



EFFICACY AND IMPACT OF L-ARGININE IN TREATING OLIGOHYDRAMNIOS DURING THE SECOND TRIMESTER: AN AMBISPECTIVE OBSERVATIONAL STUDY IN A TERTIARY CARE HOSPITAL

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Abstract

Oligohydramnios, which causes fetomaternal morbidity and mortality, is becoming more common throughout the world and is a serious public health concern. Amniotic fluid, which is high in water during the early phases of pregnancy, is the fluid that makes up the amniotic sac. In subsequent stages, nutrients, hormones, antibodies, and the baby's urine progressively begin to show up. It protects against bacteriostatic infections and provides the growing fetus with its primary source of nutrients. An Ambispective observational study was conducted for 6 months in a tertiary care hospital, involving 143 patients with Oligohydramnios. Data was collected through a data collection form and stress was analyzed by using Perceived stress scale.

The majority of participants have seen a rise in AFI of 2 cm following L-arginine use. There is more proof that stress can lead to oligohydramnios. Stress (27.27%) is the primary risk factor in the majority of individuals. Our study's results indicate that L-arginine has a potential effect on pregnant women with oligohydramnios who are in their second trimester. Amniotic Fluid Index (AFI) is higher as a result of the L-arginine 5g sachets' ingestion. Stress is the main risk factor for oligohydramnios in the majority of females. Our analysis suggests that people receiving L-arginine TID with appropriate adherence have increased amniotic fluid, however the clinical manifestations differ between studies.



INTRODUCTION

Amniotic membrane fluid has a water-like consistency. 99–98% of the AF is composed of water. The remaining 1–2 percentile changes in composition during gestation. Early in pregnancy, the AF has very little protein and is isotonic with both maternal and foetal plasma. Early in gestation, there are notable levels of AF before the fetus starts to produce urine. For the surge in AFV to occur early in pregnancy, there must be a net movement of water from the mother's bloodstream to the foetal compartment. There are several uses for amniotic fluid. Because of its bacteriostatic qualities, it serves as the main source of nutrients for the developing fetus and guards against infection. It relieves pressure, keeps things from drying out, and cushions. Normal growth requires a sufficient amount of fetal fluid.^[1]

Throughout pregnancy, the unborn child grows in the amniotic sac, sometimes known as the "bag," inside the uterus (womb). There is amniotic fluid within the sac. This sac forms about 12 days after a woman becomes pregnant. The liquid behaves as follows:

- Cushions and shields the youngster.
- Keeps the baby's body temperature steady, which helps the baby's lungs grow as they inhale the liquid; also, because the baby eats the liquid, it helps the baby's digestive system grow.
- Enables the child to move around in the liquid, which promotes the growth of its bones and muscles.
- Prevents pinching of the umbilical chord, which provides the kid with oxygen and nourishment from the placenta.^[2]

Reduced amniotic fluid content is associated with meconium aspirations syndrome, stillbirth, intrauterine and newborn mortality, non-reassuring fetal heart rate, and an increased labor induction rate. It is also connected to a decrease in the volume of amniotic fluid during labor. Up until 34 to 36 weeks of gestation, when the AFV levels out (around 400 ml) and remains constant until term, the volume of amniotic fluid fluctuates throughout pregnancy and increases linearly.^[9] Post-term gestations have a lower capacity since the AFV gradually starts to decline after 40 weeks of gestation. This pattern enables clinical assessment of AFV during pregnancy using ultrasound scanning and fundal height measurements. Low amniotic fluid may be a sign of a child's underlying illness or health problems. These ailments may have an impact on the baby's growth or result in difficulties giving birth.^[9]

The uterus's amniotic sac, sometimes known as the "bag," is where the developing fetus grows throughout pregnancy. The sac is filled with amniotic fluid. The formation of this sac occurs approximately 12 days after conception. This is how the fluid behaves:

- Shields and supports the child.
- Keeps the baby's temperature steady, which encourages the development of their lungs as they inhale the liquid.
- The baby's digestive system develops as a result of the liquid they drink.
- The ability to move around in the fluid helps the child's muscles and bones grow.
- Keeps from pinching the umbilical cord, which carries nourishment and oxygen from the placenta to the child.^[8]

The maternal abdomen was divided into four quadrants using the umbilicus and linea nigra as markers. The amniotic fluid index (AFI) is calculated by adding the anteroposterior diameters of the largest empty fluid pocket in each quadrant, excluding any fetal components or the umbilical

cord. AFI typically ranges from 5 to 25 cm. The dimensions of each individual fluid pocket should also range from two to eight cm. The sum of these four figures yielded the AFI without the usage of the fetal components or umbilical cord.^[3]

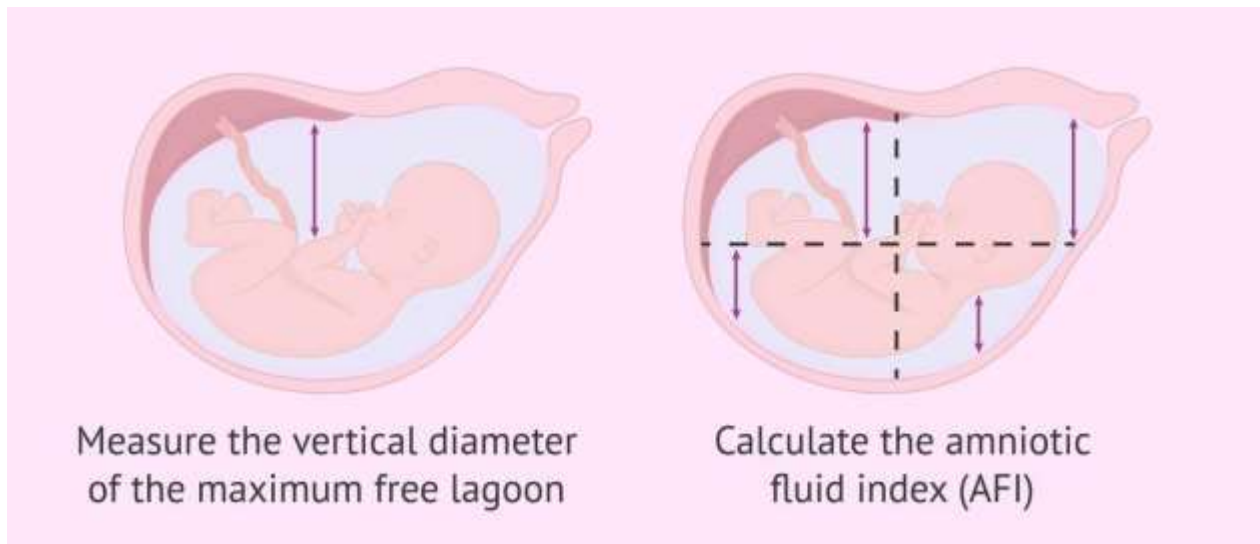


FIGURE 1: Measurement of AFI

- Less than 5cm is called oligohydramnios
- Greater than 25cm is called Polyhydramnios

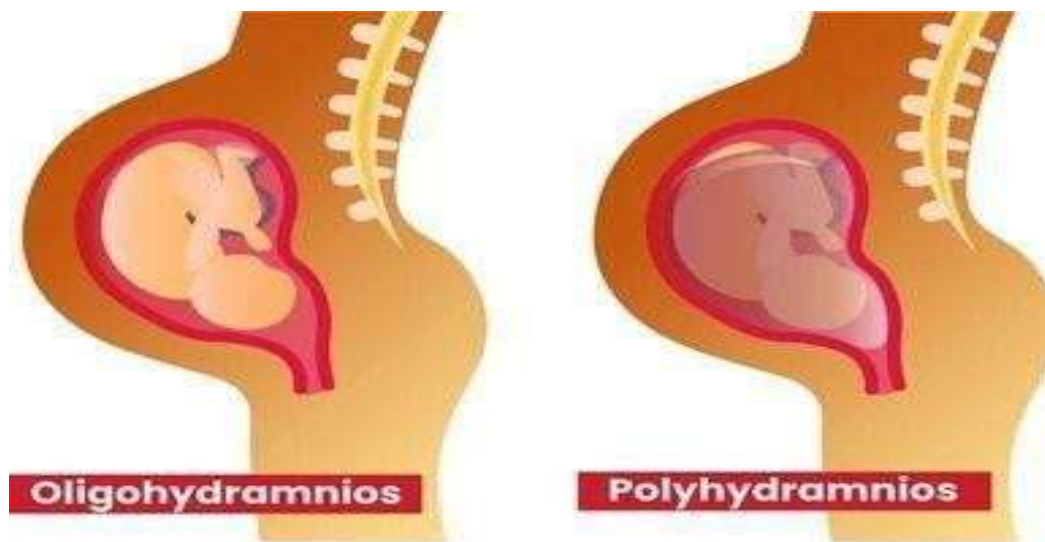


FIGURE 2: OLIGOHYDRAMNIOS vs POLYHYDRAMNIOS

Oligohydramnios complicates matters in 4.4% of all term pregnancies. Oligohydramnios, which is usually caused by either an early rupture of the foetal membranes or insufficient foetal urine production as a result of foetal urinary tract abnormalities, such as renal agenesis or dysplasia. A decrease in amniotic fluid can be caused by a number of things, such as altitude, maternal medications, and dehydration. The second most frequent reason for decreased AF production is impaired uteroplacental blood flow. abnormalities of the foetal urinary tract, such as polycystic kidneys, posterior urethral valves, renal agenesis, and any lesion blocking the urine. Clinical



presentations include amniotic fluid leakage, a smaller uterus, less movements of the foetus, discomfort in the abdomen, abrupt reduction in the fetus's heart rate, premature rupture of the membranes before term, not putting on adequate weight while pregnant, Lack of water .^[4,5]

EFFECTS OF OLIGOHYDRAMNIOS:

- An early rupture of the membranes (PROM). It is at this point, shortly before labor starts, when the amniotic sac around the baby ruptures.
- Premature pregnancy (sometimes referred to as post-term pregnancy). This baby is born at 42 weeks and 0 days. A full-term pregnancy stretches from 39 weeks and 0 days to 40 weeks and 6 days.
- Birth defects, especially those affecting the fetus's kidneys, stomach, bladder, or urethra.
- Problems with the placenta, which provides the fetus with oxygen and nutrition through the umbilical cord^[6]

L-arginine promotes intrauterine growth of the foetus by increasing the bioavailability of endothelial nitric oxide (NO) production and improving umbilical artery flow in pregnant women with pregnancy-induced hypertension and fetal growth limitation.

Furthermore, it has been demonstrated that l-arginine promotes growth hormone secretion, which raises plasmatic growth hormone and affects somatic growth. Quality of life and medication adherence are required to maintain amniotic fluid in normal range^[7]

METHODS:

It is a hospital based Ambispective observational study which is conducted for 6 months in 143 Oligohydramnios subjects. Data was analyzed by using data collecting form. Risk factors, Increase in AFI was evaluated by statistical tests. Stress was analyzed by using Perceived Stress scale.

INCLUSIONCRITERIA:

- 2nd trimester pregnant women
- Women diagnosed with Oligohydramnios.
- Women who cooperate for follow up during study.
- Women with other comorbidities

EXCLUSIONCRITERIA:

- Women with 1st and 3rd trimesters of pregnancy.
- Lactating women.

This study screened patients based on inclusion and exclusion criteria focusing on Oligohydramnios condition. Data was collected using a valid Questionnaire and analyzed using statistical tests, MS Excel and Stress was evaluated through Perceived Stress Scale

RESULTS:

We included 143 participants in our study diagnosed with Oligohydramnios and the results were analyzed by using validated statistical tests. Data was expressed as percentage

TABLE 1

CHARACTERISTICS	NUMBER	PERCENTAGE
Major risk factor: Stress	48	33.5%
Frequency of L-Arginine of TID	84	58.7%
L-Arginine consuming month 4 th month	121	84.61%
Frequency of L-Arginine of TID	84	58.7%
AFI increase after taking L-Arginine	125	87.4%
Normal Foetal moments after consuming L-Arginine	118	82.51%
Water consumption of 3 Litre	66	46.15%
Working women	123	86%

TABLE 2: DISTRIBUTION OF SUBJECTS BASED ON RISK FACTORS

Table 2 depicts information regarding risk factor causing Oligohydramnios. In Majority of the cases the most common risk factor is Stress (27.27%) followed by Leaking of amniotic fluid (19.58%), Dehydration (18.18%), no risk factor (12.58%), PROM (11.88%), placental abruption (10.48%) which is graphically represented in the figure (3).

Risk Factors	Number of subjects	Percentage%
Stress	39	27.27%
PROM	17	11.88%
Placental abruption	15	10.48%
Leaking of amniotic fluid	28	19.58%
Dehydration	26	18.18%
No	18	12.58%

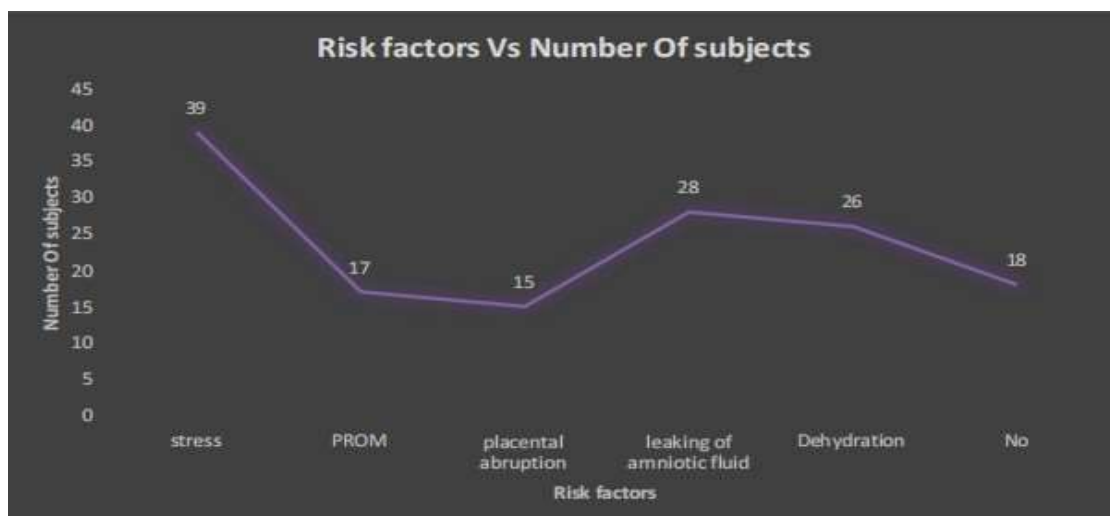


FIGURE 3: DISTRIBUTION OF SUBJECTS BASED ON RISK FACTORS

TABLE 3: DISTRIBUTION OF SUBJECTS BASED ON STRESS LEVEL

Table 3 depicts information regarding stress level. Majority of the cases are with moderate stress level (48.25%), followed by highly perceived (47.55%), low (4.19%) which is graphically

represented in the figure (4).

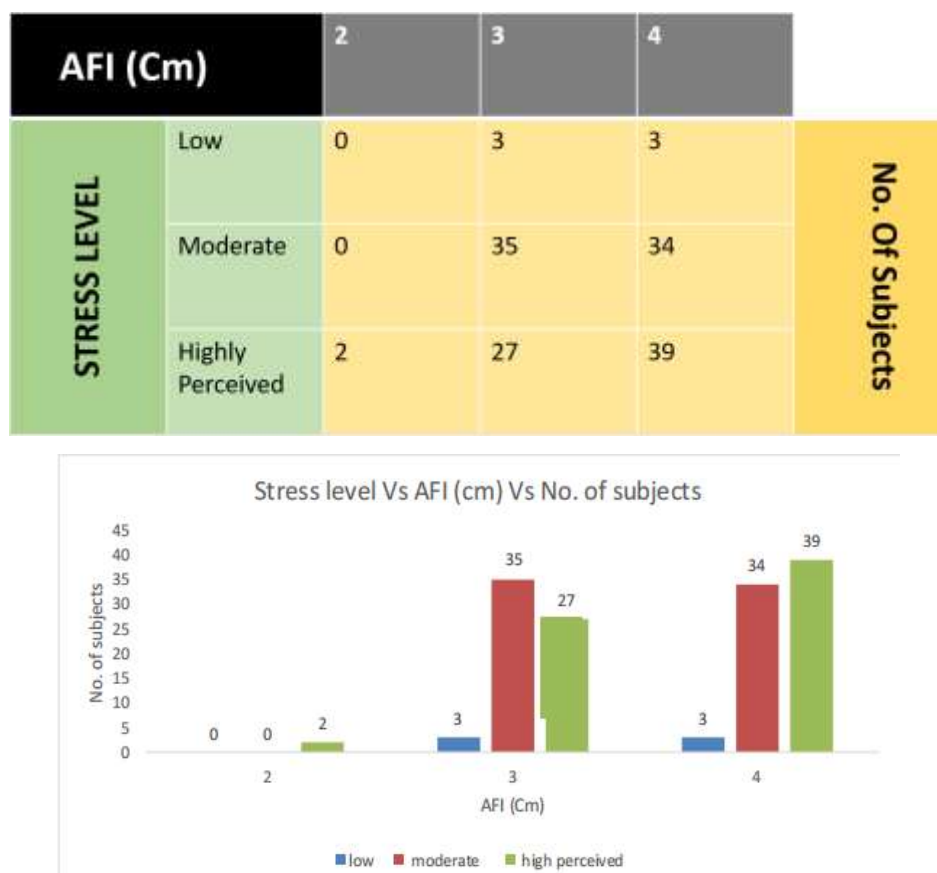


FIGURE 4: STRESS LEVEL Vs NUMBER OF SUBJECTS

TABLE 4: DISTRIBUTION OF SUBJECTS BASED ON WATER CONSUMPTION

Table 4 depicts information regarding water consumption per day. Majority of the cases are consuming 3lt of water per day (46.15%), followed by 2lt (26.57), 4lt (21.67%), >4lt (4.19%), 1 lt (1.39%) which is graphically represented in the figure (5).

Water consumption per day (litres)	Number of subjects	Percentage %
1	2	1.39%
2	38	26.57%
3	66	46.15%
4	31	21.67%
>4	6	4.19%

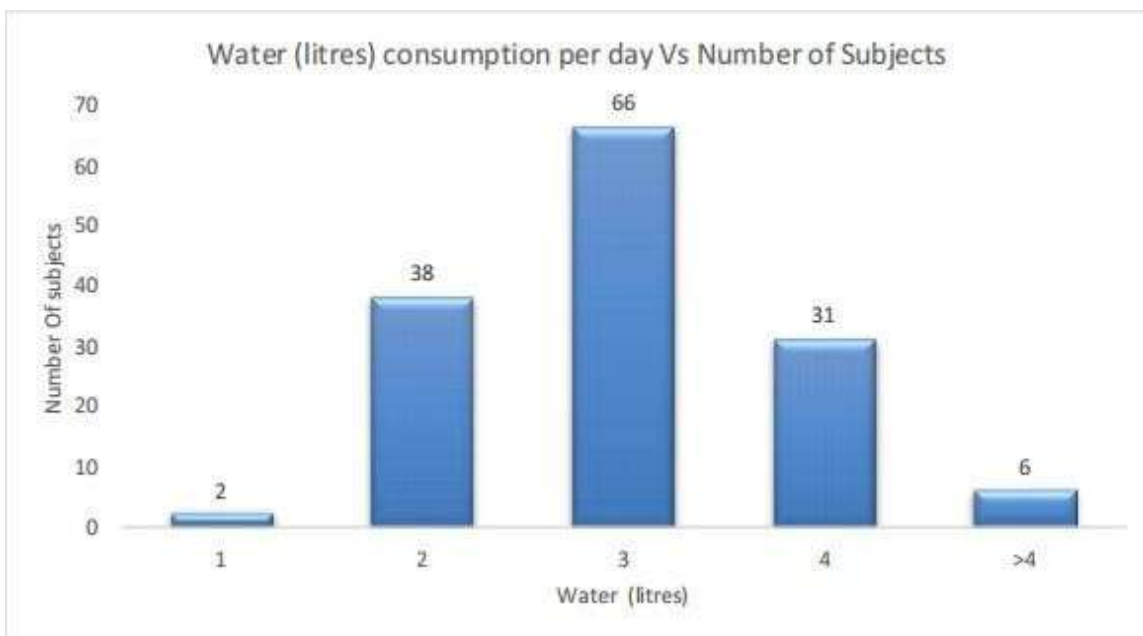


FIGURE - 5: WATER CONSUMPTION Vs NUMBER OF SUBJECTS

DISCUSSION:

We included 143 participants with oligohydramnios in the second trimester (13–26 weeks) whose USG abdominal findings indicated an AFI range of less than 5 cm. We looked at individuals in the fourth and fifth months whose AFI was less than five centimeters. We gave them L-arginine 5g sachets twice, three times, or four times a day depending on their AFI range, and we saw that the subjects' AFI range increased in the sixth month. The Perceived Stress Scale is used to analyze stress and is divided into three categories: low (0–13), moderate (14–26), and severely perceived (27–40). We saw that women who are working with poor levels of physical activity and women with low hydration are more likely to develop oligohydramnios.

In majority of the subjects stress was the major cause for Oligohydramnios. A significant rise in AFI value was observed in the majority of participants with AFI 2cm-3cm using 5g of L-arginine TID (58.74%) with appropriate medication adherence, followed by QID (33.56%) without appropriate medication adherence.

CONCLUSION:

L-arginine has a positive effect on pregnant women with oligohydramnios who are in their second trimester. Amniotic Fluid Index (AFI) was increased in women due to the administration of L-Arginine which is a nitric oxide donor which leads to increased placental perfusion and vasodilation and finally leads to increase in the amniotic fluid volume. Amniotic fluid index was increased as a result of the L-arginine 5g sachets' ingestion. Stress is the main risk factor for oligohydramnios in the majority of females. Low-physical-activity and working women are more susceptible to oligohydramnios.

ABBREVIATIONS:

AFI : Amniotic fluid index

PROM : Premature rupture of membranes



AF : Amniotic fluid

TID: Three times a day

QID: Four times a day

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LIMITATIONS:

This study contains small sample size. So, this can be further extended with number of patients to derive a better conclusion

CONFLICT OF INTEREST:

The authors declare that there is no conflict of interest.

REFERENCES:

1. Nash, P. (2013). Amniotic fluid index. Neonatal Network The Journal of Neonatal Nursing, 32(1), 46–49. <https://doi.org/10.1891/0730-0832.32.1.46>
2. Amniotic fluid. (n.d.). Marchofdimes.org. Retrieved March 11, 2024, from <https://www.marchofdimes.org/find-support/topics/pregnancy/amniotic-fluid>
3. Sciencedirect.com. Retrieved March 11, 2024, from <https://www.sciencedirect.com/topics/medicine-and-dentistry/amniotic-fluid-index>
4. Sciencedirect.com. Retrieved March 11, 2024, from <https://www.sciencedirect.com/topics/nursing-and-health->
5. Keilman, C., & Shanks, A. L. (2022). Oligohydramnios. StatPearls Publishing.
6. Oligohydramnios. (n.d.-d). Marchofdimes.org. Retrieved March 11, 2024, from <https://www.marchofdimes.org/find-support/topics/planning-baby/oligohydramnios>
7. Soni A, Garg S, Patel K, Patel Z. Role of l-Arginine in Oligohydramnios. J Obstet Gynaecol India. 2016 Oct;66(Suppl 1):279-83. doi: 10.1007/s13224-016-0853-7. Epub 2016 May 3. PMID: 27651617; PMCID: PMC5016450.
8. Amniotic fluid. (n.d.-b). Marchofdimes.org. Retrieved April 18, 2024, from <https://www.marchofdimes.org/find-support/topics/pregnancy/amniotic-fluid>
9. Iqbal, Suhail, et al. (2021) "Effect of oral L-arginine versus intravenous hydration on maternal and fetal outcome in idiopathic oligohydramnios.