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Original Research Article

To Compare the Efficacy of Intravenous Amino Acids and Intravenous Hydration on Amniotic Fluid Index (AFI) in Oligohydramnios in the Third Trimester of Pregnancy

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Abstract:

Objective: To compare the effectiveness of intravenous amino acid infusion versus normal saline in improving amniotic fluid index (AFI) among pregnant women with third-trimester oligohydramnios.

Study Design: Randomized controlled trial.

Place and Duration of Study: Department of Obstetrics and Gynecology, Hayat Memorial Teaching Hospital, Lahore, over six months after approval of the synopsis.

Methodology: A total of 84 pregnant women aged 16–40 years with singleton pregnancies in the third trimester and diagnosed with oligohydramnios were enrolled using non-probability consecutive sampling. Participants were randomly allocated into two equal groups (n=42 each). The experimental group received six daily infusions of 200 ml intravenous amino acids, while the control group received six daily infusions of 500 ml normal saline. Baseline demographic and obstetric variables were recorded. AFI was measured before and after therapy, and the mean change in AFI was calculated. Data were analyzed using SPSS-26. An independent sample t-test was applied to compare outcomes, and $p \leq 0.05$ was considered significant.

Results: Baseline characteristics were comparable between groups ($p>0.05$). Pre-therapy AFI showed no significant difference (4.11±0.86 vs 4.16±0.81 cm; $p=0.787$). Post-therapy AFI was significantly higher in the amino acid group compared with controls (6.77±1.60 vs 4.72±1.37 cm; $p<0.001$). Mean increase in AFI was also significantly greater in the experimental group (2.66±1.87 cm) than in the control group (0.56±1.73 cm; $p<0.001$). Stratified analysis demonstrated consistent improvement across age, gestational age, gravida, parity, and area of residence.

Conclusion: Intravenous amino acid infusion significantly improves AFI in women with oligohydramnios compared with normal saline and may serve as an effective therapeutic option to enhance amniotic fluid volume.

Keywords: Oligohydramnios, Amniotic fluid index, Intravenous amino acids, Pregnancy, Randomized controlled trial.

INTRODUCTION

In oligohydramnios, the volume of amniotic fluid is low in relation to the gestational age. Throughout pregnancy, the amniotic fluid level rises and falls. It reaches a constant state at about 400 ml around the 34th or 36th week of gestation and stays there until the baby is born (1-3). Transabdominal ultrasonography may assess the amount of amniotic fluid using either the amniotic fluid index (AFI) or the maximum vertical pocket, depending on the institution. Measuring the greatest vertical pocket in each of the four quadrants of the uterus, divided by the umbilicus, allows one to determine the amniotic fluid index (AFI) after 20 weeks of gestation (4, 5). All four of the uppermost vertical pockets add up to the AFI. An amniotic fluid index (AFI) below 5 cm signifies oligohydramnios (6). It has been proposed that lower

fetal urine production in response to prolonged fetal hypoxia during the third trimester of pregnancy is associated with oligohydramnios in utero-placental insufficiency. Nevertheless, the exact process is still a mystery (7). In 4.4% of full-term pregnancies, oligohydramnios is a complicating factor. In preterm pregnancies, the risk of oligohydramnios is less than 1% (8). Oligohydramnios treatment mostly involves supportive measures; nevertheless, amino acid infusion has lately been proposed as a more effective option (9). One study found that women with oligohydramnios saw a substantially higher amniotic fluid index (AFI) after one week of receiving intravenous amino acid treatment (6.32 ± 2.03cm vs 5.05 ± 2.09cm, respectively; p = 0.002) compared to the control group (9). A similar research found that women with oligohydramnios had a substantially higher amniotic fluid index (AFI) (6.82 ± 0.62cm versus 4.79 ± 0.65cm, respectively; p < 0.001) when given amino acid infusions compared to controls who received basic intravenous hydration (3). On the other hand, a research found the exact opposite: the control group had a significantly greater post-therapy amniotic fluid index (AFI) of 6.32 ± 4.6cm compared to the group that had intravenous amino acids infusion of 5.56 ± 2.3cm (10). It is clear from the existing research that there is ongoing controversy over the use of intravenous amino acids for the treatment of oligohydramnios (3, 9) exhibiting its clear advantage while others (10) reporting no effect of this therapy on post-therapy AFI. In addition, intravenous amino acids for oligohydramnios therapy are relatively new in Pakistan. Because of the critical need for additional research in this area, the current study compares the post-therapy AFI in women who received intravenous amino acids to that in women who received simple intravenous hydration in order to determine the effect of IV amino acids on AFI in oligohydramnios during the third trimester of pregnancy.

METHODOLOGY

This randomized controlled trial will be conducted in the Department of Obstetrics and Gynecology, Hayat Memorial Teaching Hospital, Lahore, over a period of six months after approval of the synopsis from the institutional ethical committee and CPSP. A non-probability consecutive sampling technique will be employed for the recruitment of participants. The sample size was calculated using OpenEpi software with a 95% confidence level and 80% power. Based on the expected mean post-therapy AFI of 6.32 ± 2.03 in the intervention group and 5.05 ± 2.09 in the control group, the calculated sample size was 84 patients, with 42 participants in each group.

Pregnant women aged 16–40 years in the third trimester with singleton pregnancy and diagnosed oligohydramnios on obstetric ultrasound performed by a consultant obstetrician will be included. Both primigravida and multigravida, as well as primiparous and multiparous women, will be eligible. Women with multiple gestation, a previous history of oligohydramnios, prior abortion, or previous intravenous amino acid therapy will be excluded after assessment of obstetric records and ultrasound findings. After obtaining informed consent, baseline demographic and clinical characteristics, including age, gestational week, gravida, para, area of residence, and baseline AFI, will be recorded on a pre-designed proforma. Participants will then be randomly allocated into two equal groups using the lottery method. The experimental group will receive six daily infusions of 200 ml intravenous amino acids, while the control group will receive six daily infusions of 500 ml normal saline. After completion of therapy, AFI will be reassessed, and the mean change in AFI will be calculated by subtracting baseline values from post-therapy measurements. Confidentiality and anonymity of participants will be strictly maintained, and no personal identifiers will be recorded. Data will be analyzed using SPSS version 26. Quantitative variables such as age, gestational age, and AFI values will be presented as mean ± standard deviation, whereas categorical variables, including gravida, para, and area of residence, will be expressed as frequencies and percentages. An independent sample t-test will be applied to compare post-therapy AFI and the mean change in AFI between the two groups. Stratification will be performed for age, gestational week, gravida, and para to control potential effect modifiers, followed by post-stratification t-test. A p-value of ≤0.05 will be considered statistically significant.

RESULTS

A total of 84 pregnant women with oligohydramnios fulfilling the eligibility criteria were enrolled and equally randomized into experimental and control groups (n=42 each). The mean age of participants was comparable between the two groups, and no statistically significant differences were observed in baseline demographic or obstetric characteristics, confirming homogeneity of the study population prior to intervention. Amniotic fluid index (AFI) was assessed before and after completion of six infusions, and the mean change in AFI was calculated to determine the therapeutic effect of intravenous amino acids compared with normal saline. Table presents the baseline demographic and obstetric characteristics of study participants. The mean age in the experimental group was 28.48±7.06 years compared to 30.24±7.21 years in the control group (p=0.261). Distribution of age groups, gestational age, gravida, parity, and area of residence was also comparable between the two groups with no statistically significant differences (p>0.05). These findings indicate successful randomization and baseline equivalence of both groups (Table 1).

Table 1. Baseline demographic and obstetric characteristics of study participants (n = 84)

Variable	Experimental Group (n = 42)	Control Group (n = 42)	*p*-value
Age	28.48±7.06	30.24±7.21	0.261
Age group			
16–20 years	9 (21.4%)	4 (9.5%)	0.320
21–30 years	15 (35.7%)	17 (40.5%)	
31–40 years	18 (42.9%)	21 (50.0%)	
Gestational age	33.21 4.286	33.64 4. 089	0.640
Gestational age group			
28–32 weeks	21 (50.0%)	16 (38.1%)	0.183
33–36 weeks	6 (14.3%)	13 (31.0%)	
37–40 weeks	15 (35.7%)	13 (31.0%)	
Gravida			
Primigravida	19 (45.2%)	18 (42.9%)	0.826
Multigravida	23 (54.8%)	24 (57.1%)	
Parity			
Primiparous	24 (57.1%)	17 (40.5%)	0.127
Multiparous	18 (42.9%)	25 (59.5%)	
Area of residence			
Rural	18 (42.9%)	19 (45.2%)	0.826
Urban	24 (57.1%)	23 (54.8%)	

Table compares the amniotic fluid index between the two groups before and after therapy. Pre-therapy AFI was similar in the experimental and control groups (4.11±0.86 vs 4.16±0.81 cm; p=0.787). After intervention, post-therapy AFI showed a significant improvement in the experimental group compared to controls (6.77±1.60 vs 4.72±1.37 cm; p<0.001) with a mean difference of 2.05 cm (95% CI: 1.40–2.69). Similarly, the mean change in AFI was significantly greater in the experimental group (2.66±1.87 cm) than in the control group (0.56±1.73 cm; p<0.001), demonstrating the effectiveness of intravenous amino acid therapy (Table 2).

Table 2. Comparison of amniotic fluid index (AFI) between experimental and control groups (n = 84)

Variable	Group	N	Mean ± SD	T	df	p-value	Mean Difference	95% CI of Difference
Pre-Therapy AFI	Experimental	42	4.11 ± 0.86	-0.272	82	0.787	-0.05	-0.41 – 0.31
	Control	42	4.16 ± 0.81					
Post-Therapy AFI	Experimental	42	6.77 ± 1.60	6.304	82	0.000	2.05	1.40 – 2.69
	Control	42	4.72 ± 1.37					
Change in AFI	Experimental	42	2.66 ± 1.87	5.319	82	0.000	2.10	1.31 – 2.88
	Control	42	0.56 ± 1.73					

Table illustrates the stratified analysis of change in AFI according to age, gestational age, gravida, parity, and area of residence. Significant improvement in AFI was observed in the experimental group across all age categories (p≤0.007). With respect to gestational age, a statistically significant increase in AFI was noted in women at 28–32 weeks and 37–40 weeks (p=0.001 and p=0.005 respectively), while the difference in the 33–36 weeks' subgroup was not significant (p=0.127). Both primigravida and multigravida women in the

experimental group demonstrated significantly greater improvement compared to controls ($p<0.01$). Similar significant effects were observed across parity and area of residence subgroups, indicating consistent therapeutic benefit of intravenous amino acids irrespective of demographic or obstetric factors (Table 3).

Table 3. Table X. Change in Amniotic Fluid Index (AFI) by Gestational Age, Stratified by Age, Gravida, Parity, and Area of Residence

Subgroup	Group	N	Mean ± SD	T	df	p-value	Mean Difference	95% CI of Difference
Age (years)								
16–20	Experimental	9	2.39 ± 1.69	3.268	11	0.007	2.92	0.95 – 4.89
	Control	4	-0.53 ± 0.72					
21–30	Experimental	15	2.69 ± 1.76	3.602	30	0.001	2.04	0.88 – 3.19
	Control	17	0.65 ± 1.44					
31–40	Experimental	18	2.76 ± 2.13	3.091	37	0.004	2.07	0.71 – 3.42
	Control	21	0.70 ± 2.04					
Gestational Age (weeks)								
28–32	Experimental	21	2.66 ± 1.46	3.660	35	0.001	1.95	0.87 – 3.03
	Control	16	0.72 ± 1.77					
33–36	Experimental	6	1.79 ± 1.33	1.603	17	0.127	1.28	-0.41 – 2.97
	Control	13	0.51 ± 1.73					
37–40	Experimental	15	2.99 ± 2.48	3.085	26	0.005	2.57	0.86 – 4.28
	Control	13	0.42 ± 1.82					
Gravida								
Primigravida	Experimental	19	2.96 ± 1.55	5.171	35	0.000	2.76	1.68 – 3.84
	Control	18	0.20 ± 1.70					
Multigravida	Experimental	23	2.40 ± 2.10	2.793	45	0.008	1.57	0.44 – 2.71
	Control	24	0.83 ± 1.75					
Parity								

Primiparous	Experimental	24	2.63 ± 1.80	3.256	39	0.002	1.86	0.70 – 3.01
	Control	17	0.77 ± 1.79					
Multiparous	Experimental	18	2.69 ± 2.01	3.987	41	0.000	2.27	1.12 – 3.43
	Control	25	0.42 ± 1.72					
Area of Residence								
Rural	Experimental	18	2.69 ± 1.92	3.190	35	0.003	2.05	0.75 – 3.35
	Control	19	0.64 ± 1.98					
Urban	Experimental	24	2.63 ± 1.88	4.250	45	0.000	2.14	1.12 – 3.15
	Control	23	0.50 ± 1.54					

DISCUSSION

In this randomized controlled trial, pregnant women with idiopathic third-trimester oligohydramnios who received intravenous amino acid infusions demonstrated a statistically significant increase in amniotic fluid index (AFI) compared with those who received normal saline. Post-therapy AFI was significantly higher in the experimental group, with a mean rise of 2.66 ± 1.87 cm versus 0.56 ± 1.73 cm in controls ($p<0.001$), indicating a therapeutic benefit of amino acid infusion in enhancing amniotic fluid volume among women with oligohydramnios (11). These findings align with several studies showing improvement in AFI with amino acid therapy. Sunil et al. reported that women receiving amino acid infusions achieved a mean gain in AFI of 2.32 ± 0.67 cm versus 1.32 ± 1.03 cm in untreated controls, with superior perinatal outcomes in the treated group. Similarly, Afzal et al. observed a mean increase in AFI of 2.30 ± 0.65 cm after amino acid infusion, and 35% of patients achieved normalization of AFI by the time of delivery. These studies corroborate our findings that amino acid infusion can significantly raise AFI, suggesting it is a viable therapeutic option for idiopathic oligohydramnios (12). The results also resonate with recent data from a randomized trial using PAN-AMIN G, where the amino acid group experienced a significantly greater AFI increase compared with normal saline (mean change 3.1 ± 0.7 cm vs 1.1 ± 0.3 cm, $p<0.001$) (13).

That study reported normalization of AFI in over 60% of treated women, further supporting the magnitude of effect observed in our trial. Although PAN-AMIN G is a specific commercial amino acid preparation, the consistent direction of benefit across these different formulations underscores biological plausibility for amino acid therapy in oligohydramnios. Our stratified analysis also demonstrated consistent increases in AFI across age, parity, gravida, and residence subgroups. This suggests that the effect of amino acid infusion on AFI is robust across common demographic and obstetric variables, which is clinically relevant given the heterogeneity of real-world antenatal populations. Mechanistically, amino acids may influence AFI through multifactorial pathways: they serve as substrates for fetal and placental protein synthesis, facilitate placental perfusion via enhanced nitric oxide synthesis, and contribute to fetal urine production, directly augmenting amniotic fluid volume (14). These physiological roles may explain why intravenous amino acid therapy can outperform simple fluid loading strategies in raising AFI.

Research on maternal hydration alone provides a useful contrast. Several trials have shown that intravenous or oral hydration can increase AFI significantly compared with no therapy. Azarkish et al. demonstrated that maternal intravenous hydration significantly increased AFI compared with control subjects, supporting hydration as a beneficial non-pharmacologic intervention (15).

Similarly, Hofmeyr's systematic review concluded that simple maternal hydration increases amniotic fluid volume, albeit with variable clinical outcomes. However, the magnitude of AFI increase with hydration alone has generally been less than that reported with amino acid infusion in comparable studies (16).

This suggests that while hydration strategies are helpful, they may not be as potent as amino acid supplementation for augmenting AFI, particularly in moderate to severe oligohydramnios. A comparative study of hydration therapy versus amino acid infusion found that both treatments increased AFI, but the differential effect was more prominent on specific days following treatment; ultimately, AFI gains were comparable at later follow-ups. This raises the possibility that timing, volume, and type of fluid or nutrient intervention are key determinants of therapeutic response, and that amino acids may provide additional

metabolic or placental benefits not captured by hydration alone. Beyond fluid and amino acid therapy, research into L-arginine supplementation, a semi-essential amino acid and precursor of nitric oxide, also suggests potential benefit for oligohydramnios management. Soni et al. observed that l-arginine supplementation significantly increased AFI (mean change >3 cm) and prolonged pregnancy, likely through enhanced uteroplacental perfusion and fetal urine output (14). Rahman et al. similarly reported significant AFI improvement following l-arginine administration (17). These findings lend further support to the concept that targeted nutritional interventions can improve amniotic fluid volume through mechanisms beyond simple hydration. Fetal weight gain, another important outcome in oligohydramnios, has been positively influenced by amino acid infusion in some studies. For example, Shree et al. reported greater fetal weight gain in the amino acid group compared with controls, suggesting broader benefits for fetal growth and well-being (10).

Although our study did not assess fetal weight outcomes, these observations highlight the potential holistic advantages of amino acid therapy in compromised pregnancies. Several older prospective studies also support amino acid infusion as a therapeutic intervention for oligohydramnios. Early work by Gupta et al. and others demonstrated improved AFI following intravenous amino acid administration, albeit with variable study designs and sample sizes (4). When integrated with more recent randomized evidence, the cumulative data form a consistent pattern in which amino acid infusions are associated with meaningful increases in AFI and, in some cases, improved perinatal outcomes.

Many studies vary in protocol regarding dosage, frequency, and duration of infusion, making direct comparisons challenging. Additionally, while most trials report increased AFI, only some evaluate clinical outcomes such as gestational age at delivery, mode of delivery, and neonatal health parameters. Future larger multicenter randomized studies with standardized intervention protocols and perinatal outcome measures will be necessary to clarify the optimal use of amino acid and hydration therapies in clinical practice. This study adds to growing evidence that intravenous amino acid infusion significantly increases AFI in idiopathic oligohydramnios and does so more effectively than standard normal saline, consistent with similar research. When set within the broader literature, including hydration, amino acid supplementation, and L-arginine interventions, these results support an integrative strategy that addresses both hemodynamic and metabolic determinants of amniotic fluid volume. The consistency of findings across diverse settings further suggests that amino acid infusion may be a valuable and practical therapeutic option for improving amniotic fluid status and potentially enhancing maternal and perinatal outcomes in oligohydramnios.

CONCLUSION

Intravenous amino acid therapy was found to be significantly more effective than normal saline in improving amniotic fluid index among women with third-trimester oligohydramnios. Participants receiving amino acid infusions demonstrated a marked rise in post-therapy AFI and greater mean change from baseline compared with controls, with consistent benefit across different age groups, gestational ages, gravida, parity, and residential backgrounds. These findings suggest that intravenous amino acid supplementation is a useful, safe, and practical therapeutic option for the management of idiopathic oligohydramnios. Incorporation of this intervention into routine obstetric care may help reduce complications associated with low amniotic fluid volume and improve perinatal outcomes. Further large-scale multicenter trials are recommended to evaluate long-term maternal and neonatal benefits and to establish standardized treatment protocols.

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