other fetuses too. Hence, reduction of the fetus in the sac overlying the internal cervical os is usually avoided unless abnormalities are noted in that fetus (lagging crown-rump length, significantly smaller sac, markers of aneuploidy, or an obvious anomaly). Embryo reduction and fetal reduction can both be safely done trans-abdominally. Embryo reduction is carried out at 6–8 gestational weeks, whereas fetal reduction is performed after 11 weeks of gestation. The benefit of fetal reduction over embryo reduction is that if any spontaneous loss of a non-viable pregnancy occurs during the embryonic period, such cases would be automatically avoided[26]. An added advantage is that by 11 weeks of gestation, we would be able to do a good fetal anatomic survey so that if one

or more fetuses appear abnormal, then they can be selectively reduced. Moreover, sometimes, before 10 weeks it is technically more difficult because of the small size of the embryo and greater distance from the maternal abdominal wall[27]. In cases of late fetal reductions, that is beyond 15 weeks of gestation, possibilities of incomplete resorption of the reduced fetus remain which might sometimes lead to grave complications such as disseminated intravascular coagulation (DIC)[28]. Dural *et al.*[29]. recommend selective termination of the fetus with an anomaly in dichorionic pregnancy in the third trimester rather than the first or second trimester. In their study, they concluded that unexpected pregnancy loss and preterm birth rates are high if selective termination is done before 24 weeks of gestation. The risk of miscarriage associated with fetal reduction has been a controversial issue. There were earlier studies that reported that the risk of miscarriage was increased after the procedure; however, more recent reviews have reported a similar risk of pregnancy loss before 24 weeks for reduced and non-reduced pregnancies[4,30].

At present, there is no law in our country regarding fetal reduction. We have performed most of the cases within 12 weeks of gestation, which is as per legal provision for abortion in our country. MFPR performed beyond 12 weeks of gestation was done in fetuses with congenital malformation, which is also as per the legal provision of abortion in the country. We recommend the formulation of a law on fetal reduction at the earliest. With increasing MFP, MFPR is going to increase shortly.

Talwar *et al.*[20]. have shared their experience of transvaginal ultrasound-guided embryo reduction in 51 MFP. They performed MFPR within the tenth week of gestation. All the reductions were successful in a single attempt, which is better than our experience. The average time required for the procedure was 5 min for early pregnancy and 8.5 min for late pregnancy. Compared to our experience, the time required is less. Kim *et al.*[31]. shared the experience of 124 cases of trans-abdominal fetal reduction. They performed the procedure at a mean gestational age of 12 + 6 weeks which is higher than our study. Procedure-related pregnancy loss rate was 0.8%, the overall pregnancy loss rate was 2.4%, and the fetal loss rate was 1.6%. Their experience is similar to ours. Patel *et al.*[32]. shared their 25 years experience of MFPR. A total of 975 procedures were performed during the period of which 805 were done by trans-abdominal approach and 170 by transvaginal approach. The pregnancy loss rate with the transvaginal approach was significantly higher. No pregnancy loss was seen in our study. The fetal loss rate in our procedure is 0.92%, which is less compared to these studies.

Only a few pieces of literature are published describing the experience of fetal reduction in the country. We could find only two manuscripts. Acharya *et al.*[33]. were the first to share their experience of fetal reduction in the country. They shared the outcome of a fetal reduction in 11 pregnancies with 38 fetuses. They did an intracardiac injection of KCl under ultrasound guidance. They reduced 16 fetuses, two patients had spontaneous abortions, one had missed abortion at 26 weeks gestation and the rest gave birth to a healthy newborn. Another study is published by Pradhan *et al.*[34]. In this study, they share the experience of fetal reduction in 22 pregnancies by trans-abdominal as well as transvaginal ultrasound-guided intracardiac fetal KCl injection technique. Sixteen MFPRs were done using the trans-abdominal approach, and the rest six using the transvaginal approach. All but one patient conceived by IVF. 16 patients delivered at term, 4 had miscarriages and the remaining 2 were awaiting delivery. The majority of the patients had a cesarean section for delivery.

Intracardiac KCl injection should be avoided if the reduction is to be attempted in twins sharing the same placenta. Due to shared circulation, the chance of the inadvertent demise of the second twin is high which is seen in our study as well. In a study by Evans *et al.*[35]. after intracardiac KCl injection, there was the demise of the second twin in all monochorionic twin reduction. Alternative methods like bipolar coagulation and intrafetal laser should be considered in such cases[36].

Strength and limitations

The biggest strength of our study is being one of the first kinds describing the experience of trans-abdominal ultrasound-guided fetal reduction in our country. Only few manuscripts have been written about fetal reduction in the country. A sample size of our study is also good. We have used clinically focused data of elective fetal reduction. There are few limitations of our study. We could follow only four patients after the procedure since the majority of the patients were referred from different other hospitals and IVF centers across the country. If we had followed all patients till delivery, we could have assessed the maternal and fetal outcomes of MFPR and established the beneficial or harmful effects of MFPR. We conducted fetal reduction in all patients by trans-abdominal route using KCl. Hence, we could not do a comparision with fetal reduction via the transvaginal route or other alternative methods of fetal reduction without using KCl.

Conclusion

Trans-abdominal ultrasound-guided embryo/fetal reduction performed between the seventh and twelfth weeks of gestation is safe and effective. Intracardiac injection of KCl in monochorionic twins should be avoided. An alternative method of fetal reduction is advised in monochorionic twin pregnancy. The law regarding fetal reduction should be formulated in the country at the earliest.

Ethical approval

Ethical approval has been obtained from institutional review committee Grande International Hospital, Tokha, Kathmandu. Reference number of the IRC letter: 20/2020.

Consent

The consent was waived by the institutional review committee since the study was retrospective in nature.

Source of funding

There is no external source of funding for the research. The expenses that occurred were born by the authors.

Author contribution

S.P.: study concept, data collection, manuscript writing. P.D.: data collection, manuscript writing. P.R.P.: data curation. N.S.: data curation.

Conflicts of interest disclosure

There is no conflict of interest of authors to disclose.

Research registration unique identifying number (UIN)

NCT06251440.

Guarantor

The principal author Sharma Paudel accepts full responsibility for the work and conduct of the study. I have access to the data and control the decision to publish.

Data availability statement

The datasets generated during and/or analyzed during the current study publicly available in https://www.clinicaltrials.gov/ with UIN: NCT06077929.

Provenance and peer review

Paper was not invited.

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