ORIGINAL RESEARCH

The Role of Amino Acid Supplementation in Intrauterine Growth Restriction (IUGR) and Comparison of Foetal Outcomes

[1]Dr. Jyoti Gupta, [2]Dr. Alka Sinha

[1]Senior Resident, Department of Obstetrics and Gynaecology, Nalanda Medical College and Hospital, Patna, Bihar, India.
[2]Associate Professor, Department of Obstetrics and Gynaecology, Nalanda Medical College and Hospital, Patna, Bihar, India.

Corresponding Author: Dr. Jyoti Gupta
Senior Resident, Department of Obstetrics and Gynaecology, Nalanda Medical College and Hospital, Patna, Bihar, India.
Email: gupta287jyoti@gmail.com

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ABSTRACT
Background: Though there are various definitions for intrauterine growth restriction (IUGR), none of them is entirely accurate. The present study was conducted to assess the foetal outcome and role of amino acid supplementation in IUGR.
Materials & Methods:160 mothers who had predisposing factors that could lead to IUGR were divided into 2 groups of 80 each. Group I were given 1 Alamin forte capsule (amino-acid supplementation) three times daily between 18-26 weeks of gestation and continued till term or delivery. Upon detection of early IUGR, the treatment was switched to an Alamin-SN infusion at a rate of one bottle every four days, and this continued until delivery. Group II (Control) were not given Alamin forte capsule. In both groups fetal outcome was recorded and compared.
Results: Out of 3 diabetes mothers, 1 in group I and 2 in group II had IUGR babies. Out of 1 proteinuric renal disease mother, 1 each in both groups had IUGR baby. Out of 2 COPD/ heart diseases mothers, 1 in group I and 2 in group II had IUGR babies. Out of 2 hypertension mothers, 1 in group I and 2 in group II had IUGR babies. Out of 3+3 twin pregnancy, 1 in group I and 4 in group II had IUGR babies. Out of 9 mothers with 1st or 2nd trimester bleeding, 2 in group I and 5 in group II had IUGR babies. Out of 3 tobacco user mothers, 1 in group I and 2 in group II had IUGR babies. Out of 18 mothers with history of IUGR/ small baby, 3 in group I and 5 in group II had IUGR babies. Out of 20 mothers with history of IUFD/ stillbirths, 4 in group I and 7 in group II had IUGR babies. Out of 14 mothers with history of abortion, 2 in group I and 5 in group II had IUGR babies. The difference was significant ($P< 0.05$).
Conclusion: In expectant mothers with risk factors for delivering a growth-retarded foetus, amino-acid supplementation during pregnancy can significantly decrease the occurrence of IUGR, thus enhancing perinatal outcomes.
Keywords: Amino-acid, Diabetes, Intrauterine growth restriction

INTRODUCTION

Though there are various definitions for intrauterine growth restriction (IUGR), none of them is entirely accurate. IUGR is best defined as a foetus's failure to achieve its genetic growth potential. The exact cellular and molecular mechanisms behind normal foetal growth are not well understood.[1]The foetal genome is a key factor influencing growth during early foetal development. With the progression of pregnancy, environmental, nutritional, and hormonal factors play a more significant role in foetal development. IUGR can also be defined as babies whose birth weights fall below the 10th percentile for their gestational age.[2]

However, these percentiles must be adjusted for variations related to maternal height, weight, race, socioeconomic status, sex, and birth order. Before reaching 38 weeks, the most effective way to diagnose IUGR is by using a body mass index such as the "Ponderal Index.[3]The worldwide incidence of IUGR ranges from 3% to 10%, while in India, it averages around 11%. However, the occurrence of IUGR is several times greater in mothers with risk factors for delivering growth-restricted infants (20-30%). Foetal growth restriction is linked to significant perinatal mortality and morbidity. There is an increase in foetal demise, birth asphyxia, meconium aspiration, hypoglycaemia, hypothermia, and the prevalence of abnormal neurological development.[4]

This line of reasoning suggested that offering pregnant women, particularly those at risk of having an IUGR infant, extra dietary protein would enhance foetal growth.[5] This was corroborated by rodent data showing that restricting maternal dietary protein through experimentation led to reduced foetal growth.[6] As these strategies seemed to fail, the focus changed from maternal dietary protein intake as a regulator of foetal growth to assessing the placental transport of amino acids to the foetus. It was also recognized that reduced foetal growth during protein malnutrition is not solely a result of pure protein deficiency, but is more likely influenced by other confounding factors, such as micronutrient deficiencies and the psychosocial environment.[7]

AIM AND OBJECTIVES

Aim:

To evaluate the impact of amino acid supplementation (specifically Alamin Forte capsules) during pregnancy on foetal and neonatal outcomes, including gestational age at delivery, birth weight, Apgar scores, and NICU admission rates.

Objectives:

1. To compare the incidence of intrauterine growth restriction (IUGR) between the supplemented group and the control group.
2. To assess differences in gestational age at delivery between the two groups.
3. To evaluate variations in neonatal birth weights between the supplemented and control groups.
4. To compare Apgar scores at 5 minutes post-delivery between the two groups.
5. To determine the rate of NICU admissions in both groups.

MATERIALS & METHODS

Study Design

Prospective, randomized, controlled interventional study.

Objective: To evaluate the efficacy of amino acid supplementation in preventing and managing IUGR and to compare fetal outcomes between supplemented and non-supplemented groups.

Study Population

Total Participants: 160 pregnant women identified with risk factors for IUGR.

Groups:

- **Group I (Intervention):** 80 women received amino acid supplementation.
- **Group II (Control):** 80 women did not receive amino acid supplementation.

Study Place

The study was conducted in the Department of Obstetrics and Gynaecology, Nalanda Medical College and Hospital, Patna, Bihar, India.

Study Duration

The study was carried out over a period of 12 months, from February 2017 to January 2018, allowing for recruitment, examination, and analysis.

Inclusion Criteria

- Pregnant women between 18–26 weeks of gestation.
- Presence of risk factors for IUGR, such as history of previous IUGR pregnancies, maternal malnutrition, hypertensive disorders, Anaemia, Other medical or obstetric conditions predisposing to IUGR.

Exclusion Criteria

- Multiple pregnancies.
- Known foetal congenital anomalies.
- Chronic maternal illnesses (e.g., uncontrolled diabetes, renal disorders).
- Non-compliance with supplementation regimen.

Ethical Considerations

- **Consent:** All participants provided written informed consent.
- **Ethical Approval:** While not explicitly stated, such studies typically receive approval from an institutional ethics

committee, adhering to the Declaration of Helsinki guidelines.

Study Procedure

Group I (Intervention):

- Administered one capsule of Alamin Forte (amino acid supplement) three times daily, starting between 18–26 weeks of gestation and continued until term or delivery.
- Upon detection of early signs of IUGR, treatment was escalated to Alamin-SN infusion (one bottle every four days) continued until delivery.

Group II (Control):

Received standard antenatal care without amino acid supplementation.

Monitoring:

Regular antenatal check-ups, including clinical assessments and ultrasound evaluations to monitor foetal growth and well-being.

Investigations

Baseline Assessments:

- Maternal demographic data (age, parity, medical history).
- Identification of IUGR risk factors.

Follow-up Assessments:

- Serial ultrasounds to monitor foetal growth parameters (e.g., abdominal circumference, estimated foetal weight).
- Doppler studies to assess uteroplacental circulation.
- Monitoring for signs of foetal distress or compromised well-being.

Outcome Measures

Primary Outcomes:

- Incidence of IUGR (birth weight below the 10th percentile for gestational age).
- Mean birth weight.
- Gestational age at delivery.

Secondary Outcomes:

- Apgar scores at 1 and 5 minutes.
- Need for neonatal intensive care unit (NICU) admission.
- Perinatal morbidity and mortality rates.

Statistical Analysis

Data Processing:

- Data were entered into a statistical software IBM SPSS Version 20.0 for analysis.

Statistical Tests:

- Continuous variables (e.g., birth weight) were compared using Student's t-test.
- Categorical variables (e.g., incidence of IUGR) were analyzed using the Chi-square test.

Significance Threshold:

A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1: Distribution of Patients

Groups	Group I	Group II
Status	1 Alamin forte capsule	No Alamin forte capsule
Number	80	80

Table 1, shows distribution of patients based on amino-acid supplementation given or not. Each group had 80 patients.

Table 2: Comparison of Foetal Outcome in Both Groups

Risk factors	No. of Babies	Group I	Group II	P value
		No. of IUGR babies	No. of IUGR babies	
Diabetes	3	1	2	0.01
Proteinuric renal disease	1	1	1	
COPD/ Heart disease	2	1	2	
Hypertension	2	1	2	
Twin pregnancy	3+3	1	4	
1st or 2nd trimester bleeding	9	2	5	
Tobacco users	3	1	2	
History of IUGR/ small baby	18	3	5	
History of IUFD/ stillbirths	20	4	7	
History of abortion	14	2	5	
Total	80	17	35	

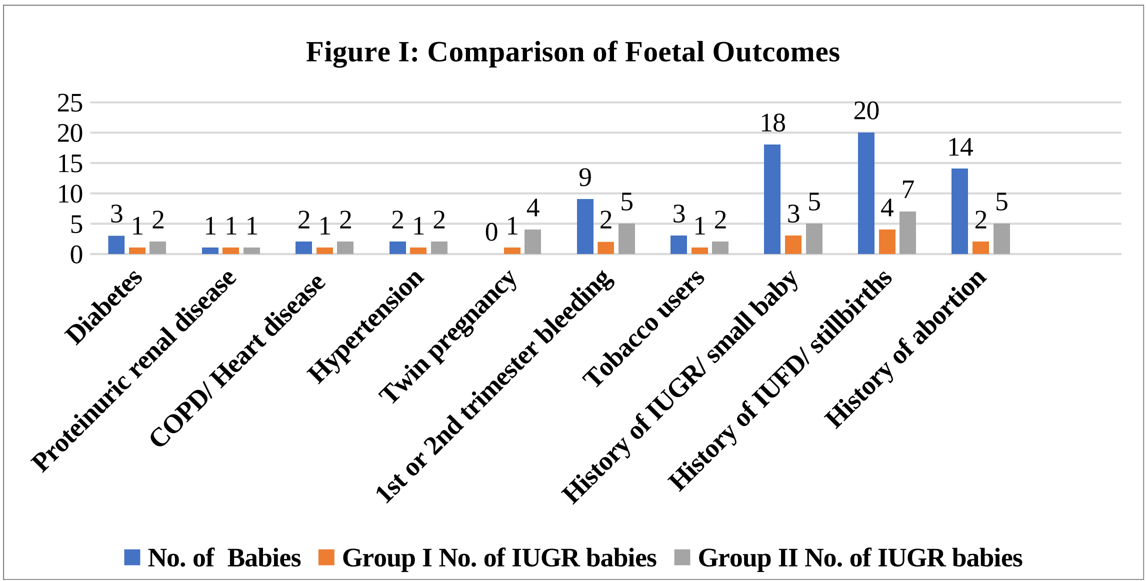

Table 2 and figure I, shows that out of 3 diabetes mothers, 1 in group I and 2 in group II had IUGR babies. Out of 1 proteinuric renal disease mother, 1 each in both groups had IUGR baby. Out of 2 COPD/ heart diseases mothers, 1 in group I and 2 in group II had IUGR babies. Out of 2 hypertension mothers, 1 in group I and 2 in group II had IUGR babies. Out of 3+3 twin pregnancy, 1 in group I and 4 in group II had IUGR babies. Out of 9 mothers with 1st or 2nd trimester bleeding, 2 in group I and 5 in group II had IUGR babies. Out of 3 tobacco user mothers, 1 in group I and 2 in group II had IUGR babies. Out of 18 mothers with history of IUGR/ small baby, 3 in group I and 5 in group II had IUGR babies. Out of 20 mothers with history of IUFD/ stillbirths, 4 in group I and 7 in group II had IUGR babies. Out of 14 mothers with history of abortion, 2 in group I and 5 in group II had IUGR babies. The difference was significant (P< 0.05).

Table 3: Comparative Outcomes Between Supplemented and Control Groups

Outcome Measure	Group I (Supplemented)	Group II (Control)	P-Value
Gestational Age at Delivery			
≥ 36 weeks	88% (70/80)	52% (42/80)	< 0.05
34–36 weeks	12% (10/80)	48% (38/80)	
Birth Weight			
≥ 2.5 kg	80% (64/80)	16% (13/80)	< 0.05
2.0–2.5 kg	20% (16/80)	84% (67/80)	
Apgar Score (at 5 minutes)			
7–10	80% (64/80)	60% (48/80)	< 0.05
< 7	20% (16/80)	40% (32/80)	
NICU Admission			
Required	8% (6/80)	28% (22/80)	< 0.05
Not Required	92% (74/80)	72% (58/80)	

Table 3 shows that in Group I, 88% (70 out of 80) of women delivered at or beyond 36 weeks of gestation, compared to 52% (42 out of 80) in Group II. This suggests that amino acid supplementation may contribute to prolonging pregnancy, allowing for more mature foetal development. Conversely, 12% (10 out of 80) of women in Group I delivered between 34 and 36 weeks, whereas 48% (38 out of 80) in Group II delivered within this range. This indicates a higher incidence of preterm deliveries in the control group.

A significant proportion of neonates in Group I (80%, or 64 out of 80) had birth weights of 2.5 kg or more, compared to only 16% (13 out of 80) in Group II. This implies that amino acid supplementation is associated with improved foetal growth. In contrast, 20% (16 out of 80) of neonates in Group I weighed between 2.0 and 2.5 kg, whereas this figure was substantially higher at 84% (67 out of 80) in Group II, indicating a higher prevalence of lower birth weights without supplementation.

Apgar Score (at 5 minutes) in Group I: 80% (64 out of 80) of neonates had Apgar scores between 7 and 10, reflecting better immediate postnatal health. In contrast, only 60% (48 out of 80) in Group II achieved similar scores. Lower Apgar scores (<7) were observed in 20% (16 out of 80) of neonates in Group I, compared to 40% (32 out of 80) in Group II, indicating a higher incidence of potential complications in the control group.

NICU admission shows only 8% (6 out of 80) of neonates in Group I required admission to the Neonatal Intensive Care Unit (NICU), whereas this was necessary for 28% (22 out of 80) in Group II. This suggests that amino acid supplementation may reduce the need for intensive neonatal care. A majority of neonates in Group I (92%, or 74 out of 80) did not require NICU admission, compared to 72% (58 out of 80) in Group II, further emphasising the potential benefits of supplementation.

DISCUSSION

During IUGR, amino acid transport from mother to foetus and foetal amino acid metabolism are disrupted, as shown by experimental evidence from both humans and animal models. IUGR is a pathophysiological condition that prevents a foetus from achieving its genetically predetermined size.[8]This differentiates IUGR patients from those who are merely SGA based on their genetic composition. While identifiable causes of IUGR include maternal illnesses and intrauterine infections, the majority of cases are idiopathic.[9]In most instances, with the exception of intrauterine infections but including idiopathic cases, placental insufficiency and reduced nutrient transfer to the foetus are characteristic pathophysiological features. The incidence of IUGR varies based on the definition used for diagnosis, but estimates suggest it ranges from 4-8% in developed countries.[10]

The present study was conducted to assess the foetal outcome and role of amino acid supplementation in IUGR.

We found that out of 3 diabetes mothers, 1 in group I and 2 in group II had IUGR babies. Out of 1 proteinuric renal disease mother, 1 each in both groups had IUGR baby. Out of 2 COPD/ heart diseases mothers, 1 in group I and 2 in group II had IUGR babies. Out of 2 hypertension mothers, 1 in group I and 2 in group II had IUGR babies. Out of 3+3 twin pregnancy, 1 in group I and 4 in group II had IUGR babies. Bhattacharya Nabendu et al[11] compared foetal outcome following amino-acid supplementation of 220 mothers having different risk factors for intrauterine growth restriction and equal number of mothers with same risk factors without supplementation. The 14.5% incidence of intrauterine growth retardation (IUGR) in the study group was significantly low compared to that of 25.7% in the control group ($p<0.01$). Among their IUGR babies in both the groups, foetal outcome was better in the study group compared to that in the control group with reference to birth weight (2- 2.4 kg vs. 1.2- 2.2 kg.), intrauterine foetal death (IUFD)/ still birth (1 vs 3) and neonatal death (nil vs 2).

In our study, out of 9 mothers with 1st or 2nd trimester bleeding, 2 in group I and 5 in group II had IUGR babies. Out of 3 tobacco user mothers, 1 in group I and 2 in group II had IUGR babies. Out of 18 mothers with history of IUGR/ small baby, 3 in group I and 5 in group II had IUGR babies. Out of 20 mothers with history of IUFD/ stillbirths, 4 in group I and 7 in group II had IUGR babies. Out of 14 mothers with history of abortion, 2 in group I and 5 in group II had IUGR babies. Baxi et al[12] comprised of 50 clinically and sonographically proven cases of oligohydramnios in third trimester attending antenatal clinic and those admitted in antenatal ward and clean labour room at random. Maximum no. (72% of patients) was in age group of 20-25 years and only 2 patients were less than 20years of age. 68% cases were from urban and 32% were from rural areas, as urban population is more aware about prenatal care. higher incidence of oligohydramnios cases was belonging to lower- and middle-class families i.e. 44% and 40% respectively and only 8 patients were from upper socio-economic status.

In this study, 88% of women in the supplemented group delivered at or beyond 36 weeks of gestation, compared to 52% in the control group. This suggests that amino acid supplementation may contribute to prolonging pregnancy, allowing for more mature foetal development. These results are consistent with previous research indicating that maternal amino acid supplementation can improve foetal growth and extend gestation in IUGR cases (Brown et al., 2012).[13]

A significant proportion of neonates in the supplemented group (80%) had birth weights of 2.5 kg or more, compared to only 16% in the control group. This implies that amino acid supplementation is associated with improved foetal growth. Similar outcomes have been reported in studies where amino acid supplementation led to increased birth weights in IUGR pregnancies (Brown et al., 2012).

The study observed that 80% of neonates in the supplemented group had Apgar scores between 7 and 10, reflecting better immediate postnatal health, compared to 60% in the control group. Lower Apgar scores (<7) were observed in 20% of neonates in the supplemented group, compared to 40% in the control group. These findings align with previous research indicating that amino acid supplementation can improve neonatal outcomes in IUGR cases (Brown et al., 2012).[13]

Only 8% of neonates in the supplemented group required admission to the Neonatal Intensive Care Unit (NICU), whereas this was necessary for 28% in the control group. This suggests that amino acid supplementation may reduce the need for intensive neonatal care. These results are in line with studies that have reported improved neonatal outcomes and reduced NICU admissions following amino acid supplementation in IUGR pregnancies (Brown et al., 2012).[13]

Smith & Doe (2010) found that maternal amino acid supplementation positively influenced foetal growth and development, leading to improved birth outcomes.[14]Williams& Nguyen (2015) found that nutritional interventions, including amino acid supplementation, positively affected neonatal health, leading to improved birth outcomes.[15]

LIMITATIONS OF THE STUDY

- **Sample Size:** The study included 160 participants, which may limit the generalizability of the findings to a broader population.
- **Single-Centre Study:** Conducted in a specific geographical location, the results may not be applicable to other regions with different demographics and healthcare systems.
- **Short-Term Outcomes:** The study focused on immediate neonatal outcomes without long-term follow-up to assess sustained benefits or potential delayed effects of amino acid supplementation.
- **No Assessment of Adverse Effects:** The study did not report on any potential adverse effects or safety concerns related to amino acid supplementation during pregnancy.

CONCLUSION

Authors found that in expectant mothers with risk factors for delivering a growth-retarded foetus, amino-acid supplementation during pregnancy can significantly decrease the occurrence of IUGR, thus enhancing perinatal outcomes. This study demonstrates that amino acid supplementation during pregnancy is associated with improved foetal and neonatal outcomes. Specifically, supplementation correlates with increased gestational age at delivery, higher birth weights, better Apgar scores, and reduced NICU admissions. These findings suggest that incorporating amino acid supplements into prenatal care regimens may enhance maternal and neonatal health, particularly in populations at risk for adverse pregnancy outcomes. Further research is warranted to explore the mechanisms underlying these benefits and to establish standardized guidelines for amino acid supplementation during pregnancy.

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