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Intra Cardiac Injection of Autologous Amniotic Fluid versus Potassium Chloride for Multifetal Pregnancy Reduction

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ABSTRACT

Background: Multifetal pregnancy reduction (MFPR) is a widely practiced procedure aimed at improving pregnancy outcomes and reducing maternal and perinatal complications. Potassium chloride (KCl) injection is the conventional method for MFPR, however its use carries certain risks. Autologous amniotic fluid (AF) injection has been proposed as a potentially safer alternative.

Aim: This study aimed to compare the efficacy and safety of intra-cardiac injection of autologous amniotic fluid versus potassium chloride for multifetal pregnancy reduction.

Methods: A randomized prospective study was conducted on 42 women with multifetal pregnancies (≥ triplets) undergoing MFPR between 8–12 weeks of gestation. Patients were randomized into two groups: Group A (n=21), received intra-cardiac AF injection and group B (n=21), received KCl injection. The primary outcome was the success rate of fetal reduction, defined as achieving twin pregnancy post-procedure. Secondary outcomes included miscarriage rates, gestational age at delivery, neonatal birth weight, and procedure-related complications.

Results: Both techniques were equally effective in achieving successful reduction to twins. The KCl group required significantly lower doses and shorter time to achieve asystole. However, the AF group demonstrated better pregnancy outcomes, including higher mean gestational age at delivery and increased neonatal birth weight. Early and late miscarriage rates, as well as take-home baby rates, were comparable between the two groups.

Conclusion: Intra-cardiac injection of autologous amniotic fluid was a safe and effective alternative to potassium chloride for multifetal pregnancy reduction. Although KCl achieved faster procedural success, AF injection was associated with more favorable perinatal outcomes. Larger multicenter studies are needed to validate these findings and assess long-term neonatal outcomes.

Keywords: Multifetal pregnancy reduction, Potassium chloride, Amniotic fluid injection.

INTRODUCTION

Multiple pregnancies are recognized as high-risk conditions for both mothers and fetuses. While, the spontaneous occurrence of higher-order multiple gestations (HOMPs) is rare, the use of ovulation induction agents such as clomiphene citrate, follicle-stimulating hormone (FSH), and human menopausal gonadotropin (hMG) significantly increases the likelihood of multiple ovulations, particularly when combined with timed intrauterine insemination [(1)].

Multiple gestations, defined as pregnancies with two or more fetuses, are strongly associated with maternal and fetal complications. In mothers, common risks include hypertensive disorders, postpartum depression, anemia, postpartum hemorrhage, pre-eclampsia, gestational diabetes, and elevated incidence of Cesarean sections. Intrauterine growth restriction (IUGR), preterm, and higher mortality are among the issues that can occur in fetuses, the risks rise in proportion to the number of fetuses. Compared to singleton pregnancies, the risk of perinatal death is fivefold higher in twins, and increases to 12-fold in triplets and 26-fold in quadruplets [(2)]. Preterm birth accounts for approximately 75% of perinatal complications and contributes to more than 50% of long-term morbidity, including neurological, respiratory, and gastrointestinal sequelae [(3)].

Multifetal pregnancy reduction (MFPR) is a widely accepted intervention aimed at improving pregnancy outcomes in high-order multiple gestations by selectively reducing the number of fetuses [(4, 5)]. However, MFPR itself carries risks, including miscarriage, intrauterine demise of remaining fetuses, and preterm delivery. Miscarriage before 24 weeks, stillbirth after 24 weeks, preterm birth before 28, 32, or 37 weeks, live birth rate, and gestational age at delivery are the main outcomes that are usually assessed. Maternal difficulties such as preterm prelabor rupture of membranes (PPROM), preeclampsia, placental issues, and neonatal birthweight are examples of secondary outcomes [(6)].

Induced fetal demise can be achieved through intracardiac, intra-amniotic, intraumbilical, or intrafetal injection of agents such as potassium chloride (KCl), digoxin, or lidocaine [(7)]. Timing is another critical variable, with first-trimester procedures (<14 weeks) associated with different risk profiles compared with later reductions (>14 weeks) [(8, 9)]. Selective termination (ST), performed for fetuses with genetic or structural anomalies, shares the same rationale of improving

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outcomes for the remaining fetuses and reducing maternal complications [10].

Despite its widespread use, KCl injection is not without complications. Reported adverse outcomes include pregnancy loss, PPROM, preterm delivery, and rarely, congenital anomalies such as limb reduction defects and anencephaly. KCl may also diffuse beyond the target fetal heart, affecting adjacent sacs [11]. As an alternative, intracardiac injection of autologous amniotic fluid (AAF) has been suggested to achieve comparable success with fewer complications. Reported benefits include higher gestational age at delivery, increased take-home baby rates, lower rates of infection and spotting, and shorter procedural times [11].

Aim of the work: The aim of this study was to evaluate the efficacy and safety of intracardiac/or intrathoracic injection of autologous amniotic fluid compared to potassium chloride, administered under transvaginal ultrasound guidance at 8–12 weeks of gestation, in achieving successful multifetal pregnancy reduction.

Methods: This was an interventional study, designed as a randomized controlled clinical trial, and carried out at a private center (Sarhan Fertility Centre). The study was carried over the course of four years, from January 2021 to December 2024, and Forty-two pregnant women with high-order multifetal gestations were enrolled in the study. In two equal groups, participants were assigned at random: 21 patients received intracardiac/or intrathoracic injections of potassium chloride (KCl), and the remaining 21 patients received intracardiac/or intrathoracic injections of autologous amniotic fluid.

Inclusion criteria: High-order multiple pregnancies (defined as more than two fetuses), irrespective of the mode of conception. Gestation age were between 8 and 12 weeks provided informed consent for the fetal reduction procedure after thorough counseling of both the patient and her family.

Exclusion criteria: Monochorionic gestations, as well as evidence of intrauterine or pelvic infections. Women presenting with threatened abortion, or with systemic conditions rendering them unfit for surgical intervention such as morbid obesity, heart failure, sepsis, or liver failure. In addition, patients with contraindications to KCl administration, including hypersensitivity to the drug or pre-existing hyperkalemia.

Sample size: The sample size was calculated using *Epi Open* software. Based on a mean procedure time of 3.4 ± 2.22 minutes for KCl injection compared to 5.64 ± 2.82 minutes for autologous amniotic fluid injection, a sample of 42 cases was required to achieve 80% study power at a 95% confidence interval.

Pre-procedural assessment: All patients underwent a detailed pre-procedural evaluation. A comprehensive history was obtained with emphasis on maternal age, parity, duration of infertility, use of assisted reproductive technologies or fertility drugs, smoking, and associated medical conditions such as diabetes mellitus, hypertension, and cardiac disease. General and abdominal examinations were performed, including assessment of body mass index (BMI), vital signs, and systemic signs (pallor, jaundice, thyroid enlargement, lower limb edema and varicosities). Abdominal inspection and palpation were also carried out to identify scars, tenderness, organomegaly, or pelvic masses, and the uterine fundal level was documented. Comprehensive counseling was provided to all patients and their families about the possible risks of multifetal pregnancy, the advantages and disadvantages of multifetal pregnancy reduction (MFPR), and the associated ethical issues. Every participant provided written informed permission.

Procedure technique: Before the procedure, all women underwent ultrasonographic assessment to confirm the number, location, and size of gestational sacs and to document fetal cardiac activity. Between weeks 8 and 12, multifetal pregnancy reduction was carried out. Procedures were performed with 1% propofol and general anesthesia. After the patients were placed in lithotomy, the vagina was cleaned with 10% povidone iodine and rinsed with sterile saline.

Under real-time sonographic guidance (GE Logiq F6, 8 MHz transducer), a 17-gauge oocyte pickup needle (Reproline follicle puncture system, Germany) was introduced transvaginally through the posterior or lateral fornix into the uterus. The most accessible fetus was generally selected for reduction. Alternatively, fetuses with smaller crown-rump length, increased nuchal translucency, abnormal morphology, or location farthest from the internal os were chosen.

In group A (amniotic fluid group), 2 mL of amniotic fluid was aspirated (1 mL in the needle and its connecting tube, and the remaining 1 mL in a 1 mL syringe). Under ultrasound guidance, the needle was advanced to the area around fetal heart, and 0.2 mL aliquots were injected sequentially until cardiac activity ceased. In group B (potassium chloride group), the needle and its connecting tube were primed with 1 mL of potassium chloride solution (2 mEq/mL 15%, EIPICO). A volume of 0.5–2 mL was then injected adjacent to the fetal heart. If cardiac activity persisted after the initial 0.5 mL, additional 0.2 mL aliquots were administered until asystole was achieved. After confirming the absence of fetal cardiac activity for at least one minute, the needle was withdrawn. In cases of quadruplet or quintuplets pregnancy, the procedure was repeated for the additional gestational sacs as required.

Post-procedural care and follow-up

All patients received prophylactic antibiotics (ceftriaxone 1 g daily, starting the day before the procedure and continued for 7 days) and postoperative intramuscular progesterone (100 mg daily for 7 days). Ultrasound assessment was performed immediately before discharge to confirm viability of the remaining fetuses. Follow-up sonography was repeated after 2 hours, at 1 week, and subsequently during antenatal care.

Patients were monitored until delivery for early complications such as vaginal spotting, infection, or miscarriage, as well as later pregnancy complications including gestational diabetes, hypertension, and preeclampsia.

Measurements of outcomes: The **primary outcomes** of the study were related to the success and safety of the MFPR procedure. Procedural success was defined as achieving the desired reduction while maintaining two viable embryos in utero. Clinical outcomes assessed included the occurrence of vaginal bleeding, abdominal cramps, early miscarriage, the take-home-baby rate and the pregnancy loss rate. Fetal loss within four weeks following the operation was deemed an early miscarriage, and these instances were classified as procedure-related losses. Fetal loss that happens after four weeks following the surgery but before 24 weeks of gestation is referred to as a late miscarriage. The live birth rate per patient was used to calculate the take-home-baby rate [(12)].

The secondary outcomes centered on obstetric factors, such as neonatal birth weight, gestational age at delivery, and pregnancy-related issues like preeclampsia, gestational diabetes, and hypertension. Delivery before the full 28 weeks of pregnancy was considered very preterm birth [(13)]. Membrane rupture that occurs before the start of labor and before 37 weeks of gestation is known as preterm prelabor rupture of membranes (PPROM) [(14)].

Ethical approval: Zagazig University's Institutional Review Board (IRB) approved the study protocol (IRB #6178/29-6-2020). Prior to enrollment, all individuals provided written informed consents. The Declaration of Helsinki's ethical guidelines were followed when conducting the study.

Statistical analysis

Version 27 of the Statistical Package for the Social Sciences (SPSS) was used to analyze the data. When all anticipated cell counts were ≥ 5, categorical variables were displayed as absolute frequencies and compared using the Chi-square test (χ^2). Fisher's exact test was used when anticipated frequencies were less than five, which was especially pertinent in this investigation because certain categories had few observations. The Shapiro-Wilk test was used to determine whether quantitative variables were normal. Data with a non-normal distribution were presented as medians with ranges, and variables with a normal distribution were summarized as means with standard deviations. When continuous variables showed a normal distribution, the independent samples t-test was employed for group comparisons. Results were deemed highly significant at $p \leq 0.001$ and statistical significance was established at a p-value ≤ 0.05.

RESULTS

42 women in all were recruited and divided into two groups at random: The potassium chloride (KCL) group (n=21) and the amniotic fluid (AF) group (n=21). Maternal age, body mass index (BMI), and place of residence did not differ statistically significantly between the two groups (p>0.05), according to table (1). The AF and KCL groups had mean ages of 26.9 ± 4.82 and 28.4 ± 4.01 years and mean BMIs of 26.2 ± 3.31 and 24.9 ± 3.78 kg/m² respectively.

Table (1): Distribution of demographic data among participants of the two studied groups

	AF group [n=21]	**KCL group [n=21]**	**χ^2**	**P**
Residence				
Rural	13(61.9%)	11 (52.4%)		
Urban	8 (38.1%)	10 (47.6%)	0.389	0.533
	Mean ± SD	**Mean ± SD**	**T**	**P**
Age (year)	26.9 ± 4.82	28.43 ± 4.01	-1.115	0.272
BMI (kg/m^2)	26.23 ± 3.31	24.93 ± 3.78	1.18	0.245

Table (2) showed that significant difference was observed in the mean injection volume, which was higher in the AF group (1.44 ± 0.44 ml) compared to the KCL group (1.16 ± 0.43 ml; p=0.041). Similarly, the duration of injection was significantly longer in the AF group (5.45 ± 1.19 minutes) compared to the KCL group (4.69 ± 0.75 minutes; p=0.018). However, total operative time did not differ significantly (p=0.39).

Table (2): Comparison of procedural data between the two studied groups

	AF group [n=21]	KCL group [n=21]		
	Mean ± SD	**Mean ± SD**	**χ2**	**P**
Number of pricks **One** **two** **three**	 10 (47.6%) 7 (33.3%) 4 (19.0%)	 13 (61.9%) 6 (28.6%) 2 (9.5%)	Fisher's exact test	0.57
	Mean ± SD	**Mean ± SD**	**T**	**P**
Procedural gestational age (week)	8.62± 0.8	8.81± 1.08	-1.59	0.11
Volume (ml)	1.44 ± 0.44	1.157 ± 0.431	2.11	0.041*
Duration of injection (minute)[a]	5.45 ± 1.19	4.69 ± 0.75	2.478	0.018*
Operative time (minute)[b]	8.10 ± 1.17	7.83 ± 0.81	0.87	0.39

[a] **Duration of injection:** Fetal reduction procedure Time, [b] **operative time:** Total operative and anaesthesia time. ***p<0.05:** Statistically significant.

The distribution of gestational age categories at the time of the procedure (8–<9 weeks, 9–<10 weeks, and 10–12 weeks) was similar between the two groups, with no statistically significant difference (p=0.91). The most common procedural age was 8–<9 weeks in both groups as shown in table (3).

Table (3): Gestational age distribution at the time of procedure in the two studied groups

Gestational age	AF group [n=21]	KCL group [n=21]	χ^2	P
8 – <9 weeks	11 (47.6%)	11 (52.4%)	Fisher's exact test	0.91
9 – <10 weeks	8 (42.9%)	7 (33.3%)		
10 – 12 weeks	2 (9.5%)	3 (14.3%)		

Early complications, including miscarriage, vaginal bleeding, leakage, fever, and subchorionic hematoma, occurred at comparable frequencies across the two groups. No statistically significant differences were detected (p > 0.05 for all). Vaginal bleeding was observed in 23.8% of the AF group and 42.9% of the KCL group, while early miscarriage occurred in 4.8% of cases in both groups as shown in table (4).

Table (4): Comparison between the two studied groups regrading early post-procedure complications

	AF group [n=21]	KCL group [n=21]	χ^2	P	RR (95% CI)
Early miscarriage **No** **Yes**	20 (95.2%) 1 (4.8%)	20 (95.2%) 1 (4.8%)	Fisher's Exact Test	0.999	1(0.06 – 15.6)
Vaginal spotting/bleeding **No** **Yes**	16 (76.2%) 5 (23.8%)	12 (57.1%) 9 (42.9%)	1.71	0.19	0.56(0.22 – 1.38)
Leakage No Yes	21(100%) 0 (0%)	20 (95.2%) 1 (4.8%)	Fisher's Exact Test	0.999	0 (0.01 – 6.53)
Fever No Yes	20 (95.2%) 1 (4.8%)	21(100%) 0 (0%)	Fisher's Exact Test	0.999	∞ (undefined)
Subchorionic hematoma No Yes	21(100%) 0 (0%)	20 (95.2%) 1 (4.8%)	Fisher's Exact Test	0.999	0 (0.01 – 6.53)

Table (5) showed that no statistically significant differences were found between the two groups regarding late complications such as gestational hypertension, preeclampsia, diabetes mellitus, intrauterine growth restriction, late miscarriage, extreme prematurity, or preterm premature rupture of membranes (PPROM). Hypertension (16.7% vs. 26.3%) and PPROM (36.8% vs. 40%) were more frequent in the KCL group, while extreme prematurity occurred more often in the AF group (5.3% vs. 5%). However, none of these differences reached statistical significance.

Table (5): Comparison of late pregnancy complications between the two studied groups

	AF group	KCL group	χ^2	P	RR (95% CI)
Hypertension No Yes	**n=18** 15 (83.3%) 3 (16.7%)	**n=19** 14 (73.7%) 5 (26.3%)	Fisher's Exact Test	0.69	0.63 (0.15 – 2.69)
Preeclampsia No Yes	**n=18** 17 (94.4%) 1 (5.6%)	**n=19** 19 (100%) 0 (0%)	Fisher's Exact Test	0.999	∞ (undefined)
DM No Yes	**n=18** 18 (100%) 0 (0%)	**n=19** 18 (94.7%) 1 (5.3%)	Fisher's Exact Test	0.999	0 (0.01 – 7.3)
SGA/IUGR **No** **Yes**	**n=18** 17 (94.4%) 1 (5.6%)	**n=19** 19(100%) 0 (0%)	Fisher's Exact Test	0.999	∞ (undefined)
Late miscarriage[a] **No** **Yes**	**n=20** 19 (95%) 1 (5%)	**n=20** 20 (100%) 0 (0%)	Fisher's Exact Test	0.999	∞ (undefined)
Extreme prematurity[b] **No** **Ye**	**n=19** 18 (94.7%) 1 (5.3%)	**n=20** 19 (95%) 1 (5%)	Fisher's Exact Test	0.999	1.06 (0.071 to 15.62)
PPROM [c] **No** **Yes**	**n=19** 12 (63.2%) 7 (36.8%)	**n=20** 12 (60%) 8 (40%)	0.041	0.839	0.92(0.42 – 2.04)

[a] **Late miscarriage:** fetal loss after 4 weeks of procedure and before 24 weeks of gestation, [b] **Extreme prematurity:** babies born alive before 28 weeks of gestation, [c] **PPROM:** preterm premature rupture of membranes

Gestational age at delivery and estimated neonatal birth weight did not differ significantly between groups. The mean gestational age at birth was 34.5 ± 2.5 weeks in the AF group versus 33.5 ± 2.97 weeks in the KCL group (p=0.25), and the mean birth weight was 2018.4 ± 385.6 g versus 1951.0 ± 489.3 g respectively (p=0.63). Mode of delivery (vaginal vs. Cesarean) and rates of NICU admission were also comparable. Take-home baby rates were nearly identical (94.7% in AF vs. 95% in KCL) (Table 6).

Table (6): Comparison between the two studied groups regarding birth data.

	AF group [n=19]	KCL group [n=20]	Statistical test	P
	Mean ± SD	**Mean ± SD**		
Gestational age at birth (week)	34.53 ± 2.5	33.5 ± 2.97	t =1.16	0.25
Estimated birth weight (g)	2018.42±385.58	1951.0±489.32	t =0.47	0.63
Mode of delivery: **VD** **CS**	 7 (36.8%) 12 (63.2%)	 6 (30%) 14 (70%)	Fisher's Exact Test	0.73
NICU admission **No** **Yes**	 11 (57.9%) 8 (42.1%)	 12 (60%) 8 (40%)	$\chi^2 = 0.018$	0.893
Take- home baby No Yes	 1 (5.3%) 18 (94.7%)	 1 (5%) 19(95%)	Fisher's Exact Test	0.999
Survived fetuses **No survivor** **One survivor** **Two survivors**	n=19 1 (5.3%) 1 (5.3%) 17 (89.4%)	n=20 1 (5%) 0 (0%) 19 (95%)	Fisher's Exact Test	0.801

The distribution of gestational age at birth showed no significant differences between groups (p=0.75). The majority of deliveries in both groups occurred between 32–36 weeks, with fewer cases delivering before 28 weeks or beyond 36 weeks (Table 7).

Table (7): Gestational age distribution at birth in the two studied groups

	AF group [n=19]	KCL group [n=20]	χ^2	P
Gestational age				
24 – <28 weeks	1 (5.3%)	2 (10%)		
28 – <32 weeks	2 (10.5%)	3 (15%)	Fisher's	0.75
32 – 36 weeks	10 (52.6%)	12 (60%)	exact test	
>36 weeks	6 (31.6%)	3 (15%)		

DISCUSSION

Table (1) revealed that the two groups under study did not differ statistically in terms of residence (p = 0.533), body mass index (BMI, kg/m^2) (26.23 ± 3.31 in the AF group vs. 24.93 ± 3.78 in the KCL group, p = 0.245), or maternal age (26.9 ± 4.82 years in the AF group vs. 28.43 ± 4.01 years in the KCL group, p = 0.272). **Table (2)** showed that the number of pricks ("bricks") used in the study was single 47.6% of cases of AF group and 61.9% of cases of KCL group with no statistically significant difference between the groups (p = 0.567). The mean volume of the reduction agent was significantly higher in the AF group than in the KCL group (1.44 ± 0.44 ml vs. 1.16 ± 0.43 ml, p = 0.041*), and the mean injection time was also longer with AF (5.45 ± 1.19 minutes vs. 4.69 ± 0.75 minutes, p = 0.018*). In contrast, the mean operative time did not differ significantly between the two groups (8.10 ± 1.17 minutes vs. 7.83 ± 0.81 minutes, p = 0.39). Similarly, **Namrata *et al.*** [16] conducted a prospective cohort study to compare the use of intracardiac autologous amniotic fluid versus potassium chloride (KCl) for fetal reduction between 11 and 13 weeks of gestation. A total of 50 patients were enrolled, with 25 undergoing instillations of autologous amniotic fluid and 25 receiving potassium chloride. they reported that a single prick was used in 52% of cases in the amniotic fluid (AF) group and 64% of cases in the KCL group, which was not statistically significant (p = 0.649). They also observed significantly higher injection volumes in the AF group compared to the KCL group (0.56 ± 0.17 ml vs. 0.33 ± 0.18 ml, p < 0.001) and longer mean injection times with AF (5.64 ± 1.81 minutes vs. 3.41 ± 1.22 minutes). Compared to the present study, **Namrata *et al.*** [16] reported lower injection volumes and shorter KCl injection times, while AF injection times were similar; in both studies, the difference between AF and KCl remained significant.

Also, table (2) revealed that there was no statistically significant difference between the two groups (p = 0.11), with the mean gestational age at the time of the surgery being 8.62 ± 0.8 weeks for the amniotic fluid (AF) group and 8.81 ± 1.08 weeks for the KCL group. By contrast, **Dasgupta *et al.*** [17] reported later procedural timing in a case series of 20 women with quadruplet pregnancies, where, between weeks 11 and 15 weeks of gestation, potassium chloride was injected intracardiac to perform MFPR transabdominally. The average gestational age at fetal reduction in their study was 11.9 ± 0.94 weeks. Differences in inclusion criteria and the timing of the procedure at a later gestational age could be the cause of this disparity.

Table (3) described the gestational age distribution at the time of the procedure. In the AF group (n = 21), 11 cases (47.6%) were performed between 8 and < 9 weeks, 8 cases (42.9%) between 9 and < 10 weeks, and 2 cases (9.5%) between 10 and 12 weeks. Similarly, in the KCL group (n = 21), 11 cases (52.4%) were between 8 and < 9 weeks, 7 cases (33.3%) between 9 and < 10 weeks, and 3 cases (14.3%) between 10 and 12 weeks. Statistical analysis showed no significant difference in gestational age distribution between the two groups (p = 0.91). Different number and percentage were reported by **Paudel *et al.*** [18] who performed a retrospective cohort research on 108 women who received a transabdominal intracardiac injection of potassium chloride (KCl) for multifetal pregnancy reduction (MFPR). The timing of the procedure varied across gestational ages: 1 case (0.93%) was performed between the 7th and 8th weeks, 13 cases (12.03%) between the 8th and 9th weeks, 44 cases (40.7%) between the 9th and 10th weeks, 30 cases (27.7%) between the 10th and 11th weeks, 15 cases (13.9%) between the 11th and 12th weeks, 2 cases (1.85%) between the 13th and 14th weeks, and 1 case (0.93%) each between the 14th–15th and 15th–16th weeks of gestation.

Table (4) showed early post-procedure complications. early miscarriage, defined as procedure-related loss occurring within four weeks of the procedure, was observed in one case in each group (4.8%), with no significant difference between the AF and KCl groups (p = 0.999), indicating a comparable early safety profile for both techniques. Different results

were reported by a study carried out by **Latha *et al.* [19]**. The study reported that five cases (16%) of complete fetal loss occurred within one week of the procedure, while the majority of losses (48.3%) occurred eight weeks post-procedure. No losses were observed between 2 to 4 weeks or after 15 weeks. In comparison, the current study reported a lower early pregnancy loss rate of 4.8% in each group (AF group and KCL group). Also, **Lee *et al.* [12]** discovered that, while not statistically significant, the non-KCl groups had lower rates of immediate pregnancy loss than the KCl groups (5.6% vs. 10.5%). This suggests a trend toward fewer early losses with non-KCl techniques, though without conclusive evidence of superiority. The current study demonstrated more comparable outcomes between both methods, suggesting a similar early safety profile.

Also, table (4) presented other postoperative complications including vaginal spotting, leakage, fever and subchorionic hematoma. Vaginal spotting occurred less frequently in the AF group compared to the KCl group (23.8% vs. 42.9%). Leakage and subchorionic hematoma occurred within one case (4.8%) of KCL group for each complication and fever occurred within only one case (4.8%) of AF group. Overall, these problems did not differ statistically significantly between the two groups ($p > 0.05$), indicating similar safety in terms of mild post-procedural occurrences. As an alternative, **Nurzadeh *et al.* [10]** reported procedure-related adverse outcomes, with vaginal bleeding or spotting occurring in 19% of early reductions and 25% of late reductions, and leakage observed in 13% and 7% respectively, though these differences were not statistically significant ($p = 0.863$). **Kim *et al.* [20]** also evaluated procedure-related adverse outcomes and reported a markedly higher incidence of subchorionic hematoma (SCH), particularly in embryo reductions (45.3% within one week and 40.2% within four weeks), compared to lower rates in fetal reductions (25.0% and 6.4%, respectively). In contrast, the present study observed a much lower incidence of SCH.

Table 5 summarized late pregnancy complications in the two studied groups. Hypertension was less frequent in the AF group compared to the KCL group (16.7% vs. 26.3% respectively). However, this difference was not statistically significant ($p = 0.69$). Other complications included GDM, was observed only in the KCL group (5.3%), preeclampsia that occurred in 5.6% of cases in the AF group and selective fetal growth restriction (sFGR) also was reported in 5.6% of cases in the AF group. None of these complications reached a statistically significant difference ($p = 0.999$). Compared to the current study, **Nurzadeh *et al.* [10]** reported slightly lower rates of hypertension (9% in early and 15% in late fetal reductions), higher rates of GDM in embryo reductions (18% vs. 5.3% in the KCL group), and similar rates of IUGR (4% vs. 5.6% in the AF group). None of these differences reached statistically significant level ($p > 0.05$). Also, **Kim *et al.* [20]** reported that hypertensive disorders in 6.1% of cases undergoing embryo reduction and 5.2% of cases undergoing fetal reduction, with GDM observed in 8.8% of the embryo reduction group and 5.2% of the fetal reduction group. None of these differences reached statistical significance ($p > 0.05$). However, the rate of GDM in the fetal reduction group was comparable to that in the current study's KCL group (5.2% vs. 5.3% respectively). Additionally, different results were reported by **Hass *et al.* [21]** in which they conducted a retrospective cohort study comparing 83 early (6–8 weeks) transvaginal MFPRs with 125 late (11–14 weeks) transabdominal MFPRs. Early reductions were performed via transvaginal cardiac puncture with aspiration of amniotic fluid and fetal parts, while late reductions used transabdominal intracardiac or intrathoracic KCl injection. The study found hypertensive disorders in 0% of early versus 20% of late reductions, GDM in 13% versus 10.5%, and SGA infants in 5.3% versus 20%. However, none of these differences reached statistical significance ($p > 0.05$). Compared to the current study, different techniques and case selection may account for the variation in outcomes. However, the rate of SGA in the AF group (5.6%) was similar to that reported by **Hass *et al.* [21]** (5.3%).

Also, table (5) revealed that with regard to late miscarriage, which happened in one instance (5%) in the AF group and none (0%) in the KCL group, there was no statistically significant difference between the two groups. Similar results were published by **Dasgupta *et al.* [17]** who observed no pregnancy loss before 24 weeks, which is consistent with the absence of late miscarriage in the KCL group of the current study. **Nurzadeh *et al.* [10]** also reported complete pregnancy loss before 24 weeks in 1% of early fetal reductions (11–14 weeks) and none in late fetal reductions (15–19 weeks), similar to the KCL group of the current study. In contrast, **Kim *et al.* [20]** reported late miscarriage in 13.3% of embryo reductions (6–8 weeks) and 5.2% of fetal reductions (11–20 weeks), the latter rate is comparable to the AF group of the current study (5%).

Furthermore, table (5) indicated that the method of fetal reduction had no significant effect on the risk of extreme preterm birth, as there was no statistically significant difference between the two groups regarding extreme prematurity, which occurred in 5.3% of cases in the AF group and 5% of cases in the KCL group ($p = 0.999$). In a similar vein, **Dasgupta *et al.* [17]** reported extreme prematurity in approximately 5% of cases, which is consistent with the findings in both groups of the current study. In contrast, **Lee *et al.* [12]** observed extreme prematurity in 2.5% of cases in the late KCL group (reductions after 8 weeks) compared to 0% in the

late non-KCL group, suggesting a possible association between KCL use and an increased risk of earlier delivery.

Additionally, table (5) showed that, with 7 instances (36.8%) in the AF group and 8 cases (40%) in the KCL group, there was no statistically significant difference in PPROM between the two groups (p = 0.839). The AF group experienced somewhat fewer PPROMs, although the difference was not statistically significant (RR = 0.92). According to **Dasgupta *et al.*** [17], the total incidence of PPROM was 20% lower. Similarly, **Hass *et al.*** [21] observed PPROM in 12% of early fetal reductions and 20% of late reductions, with no significant difference between groups ($p > 0.05$). In contrast, **Lee *et al.*** [12] reported PPROM in 27.6% of cases in the KCL group compared to 9.7% in non-KCL cases, suggesting a possible association between KCL use and increased risk of PPROM.

Table (6) revealed that neither the estimated birth weight nor the gestational age at birth differed statistically significantly between the AF and KCL groups. At birth, the AF group's mean gestational age was 34.53 ± 2.5 weeks, while the KCL group's was 33.5 ± 2.97 weeks (mean difference 1.03 weeks; p = 0.251). In the AF group, the mean estimated birth weight was 2018.42 ± 385.58 g, while in the KCL group, it was 1951.0 ± 489.32 g (p = 0.637). Comparable outcomes were reported by **Namrata *et al.*** [16] who found a mean gestational age at delivery of 35 ± 7 weeks in the AF group and 36 ± 7 weeks in the KCL group. The mean birth weights were 1840 ± 200 g in the AF group and 1832 ± 230 g in the KCL group. **Hass *et al.*** [21] also reported comparable outcomes, with mean gestational ages of 35.5 ± 2.8 weeks in the early fetal reduction group and 35.7 ± 2.5 weeks in the late group, and mean birth weights of 2183 ± 630 g and 2167 ± 377 g respectively.

As well, table (6) revealed that there was no statistically significant difference between the groups (p = 0.73), with CS being the mode of delivery in 63.2% of instances in the AF group and 70% in the KCL group. Similar results were published by **Zhang *et al.*** [15] who conducted a study on 363 patients undergoing transabdominal ultrasound-guided fetal reduction between 12 and 14 weeks of gestation. They compared intracranial and intrathoracic injections of KCl and observed Cesarean section (CS) rates of 76.9% and 76.3% respectively. In contrast, **Namrata *et al.*** [16] reported that all cases in both groups of MFPR were delivered via Cesarean section.

In addition, table (6) showed that with respect to NICU admission, there was no statistically significant difference between the two groups, with 42.1% of cases in the AF group and 40% in the KCl group requiring NICU care. **Nurzadeh *et al.*** [10] reported NICU admission rates of 49% in the early reduction group and 18.5% in the late reduction group. Compared to the current study, the NICU admission rate in the early reduction group was similar to both the AF (42.1%) and KCL (40%) groups, while the rate in the late reduction group (18.5%) was notably lower than in both groups of the current study.

Furthermore, table (6) reported that there was no statistically significant difference between the studied groups regarding take-home baby (p = 0.999). Eighteen cases (94.3%) in the AF group and nineteen cases (95%) in the KCL group with one case in the AF group experienced perinatal death. Similar results were obtained by **Namrata *et al.*** [16] in which they reported that both fetal reduction groups (amniotic fluid and potassium chloride) had a similar take-home baby rate of 85%, which is slightly lower than both studied groups in the current study (94.8%). Different results were obtained by **Dasgupta *et al.*** [17] who reported that the take-home baby was 100%. Also, **Lee *et al.*** [12] reported a take-home baby rate of 69.7% in the KCL groups and 86.1% in the non-KCL groups. In comparison, the current study demonstrated higher take-home baby rates in both groups.

Additionally, table (6) exhibited that there was no statistically significant difference between the groups regarding take-home baby rates (p=0.999). Take-home baby was achieved in 18 cases (94.3%) in the AF group and 19 cases (95%) in the KCL group, with one perinatal death reported in the AF group. Lower take-home baby rates were reported by **Namrata *et al.*** [16]**,** who observed 85% in both AF and KCL groups while, **Lee *et al.*** [12] reported rates of 69.7% in the KCL group and 86.1% in the non-KCL group. Overall, the current study demonstrated higher take-home baby rates in both groups compared to previous studies.

Table (6) also described fetal perinatal survival following reduction. In AF group, there was no survivors in 5.3% of cases, one survivor in 5.3%, and two survivors in 89.4%. In KCL group, there were no survivors in 5% of cases, one survivor in 0%, and two survivors in 95% of cases. There was no statistically significant difference between the groups regarding fetal survival after reduction (p = 0.801). Similar results were reported by **Dasgupta *et al.*** [17] who found no survivors in 0% of cases, one survivor in 10%, and two survivors in 90% showing a pattern comparable to the AF group in the current study. Furthermore, **Hass *et al.*** [21] reported fetal survival rates after early fetal reduction as 4.8% with no survivors, 6% with one survivor and 89.2% with two survivors, while late fetal reduction showed 2.4% with no survivors, 0.8% with one survivor, and 96.8% with two survivors. Compared to the current study, the AF group showed outcomes similar to early reduction, and the KCL group demonstrated outcomes comparable to

late reduction.

Table (7) showed that the distribution of birth gestational age in both groups at the time of birth was as follows: 24 – < 28 weeks; 5.3% in AF group versus 10 % in KCL group, 28 – < 32 weeks; 10.5 % in AF group versus 15 % in KCL group, 32 – 36 weeks; 52.6% in AF group versus 60% in KCL group and > 36 weeks; 3 1.6% in AF group versus 15 % in KCL group. Similar results were reported by **Dasgupta *et al.* [17],** who observed that the birth gestational was as follows: one woman (5%) delivered between 24 and 27 weeks + 6 days, three women (15%) between 28 and 30 weeks + 6 days, three women (15%) between 31 and 34 weeks + 6 days, and 11 women (55%) between 35 and 36 weeks + 6 days. Different results were reported by **Kim *et al.* [20]** who described that the birth gestational age was as follows: 24–< 34 weeks in 12.7% of the embryo reduction group versus 5.2% of the fetal reduction group; ≥ 34 to < 37 weeks in 36.5% of the embryo reduction group versus 37.4% of the fetal reduction group and ≥ 37 weeks in 42% of the embryo reduction group versus 54.8% of the fetal reduction group. Furthermore, **Namrata *et al.* [16]** reported that the birth gestational age was distributed as follows: < 32 weeks in 8% in both groups; 32–34 weeks in 4% of the AF group versus 8% of the KCL group, > 34–37 weeks in 48% of the AF group versus 44% of the KCL group and > 37 weeks in 8% of the AF group versus 4% of the KCL group.

LIMITATIONS: This study had several limitations. First, the absence of a control group reduces the overall strength of the findings. However, there was less chance of selection bias because clinical factors including maternal age and the number of fetuses before and after the surgery were similar among the groups. Second, the comparatively small sample size limits the capacity to make definitive inferences, emphasizing the necessity of larger research projects carried out in collaborative multicenter settings. Lastly, while triplet, quadruplet, and quintuplet cases were included in the study, there were only a few cases in each subgroup, which might have an impact on how broadly the findings can be applied. To confirm these results, other studies with bigger and more evenly distributed subgroups are needed.

CONCLUSION

This study demonstrates that both amniotic fluid injection and potassium chloride (KCL) injection are effective methods for multifetal pregnancy reduction. However, the findings suggested that amniotic fluid injection may provide more favorable perinatal outcomes, particularly in terms of achieving a higher gestational age at delivery and increased neonatal birth weight. The amniotic fluid injection method seemed to have a better safety profile with fewer procedure-related concerns, even though the KCL group's systole time and dosage were noticeably lower. These findings should be regarded cautiously due to the study's comparatively small sample size. To confirm these findings and develop evidence-based guidelines for the best practices in multifetal pregnancy reduction, larger, multicenter collaborative trials are necessary.

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