



Effects of Amino Acid Infusion on Amniotic Fluid Volume and Perinatal Outcomes in Oligohydramnios Patients: An Evidence-Based Case Report

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Abstract: Oligohydramnios is associated with perinatal morbidity and mortality. Intravenous (IV) amino acid infusion is a proposed management strategy to improve amniotic fluid volume and fetal nutrition. This evidence-based case report evaluates the efficacy of IV amino acid infusion versus standard IV hydration on Amniotic Fluid Index (AFI) and perinatal outcomes. This was a systematic search conducted on PubMed, Scopus, Cochrane, and Google Scholar for randomized controlled trials or semi-experimental studies. Critical appraisal was performed using OCEBM criteria. The results showed that literature screening process yielded three eligible studies, comprising one RCT and two semi-experimental studies. Two of these studies reported a statistically significant increase in AFI among patients in the amino acid infusion group ($p < 0.001$), while one study observed no significant difference compared to standard IV hydration. However, all three studies consistently demonstrated significant clinical improvements in estimated fetal weight gain and the prolongation of gestational age. Additionally, the need for NICU admission and perinatal mortality rates were lower in the amino acid groups. A notable methodological limitation identified across the appraised studies was the absence of reported confidence intervals. In conclusion, intravenous amino acid infusion serves as a potential and effective adjuvant therapy for patients with oligohydramnios. While evidence showing superior AFI improvement remains inconsistent across the studies, the intervention consistently improves fetal weight gain, reduces the risk of preterm birth, and enhances overall perinatal survival rates.

Keywords: amino acid infusion; amniotic fluid index (AFI); oligohydramnios; perinatal outcome

INTRODUCTION

Amniotic fluid is a clear fluid that is present in amniotic sac and surrounds the fetus.¹ Amniotic fluid provides protection for the growing foetus. It supplies nutrients to the foetus while providing a cushion against mechanical and biological injury as well as a barrier against infection. Regulation of amniotic fluid is balanced by the production lung fluid and fetal urine, and its absorption by intramembranous flow and foetal swallowing.² Adequate amniotic fluid allows normal fetal movements and growth and cushions the fetus and umbilical cord.³

Oligohydramnios is defined as an amniotic fluid volume less than the minimum expected for gestational age. More specifically, it occurs when the index is below the 5th percentile for gestation, the amniotic fluid index (AFI) is <5 cm, or there is no pocket of amniotic fluid ≥ 2 cm.^{3,4,5} Data indicates that oligohydramnios is observed in approximately 7–8% of pregnancies, although a recent study reports a prevalence of 1–5%.^{6,7} Oligohydramnios is associated with perinatal morbidity and mortality. It can lead to chronic placental insufficiency, cord compression, which in turn can lead to fetal hypoxia, poor lung development, intrauterine growth restriction, abnormal fetal heart patterns during labor, meconium aspiration syndrome, low APGAR score, neonatal intensive care unit (NICU) admission, and stillbirth.⁸

Treatment of oligohydramnios includes hospitalization, specialist consultation, bed rest, oral rehydration, IV hydration, and IV amino acids.⁹ In literature whereas few studies have shown that improvement of AFI either by IV hydration or amino acid infusion is comparable, other studies have shown that IV amino acids are better than IV hydration.^{9,10,11} Amino acid is often prescribed for the treatment of oligohydramnios. As they constitute the carbon and nitrogen requirement for the placenta and foetus. Amino acid acts as regulators of the development of the foetus and placenta. They are a source of protein building blocks in the foetus and they also influence metabolic cyclic pathways between placenta and foetus. These are shown to improve vascularity through nitric oxide and stimulate insulin secretion leading to foetal growth.¹² Most oral and IV interventions are proven to be effective, but any comprehensive study on one modality's guaranteed effectiveness and dosage has yet to be implemented. Therefore, this evidence-based case report aims to compare the efficacy of intravenous amino acid infusion versus intravenous hydration in cases of oligohydramnios and FGR, specifically assessing their impact on the amniotic fluid volume and index also perinatal outcomes.

CASE REPORT

A 25-year-old primigravida, Mrs. A, presented with a primary complaint of a fundal height smaller than expected for her gestational dates, which was noted during a routine antenatal check-up at 32 weeks of gestation. She had no history of premature rupture of membranes (PROM), hypertensive disorders of pregnancy, or diabetes mellitus, and her anomaly scan at 20 weeks had been unremarkable. The patient's clinical history revealed no known maternal comorbidities, though she reported a subjective decrease in fetal movements over the preceding week. Comprehensive history taking, physical examination, and obstetric ultrasonography were performed. The patient was subsequently diagnosed with oligohydramnios and fetal growth restriction (FGR). Based on her ultrasonographic evaluation, the patient had an Amniotic Fluid Index (AFI) of 4.2 cm, falling below the 5th percentile, and an estimated fetal weight (EFW) indicating growth restriction. Doppler velocimetry of the umbilical artery was within normal limits, ruling out severe placental insufficiency. Management consisted of bed rest in the left lateral position and hydration monitoring. Additionally, to address the oligohydramnios and improve fetal nutritional status, the patient was prescribed an intravenous amino acid infusion (200 mL administered on alternate days for two weeks). Follow-up assessment at 14 days showed a significant therapeutic response, with the AFI increasing to 7.5 cm and a documented increase in estimated fetal weight.

Problem formulation is as follows: In pregnant women diagnosed with oligohydramnios, is amino acid infusion increase amniotic fluid volume and improve perinatal outcomes?

Based on the clinical question, the following PICO was created. Patients were pregnant women with diagnosis of oligohydramnios; intervention of parenteral amino acid infusion; comparison was intravenous fluid infusion; and outcome of AFI or amniotic fluid volume increase and perinatal outcomes.

METHODS

The literature search was conducted independently across four databases: PubMed, Scopus, Cochrane, and Google Scholar. The search was performed using advanced search strategies by combining MeSH terms and title/abstract keywords from each component of PICO and the study design, as well as using the Boolean operator “OR” to increase sensitivity and “AND” to increase specificity (Table 1). The keywords used were oligohydramnios, perinatal outcomes, parenteral nutrition, amino acid, infusion, intravenous fluid.

The eligibility criteria are pregnant patients diagnosed with oligohydramnios; studies designed as Randomized Controlled Trials (RCTs) or systematic reviews/meta-analyses including RCTs; intervention groups receiving amino acid infusion; control groups receiving placebo or standard intravenous therapy; studies reporting clinical outcomes regarding Amniotic Fluid Index (AFI) or amniotic fluid volume and perinatal outcomes; dan articles published in English or Indonesian. Meanwhile, the exclusion criteria are studies not conducted on human subjects (animal or *in vitro* studies) and studies where the full-text manuscript is not accessible.

The titles and abstracts of all retrieved articles were reviewed to assess their relevance to the clinical question. Studies that met the eligibility criteria were further screened. A critical appraisal of the included studies was conducted using the Oxford Centre for Evidence-Based Medicine (OCEBM) assessment tool, evaluating each article for Validity, Importance, and Applicability (VIA).

RESULTS

A total of 25 articles were retrieved from PubMed, Cochrane, Scopus, and Google Scholar (Table 1). These articles were subsequently filtered to assess the relevance of their titles and abstracts in relation to the PICO framework. After screening, three studies met the eligibility criteria (Figure 1), including three of randomized controlled trials (RCTs) studies. Detailed study characteristics, including research design, population, intervention, and outcomes assessed, are summarized in Table 2.

Critical evaluations of each study are provided in Tables 3, 4, and 5.

Table 1. Search strategy method

Database	Search strategy	Number	Selected
Pubmed	("Oligohydramnios"[Mesh] OR "Oligohydramnios") AND ("Parenteral Nutrition"[Mesh] OR "Fluid Therapy"[Mesh] OR "amino acid infusion" OR "intravenous amino acids" OR "intravenous fluids")	12	1
Cochrane	#1 MeSH descriptor: [Oligohydramnios] #2 MeSH descriptor: [Parenteral nutrition] #3 (AFI) OR ("amniotic fluid index") #4 #1 AND #2 AND #3	2	0
Scopus	TITLE-ABS-KEY (oligohydramnio*) AND TITLE-ABS-KEY ("amino acid infusion" OR "intravenous amino acid*" OR "IV amino acid*") AND NOT TITLE-ABS-KEY (rat OR mouse OR mice OR sheep OR ovine OR rabbit OR animal*)	1	0
Google Scholar	oligohydramnios "intravenous amino acids" AFI - animal	10	2

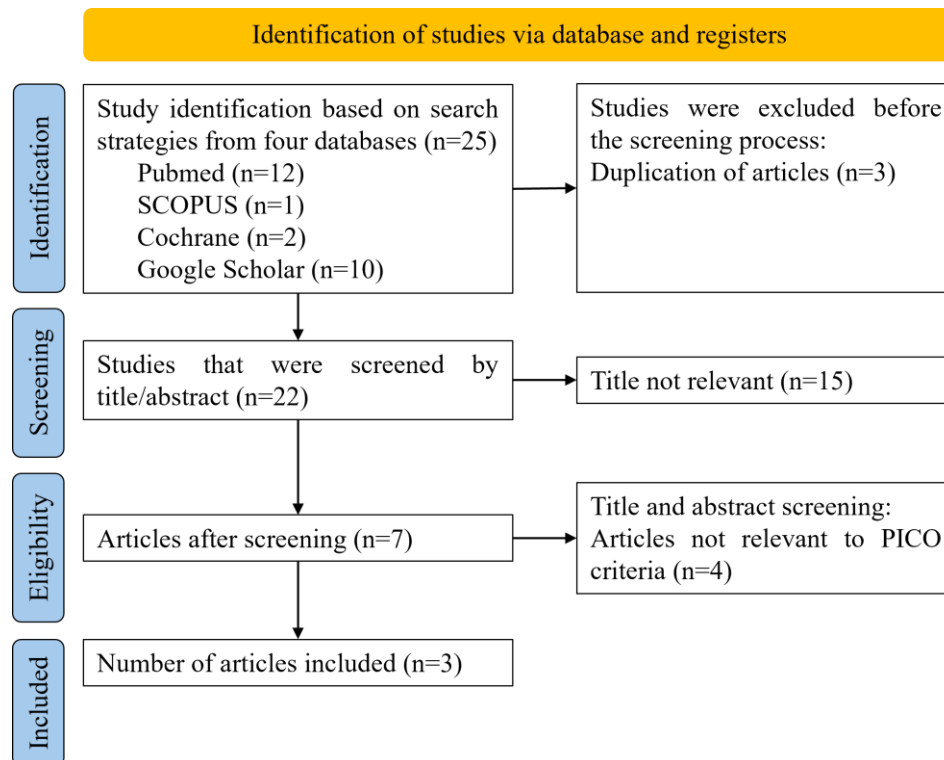


Figure 1. Flowchart of literature search.

DISCUSSION

The literature search identified three relevant studies addressing the clinical question concerning the impact of intravenous (IV) amino acid supplementation on amniotic fluid volume and perinatal outcomes. Of these, two were semi-experimental studies, and one was a randomized controlled trial (RCTs). These three studies were subsequently analysed to evaluate the effectiveness of amino acid infusion compared to standard IV hydration in patients with oligohydramnios. Across all three studies, IV amino acid infusion demonstrated a substantial effect on increasing the AFI. In Shinde et al,¹³ the mean AFI increased significantly to 7.52 ± 2.04 cm compared to 5.89 ± 2.20 cm in the hydration group ($p < 0.0001$). Similarly, Bhargava et al¹⁵ reported a dramatic rise from a baseline of 5.2 cm to 9.1 cm, whereas the control group only reached 5.8 cm.

The validity of the evidence presented in the three studies warrants careful consideration. The study by Shinde et al¹³ employed a semi-experimental design rather than a pure randomized controlled trial, which introduces a higher potential for selection bias compared to the other included studies. A critical methodological limitation observed across all three studies was the failure to report 95% confidence intervals (CI) for the mean differences in outcomes. This lack of reporting limits the ability to assess the precision of the treatment effect, even when statistically significant p-values were provided.¹⁴ Furthermore, the study by Kumar et al⁹ had a relatively small sample size ($n=30$), which may have resulted in insufficient statistical power (Type II error) to detect a significant difference in AFI between the intervention groups.⁹

The study by Bhargava et al¹⁵ demonstrated that amino acid infusion resulted in a significant reduction in oligohydramnios, marked by a substantial increase in the AFI compared to the control group ($p < 0.001$). Similarly, Shinde et al¹³ reported a statistically significant improvement in AFI on the 14th day in the amino acid group (7.52 ± 2.04 cm) compared to the hydration group (5.89 ± 2.20 cm). In contrast, the study by Kumar et al⁹ reported an increase in AFI following the intervention, but the results were not statistically significant when comparing the amino acid group to the normal saline group ($p=0.677$). Despite this inconsistency regarding AFI, all three studies consistently reported significant improvements in fetal weight gain and a reduction in the proportion of low-birth-weight infants in the amino acid groups. These findings are further

corroborated by the study of Habib et al., which demonstrated the superior efficacy of amino acid therapy over standard hydration. In their methodology, the control group received 500 ml of intravenous normal saline, while the study group was administered 200 ml of IV amino acid infusion on alternate days for a total of six doses. The results indicated that the mean AFI following the intervention was significantly higher in the amino acid group compared to the control group (6.82 ± 0.62 vs. 4.79 ± 0.65 , respectively; $p < 0.001$).¹⁶

The studies included populations with heterogeneous clinical characteristics, which complicates the generalizability of the results. Shinde et al. and Bhargava et al. specifically recruited patients with oligohydramnios associated with FGR or IUGR, suggesting a study population with pre-existing placental insufficiency. In contrast, Kumar et al.⁹ focused on "idiopathic" oligohydramnios, where cases with a recognizable underlying etiology or established fetal growth issues were not a mandatory inclusion criterion.^{9,13,15} This distinction is crucial, as the presence of FGR/IUGR indicates a baseline of compromised fetal nutrition, whereas idiopathic cases represent a population without a clearly identified cause for the reduced liquor volume.^{17,18} The fact that amino acid infusion showed efficacy in both subtypes suggests a robust physiological benefit that transcends the specific etiology of the fluid reduction, likely by addressing lower serum amino acid concentrations found in these fetuses and improving vascularity via nitric oxide pathways.^{19,20}

The therapy's effect on fetal growth was equally pronounced. Shinde et al. observed a mean increase in EFW of 338.73 g over 14 days. This is supported by Bhargava et al.¹⁵ where 63.3% of newborns in the amino acid group achieved a birth weight >2.5 kg, a stark contrast to only 25% in the hydration-only group.^{9,15} A theoretical framework supports the role of amino acids in modulating amniotic fluid volume and fetal growth. Amino acids cross the placenta via active transport systems, maintaining higher concentrations in the fetus than in the mother.¹³ Physiologically, specific amino acids like L-Arginine serve as precursors for nitric oxide (NO) synthesis.²¹ Nitric oxide promotes vasodilation of the uteroplacental vasculature, thereby enhancing blood flow to the fetus.²⁰ This improved perfusion increases fetal renal blood flow and glomerular filtration rates, leading to increased fetal urine production which acts as the primary source of amniotic fluid in the third trimester.¹⁰ Additionally, improved maternal nutritional status through supplementation addresses the fetal nutrient deficit that often accompanies oligohydramnios, directly contributing to the observed weight gain.²²

Regarding perinatal outcomes, the effect size of intravenous amino acid supplementation was clinically significant in reducing neonatal morbidity and improving survival rates. Kumar et al. demonstrated a substantial decrease in NICU requirements, noting that the need for admission was significantly lower in the amino acid group at 14%, compared to 38% in the hydration group.¹³ This is further corroborated by Bhargava et al.¹⁵ who highlighted a significant reduction in perinatal mortality ($p < 0.05$). These findings suggest that parenteral nutritional support does not only restore amniotic fluid volume but directly enhances neonatal survival chances by mitigating the risks associated with restricted fetal growth and chronic hypoxia.^{9,15}

The evidence regarding the efficacy of IV amino acid supplementation in increasing AFI remains somewhat inconsistent due to the non-significant findings in the Kumar et al.'s study.⁹ However, the consistent positive impact on fetal weight and the prolongation of gestational age suggests a clinical benefit. The limitations of the current evidence base, particularly the lack of reported precision (confidence intervals) and the small sample sizes in some trials, highlight the need for larger, high-quality RCTs to confirm the magnitude of the effect.

CONCLUSION

Clinical evidence from the case demonstrates that intravenous amino acid infusion is highly effective in increasing amniotic fluid volume and successfully improving the nutritional status of a growth-restricted fetus (FGR). The review of the three selected studies indicates that intravenous amino acid infusion is a potentially effective adjuvant therapy for oligohydramnios. In summary,

the magnitude of the effect is consistent across the literature; IV amino acid supplementation not only effectively restores amniotic fluid volume but also significantly enhances fetal weight gain and improves overall perinatal survival compared to conventional hydration therapy. Given the safety profile and the potential for fetal salvage, amino acid infusion can be recommended, particularly in cases where fetal growth restriction is a concern.

Conflict of Interest

The authors declare that there are no conflicts of interest related to the studies in this manuscript.

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Table 2. Study characteristics

Authors	Study designs	Population	Intervention	Comparison	Results
A Shinde (2023)	Semi-experimental hospital-based study	Singleton pregnancy, gestational age between 28-36 weeks, amniotic fluid index (AFI) less than or equal to seven, and FGR grade one on obstetric ultrasonography	Group A patients received an amino acid IV infusion of 200 ml three times in one week, preceded by the administration of 500 ml of dextrose 5% solution for two consecutive weeks	Group B patients received intravenous (IV) fluid (1 dextrose 10%, 2 ringer lactate) on an alternate day for two consecutive weeks	In both groups, the mean AFI at admission was observed at 4.93 ± 2.03 cm and 4.22 ± 2.00 cm, respectively. The mean AFI on the 14th day in the IV amino acid group was 7.52 ± 2.04 , and in the IV hydration group, 5.89 ± 2.20 with a significant p-value of <0.0001 . The mean increase in EFW after seven and 14 days was 149.42 g and 338.73 g in IV amino acid group. The mean increase after 14 days was statistically significant compared to seven days in amino acid group. The need for NICU admission was greater in 18 (34.61%) of the IV hydration group than in 11 (21.2%) of the IV amino acid group, although it did not differ significantly between two intervention groups.
P Kumar (2016)	Experimental study	All healthy pregnant women with AFI <8 between gestational age of 28–34 weeks with oligohydramnios and willing to deliver in Bharati Hospital, Maharashtra, India	Selected cases were administered I.V. normal saline drip (500 ml)-6 drips (1 drip/day)	Other cases were administered I.V. amino acid drip (200 ml)-6 drips (1 drip/day)	The mean AFI at the end of 6 drips did not differ significantly between two intervention groups (P-value >0.05). Significantly higher proportion of cases from amino acid group had larger birth weight (p-value <0.001) and lower NICU stay (p-value <0.01).
A Bhargava (2015)	A prospective randomized controlled study	Women who were clinically and sonographically proven cases of oligohydramnios and/or IUGR in third trimester of pregnancy who visited the Department of Obstetrics & Gynaecology, LN Medical College and J.K. Hospital, (M.P.) during the period of August 2012 to April 2014.	Study group received intervention in the form of IV fluids and IV amino acids 200 cc on alternate days for ten days. On the other days, 3 units of IV fluids were infused. Repeat USG was performed at the end of 2 weeks and 4 weeks. Repeat infusions were given if required after 3-4 weeks. Oral iron, calcium and multivitamins were also given.	Control group received intervention in the form of IV fluids for days for ten days. Repeat infusions were given if required after 3-4 weeks. Oral iron, calcium and multivitamins were also given.	In both groups, the mean AFI at admission was observed at 5.2 cm and 5.4 cm, respectively. The mean AFI after treatment in the IV amino acid group was 9.1 cm, and in the IV hydration group, 5.8 cm with a significant p-value of <0.001 . The percentage of babies born with a birth weight >2.5 kg was significantly higher in the IV amino acid group (63.3%) compared to the IV hydration group (25%). The need for NICU admission and the rate of perinatal mortality were lower in the IV amino acid group than in the IV hydration group



Table 3. Summary of validity critical review

Questions	Shinde (2023)	Kumar (2016)	Bhargava (2015)
Were study participants randomized? And is the randomization table hidden?	-	+	+
Were the characteristics of the two groups comparable before the intervention?	+	+	+
Was each group given the same treatment?	-	-	-
Were all the patients who participated in the clinical trial included in the final analysis?	+	+	+
Are measurements made objectively or are both patients and doctors blind to therapy provided?	-	-	-

Table 4. Summary of importance critical review

Question	A Shinde (2023)	P Kumar (2016)	A Bhargava (2015)
How big is the effect of the therapy?	The mean AFI on the 14th day in the IV amino acid group was 7.52 ± 2.04 , and in the IV hydration group, 5.89 ± 2.20 with a significant p-value of <0.0001 . The mean increase after 14 days was statistically significant compared to seven days in the amino acid group. The need for NICU admission was greater in IV hydration group, although it did not differ significantly between the two intervention groups.	The mean AFI after treatment in the IV amino acid group was 8.9 cm, and in the IV hydration group, 7.5 cm with a significant p-value of <0.001 . The mean birth weight was significantly higher in the IV amino acid group with a p-value of <0.001 . The need for NICU admission was significantly lower in the IV amino acid group (14%) than in the IV hydration group (38%), and the duration of NICU stay was also reduced in the amino acid group.	The mean AFI after treatment in the IV amino acid group was 9.1 cm, and in the IV hydration group, 5.8 cm with a significant p-value of <0.001 . The percentage of babies born with a birth weight >2.5 kg was significantly higher in the IV amino acid group (63.3%) compared to the IV hydration group (25%). The rate of perinatal mortality was significantly lower in the IV amino acid group compared to the IV hydration group with a p-value of <0.05 .
How precise is the estimate of the therapeutic effect?	The precision cannot be evaluated since the study did not report confidence intervals, even with a significant result.	The precision cannot be evaluated since the study did not report confidence intervals	The precision cannot be evaluated since the study did not report confidence intervals, even with a significant result

Table 5. Summary of applicability critical review

Question	Shinde (2023)	Kumar (2016)	Bhargava (2015)
Are your patients very different from the study population?	No	No	No
Is the therapy available at your facility?	Yes	Yes	Yes
Will the benefits of the therapy outweigh the harms for your patients?	Yes	Yes	Yes

