

Feto-maternal Outcomes in Patients of Oligohydramnios: A Prospective Observational Study

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Cite this paper as: Snehal S Anturlikar, Haresh A Desai, (2025) Feto-maternal Outcomes in Patients of Oligohydramnios: A Prospective Observational Study. *Journal of Neonatal Surgery*, 14 (13s), 1060-1065.

ABSTRACT:

Background: Oligohydramnios referred to as decreased amniotic fluid index (AFI) <5 cm [1] is a serious disorder affecting 4.4% of pregnancies [2]. Borderline oligohydramnios, i.e. AFI between 5.1 to 8 cm also can lead to unwanted outcomes in pregnancy. Less than normal amount of amniotic fluid may lead to complications like restricted growth, underdeveloped organs, fetal distress, less birth weight, preterm birth, prolonged labor, uteroplacental insufficiency, etc. [3] L-arginine, a semi-essential amino acid is suggested to improve amniotic fluid index. [2] Hence our study was planned to know effect of L-arginine in oligohydramnios patients at our centre.

Materials and Methods: This was a prospective observational study undertaken in a tertiary care teaching hospital which included 200 patients diagnosed with oligohydramnios from 1st January 2023 to 31st October 2024. Institutional ethics committee permission (PUIECHR/PIMSR/00/081734/5306) was obtained before data collection. All pregnant women with singleton pregnancies diagnosed with oligohydramnios and satisfying inclusion criteria were included and data was recorded for those who received L-arginine along with those who came directly for delivery without receiving L-arginine.

Results: Out of 200 patients diagnosed with oligohydramnios, 100 patients received L-arginine and 100 patients came directly for delivery and did not receive L-arginine. Of those receiving L-arginine, the average gestational age of starting L-arginine therapy was 35.3 ± 2.1 weeks while gestational age at delivery was 37.4 ± 1.82 . Hence, there was an increase of 2.1 ± 0.27 weeks of gestational age at an average. The increase in AFI after treatment with L-arginine was 0 to 3 cm with a mean of 0.735 cm.

Conclusion: Our study showed a significant increase in gestational age as well as an increase in AFI with the administration of L-arginine. For establishing beneficial role of L-arginine in oligohydramnios, more such studies with bigger sample size are needed.

Keywords: *Oligohydramnios, maternal outcomes, fetal outcomes, L-arginine*

1. INTRODUCTION

L-arginine, an endogenous precursor of nitric oxide is a semi-essential amino acid and an important regulator of placental perfusion. It is suggested to improve the amniotic fluid index in oligohydramnios by promoting fetal growth by improving blood flow through the umbilical artery, especially in pregnant women with pregnancy-induced hypertension and fetal growth restriction [2].

2. MATERIALS AND METHOD

This was a prospective observational study undertaken from 1st January 2023 to 31st October 2024 in a tertiary care teaching hospital and included 200 patients diagnosed with oligohydramnios.

AFI (amniotic fluid index) <5 cm is referred to as oligohydramnios [1] which affects around 4.4% of all pregnancies at term [2]. Borderline AFI is referred to as AFI between 5 to 8 cm. [4]

The amniotic fluid surrounding the fetus is important for adequate fetal growth and good fetal outcome. It also serves to protect the fetus and umbilical cord from compression [2]. It helps create physical space for fetal movement thus helping in neuromusculoskeletal maturation. By the mid-third trimester, amniotic fluid volume reaches 800 ml [4].

If amniotic fluid volume decreases, the foetus tries to acclimatize by reducing urine output by redirecting blood flow towards vital organs. Fetal movement may decrease, and foetus may assume a peculiar appearance with musculoskeletal deformities [2]. Also, oligohydramnios may lead to various fetal complications like meconium aspiration, fetal heart rate deceleration, and non-reactive fetal tracings. [5]

Maternal complications like prolonged labor due to inertia, increased incidence of operative intervention, and uteroplacental insufficiency can also occur due to oligohydramnios [6].

Institutional ethics committee permission (PUIECHR/PIMSR/00/081734/5306) was obtained before data collection.

Inclusion Criteria: All pregnant women with a singleton pregnancy between 24-36 weeks of gestation, diagnosed with oligohydramnios and having borderline AFI, consenting to take part in the study and coming to the Department of Obstetrics and Gynecology between 1st January 2023 to 31st October 2024.

Pregnant women who came for emergency delivery due to oligohydramnios to the department of obstetrics and gynecology within the study period and were not on arginine therapy were also included.

Exclusion Criteria:

Congenital anomalies, multiple pregnancies, pregnant women diagnosed with oligohydramnios in 1st trimester, premature rupture of membrane, and those who did not consent to take part in the study, were excluded.

Patients who received L-arginine sachets (3-4 sachets a day) and/or tablets (3 times a day) were observed, and a case record form was filled. Treatment with L-arginine continued till improvement in liquor/ need for emergency cesarean section.

Those patients, who came directly for emergency delivery due to oligohydramnios and were not on L-arginine therapy, their data were also recorded in case record form.

Amniotic fluid volume calculation was done by the Department of Obstetrics and Gynaecology using the four-quadrant technique by ultrasound and data was recorded in the case record form.

Data is presented as mean $\pm$ standard deviation. Fischer's exact test was used to determine the observations' statistical significance. Wilcoxon Sign Rank test was used to know if the increase in AFI after treatment with L-arginine was significant. Mann-Whitney U test was performed to know if an increase in gestational age after administration of L-arginine was significant. SPSS software version 25 was used for data analysis.

3. RESULTS:

A total of 200 pregnant females diagnosed with oligohydramnios from 1st January 2023 to 31st October 2024 were included in this study. Out of these, 100 patients received L-arginine and 100 patients came directly for delivery and were not prescribed L-arginine.

The demographic characteristics of both these groups are given below in Table I.

Table I: Demographic characteristics of pregnant ladies with oligohydramnios:

Characteristic	With arginine (100)	Without arginine (100)
Mean Age	24.86 $\pm$ 3.72 years	25.12 $\pm$ 4.10 years
Parity		
Primigravida	48 (48%)	52 (52%)
Multigravida	52 (52%)	48 (48%)
BMI		
<18.5	3 (3%)	3 (3%)
18.5-24.9	52 (52%)	24 (24%)
25-29.9	32 (32%)	18 (18%)

>30	13(13%)	7 (7%)
Mode of delivery		
Normal delivery	21 (21%)	11 (11%)
Cesarean delivery	79 (79%)	89 (89%)
Education		
Primary	12 (12%)	10 (10%)
Secondary	28 (28%)	40 (40%)
Bachelors	1 (1%)	3 (3%)
Masters	1 (%)	0 (0%)
Unknown	58 (%)	47 (47%)

Amongst the 200 patients, 100 patients were primigravida. The remaining (100/200, 50%) were multigravida. The maximum number (76/200, 38%) of patients were between 18.5 to 24.9 BMI which suggested normal weight. There were more cesarean deliveries (89/100, 89%) in patients not receiving L-arginine, compared to those who received L-arginine though it was not statistically significant. In patients treated with L-arginine, reasons for cesarean delivery were intrauterine growth retardation, pregnancy-induced hypertension, fetal distress, and Doppler changes while, in those who did not receive L-arginine, the main reason was fetal distress and Doppler changes.

Among the patients receiving L-arginine, the maximum number of women (37/100, 37%) belonged to 'O+' blood group. The duration of treatment varied from 1 to 44 days with a mean of 14.4 ± 10.9 days. In these women, the amniotic fluid index (AFI) before treatment with L-arginine was between 3.1 cm to 7.8 cm with a median AFI of 6. The increase in AFI after treatment with L-arginine was 0 to 3 cm with a mean of 0.735 cm. The median AFI post-treatment was 6.8 cm. This increase in median AFI was highly significant ($p < 0.001$) according to the Wilcoxon sign rank test showing that L-arginine was effective in increasing amniotic fluid as mentioned in Table II.

Table II: Changes in AFI in patients receiving L-arginine

n = 100	Median	Mean $\pm$ SD	SE	p - value
AFI index before starting arginine therapy	6.00	5.85 ± 1.11	0.112	<0.001
AFI index after starting arginine therapy	6.80	6.58 ± 1.21	0.122	

The average gestational age of starting L-arginine therapy was 35.3 ± 2.1 weeks while, at delivery the mean gestational age was 37.4 ± 1.8 . Hence, there was an increase of 2.1 ± 0.27 weeks of gestational age at an average which was highly significant ($p < 0.001$) according to the Mann-Whitney U test suggestive of the beneficial effect of L-arginine in increasing gestational age.

Among those patients not on L-arginine therapy and who came directly for delivery due to oligohydramnios, the maximum number of women (42/100, 42%) belonged to the 'B+' blood group. The average gestational age at delivery was 38.1 ± 2.22 weeks. AFI at delivery ranged from 1.28 cm to 7.8 cm.

Table III: Neonatal Outcomes

Outcomes	Whose mother received L-arginine (100)	Whose mother did not receive L-arginine (100)
Gender of baby		
Male	32	51
Female	68	49
Birth Weight		
<2.5 kg	45	48
>2.5 kg	55	52
NICU	7	13

admission of baby		
Death of baby	0	1
Congenital anomaly	0	2
Gestational age of baby		
<37 weeks	20	34
>37 weeks	80	66
APGAR score at 1min		
6	0	32
7	17	54
8	83	14
APGAR score at 5 min		
7	0	32
8	17	54
9	83	14

Of 200 babies born, 83 (41.5%) were male and 117 (58.5%) were female. There was a single fetal death reported due to respiratory distress by the pregnant lady who did not receive L-arginine. There was no death of babies in the L-arginine therapy group. Neonatal intensive care unit admissions were less in patients receiving L-arginine (7/100), while in those not on L-arginine therapy, it was 13/100. Babies born with birth weight less than 2.5 kg were more or less similar in both groups. The congenital anomalies were reported in 2 babies whose mother did not receive L-arginine, which were dorsal hypospadias in one baby and right rudimentary thumb along with normal thumb in another baby.

Twenty preterm babies were born in the group receiving L-arginine whereas 34 preterm babies were born in the group not receiving L-arginine. It was statistically significant according to the Chi-square test with a p-value <0.05, which may suggest that administration of L-arginine may lead to fewer premature births and may favor better neonatal outcomes.

There was a highly significant ($p < 0.001$) difference between APGAR (Appearance, Pulse, Grimace, Activity, Respiration) scores at 1 min and 5 min among both the groups according to Fischer's exact test, which showed that administration of L-arginine to mothers may have improved APGAR scores in the baby. Details of the APGAR score are mentioned in Table III.

4. DISCUSSION

Oligohydramnios may lead to adverse fetomaternal outcomes like fetal malposition, stillbirth, neonatal death, low birth weight, and preterm deliveries. [7] L-arginine facilitates vasodilatation and improves placental perfusion, [8] plays a promising role in improving amniotic fluid volume. In some studies [2,8,9,10], an increase in AFI index and gestational age were noted, leading to better fetal and maternal outcomes.

In our study, 100 patients on L-arginine therapy showed an increase in gestational age by 2.1 ± 0.27 weeks. A study conducted by Soni A et al. [2] also showed an increase in gestational age of 2.4 weeks. However, the mean age of recruitment and administration of L-arginine was 32.3 weeks, whereas in our study it was 35.3 weeks. Hence, the duration of administration of L-arginine was less compared to their study. Maybe due to that, their study saw more increase in AFI (3.332 cm).

A similar study conducted by Hebbar S et al. [9] showed an increase in AFI by 1.8 cm in 11 patients with a mean duration of treatment of 21.6 days while in our study, the mean duration of treatment with L-arginine was 14.4 days with 100 patients and showed an increase of 0.735 cm in AFI.

A study conducted by Shreedharan R et al. [11] showed an average increase of AFI of 2.03 ± 0.39 cm for an average duration of treatment with L-arginine of 23.99 days. Our study showed a lesser increase in AFI compared to this study but the average treatment duration was less (14.4 days).

The rate of cesarean section in our study was 79% (79/100) in those patients treated with L-arginine and was similar to a study conducted by Soni A et al. [2] where the number of patients receiving L-arginine was 100 and the rate of cesarean section was 72%.

Iqbal S et al. [10] conducted a similar study which showed a mean increase in gestational age by 5.93 weeks and a mean increase in AFI by 1.55 cm after treatment with L-arginine and was in accordance with our study where there was an increase in gestational age and AFI but not as high as this study. In his study, only 18% of patients underwent cesarean section after treatment with L-arginine whereas, in our study, the patient's rate of cesarean section was 79% in the L-arginine-treated group, which was much higher.

A mean increase in AFI was 2.19 ± 0.36 cm with an average treatment duration with L-arginine of 20.70 ± 5.47 days, according to a study conducted by Hatem R et al. [12]. Another study conducted by MA Begum et al. [8] showed a mean

increase in AFI of 2.6 cm with 3.23 weeks of treatment with L-arginine. In our study, the duration of treatment ranged from 1 to 44 days with a mean of 14.4 ± 10.9 days, and maybe because of that, the increase in AFI was also less (0.735 cm) in our study.

A similar study conducted by Sahay V [13] showed an increase in AFI of 3.2 cm and an increase in gestational age of about 3.1 weeks which was in accordance with our study which also showed an increase in both, though not as high as this study.

Though our study showed an increase in the amniotic fluid index and gestational age with the use of L-arginine, however, major limitations of our study might be a small sample size and less duration of therapy with L-arginine.

In our study, there were no stillbirths or intrauterine deaths recorded in either of the groups which was similar to a study conducted by MD Amirunnisa Begum et al. [8] and in contrast to a study conducted by I-Jan Hu et al. [14] where oligohydramnios was considered to be one of the important factors of stillbirth. There was one death recorded in our study due to respiratory distress after birth whose mother had not received L-arginine.

One minute APGAR score of <7 was found in 32 babies (16%), and none of them belonged to the group receiving L-arginine. A study by Guin G. et al. [15] showed that 39% of babies had APGAR scores of <7 , which was higher than ours. They also reported 12 congenital anomalies (12/140, 8.5%) in the oligohydramnios group, whereas in our study, only 2 (2/200, 1%) congenital anomalies were reported, and that too belonged to the group not receiving L-arginine.

The NICU admission in our study was less (7/100, 7%) in the group receiving L-arginine in contrast to a study conducted by Md Amirunnisa Begum et al. [8], where almost 32.6% (15/46) required NICU admission. In our study, 45% (45/100) of babies were born with low birth weight, which was similar to this study by Md Amirunnisa Begum et al. [8], where 41.3% (19/46) of babies had low birth weight.

5. CONCLUSION

From the findings of our study, we observed that L-arginine therapy showed a mean increase in amniotic fluid index of 0.735 cm for an average duration of treatment of 14.4 ± 10.9 days. Also, an increase in gestational age by 2.1 ± 0.27 weeks was noted, which may have led to fewer cesarean sections in patients receiving L-arginine as compared to those who did not receive L-arginine.

However, more studies with L-arginine in oligohydramnios with a larger sample size are needed to reach a more specific conclusion about the beneficial role of L-arginine in oligohydramnios.

Conflict of interest: None

Funding: None

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