The Egyptian Journal of Hospital Medicine (January 2023) Vol. 90 (2), Page 2161-2169

# Ischemia-Modified Albumin in Cord Blood of Preterm Infants: A Novel Indicator for Intrauterine Growth Restriction- A Prospective Case Control Study.

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## ABSTRACT

**Background:** Ischemia modified albumin (IMA) rises promptly after an ischemic event and stays elevated for several hours. However, a knowledge gap still exists in terms of the association between intrauterine growth restriction (IUGR) and IMA levels.

**Objective:** The purpose of this study is to ascertain any potential relationships between cord blood IMA levels and IUGR in preterm newborns with or without complex gestations,

**Methods:** A prospective case-control study included 80 mothers of preterm neonates (<37 gestational weeks). Based on antenatal ultrasound findings, eligible women were divided into two groups: case group including the women diagnosed antenatally with IUGR, and control group including women with normal fetal development. The analysis and quantification of the IMA levels was done using a double-antibody sandwich ELISA kit

**Results:** The albumin level was significantly lower in the case group compared to the control group (3.18 ± 0.28 versus 3.88 ± 0.49; p <0.001), while the IMA level was significantly higher in the case group compared to the other group (145 (97.5 - 210) versus 40 (25- 90); p <0.001). At a cut-off point of ≤ 3.4, the albumin had an AUC of 0.993, a sensitivity of 95%, and a specificity of 87.5% for differentiating IUGR. While the cut-off point of IMA of >50 had an AUC of 0.850, a sensitivity of 92.5%, and a specificity of 67.5% for prediction of IUGR.

**Conclusion**: The levels of IMA and albumin in the cord blood have a strong correlation with the IUGR.

**Keywords**: Intrauterine growth restriction; Ischemia modified albumin; Albumin; Ultrasound.

## INTRODUCTION

Intrauterine growth restriction (IUGR) , one of the leading causes of perinatal morbidity and mortality, was defined by the American College of Obstetricians and Gynecologists as a foetal weight estimate (EFW) that is below the 10th percentile [(1)]. The prevalence of IUGR is estimated to be 7–15% of pregnancies worldwide [(2)]. IUGR has a variety of causes, which can be classified based on whether the cause is maternal or fetal [(3)]. Preeclampsia (PE) is the most common maternal cause since it causes a generalized oxidative and hypoxic environment that contributes to the occurrence of IUGR [(4)]. Reduced umbilical artery blood flow, which appears as changes in pulsatility and resistance index on Doppler ultrasonography, is the first symptom of IUGR [(5)].

Hypertension, smoking, anemia, and placental insufficiency are all linked to IUGR because they generate an ischemic microenvironment and increase oxidative stress [(6)]. In IUGR fetuses, the risk of perinatal death was ten times higher than in normal pregnancies [(7)]. When examining these fetuses, follow-up and management are critical. Doppler examination is the key technique for fetuses' follow-up after diagnosis. The amniotic fluid level, scalp pH, fetal well-being monitoring, base excess, and Apgar score were among the biochemical and clinical indicators used to indicate perinatal asphyxia [(8)].

However, no one sign has high predictive effectiveness in detecting fetal hypoxia or ischemia. Uncertain oxidative damage at the molecular level is what causes ischemic modified albumin (IMA), but reperfusion after an ischemia event may harm serum albumin [(9)]. In the absence of aggravating clinical factors like myocardial necrosis, IMA has shown a good predictive value as a relatively novel biomarker in identifying myocardial ischemia [(10)]. IMA was reported to have a high sensitivity (>80%) compared to troponin and ECG; therefore, it played a key role in detecting myocardial ischemia in patients associated with retrosternal discomfort. A literature suggested that following an ischemic episode, IMA rised immediately and remains increased for several hours [(11)]. However, a knowledge gap still exists in terms of the association between IUGR and IMA levels. Therefore, in preterm newborns with or without complex gestations, the purpose of this study was to ascertain any potential relationships between cord blood IMA levels and IUGR.

## PATIENTS AND METHODS

Written consent was taken from the women after describing the research and its aim. Every woman had the option to leave the study at any moment, without having to give a reason.

### Study Design:

We conducted a prospective case-control study that recruited mothers of preterm neonates (<37 gestational weeks). All women were recruited from the Maternity Hospital, Ain Shams University hospital, through the



Received: 18/09/2022
Accepted: 20/11/2022

period from Sepetmber 2019 till September 2020. Based on antenatal ultrasound findings, eligible pregnant women were split into: 1) case group, which included women with antenatal diagnosis of IUGR, and 2) control group, which included women with normal fetal development. The IUGR was defined as EFW <10$^{th}$ centile for gestational age.

***Inclusion and exclusion criteria:***

Adult women were deemed eligible if they delivered preterm babies through Cesarean section (CS), regardless of their risk factors for IUGR. We excluded mothers of neonates with suspected intrinsic causes of IUGR (such as familial tendency and karyotype abnormalities, hereditarily small constitution, and developmental abnormalities), vaginal deliveries, and suspected perinatal hypoxic events. The hypoxic events were suspected based on perinatal asphyxia, persistent low Apgar Scores (<7 at 5 min), need for resuscitation, and meconium aspiration syndrome.

***Data collection:***

The following data were collected from all eligible women: demographic and socioeconomic characteristics, detailed gynecological history, history of IUGR risk factors [(12)], maternal anthropometric measures, and the results of the Enzyme-Linked Immunosorbent Assay (ELISA) assessment of IMA levels. Besides, we collected the following data from all neonates: gestational age, Apgar score, birth weight and other anthropometric measures to classify the neonates into small or appropriate for gestational age. Besides, we utilized the Poderal index to assess the extent of fetal malnutrition [(13)]. The cephalization index was used to categorise the case group's IUGR severity, according to the brain: body ratio. According to these indices, neonates were classified into symmetric (Hypoplastic small for date) and asymmetric (malnourished babies) IUGR [(14)].

***Methodology :***

Five millilitres of blood was withdrawn from the placental part of the umbilical cord and centrifuged at 1000x g for 15 minutes. The separated serum was stored at -20°C. The measurement of the IMA levels was done using a double-antibody sandwich ELISA kit (Bioassay technology, Shanghai, China). The results were calculated by drawing a curve of the average optical density using curve fitting software. The regression analysis was used to determine the best fit line.

**Ethical consideration:**

**The study was approved by the local Ethics Committee of the Pediatrics Department, Faculty of Medicine, Ain Shams University. This work has been conducted in agreement with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.**

***Statistical Analysis***

The data were analyzed using SPSS 15.0.1 for windows. According to their normality, numerical data were summarized as mean (SD) or median (interquartile range). The association between IUGR and numerical variables were assessed using unpaired t-test or Mann-Whitney test. Qualitative data were presented as frequency and percentage and compared by the Chi-Square test. The Receiver operator characteristic curve (ROC) was used to assess the diagnostic performance of IMA. A P-value less than 0.05 was considered significant.

**RESULTS**

Eighty women were included prospectively and divided into case and control groups according to the presence of IUGR. Regarding maternal characteristics, both groups were analogous in terms of age, parity, and body mass index (BMI). However, the case group had a significant shorter inter-pregnancy interval (<2 years) when compared to the control group ($p = 0.001$). Additionally, the case group's consumption of alcohol increased significantly($p = 0.021$). The case group higher prevalence of pre-eclampsia (PE) compared to the other group ($p < 0.001$). The case and control groups showed comparable environmental and social factors (marital status, education, occupation, prenatal care, residence and economic status), **Table 1.**

**Table 1: Characteristics of the included women (n =80)**

| | | Patients group | | Control group | | P-value |
|---|---|---|---|---|---|---|
| | | No. = 40 | | No. = 40 | | |
| Age (years) | Mean±SD | 30.98 ± 6.9 | | 30.65 ± 6.5 | | 0.846 |
| Parity | Median(IQR) | 2 (1 - 3) | | 2 (1 - 3) | | 0.662 |
| Inter pregnancy interval (years) | ≤ 2 | 24 (60.0%) | | 7 (17.5%) | | <0.001 |
| | >2 | 16 (40.0%) | | 33 (82.5%) | | |
| Weight (kg) | Mean±SD | 96.38 ± 13.87 | | 92.25 ± 13.32 | | 0.179 |
| Height (m) | Mean±SD | 1.66 ± 0.06 | | 1.67 ± 0.06 | | 0.528 |
| BMI (kg/m$^2$) | Mean±SD | 34.58 ± 5.23 | | 33.08 ± 4.87 | | 0.190 |
| Smoking | Active | 0 | 0.0% | 0 | 0.0% | 0.363 |
| | Passive | 35 | 87.5% | 32 | 80.0% | |
| | No | 5 | 12.5% | 8 | 20.0% | |
| **Alcohol** | No | 35 | 87.5% | 40 | 100.0% | 0.021 |
| | Yes | 5 | 12.5% | 0 | 0.0% | |
| Placenta | No abnormalities | 35 | 87.5% | 33 | 82.5% | 0.739 |
| | Placenta accrete | 3 | 7.5% | 3 | 7.5% | |
| | Placenta previa | 2 | 5.0% | 3 | 7.5% | |
| | Vilamentous insertion of placenta | 0 | 0.0% | 1 | 2.5% | |
| Umblical cord pathology (single umblical artery) | Yes | 9 | 22.5% | 5 | 12.5% | 0.239 |
| | No | 31 | 77.5% | 35 | 87.5% | |
| Uterine factors (fibroids, miomas, synequias, poor uterine vascularization) | Yes | 0 | 0.0% | 0 | 0.0% | NA |
| | No | 40 | 100.0% | 40 | 100.0% | |
| Anemia(<11 g/dl) | Negative | 31 | 77.5% | 28 | 70.0% | 0.446 |
| | Positive | 9 | 22.5% | 12 | 30.0% | |
| Mat. Pathology Factors | No | 6 | 15.0% | 29 | 72.5% | 0.000 |
| | Hypertemsion | 10 | 25.0% | 4 | 10.0% | 0.077 |
| | Diabetes Milletus | 3 | 7.5% | 4 | 10.0% | 0.692 |
| | Diabetes Mellitus& Hypertension | 3 | 7.5% | 0 | 0.0% | 0.077 |
| | Preeclampsia | 14 | 35.0% | 0 | 0.0% | 0.000 |
| | Preeclampsia &HELLP syndrome | 2 | 5.0% | 0 | 0.0% | 0.152 |
| | Preeclampsia& Diabetes Mellitus | 0 | 0.0% | 1 | 2.5% | 0.314 |
| | Diabetes Mellitus& Antiphospholipid syndrome | 1 | 2.5% | 0 | 0.0% | 0.314 |
| | Rheumatic heart/Mitral stenosis | 1 | 2.5% | 0 | 0.0% | 0.314 |
| | Urinary Infection | 0 | 0.0% | 1 | 2.5% | 0.314 |
| Marital status | Divorced | 1 | 2.5% | 0 | 0.0% | 0.314 |
| | Married | 39 | 97.5% | 40 | 100.0% | |
| Educational level | Middle school | 24 | 60.0% | 27 | 67.5% | 0.060 |
| | College | 3 | 7.5% | 0 | 0.0% | |
| | Institutionel | 2 | 5.0% | 7 | 17.5% | |
| | Illiterate | 11 | 27.5% | 6 | 15.0% | |
| Occupation | Physical | 37 | 92.5% | 35 | 87.5% | 0.456 |
| | Intellectual | 3 | 7.5% | 5 | 12.5% | |
| Prenatal care | Inadequate | 19 | 47.5% | 13 | 32.5% | 0.171 |
| | Adequate | 21 | 52.5% | 27 | 67.5% | |
| Residence | Urban | 27 | 67.5% | 32 | 80.0% | 0.204 |
| | Rural | 13 | 32.5% | 8 | 20.0% | |
| Economic status | Low | 14 | 35.0% | 7 | 17.5% | 0.075 |
| | Moderate | 26 | 65.0% | 33 | 82.5% | |

**Table 2** demonstrates that the two groups were comparable regarding maternal laboratory values, including complete blood count (CBC), liver functions, and renal functions.

**Table 2: The laboratory values of the included women (n =80)**

| | | Patients group | Control group | P-value |
|---|---|---|---|---|
| | | No. = 40 | No. = 40 | |
| **CBC** | | | | |
| RBCs (*$10^6$)/L | Mean ± SD | 4.48 ± 0.93 | 4.43 ± 1.39 | 0.846 |
| HB (g/dl) | Mean ± SD | 11.52 ± 1.16 | 11.29 ± 1.18 | 0.373 |
| WBCs ( (*$10^3$)/L) | Mean ± SD | 9.36 ± 2.53 | 8.73 ± 3.11 | 0.329 |
| PLT (*10^3)/L | Mean ± SD | 230.38 ± 58.79 | 212.50 ± 52.39 | 0.155 |
| **Liver Functions** | | | | |
| AST (IU/L) | Median (IQR) | 18 (16 - 23.5) | 17 (15 -19.5) | 0.255 |
| ALT (IU/L) | Median (IQR) | 18 (12 - 22) | 18 (13 - 22.5) | 0.893 |
| **Renal functions** | | | | |
| BUN (mg/dl) | Mean ± SD | 9.23 ± 1.10 | 9.53 ± 1.90 | 0.704 |
| Creatinine (mg/dl) | Mean ± SD | 0.77 ± 0.15 | 0.73 ± 0.17 | 0.341 |

**Mean ± SD:**for parametricdata, **Median (IQR):**for non parametric data

The neonates in the case and control groups had comparable gestational age and gender distribution. The case group contrasted with the control group by having considerably reduced weight, length, OFC, BMI, and cephalization index ($p < 0.001$ each), and significantly lower ponderal index ($p = 0.020$). We found that 40% of the neonates with IUGR were extremely low birth weight (ELBW), 22.5% were very low birth weight(VLBW), and 37.5% were low birth weight (LBW) compared to the control group, in which 22.5% were LBW, and 77.5% were normal weight. Both groups had comparable APGAR scores (**Table 3**).

**Table 3: Characteristics of the included neonates (n =80)**

| | | Patients group | Control group | P-value |
|---|---|---|---|---|
| | | No. = 40 | No. = 40 | |
| Gestational age (wks) by date of LMP | Mean ± SD | 34.20 ± 2.05 | 34.78 ± 1.07 | 0.121 |
| | Range | 29 – 36 | 32 – 36 | |
| Gestational age(wks) by antenatal U/S | Mean ± SD | 34.30 ± 1.73 | 34.45 ± 1.24 | 0.657 |
| | Range | 31 – 37 | 32 – 37 | |
| Gender | Female | 22 (55.0%) | 23 (57.5%) | 0.822 |
| | Male | 18 (45.0%) | 17 (42.5%) | |
| Weight (kg) | Mean ± SD | 1.23 ± 0.39 | 2.65 ± 0.28 | 0.000 |
| | Range | 0.7 – 2 | 2 – 3.2 | |
| Weight category (kg) | Extremely low ( <1 kg) | 16 (40.0%) | 0 (0.0%) | 0.000 |
| | Very low birth weight (1kg -< 1.5kg) | 9 (22.5%) | 0 (0.0%) | |
| | Low birth weight( 1.5kg - < 2.5kg) | 15 (37.5%) | 9 (22.5%) | |
| | Normal Weight (> 2.5kg- 4kg) | 0 (0.0%) | 31 (77.5%) | |
| Length (cm) | Mean ± SD | 36.88 ± 3.35 | 45.85 ± 1.44 | 0.000 |
| | Range | 28 – 42 | 43 – 49 | |
| OFC (cm) | Mean ± SD | 26.48 ± 1.93 | 32.00 ± 0.91 | 0.000 |
| | Range | 22 – 30 | 30 – 34 | |
| BMI ($kg/m^2$) | Mean ± SD | 8.84 ± 2.21 | 12.55 ± 1.06 | 0.000 |
| | Range | 5 – 18 | 11 – 15 | |
| Cephalization index | Mean ± SD | 23.19 ± 5.81 | 12.15 ± 1.16 | 0.000 |
| | Range | 14.5 – 35 | 10 – 15 | |
| Ponderal index | Mean ± SD | 2.43 ± 0.79 | 2.74 ± 0.20 | 0.020 |
| | Range | 1.3 – 6.4 | 2.3 – 3 | |
| APGAR score | Mean ± SD | 7.06 ± 1.25 | 7.22 ± 1.09 | 0.562 |
| | Range | 4.8 – 8.9 | 4.7 – 8.9 | |

LMP: last menstrual period; OCF: Occipitofrontal circumference; BMI: Body mass index

When plotted on the Fenton growth chart, neonates with IUGR had significantly smaller weight than the control group with a p-value < 0.001. We found that 17.5% of the studied patients (7 cases) were small asymmetrical and 82.5% of the studied patients (33 cases) were symmetrical **(Figure 1**).

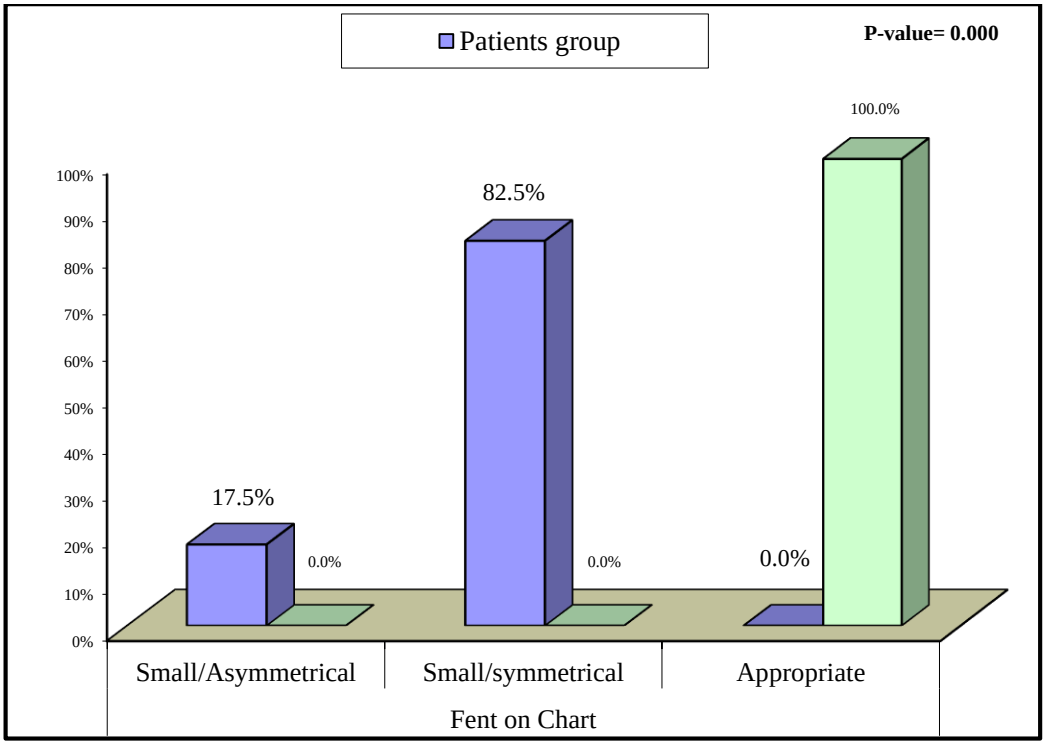


**Figure (1):** This figure shows a comparison between the two groups regarding weight when plotted on the Fenton chart

When compared to the control group, the case group's albumin level was considerably lower. (3.18 ± 0.28 versus 3.88 ± 0.49; p <0.001; **Figure 2**), while the IMA level was significantly higher in the case group compared to the other group 45 (97.5 - 210) versus 40 (25- 90); p <0.001; **Figure 3**). At a cut-off point of ≤ 3.4, the albumin had an AUC of 0.993, a sensitivity of 95%, and a specificity of 87.5% for differentiating IUGR. While the cut-off point of IMA of >50 had an AUC of 0.850, a sensitivity of 92.5%, and a specificity of 67.5% for prediction of IUGR (**Figure 4**).

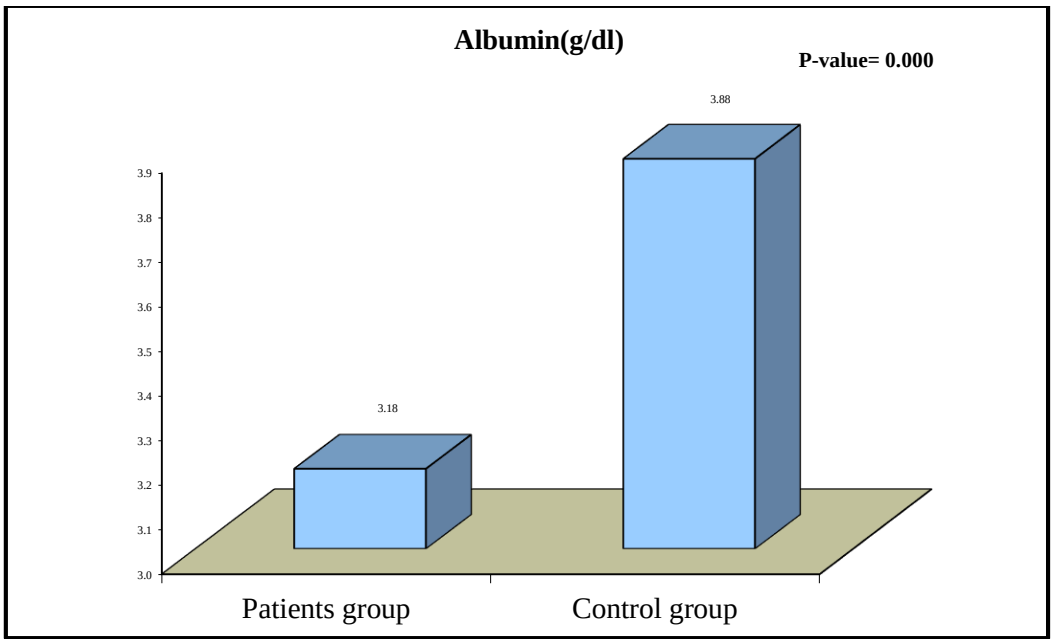


**Figure (2):** This figure shows the comparison between the two groups regarding Albumin level

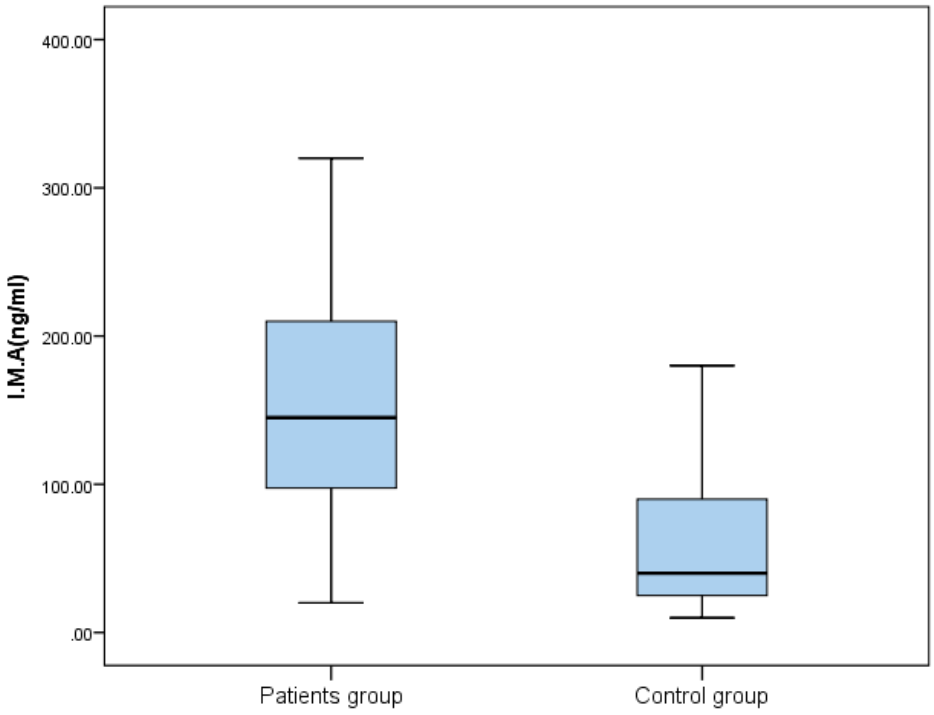


**Figure (3):** This box and whisker plot illustration shows the comparison between the two groups regarding IMA level.

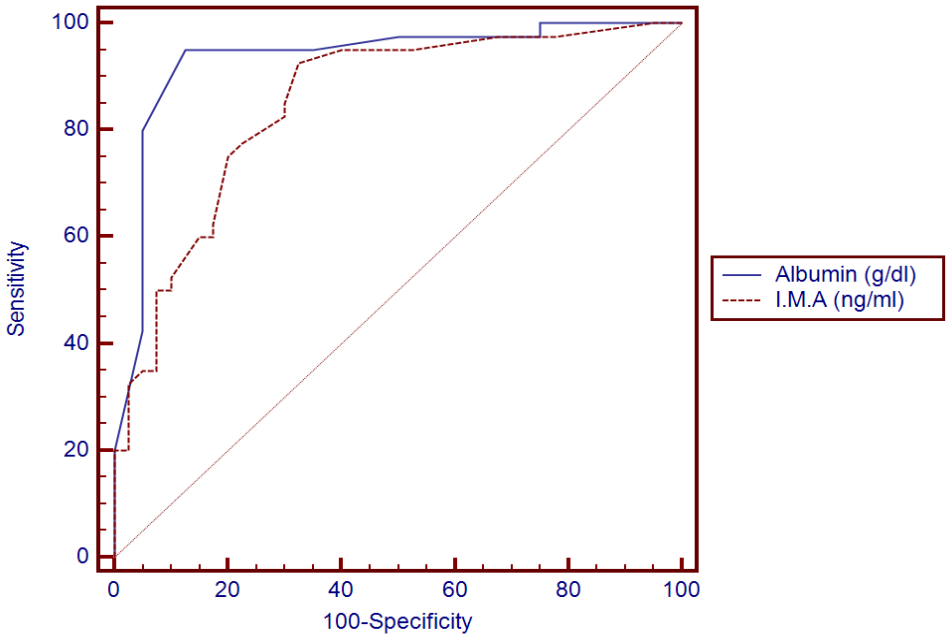


**Figure (4):** ROC curve for detection of cut off value of Albumin and IMA in IUGR preterms

There were indirect correlations between hemoglobin level and IMA level, as a decrease in HB level was associated with increased IMA level. Also, there was an inverse correlation between liver function tests (AST & ALT) and Albumin level as an increase in liver function tests (AST & ALT) was associated with a decrease in Albumin level (**Table 4**).

**Table 4: Correlation between Albumin & IMA levels with quantitative data measured (n =80)**

| | Albumin(g/dl) | | I.M.A(ng/ml) | |
|---|---|---|---|---|
| | **r** | **P-value** | **R** | **P-value** |
| Albumin(g/dl) | - | - | 0.149 | 0.358 |
| I.M.A(ng/ml) | 0.149 | 0.358 | - | - |
| Age (years) | 0.150 | 0.356 | -0.003 | 0.983 |
| Parity | 0.047 | 0.771 | 0.090 | 0.581 |
| Inter gestational period (years) | 0.211 | 0.247 | -0.056 | 0.761 |
| Gestational wks By date | 0.072 | 0.660 | -0.074 | 0.648 |
| Gestational age by U/S | -0.046 | 0.779 | -0.005 | 0.978 |
| Weight (kg) | -0.117 | 0.471 | -0.083 | 0.611 |
| Height (m) | 0.170 | 0.294 | -0.145 | 0.372 |
| BMI (kg/m$^2$) | -0.182 | 0.261 | -0.106 | 0.516 |
| RBCs (*10^6)/Ml | 0.161 | 0.320 | -0.099 | 0.545 |
| HB(g/dl) (< 11g/dl) | 0.065 | 0.691 | -0.315* | 0.048 |
| WBCs ((*10^3)/µL) | -0.129 | 0.428 | -0.020 | 0.904 |
| PLT(*10^3)/µL | -0.145 | 0.371 | -0.181 | 0.264 |
| AST(IU/L) | -0.347* | 0.028 | 0.120 | 0.460 |
| ALT(IU/L) | -0.357* | 0.024 | 0.164 | 0.311 |
| BUN (mg/dl) | -0.298 | 0.062 | 0.071 | 0.664 |
| Creatinine (mg/dl) | -0.153 | 0.347 | 0.033 | 0.842 |
| APGAR score | -0.023 | 0.889 | 0.033 | 0.842 |
| Weight (kg) | -0.056 | 0.732 | 0.142 | 0.382 |
| Length (cm) | 0.099 | 0.542 | 0.259 | 0.107 |
| OFC (cm) | 0.088 | 0.588 | 0.150 | 0.354 |
| BMI (kg/m$^2$) | -0.126 | 0.438 | -0.102 | 0.531 |
| Cephalization index | 0.053 | 0.746 | -0.127 | 0.434 |
| Pondera index | -0.176 | 0.277 | -0.304 | 0.056 |

BMI: Body mass index, OCF: Occiptofrontal circumference.

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## DISCUSSION

Antenatal detection is crucial since IUGR is a significant, common disorder that is linked to a high prevalence of neonatal morbidities and long-term consequences such perinatal hypoxia, hypothermia, hypoglycemia, hypocalcemia, hyperbilirubinemia, feed intolerance, NEC, and sepsis[15]. Ultrasound evaluation of the fetus is considered the standard diagnostic tool for IUGR antenatally [16]. IMA is elevated in most patients with cardiac ischemia, liver cirrhosis, diabetes mellitus, brain ischemia, and intrauterine ischemia. Such conditions are potent producers of free radicals [17].

It was demonstrated that the drop in albumin in plasma and the rise in IMA occurred in ischemia pregnancies as a result of inflammation and endothelial cell activity being activated. Similarly, ***Özdemir et al.*** found that cord blood IMA was significantly higher and albumin was markedly lower [18]. ***Van Rijn et al.*** explained this by impaired placental circulation, which is related to restricted fetal growth [19].

At the same time, ***Özdemir et al.*** revealed decreased albumin in plasma and higher IMA were associated with inflammation and endothelial cell activation in ischemic pregnancies[18]. ***Karadeniz et al.*** reached similar results, as they discovered that in the IUGR group, the IMA level was greater [20]. In contrast to ***Iacovidou et al***., who found no statistical difference in IMA level and albumin level between the IUGR group and AGA group, this could be because vital organs as the brain and heart were spared [21].

We found that the cut-off point for cord blood Albumin was ≤ 3.4 with AUC = 0.993, the sensitivity of 95% and specificity of 87.5%, While the cut-off point of IMA was >50 with AUC = 0.850, the sensitivity of 92.5%, and specificity of 67.5%. In addition, we have observed an indirect correlation between Hb level and IMA level. A decrease in Hb level below <11 g/dl was associated with increased IMA level. Low haemoglobin levels limit oxygen flow throughout the body, resulting in persistent hypoxia or oxidative stress, which may then lead to foetal development restriction[22].

Likewise, we found an inverse correlation between liver function tests (ALT and AST) and Albumin level. An increase in ALT and AST is associated with decreased albumin levels. This is expected as the liver is the only site for albumin synthesis. With elevated levels of AST and ALT, it is a helpful marker of hepatic function that may be compromised in chronic liver disorders [23].

Antenatal ultrasound combined with IMA represents a good predictor of IUGR, allowing better care of neonates with IUGR.

We found an interpregnancy period of less than two years was linked to an increased risk of IUGR. The WHO advised women to wait at least two years after a live delivery and six weeks after an early pregnancy loss before getting pregnant again to reduce the risk of adverse maternal and perinatal outcomes [24].

Short interpregnancy intervals may not allow adequate time for the mother to recover from dietary deficiencies, resulting in fetal-maternal competition for vital resources [25]. In terms of maternal age, we could not identify any association between it and IUGR. Similarly, ***ŞENGÜL et al.*** discovered that the risk of IUGR was not influenced by parity or age [26]. In contrast, ***Muhammad et al.*** concluded that young maternal age carried a risk for IUGR. They also found that mothers with weights around 54.2±9.7 kg, height around 1.51±0.04 m, and BMI around 22 kg/m$^2$ were significantly associated with IUGR [27].

Regarding maternal habits, alcohol intake was more prevalent in mothers of the IUGR group (87.5%) as opposed to the other group (12.5%). Similar results were reached by ***Sabra et al.*** [28] Alcohol intake during pregnancy results in alcoholic fetal syndrome, which is characterized by a reduction in fetal weight, length, occipital frontal circumference (OFC), other malformations such as facial anomalies, and developmental delay [29].

Although we expected smoking to be a risk for IUGR, we could not detect any difference between the two groups. In contrast to ***Villalbí et al.*** who stated that both active and passive smoking is strongly associated with IUGR [30]. Regarding maternal factors, we found that PE was only prevalent in the IUGR group (35%) as opposed to the other group (0%). IUGR is the result of the hypoxia and ischemia in the fetus which is caused by placental insufficiency in PE [31].

In accordance with ***Padilla et al.*** [32], we found that the IUGR group had high significantly lower weight, length, OFC, BMI, cephalization index, and ponderal index in comparison to the control group. We also found that 40% of patients were extremely low birth weight (<1 kg), 22.5% were very low birth weight (<1.5 kg), and 37.5% were low birth weight (<2.5 kg) as compared to the control group who had only 22.5% were low birth weight. Furthermore, we found that symmetrical IUGR was more common than asymmetrical IUGR (82.5% vs. 17.5%).

Similarly, ***Dashe et al.*** found that 80% were symmetrical IUGR [33]. In contrast, ***O'Connor et al.*** found that only 29% of the patients' group were symmetrical IUGR while 71% were asymmetrical IUGR [34].

## CONCLUSION

We suggest an important association between the IUGR and cord blood albumin & IMA levels, highlighting the role of combined antenatal ultrasound and serum IMA in diagnosing IUGR. In addition, a significant association between IUGR and interpregnancy interval < 2 years, alcohol intake during pregnancy, and preeclampsia was indicated. Still, to find out whether cord blood IMA levels could be used to detect prenatal asphyxia in IUGR cases, more research with bigger sample numbers is necessary.

**Acknowledgment:** Not applicable.
**Conflicts of interest:** Not found.
**Financial support and sponsorship:** None provided.

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