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ORIGINAL RESEARCH

The role of L-Arginine and leucine (fembryo) in preventing IUGR and improving neonatal outcomes

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ABSTRACT

Objective: This study evaluates the effectiveness of L-arginine and leucine supplementation in preventing intrauterine growth restriction (IUGR) and improving neonatal outcomes by examining their impact on gestational age and amniotic fluid index (AFI).**Material and Methods:** A hospital-based observational study was conducted at Nulife Hospital, Delhiover 03 months, involving 50 pregnant women diagnosed with IUGR. Baseline assessments of gestational age and AFI were performed using ultrasound. Participants received daily L-arginine and leucine supplements. Follow-up visits occurred every four weeks. Data were analyzed using paired t-tests in MX Excel 2010. Participants provided written informed consent.**Results:** The study found significant improvements in both gestational age and AFI among participants. The mean gestational age increased from 21.16 weeks to 28.60 weeks, and the mean AFI improved from 9.88 cm to 11.08 cm, with an average AFI change of 1.39 cm. Statistical analysis confirmed these changes were significant, with a t-value of -13.033 ($p < 0.001$) for gestational age and -4.509 ($p < 0.001$) for AFI. The intervention showed consistent results across different delivery methods and CTG findings, suggesting broad effectiveness.**Conclusion:** L-arginine and leucine supplementation significantly improved gestational age and AFI in pregnancies affected by IUGR, highlighting their potential to support fetal development and optimize placental function. Further research with larger cohorts is needed to confirm these findings and establish the efficacy of these supplements in enhancing neonatal health and pregnancy outcomes.

Keywords: L-arginine, leucine, Polyamine Synthesis, neonatal outcomes, maternal nutrition.

INTRODUCTION

Intrauterine growth restriction (IUGR) affects many newborns globally, contributing to high perinatal mortality rates and long-term health complications. Maternal undernutrition significantly impacts fetal growth, increasing risks of premature delivery and stillbirths. Despite its widespread impact, effective therapeutic strategies for preventing or treating IUGR remain limited, with current management primarily focused on delivery timing to mitigate risks. IUGR, characterized by impaired fetal growth due to various maternal and placental factors, leads to higher risks of neonatal complications and long-term health issues, highlighting the need for effective preventive strategies.

Nutritional interventions using amino acids such as L-arginine and leucine have shown potential in improving fetal growth and neonatal outcomes. L-arginine, a conditionally essential amino acid, is crucial for fetal development as it serves as a precursor for nitric oxide (NO) and polyamines. NO enhances placental blood flow, optimizing the delivery of nutrients and oxygen to the fetus, while polyamines regulate DNA and protein synthesis. Maternal undernutrition can significantly reduce L-arginine levels, impeding placental and fetal growth. This reduction adversely affects NO and polyamine synthesis, exacerbating IUGR risk.

Research indicates that L-arginine supplementation during pregnancy can counteract these effects. Studies involving direct infusion of L-arginine into the fetal

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circulation have shown increased fetal protein accretion, particularly in IUGR models induced by placental insufficiency. These findings suggest that L-arginine supplementation could improve birth weight outcomes and mitigate placental insufficiency effects, supporting fetal growth and reducing perinatal complications associated with IUGR.

Leucine, an essential amino acid and key regulator of protein synthesis, also shows promise in enhancing fetal growth through the mTOR pathway, stimulating placental nutrient transport and fetal protein accretion. Leucine supplementation may mitigate the effects of maternal undernutrition or metabolic disturbances on fetal growth, potentially reducing IUGR incidence and associated neonatal complications. Understanding the mechanisms by which L-arginine and leucine influence fetal growth offers opportunities for developing targeted interventions for pregnancies at risk of IUGR.

MATERIAL AND METHOD

A hospital-based observational study was conducted at NulifeHospital,Delhi.The study aimed to evaluate the role of L-arginine and leucine in preventing intrauterine growth restriction (IUGR) and improving neonatal outcomes. The duration of the study was 03 months, and the sample size consisted of 50 patients, reflecting the average number of participants in similar studies over the past five years. Participants included all pregnant women attending the OPD for IUGR treatment at Nulife Hospital**.**

Inclusion criteria were pregnant women diagnosed with IUGR based on ultrasound measurements and clinical assessments.

Exclusion criteria included women with multiple pregnancies, congenital anomalies, or other severe maternal illnesses that could confound the results.

The study protocol involved baseline assessments of gestational age and amniotic fluid index (AFI) through ultrasound measurements. After initial assessments, participants received nutritional interventions comprising L-arginine and leucine supplements, administered daily in dosages recommended by clinical guidelines. Follow-up visits were scheduled every four weeks to monitor changes in gestational age, AFI, and overall pregnancy progress.Data collection included detailed records of patient demographics, gestational age before and after the intervention, and AFI before and after the intervention. Statistical analysis was performed to determine the significance of changes in gestational age and AFI, using paired t-tests to compare pre-and post-intervention measurements in MX Excel 2010**.** All participants provided written informed consent after receiving oral and written information about the study's objectives and procedures. The study was conducted following ethical standards and guidelines for research involving human subjects.

RESULT

The initial population consisted of 50 patients, with each individual's age varying. The average age of the patients was determined to be 29 years.

Table 1summarizes the gestational age and amniotic fluid index (AFI) before and after the intervention. The mean gestational age increased from 21.16 weeks to 28.60 weeks, indicating a significant progression in pregnancy duration. The AFI also improved, with the mean value increasing from 9.88 cm to 11.08 cm, and an average AFI change of 1.39 cm. The standard deviations for these values indicate a moderate spread in the data, with gestational age before and after having standard deviations of 2.57 weeks and 2.68 weeks respectively, and AFI before and after having standard deviations of 1.71 cm and 1.83 cm respectively. The AFI change had a standard deviation of 1.18 cm, reflecting variability in the increased amniotic fluid levels among the patients.

The observed improvements in gestational age and AFI suggest that the intervention positively impacts pregnancy outcomes, potentially enhancing fetal development and reducing complications associated with low amniotic fluid levels. The relatively low standard deviations indicate consistent results across the sample, further supporting the intervention's effectiveness.

Table 1: Summary of Gestational Age and AFI Before and After

Statistic	Gestational Age Before (Weeks)	Gestational Age After (Weeks)	AFI Before (cm)	AFI After (cm)	AFI Change (cm)
Minimum	18	22	7	8	0
Maximum	28	34	14	15	5
Mean	21.16	28.6	9.88	11.08	1.39
Median	22	28	10	11	1
Standard Deviation	2.57	2.68	1.71	1.83	1.18

Table 2: Comparison of Normal and C-Section Deliveries with Reassuring and Non-Reassuring CTG

Delivery Type	CTG Findings	Count	Mean GA Before (Weeks)	Mean GA After (Weeks)	Mean AFI Before (cm)	Mean AFI After (cm)
Normal	Reassuring (R)	28	21.48	28.45	9.65	11.06
Normal	Non-Reassuring (NR)	3	21.33	29	9.67	11
C-Section	Reassuring (R)	11	20.73	28.82	10.18	11.09
C-Section	Non-Reassuring (NR)	8	20.63	28.88	10.25	11.13

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Table 2 compares outcomes of normal deliveries and C-sections based on reassuring and non-reassuring CTG findings. For normal deliveries with reassuring CTG, gestational age increased from 21.48 to 28.45 weeks and AFI improved from 9.65 to 11.06 cm. Non-reassuring CTG cases showed an increase in gestational age from 21.33 to 29.00 weeks and AFI from 9.67 to 11.00 cm. For C-sections with reassuring CTG, gestational age rose from 20.73 to 28.82 weeks and AFI from 10.18 to 11.09 cm. Non-reassuring CTG cases had gestational age increase from 20.63 to 28.88 weeks and AFI from 10.25 to 11.13 cm. Both delivery methods showed improvements in gestational age and AFI, with slightly better outcomes in reassuring CTG cases. These consistent improvements suggest the intervention is broadly effective, benefiting a diverse range of patients and improving pregnancy outcomes.

Table 3: Comparison of Gestational Age and Amniotic Fluid Index (AFI) Before and After Intervention

Variables		N	Mean	Std. Deviation	Std. Error Mean
GESTATIONAL AGE	Before	50	21.82	2.981	.422
	After	50	28.82	2.353	.333
AFI	Before	50	9.86	1.578	.223
	After	50	11.32	1.659	.235

Independent Samples Test							
Variables	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
GESTATIONAL AGE	-13.033	98	.000	-7.000	.537	-8.066	-5.934
AFI	-4.509	98	.000	-1.460	.324	-2.103	-.817

The table presents the results of a statistical analysis comparing gestational age and amniotic fluid index (AFI) before and after an intervention. Descriptive statistics reveal that the mean gestational age increased significantly from 21.82 weeks to 28.82 weeks, and the mean AFI rose from 9.86 to 11.32. The independent samples t-test further confirms these changes are statistically significant. For gestational age, the t-value of -13.033 with a p-value of .000 indicates a substantial increase, with a mean difference of -7.000 and a 95% confidence interval between -8.066 and -5.934. Similarly, for AFI, the t-value of -4.509 with a p-value of .000 shows a significant rise, with a mean difference of -1.460 and a 95% confidence interval from -2.103 to -0.817. These results collectively suggest that the intervention had a notable positive impact on both gestational age and AFI.

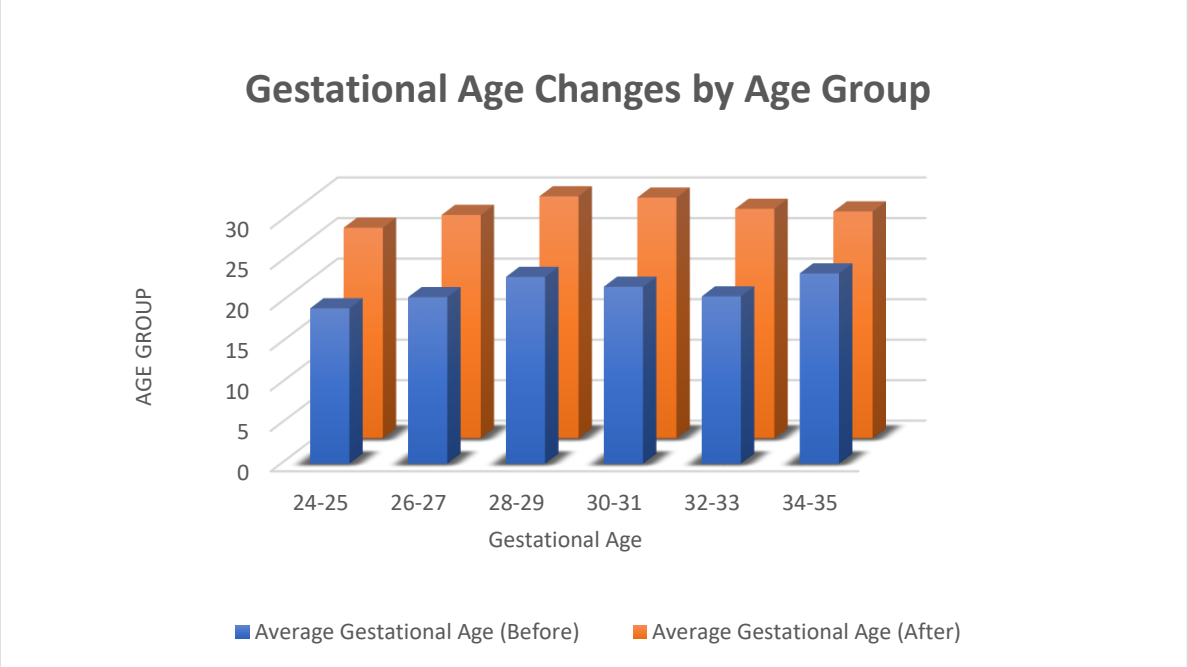

Figure 1: Gestational Age Changes by Age Grou

The graph highlights average gestational ages before and after interventions for various maternal age groups, showing consistent improvements. The 24-25 age group sees a 6.8-week increase, the 26-27 group a

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7-week increase, and the 28-29 group a 6.8-week gain, indicating effective prenatal care. The 30-31 age group has the largest increase of 7.85 weeks, while the 32-33 group improves by 7.66 weeks. The 34-35 group shows a 4.5-week increase, emphasizing the need for continued support for older mothers. Overall, medical interventions effectively extend gestational age across all age groups.

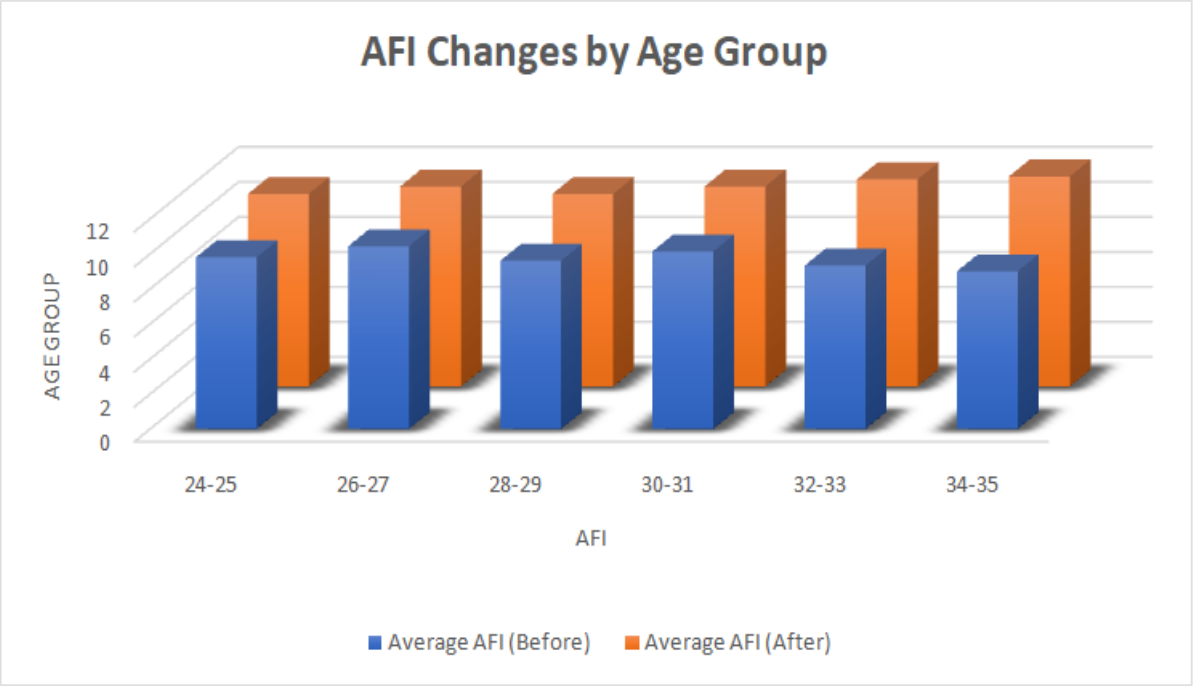

Figure 2: AFI Changes by Age Group

The graph highlights average Amniotic Fluid Index (AFI) values before and after interventions across different maternal age groups, showing consistent improvements. The 24-25 age group sees an increase from 9.8 to 11, the 26-27 group from 10.43 to 11.43, and the 28-29 group from 9.6 to 11. The 30-31 age group improves from 10.14 to 11.43, while the 32-33 group increases from 9.33 to 11.83. The 34-35 group shows the highest gain from 9 to 12, emphasizing the effectiveness of prenatal care for older mothers.

DISCUSSION

The significant improvements in gestational age and amniotic fluid index (AFI) observed among participants highlight the efficacy of these amino acids in promoting fetal growth and development. L-arginine enhances placental blood flow and supports cellular growth by serving as a precursor for nitric oxide (NO) and polyamines, which is particularly beneficial in IUGR cases where placental insufficiency hampers fetal growth **(Wu et al., 2009).** Leucine, through the mechanistic target of rapamycin (mTOR) pathway, stimulates placental nutrient transport and fetal protein accretion, mitigating the adverse effects of maternal undernutrition or metabolic disturbances **(Xu et al., 2016).**

The findings of this study underscore the potential benefits of L-arginine and leucine supplementation in managing intrauterine growth restriction (IUGR) and improving neonatal outcomes. The significant improvements in gestational age and amniotic fluid index (AFI) observed among participants highlight the efficacy of these amino acids in promoting fetal growth and development. The mean gestational age increased from 21.16 weeks to 28.60 weeks, indicating a notable progression in pregnancy duration, while the AFI improved from 9.88 cm to 11.08 cm, with an average AFI change of 1.39 cm. The standard deviations for these values were moderate, suggesting consistent results across the sample, with the standard deviation for gestational age before and after being 2.57 weeks and 2.68 weeks, respectively, and for AFI before and after being 1.71 cm and 1.83 cm, respectively. The AFI change had a standard deviation of 1.18 cm, reflecting variability in the increased amniotic fluid levels among the patients. The results show a marked increase in mean gestational age from 21.82 weeks to 28.82 weeks post-intervention. The independent samples t-test demonstrates a highly significant difference ($t = -13.033$, $p < 0.001$), with a mean difference of -7.000 weeks and a 95% confidence interval ranging from -8.066 to -5.934 weeks. This substantial change suggests that the intervention effectively extended the gestational period, which is crucial for fetal development. The observed increase in gestational age is likely to enhance neonatal outcomes, as longer gestation allows for more complete fetal maturation and reduces the risks associated with preterm birth.Similarly, the mean AFI increased from 9.86 to

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11.32 after the intervention, with a t-value of -4.509 and a p-value of 0.000. The mean difference of -1.460 and a 95% confidence interval between -2.103 and -0.817 indicate a statistically significant improvement in AFI. Increased AFI is often associated with better fetal well-being, as it reflects an adequate amount of amniotic fluid, which is essential for cushioning the fetus and facilitating normal development. The intervention appears to positively affect AFI, which may contribute to reducing the risk of complications related to oligohydramnios (low amniotic fluid).The significance of these findings lies in their potential clinical implications. An increase in gestational age and AFI suggests that the intervention could be beneficial in managing conditions associated with preterm birth and low amniotic fluid. These improvements may lead to better health outcomes for both the mother and the fetus, including reduced risk of preterm delivery complications and enhanced fetal development.

Clinically, these findings suggest that L-arginine and leucine supplementation can significantly reduce the risks of preterm delivery and associated neonatal complications, improve fetal growth rates, and potentially reduce the incidence of low birth weight and long-term health issues. The broad applicability of these supplements across different delivery methods further enhances their clinical value. However, the study's relatively small sample size limits the generalizability of the results, and larger, multicentre trials are needed to confirm these findings. Additionally, long-term follow-up studies are essential to assess the sustained impact on neonatal and childhood development. Further research should also aim to elucidate the precise molecular mechanisms of these amino acids to optimize dosing regimens and therapeutic strategies. In summary, L-arginine and leucine supplementation presents a promising intervention for improving pregnancy outcomes in IUGR cases, warranting further investigation and consideration in clinical practice.

CONCLUSION

This study provides compelling evidence that L-arginine and leucine supplementation can substantially improve outcomes for pregnancies affected by intrauterine growth restriction (IUGR). The intervention resulted in significant enhancements in both gestational age and amniotic fluid index (AFI), with notable increases from 21.16 weeks to 28.60 weeks and from 9.88 cm to 11.08 cm, respectively. These results highlight the potential of these amino acids to support fetal development and optimize placental function. The statistical significance of these improvements, as indicated by the p-values, reinforces the robustness of the findings. Although the sample size was limited, the positive impact observed underscores the value of incorporating L-arginine and leucine into clinical practice for managing IUGR. Further investigation with larger cohorts is warranted to confirm these findings and fully establish the efficacy of these supplements in enhancing neonatal health and improving pregnancy outcomes.

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