

EFFECT OF INTRAVENOUS AMINO ACID INFUSION ON FETAL OUTCOME IN OLIGOHYDRAMNIOS PREGNANCIES

Tarunibala Devi Kongkham¹, Balchand Nandeibam¹, Rakshitha G¹, Sheral Raina Tauro¹, Y. Ajitkumar Singh²

¹ Senior Resident, Department of Obstetrics & Gynaecology, RIMS, Imphal, Manipur, India

² Associate Professor, Department of Obstetrics & Gynaecology, RIMS, Imphal, Manipur, India

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Corresponding Author:

Dr. Tarunibala Devi Kongkham,
Email: bembkongs26@gmail.com

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ABSTRACT

Background: Oligohydramnios, defined sonographically as a single deepest pocket <2 cm (Manning) or Amniotic Fluid Index (AFI) <5 cm (Phelan), complicates 3-5% of pregnancies. It is associated with adverse maternal and perinatal outcomes including fetal distress, low birth weight, operative delivery, and neonatal morbidity. Intravenous amino acid infusion has been proposed as a therapeutic intervention to improve amniotic fluid volume and fetal outcome.

Materials and Methods: This non-randomised controlled trial was conducted in the Department of Obstetrics and Gynaecology, Regional Institute of Medical Sciences, Imphal, Manipur, India, from September 2019 to August 2021. Ninety pregnant women with singleton pregnancies between 28–40 weeks gestation and oligohydramnios (AFI ≤5 cm) were included. Participants were divided into two groups: Group A received intravenous amino acid infusion, while Group B did not receive amino acid therapy. Maternal characteristics, AFI changes, mode of delivery, birth weight, Apgar score, NICU admission, and neonatal complications were analysed using SPSS version 21.0. A p-value <0.05 was considered statistically significant. **Result:** Baseline demographic characteristics were comparable between groups. Following treatment, mean AFI increased significantly in Group A (from 3.7 ± 0.84 cm to 5.4 ± 1.09 cm) compared to Group B (from 3.2 ± 1.07 cm to 3.6 ± 0.9 cm) (p=0.001). Neonates weighing >2.5 kg were significantly more frequent in Group A than Group B (84.4% vs. 60.0%; p=0.018). Apgar scores ≥7 at one minute were higher in the amino acid group (97.8% vs. 86.7%; p=0.049). Caesarean section due to fetal distress and NICU admissions were more common in the group without amino acid infusion. No perinatal deaths occurred. **Conclusion:** Intravenous amino acid infusion in pregnancies complicated by oligohydramnios significantly improved AFI and was associated with better fetal growth and favourable perinatal outcomes. Amino acid supplementation may be considered a useful therapeutic option in the management of oligohydramnios. Further large-scale randomized controlled studies are recommended to confirm these findings.

INTRODUCTION

Amniotic fluid (AF) forms a dynamic milieu within the amniotic cavity, surrounding and protecting the developing embryo and fetus. As pregnancy advances, AF volume evolves predictably: it rises linearly from approximately 25 mL at 10 weeks to 400 mL at 20 weeks, driven by bi-directional diffusion across the non-keratinized fetal skin, amnion, placenta, and umbilical cord. Keratinization completes around 25 weeks, shifting this relationship; volume peaks at ~800 mL by 28 weeks, plateaus near term, and declines to ~400 mL at 42 weeks.^[1] AF, comprising 98-99% water and 1-2% solids,^[2] is primarily sourced from fetal urine (~300

mL/kg fetal weight/day) and oral/nasal/tracheal/pulmonary secretions (~60-100 mL/kg/day).^[1]

AF serves critical roles during pregnancy, including mechanical cushioning against injury, temperature regulation, facilitation of fetal movement to prevent adhesions, and bacteriostatic protection against ascending infections.^[3] It also enables diagnostic amniocentesis for maturity and disease assessment. During labour, the membranes promote cervical dilatation, store prostaglandins, prevent cord compression, and maintain an aseptic environment. Oligohydramnios, defined sonographically as a single deepest pocket <2 cm (Manning) or Amniotic Fluid Index (AFI) <5 cm (Phelan), complicates 3-5%

of pregnancies.^[1] The AFI, introduced in 1987, remains the preferred semi-quantitative ultrasound method for volume assessment.^[4] Isolated oligohydramnios occurs without growth restriction, abnormal umbilical artery Doppler, or identifiable maternal/fetal risk factors.^[5,6] It signals underlying issues like placental hypoperfusion, fetal anomalies, IUGR, malpresentation, post-maturity, and labor distress, often leading to meconium-stained liquor, abnormal fetal heart rates, caesarean deliveries, and perinatal morbidity/mortality.^[7,8] Severity correlates with placental insufficiency, hypoxia-induced shunting (reducing renal/pulmonary perfusion and urine output), and chronic IUGR.^[7]

Global trials have explored interventions like intravenous dextrose, maltose, and amino acids to augment AF volume and fetal weight, with amino acid infusions notably improving maternal nutrition and AFI.^[4] Despite these benefits, evidence on amino acid effects in oligohydramnios remains limited, particularly in resource-constrained settings. This study, conducted at a tertiary care center in Manipur, evaluates the impact of intravenous amino acid infusion on fetal outcomes in oligohydramnios pregnancies, addressing this evidence gap.

MATERIALS AND METHODS

This non-randomized controlled trial (quasi-experimental study) was conducted from September 2019 to August 2021 in the Department of Obstetrics and Gynaecology at the Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, India—a tertiary care referral centre

Inclusion Criteria

Singleton pregnancy between 28-40 weeks with Oligohydramnios (AFI \leq 5cm) irrespective of the parity with intact amniotic membrane. Only those women, who had reliable dating of pregnancy confirmed by an early 1st trimester Ultrasound examination using CRL or with known LMP and regular cycles were enrolled in the study.

Exclusion Criteria

1. Gestational age less than 28 weeks.
2. Associated fetal malformations.
3. Patient with true labour pains.
4. Oligohydramnios with medical complication like diabetes mellitus, pregnancy induced hypertension, anaemia, chronic nephritis, cardiac disease.
5. Ruptured membranes.
6. Multiple pregnancy
7. Chorioamnionitis.
8. Patients who refuse to give informed written consent.

Data collection: Prior to data collection, ethical approval was sought from the Research Ethics Board of Imphal. Informed written consent was taken from all the participants. Data were collected in predesigned proforma. The collected data were checked for completeness and consistency.

1. Pre-defined proforma consisting of the following section
 - a. Sociodemographic characteristics
 - b. Clinical history
 - c. Clinical examination findings
 - d. Laboratory investigation
2. Trans abdominal ultrasonography
3. Doppler velocimetry of umbilical artery and middle cerebral artery.

Study Variables:

Independent variable/ Predictor variables

1. Age in years
2. Parity
3. Blood pressure
4. Educational status
5. Occupation
6. Gestational age (weeks) at admission

Outcome/ Dependent Variables

1. AFI (amniotic fluid index)
2. SD Ratio
3. Mode of delivery
 - a. Vaginal
 - Spontaneous
 - Instrumental
 - Breech
 - b. Caesarean section
 - c. Indication for caesarean section
4. Fetal outcome
 - a. Gestational age at delivery
 - b. Viability _ Live born, Still born
 - c. Birth weight- <1.5kg, 1.5 to 2.5 kg, >2.5kg
 - d. Apgar score _ 7 or more, less than 7
 - e. Admission in NICU- admitted, not admitted
 - f. Any neonatal death

Statistical analysis: Data was entered and analysed using SPSS 21.0 (IBM Corp., Armonk, NY, United states) for Windows. Categorical variables like parity, educational status, occupation is presented as frequency and percentages. Continuous variable like age, AFI, SD ratio are presented as mean (SD) or median (IQR), depending on the type of distribution. Chi square test was used for comparing categorical variables and independent t-test for continuous variables. Fisher's exact test was used to determine the association between fetal outcome and the type of intervention. A p-value <0.05 was taken as significant.

RESULTS

A total of 90 pregnant women with oligohydramnios were included in the study. The patients were allotted to two group, Group A: patients on intravenous amino acid infusion and Group B: patient without amino acid infusion.

Baseline Characteristics

[Table 1] shows the mean age was similar between the groups (Group A: 28.4 \pm 6.3 years; Group B: 26.7 \pm 5.6 years; p = 0.195). [Table 2] shows Parity distribution did not differ significantly (primigravida: 51.1% vs 53.3%; p=0.833).

Socio-Demographics

Occupation (employee 46.7% vs. 26.7%; homemaker 53.3% vs. 73.3%; $p=0.49$), residence (rural 57.8% vs. 75.6%; $p=0.74$), and education ($p=0.173$) were similar across groups.

[Table 3] Gestational Age at Admission The intervention group had a higher rate of preterm admission (<37 weeks: 68.9% vs 8.9%; $p<0.05$), reflecting clinical preference for early intervention.

[Table 4] depicts The baseline mean S/D ratio was similar between groups (2.7 ± 0.36 compared to 2.9 ± 0.56 ; $p=0.141$).

[Table 5] shows Primary Outcome: Amniotic Fluid Index (AFI) Group A had a slightly higher pre-treatment AFI (3.7 ± 0.84 cm) than Group B (3.2 ± 1.07 cm; $p=0.021$). After treatment, AFI increased more in Group A (5.4 ± 1.09 cm) versus Group B (3.6 ± 0.9 cm; $p=0.001$), with mean gains of 1.7 cm and 0.4 cm, respectively.

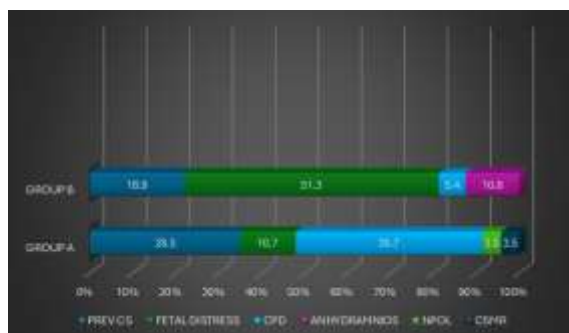


Figure 1: indications of CS

Delivery and Fetal Outcomes Term delivery rates were similar between groups (≥ 37 weeks: 93.3% versus 91.1%; $p=0.694$). Caesarean rate was lower in Group A, favoring vaginal delivery.

[Figure 1] shows Caesarean Indications ($n=65$)

Fetal distress predominated in controls (51.4% vs. 10.7%), while cephalopelvic disproportion (CPD) was common in intervention group.

Birth weight Group A had a greater proportion of births weighing over 2.5 kg (84.4%) compared to Group B (60.0%), with statistical significance ($p=0.018$). Apgar Score at 1 Minute: Group A had more scores ≥ 7 (97.8% vs. 86.7%; $p=0.049$).

Resuscitation, NICU, Complications- Routine care was administered more frequently in Group A (84.4%) than in Group B (60%), with the difference in bag/mask usage nearly reaching statistical significance ($p=0.069$). Admission to the NICU occurred less often in Group A (11.1%) compared to Group B (20%), though this did not achieve statistical significance ($p=0.245$). Rates of neonatal complications, such as respiratory distress (4.4% versus 8.9%), were similar between both groups (overall $p=0.696$). No perinatal deaths were observed.

[Figure 2] show distribution of newborn complication.

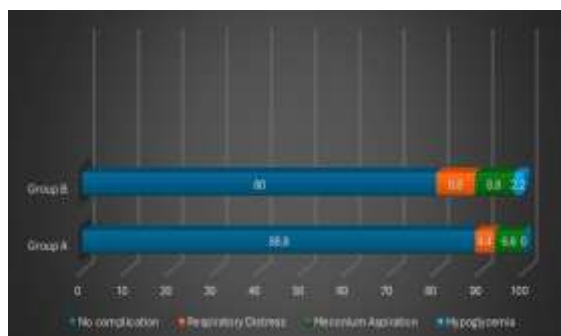


Figure 2: show distribution of newborn complication.

Table 1: Age distribution of the pregnant women with and without amino acid infusion treatment (N=90)

	Group A (intervention) N=45 Mean (SD)	Group B (Non-intervention) N=45 Mean (SD)	P- Value
Age in years	28.36 (6.3)	26.71 (5.59)	0.195

[Table 1] show that the mean age of the participant was comparable between the two group ($p=0.195$)

Table 2: Parity of the study participant (N=90)

	Group A N=45 N (%)	Group B N=45 N (%)	
Primigravida	23 (51.1)	24 (53.3)	p-value-0.833
Multigravida	22 (48.8)	21 (46.6)	

[Table 2] shows that parity was comparable between two group ($p=0.833$)

Table 3: Period of gestation at admission of the study participant (N=90)

	Group A N=45 N (%)	Group B N=45 N (%)	
<37 wks	31 (68.8)	4 (8.8)	p-value <0.05
≥ 37 wks	14 (31.1)	41 (91.1)	

[Table 3] shows that most of the intervention group admit < 37 wks and control group admit >37 wks and it is found to be statistically significant ($p\text{-value} = < 0.05$)

Table 4: Mean SD ratio at admission of Study participant (N=90)

Mean umbilical artery S/D ratio	Group A N=45 Mean (SD)	Group B N=45 Mean (SD)	
S/D Ratio	2.7 (0.36)	2.9 (0.56)	p-value=0.141

[Table 4] shows that SD ratio of both intervention and control group are comparable (p-value = 0.141)

Table 5: Mean AFI of pre and post amino acid infusion between two group (N=90)

	Group A N=45 Mean (SD)	Group B N=45 Mean (SD)	
AFI pre-treatment mean	3.7 (0.84)	3.2 (1.07)	P=0.021
AFI post-treatment mean	5.4 (1.09)	3.6 (0.9)	P=0.001

[Table 5] shows that changes in AFI is more in intervention group than control group and it is statistically significant (p-value= 0.001)

Table 6: Distribution of participant by the mode of delivery (N=90)

	Group A N=45 N (%)	Group B N=45 N (%)	
Normal vaginal delivery	17 (37.7)	5 (11.1)	
Vaginal delivery with cytology induction	0	2 (4.4)	p-value=0.013
Vaginal delivery with gel induction	0	1 (2.2)	
Caesarean section	28 (62.2)	37 (82.2)	

Table 7: Comparison of Birth weight between two group (N=90)

	Group A N=45 N (%)	Group B N=45 N (%)	
Birth wt <1.5KG	0	0	p-value = 0.018
1.5KG TO 2.5KG	7 (15.5)	18 (40)	
>2.5KG	38 (84.4)	27 (60)	

[Table 7] shows that birth weight is more in intervention group than control group) p- value= 0.018).

DISCUSSION

The amniotic fluid (AF) is a part of the baby's life support system. Amniotic fluid production begins soon after the formation of the amniotic sac, approximately 12 days after conception. In early pregnancy, the fluid is primarily derived from maternal plasma transudation across the fetal membranes. By around the 20th week of gestation, fetal urine becomes the principal source of amniotic fluid. As gestation advances, the fetus moves freely within the amniotic cavity, facilitated by this fluid environment. During the second trimester, the fetus begins swallowing and respiratory movements involving amniotic fluid, which contribute to the maturation of the gastrointestinal and respiratory systems. Amino acids constitute an essential nutritional component of amniotic fluid and play a significant role in fetal growth and development. Maternal nutritional status and caloric intake are known to influence the concentration of amino acids in amniotic fluid. The observed increase in the mean amniotic fluid index (AFI) following maternal intravenous amino acid infusion in the present study may reflect the correction of an underlying intrauterine nutritional deficiency.^[9]

Our study results are comparable to studies conducted by various authors across the country.^[1,2,6,10] A study conducted by J. Anagha et al,^[7] has shown that there was a significant increase in the post treatment AFI. This clearly proves that the amino acid infusion improves AFI in pregnant with oligohydramnios.

In the present study it was found that amino acid infusion was found to improve pregnancy outcome. The mean birth weight of newborn, percentage of

vaginal deliveries were found to be higher in amino acid infusion group. Similar results were reported by

studies conducted by Shree P et al and Ratkindra A et al.^[3,4]

In the present study, the majority of participants in the amino acid infusion group, 31 (68.8%), were admitted before 37 weeks of gestation, whereas in the group that did not receive amino acid infusion, most participants, 41 (91.1%), were admitted after 37 weeks. This difference may be explained by the fact that women in the amino acid infusion group were booked patients undergoing regular antenatal follow-up, which enabled earlier detection of oligohydramnios. In contrast, participants in the non-amino acid group were more frequently diagnosed at a later gestational age, resulting in a higher proportion of admissions after 37 weeks.

With regard to birth weight, neonates weighing more than 2.5 kg were more frequent in the amino acid infusion group, accounting for 38 (84.4%) of 45 births. In contrast, low birth weight (<2.5 kg) was more commonly observed in the group that did not receive amino acid infusion, with 18 (40%) of 45 neonates falling into this category. This difference was found to be statistically significant (p < 0.05). These findings are consistent with randomized controlled trial conducted by Shree P et al,^[3] who demonstrated that intravenous amino acid infusion significantly improved fetal birth weight. Similarly, Kumar P et al,^[10] reported that amino acid infusion therapy resulted in a significant increase in birth weight in pregnancies complicated by oligohydramnios.

Normal vaginal delivery with spontaneous onset of labour was significantly higher in the amino acid infusion group (p = 0.013). Caesarean section was more common in the group that did not receive amino acid infusion, with fetal distress being the most frequent indication. In contrast, among women who received intravenous amino acid infusion, the most common indications for caesarean section were cephalopelvic disproportion (CPD) followed by multiparity with previous caesarean section. These results are consistent with observations reported in

several previous studies, which also demonstrated a higher incidence of fetal distress and operative delivery among patients who did not receive amino acid therapy.^[3,10-12]

The Apgar score at 1 minute was significantly higher among neonates born to mothers who received intravenous amino acid infusion ($p = 0.049$). In addition, NICU admission was more frequent among neonates in the group that did not receive amino acid therapy. These findings are consistent with observations reported in previous studies.^[5,10] Neonatal complications were slightly higher in the group that did not receive amino acid infusion ($p = 0.696$). In the amino acid infusion group, respiratory distress was observed in 2 neonates and meconium aspiration in 3 neonates. In contrast, in the group without amino acid infusion, respiratory distress occurred in 4 neonates, meconium aspiration in 4 neonates, and hypoglycaemia in 1 neonate.

Overall, these findings suggest that maternal amino acid infusion may contribute to improved amniotic fluid index (AFI), which in turn may positively influence birth weight and perinatal outcomes, including better neonatal condition at birth and reduced need for NICU admission

Limitations: A key strength of the present study is the inclusion of a representative study population, which improves the generalizability of the findings to similar clinical settings. However, certain limitations should be acknowledged. In particular, quantitative estimation of amino acid levels in maternal serum or amniotic fluid was not performed, which might have provided a more objective evaluation of the biochemical impact of amino acid supplementation and further strengthened the study conclusions.

CONCLUSION

In conclusion, intravenous amino acid infusion in pregnancies complicated by oligohydramnios was associated with a significant improvement in amniotic fluid index (AFI) and showed favourable effects on fetal growth and perinatal outcomes. Women receiving amino acid therapy demonstrated higher AFI, better birth weight distribution, improved Apgar scores, and fewer incidences of fetal distress and NICU admissions compared with those who did not receive amino acid infusion.

These findings suggest that maternal amino acid supplementation may be a useful therapeutic intervention for improving amniotic fluid volume and optimizing maternal and neonatal outcomes in pregnancies with oligohydramnios. However, further large-scale randomized controlled studies with biochemical assessment of amino acid levels are recommended to validate these findings and establish definitive clinical guidelines.

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