https://doi.org/10.15360/1813-9779-2024-5-31-36

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Pancreatic Ultrasound in High-risk Neonates

Safaa A. ELMeneza[1]*, Naglaa F. Hassan[1], Aisha R. Mohamed[2]

Pediatrics[1] and Radiodiagnosis[2] departments, Faculty of Medicine for Girls, Al-Azhar University, Elmokaiam Eldaym Str., 6 district, 1141 Nasr city, Cairo, Egypt

For citation: *Safaa A. ELMeneza, Naglaa F. Hassan, Aisha R. Mohamed.* Pancreatic Ultrasound in High-risk Neonates. *Obshchaya Reanimatologiya = General Reanimatology.* 2024; 20 (5): 31–36. https://doi.org/10.15360/1813-9779-2024-5-31-36 [In Engl.]

***Correspondence to:** Safaa A. ELMeneza, Safaa5@hotmail.com, safaaelmeneza@azhar.edu.eg

Summary

Pancreatic ultrasound is employed to assess the structure of the organ and diagnose various conditions. However, analyses of pancreatic images of high-risk newborn infants are scarce.

Aim of the study: to investigate pancreatic echogenicity in high-risk neonates and evaluate the association between pancreatic echogenicity and clinical diagnosis.

Materials and methods. This prospective observational case-control ultrasound study included 105 neonates admitted to the neonatal intensive care unit or outpatient. The patients were divided into two groups: group 1 (high-risk), which included 55 high-risk neonates, and group 2 (control), which included 50 neonates of comparable age with no history of high-risk pregnancy or delivery who were presented for medical consultation. Abdominal ultrasound examinations were performed, with a focus on the pancreas. Pancreatic echogenicity was classified as hyperechoic, isoechoic, or hypoechoic, relative to the liver.

Results. No significant difference in pancreatic size was observed between the high-risk and control groups. A significant predominance of hyperechogenicity over hypoechogenicity or isoechogenicity was found in the high-risk group. A significant difference in echogenicity was found between the high-risk and control groups (P=0.0001). Neonates in the control group were more likely to have pancreatic isoechogenicity (60%) compared to hyperechogenicity (34%) or hypoechogenicity (6%). In the high-risk group, neonates had a higher frequency of pancreatic hyperechogenicity (72.72%) compared to hypoechogenicity (10.9%) or isoechogenicity (16.36%). Notably, 83.3% of infants born to diabetic mothers had a hypoechogenic pattern. Certain high-risk infants, such as preterm infants and those with perinatal asphyxia, had a higher frequency of hyperechogenicity (83.3%). The percentage of hypoechoic pattern was comparable in male and female newborns (50%); isoechoic pattern was more prevalent in females (77.3%) than in males (22.2%), while males had a more frequent hyperechoic pattern (57.5%).

Conclusion. Evaluation of the pancreas in high-risk neonates and monitoring of long-term outcomes are of critical importance, especially in the infants of diabetic mothers.

Keywords: high-risk neonates; pancreas; ultrasound; hyperechogenicity; isoechogenicity; hypoechogenicity; neonates

Conflict of interest. The authors declare no conflict of interest.

Financial support. This study did not receive financial support.

Acknowledgments. We thank the parents of the neonates for their cooperation in this study.

Ультразвуковое исследование поджелудочной железы у новорожденных из группы высокого риска

Сафаа А. Эль-Менеза[1]*, Наглаа Ф. Хассан[1], Аиша Р. Мохамед[2]

Отделения педиатрии[1] и лучевых методов исследования[2], Факультет медицины для девушек, Университет Аль-Азхар, Египет, г. Каир, г. Наср, 1141, 6 округ, ул. Эльмокаям Эльдайм

Для цитирования: *Safaa A. ELMeneza, Naglaa F. Hassan, Aisha R. Mohamed.* Pancreatic Ultrasound in High-risk Neonates. *Общая реаниматология.* 2024; 20 (5): 31–36. https://doi.org/10.15360/1813-9779-2024-5-31-36 [На русск. и англ.]

***Адрес для корреспонденции:** Сафаа А. Эль Менеза, Safaa5@hotmail.com, safaaelmeneza@azhar.edu.eg

Резюме

Ультразвуковое исследование поджелудочной железы (ПЖ) применяют для оценки структуры органа и диагностики различных заболеваний. При этом опубликованных результатов анализа ультразвукового исследования ПЖ новорожденных из группы высокого риска очень мало.

Цель исследования — изучить особенности эхогенности ПЖ у новорожденных из группы высокого риска и оценить связь между паттерном эхогенности ПЖ и клиническим диагнозом.

Материалы и методы. В проспективное обсервационное ультразвуковое исследование типа «случай–контроль» включили 105 новорожденных, которых разделили на две группы. В 1-ю группу (высокого риска) включили 55 пациентов отделения интенсивной терапии новорожденных, во 2-ю группу (сравнения) — 50 новорожденных, доставленных на амбулаторный прием без информации об осложнениях беременности или родов в анамнезе. Провели ультразвуковое исследование брюшной полости

с акцентом на ПЖ. Эхогенность ПЖ оценивали по отношению к печени как гиперэхогенную, изоэхогенну или гипоэхогенную.

Результаты. Размеры ПЖ у новорожденных обеих групп существенно не различались. У пациентов из группы высокого риска выявили значительное преобладание гиперэхогенности над гипоэхогенностью или изоэхогенностью. Установили межгрупповое различие в эхогенности ПЖ (p=0,0001). У новорожденных группы сравнения преобладала изоэхогенность ПЖ (60%), реже обнаруживали гиперэхогенность (34%) и гипоэхогенность (6%). У новорожденных из группы высокого риска чаще выявляли гиперэхогенность ПЖ (72,72%) и значительно реже — гипоэхогенность (10,9%) и изоэхогенность (16,36%). У 83,3% младенцев, рожденных от матерей, страдающих сахарным диабетом, наблюдали гипоэхогенность ПЖ. Высокую частоту гиперэхогенности (83%) в группе высокого риска отметили среди недоношенных новорожденных и переживших перинатальную асфиксию. Гипоэхогенность ПЖ встречали с равной частотой у новорожденных мальчиков и девочек (50%); изоэхогенный паттерн преобладал у девочек (77,3%) по сравнению с мальчиками (22,2%), а гиперэхогенный - чаще встречался у мальчиков (57,5%).

Заключение. Оценка состояния ПЖ у новорожденных из группы высокого риска и мониторинг отдаленных исходов имеют решающее значение, особенно у детей, чьи матери страдают сахарным диабетом.

Ключевые слова: новорожденные группы высокого риска; поджелудочная железа; ультразвуковое исследование; гиперэхогенность; изоэхогенность; гипоэхогенность; новорожденные

Конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.

Финансовая поддержка. Данное исследование провели без финансовой поддержки.

Introduction

The pancreas, an organ located in the abdomen, performs both endocrine and exocrine functions. It produces hormones that regulate blood glucose levels and secretes fluids containing bicarbonate and enzymes for digestion. While pancreatic disorders are difficult to detect using imaging techniques, ultrasound can detect a variety of conditions including pancreatitis, pancreatic insufficiency, cystic formations, and pancreatic tumors [1]. Pancreatic insufficiency is a condition in which the pancreas does not produce enough digestive enzymes to break down food in the digestive system [2].

Although challenging, imaging of the pancreas can provide valuable information about morbidity and mortality. Ultrasound is particularly useful for examining the pancreas in children because it is non-invasive, does not require sedation, and does not expose children to ionizing radiation. The effectiveness of ultrasound in evaluating the pediatric pancreas is well documented, with children having an optimal acoustic window due to their minimal adipose tissue and large left hepatic lobe [3].

The pancreas can be affected by a variety of diseases, both focal and diffuse.

Transabdominal ultrasound can detect acute pancreatitis, congenital anomalies, cysts, and tumors. However, assessing the pancreatic images may be limited because of the variation of pancreatic area in echogenicity and size. Although the ultrasound investigation provides a rapid, noninvasive, and safe method of examining multiple organs in the NICU, the knowledge of the neonatal pancreas remains limited. Studies on the echogenicity of the neonatal pancreas are still limited. While the echogenicity of a normal adult pancreas increases with age [4], it may appear isoechoic or hypoechoic in children [3]. A marked increase in echogenicity in children may indicate conditions such as cystic fibrosis [5]. High-risk infants, including those born prematurely or with health problems at birth, have an increased risk of morbidity and mortality regardless of gestational age or birth weight. These newborns are vulnerable to both immediate and long-term health and developmental problems. Although high-risk neonates may present with varying degrees of pancreatic disease, few studies have focused on pancreatic imaging in NICU patients. Understanding the diverse pancreatic imaging patterns in high-risk neonates may facilitate early detection of a pancreatic pathologic pattern(s) and personalize treatment to improve outcomes.

The aim of the study was to investigate pancreatic echogenicity in high-risk neonates and evaluate the association between pancreatic echogenicity and clinical diagnosis in high-risk neonates.

Material and Methods

The study was conducted at AL Zhrraa University Hospital. It was an observational case-control study. The study was approved by the Ethics Committee of the Faculty of Medicine for Girls (registration number RHDIRB 2018122002 and OHHP Reg.No. IRB00012239 / study number 2461).

Informed consent statement. Informed consent was obtained from the parents of the neonates enrolled in the study.

The study period was from November 2023 to June 2024. We hypothesized that neonates and high-risk neonates have specific patterns of pancreatic echogenicity and that high-risk neonates may have a different pattern than other normal neonates that can be detected by US examination. The power was set at 0.8 (80%) to avoid false-negative results, with 80% representing a reasonable balance between alpha and beta risk.

Sample size was estimated using the equation:

$$n = \frac{z^2 \times \hat{p}(1-\hat{p})}{\varepsilon^2}$$

A minimum sample size of 101 patients was required to achieve a 95% confidence level. The study prospectively enrolled 105 patients, including neonates admitted to the NICU and controls brought in for consultation. Participants were divided into two groups: Group 1 (high-risk) with 55 neonates and Group 2 (control) with 50 neonates. The high-risk group included preterm infants, infants of diabetic mothers (IDM), and those with perinatal asphyxia (PA), jaundice, meconium aspiration (MA), sepsis, intrauterine growth retardation (IUGR), and neonates from post-date pregnancies. To ensure optimal abdominal visualization, infants with major congenital anomalies, liver disease, and necrotizing enterocolitis were excluded [6]. The control group consisted of normal neonates of comparable age with no history of high-risk pregnancy or delivery who were presented for medical consultation. The patient selection process is illustrated in a flow chart (Figure).

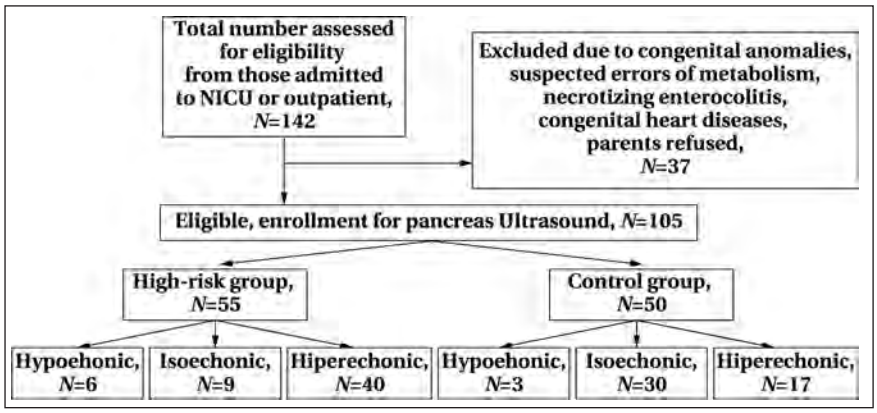

Fig. Study flow diagram.

In addition, laboratory tests were performed for blood gases, electrolytes, blood glucose, complete blood count, and C-reactive protein (CRP).

Pancreatic ultrasound examinations were performed using a SIEMENS Sonoline Elegra unit with a 3.5 curvilinear transducer. Patients were positioned in the supine position with the option to move to either side for improved visualization. The echogenicity of the pancreas was assessed in relation to the liver, which served as a reference point [7–8]. Pancreatic images were categorized as hyperechoic, isoechoic, or hypoechoic compared to the liver at a similar depth. The examining radiologist was blinded to the clinical diagnoses of the patients.

Data analysis. The collected data were coded and processed. All analyses were performed with IBM SPSS version 25.

Qualitative variables were presented as numbers and percentages, while quantitative variables were expressed as means with standard deviations *(SD)*.

The data exhibited a normal distribution, allowing the use of Student's *t*-test to compare group means. Chi-squared test was used to determine statistical significance between categorical variables.

A *P* value of less than 0.05 was considered statistically significant. The study used a 95% confidence interval and accepted a 5% margin of error. Therefore, two-tailed *P* values of 0.05 or less were considered statistically significant.

Results

The results are presented in Tables 1–6.

Demographic and clinical features of the groups. While no significant differences were observed between high-risk and control infants with respect to gestational age, sex, body length, head circumference, and mode of delivery, significant differences were found in birth weight, postnatal age, and Apgar scores at 1 and 5 minutes in high-risk infants.

The corresponding *P* values were 0.003, 0.0029, 0.0001, and 0.0001 (Table 1).

Table 2 shows the clinical diagnoses and their frequencies among the patients. In the high-risk group, each of the following conditions accounted for 10.9% of cases: preterm birth, infants born to diabetic mothers, perinatal asphyxia, meconium aspiration, sepsis, intrauterine growth retardation, and

Table 1. The characteristics of the studied groups.

Parameters	Values in groups		*P*-value
	High-risk, *N*=55	Control, *N*=50	
Gestational age, weeks	38.15±3.05 30–44	38.5±1.5 37–41	t=0.734*, *P*=0.46
Birth weight, kg	3.07±0.61 1.800–4.300	3.34±0.18 3.100–3.500	3.012*, *P*=0.003
Gender, male/female	28/27	30/20	χ^2=0.8671, *P*=0.35
Postnatal age, day	5.89±3.02 3–11	7.9±3.73 3–5	t=3.047*, *P*=0.0029
Body length, cm	48.82±1.44	49.1±0.88	1.188*, *P*=0.237
Head circumference, cm	34.33±0.68	34.5±0.47	t=1.476*, *P*=0.143
Mode of delivery			
Normal vaginal	39	28	t=2.4970, *P*=0.114
Cesarean section	16	22	
Apgar score at 1 min	4.8±2.03	7.9±1.34	9.137*, *P*=0.0001
Apgar score at 5 min	6.49±1.95	8.5±1.35	t=6.082*, *P*=0.0001

Note. * — *t*-Student *t*-test; χ^2 — chi-square test.

post-term pregnancy. In addition, jaundice was observed in 12.72% of the high-risk infants (Table 2).

Laboratory findings. The high-risk group had significant decreases in hemoglobin, RBCs, platelets, and blood glucose (*P*=0.0001, 0.0001, 0.023, and 0.0001, respectively). In contrast, the control group showed significant increases in WBCs and bilirubin (*P*=0.039 and 0.0001, respectively) (Table 3).

Ultrasonographic evaluation of the pancreas. Ultrasonography revealed that the pancreas of the studied neonates had well-demarcated borders and consistent echogenicity. Pancreatic dimensions did not differ significantly between the high-risk and control groups (Table 4).

In the control group, isoechogenicity was observed in 60% of patients, while hyperechogenicity and hypoechogenicity were observed in 34% and 6%, respectively. Conversely, high-risk infants had a higher proportion of hyperechogenicity (72.72%), followed by isoechogenicity (16.36%) and hypoechogenicity (10.9%). The high-risk group showed a significant prevalence of hyperechogenicity compared to the other patterns. Post hoc power analysis for dichotomous data (alpha=0.05) in high-risk infants showed 100% power for hyperechogenicity versus isoechogenicity and hypoechogenicity. However, a low power of 12.9% was observed between hypoechoic and isoechoic patterns.

Table 2. Diagnoses of high-risk newborns and their frequency.

Diagnoses	Values, *N* (%)
Hyperbilirubinemia	7 (12.72)
Infant of diabetic mother	6 (10.9)
Perinatal asphyxia	6 (10.9)
Meconium aspiration	6 (10.9)
Premature rupture of membranes	6 (10.9)
Sepsis	6 (10.9)
Prematurity	6 (10.9)
Intrauterine growth retardation	6 (10.9)
Postdate pregnancy	6 (10.9)

A significant difference in echogenicity was found between the high-risk and control groups (*P*=0.0001). The control group showed predominantly isoechogenicity compared to hyper- and hypoechogenicity. Post hoc power analysis for dichotomous data (alpha=0.05) in the control group showed a 100% probability for isoechogenicity versus hypoechogenicity and hypo- and hyperechogenicity combined. In addition, there was a 96.8% probability for isoechogenicity versus hyperechogenicity.

However, the hypoechoic pattern was prevalent (83.3%) in infants born to diabetic mothers. Certain high-risk infants, including those born prematurely or with perinatal asphyxia, had a higher frequency of hypoechoic patterns (83.3%) (Table 5).

The occurrence of hypoechoic patterns was equally distributed between male and female new-

Table 3. Laboratory findings in the studied groups.

Parameters	Values in groups		*P*-value
	High-risk, *N*=55	Control, *N*=50	
Hemoglobin, g/dL	14.74±1.5	16.8±1.9	t=6.194, *P*=0.0001
RBC, 10^6/mm³	4.39±0.85	5.01±0.04	t=5.150, *P*=0.0001
WBC, 10^6/mm³	14.32±6.27	12.42±1.46	t=-2.091, *P*=0.039
Platelets, 10^3/μL	192.93±85.71	225.8±56.23	t=2.299, *P*=0.023
Blood glucose, mg/dL	56.89±9.75	67.3±4.08	t=7.010, *P*=0.0001
Serum bilirubin, mg/dL	6.03±4.56	1.69±0.096	t=-6.726, *P*=0.0001

Note. t — Student's *t*-test.

Table 4. Comparison of pancreatic dimensions between the control and high-risk groups.

Parameters	Values in groups		*P*-value
	High-risk, *N*=55	Control, *N*=50	
Head, cm	1.1±0.4	0.94±0.4	t=1.28, *P*=0.2
Body, cm	0.6±0.04	0.6±0.15	t=0.00, *P*=1.00
Tail, cm	0.97±0.14	1 ±0.14	t=–1.09, *P*=0.27

Note. t — Student's *t*-test.

Table 5. The echogenicity of pancreas in the studied groups.

Groups	Values in groups, *N* (%)			*P*-value
	Hypoechoic	Isoechoic	Hyperechoic	
High-risk:				
Hyperbilirubinemia	1 (14.3)	1 (14.3)	5 (71.4)	χ^2= 38.06, *P*=0.0001
Infants of diabetic mother	5 (83.3)	0 (0)	1 (16.7)	
Perinatal asphyxia	0 (0)	1 (16.7)	5 (83.3)	
Meconium aspiration	0 (0)	2 (33.3)	4 (66.7)	
Premature rupture of membranes	0 (0)	0 (0)	6 (100)	
Sepsis	0 (0)	2 (33.3)	4 (66.7)	
Prematurity	0 (0)	1 (16.7)	5 (83.3)	
Intrauterine growth retardation	0 (0)	0 (0)	6 (100)	
Post-date pregnancy	0 (0)	2 (33.3)	4 (66.7)	
Total	6 (10.9)	9 (16.36)	40 (72.72)	
Control	3 (6)	30 (60)	17 (34)	χ^2 =20.9818, *P*=0.0001
High risk — Control	χ^2= 21.3988			*P*=0.0001

Table 6. The echogenicity of the pancreas concerning sex in the high-risk group.

Sex	Values, *N* (%)		
	Hypoechoic	Isoechoic	Hyperechoic
Male	3 (50)	2 (22.2)	23 (57.5)
Female	3 (50)	7 (77.3)	17 (42.5)
Total	6 (100)	9 (100)	40 (100)

borns (50%). Isoechoic patterns were more common in females (77.3%) than in males (22.2%), whereas hyperechoic patterns were more common in males (57.5%) than in females (42.5%) (Table 6).

Discussion

Ultrasound examination of the pancreas has proven valuable in both adults and children. The pancreas develops around the fifth week of pregnancy, arising from the endodermal lining of the duodenum as separate ventral and dorsal buds. As a result, this organ is susceptible to several intrauterine risk factors, including infection, blood glucose fluctuations, and oxygen deprivation. Limited research has focused on the pancreas during the neonatal period, with no studies specifically examining high-risk neonates, except for a 1990 investigation of premature infants [9]. Our study aimed to characterize the sonographic features of the pancreas in high-risk neonates admitted to the NICU.

The study found no significant differences in pancreatic dimensions in the head, body, and tail regions between the high-risk and control groups. These findings are consistent with previous research in healthy neonates [10–11], although D. S. Raut et al. [12] reported lower values.

The study revealed a marked prevalence of pancreatic hyperechogenicity in the high-risk neonatal group, whereas isoechogenicity predominated in the control neonatal group. Pancreatic echogenicity was assessed using the liver as a reference point.

In the high-risk group, 72.72% of patients had hyperechogenic pancreas, 16.36% had isoechogenic pancreas, and 10.9% had hypoechogenic pancreas. In the control group, 34% of neonates had hyperechogenic pancreas, 60% had isoechogenic pancreas, and 6% had hypoechogenic pancreas. A previous study found that 60% of healthy newborns had a hyperechogenic pancreas [9], while another study of newborns, infants, and children up to 19 years of age revealed low echogenicity in 10%, isoechoic pancreas in 53%, and high echogenicity in 37% [10]. Typically, the pancreas in neonates and infants is described as slightly more echogenic than the liver. However, one study contradicted this and reported that the neonatal pancreas was relatively hypoechoic [11].The echogenicity and tissue reflectivity of the pancreas may be influenced by the interaction of external and internal factors. Increased pancreatic echogenicity is attributed to the amount of intra- and peripancreatic fat, connective tissue septa between lobules, and reticular tissue [13]. In addition, the densely packed cellular elements in the pancreas of newborns and infants contribute to increased echogenicity, as it occurs in the kidneys [14]. In older children and adults, increased echogenicity may result from fibrosis, lipomatosis, hemosiderosis, medications, congestive changes, fatty infiltration, and calcification [11].

Hyperechogenicity may not necessarily indicate disease, especially in preterm infants. A study by E. Walsh showed that pancreatic hyperechogenicity changes to an isoechoic pattern with age [9]. In this study, analysis of echogenicity in various high-risk infants showed that preterm infants, neonates with perinatal asphyxia or delivered after premature rupture of membranes, and infants with IUGR had a predominance of hyperechoic pancreatic parenchyma. This may be due to exposure to risk factors during the intrauterine and perinatal period that could affect blood flow and tissue perfusion or cause energy depletion and oxidative stress that alter organ structure and metabolism. Pancreatic echogenicity in children is related to the volume of parenchymal tissue [15].

Preterm infants have relatively small amounts of subcutaneous tissue and intra-abdominal fat, which facilitates the examination of abdominal organs. The pancreas was hyperechoic in 83.3% of preterm infants and isoechoic in 17.7%, which is comparable to the data of E. Walsh et al. who reported that normal pancreatic parenchyma in preterm and term infants is hyperechoic with respect to the liver [9]. This appearance is related to prominent septa within the lobules, large amounts of glandular tissue, and supportive reticular tissue within the lobules. The shift from predominantly hyperechoic patterns in preterm infants to isoechoic patterns in term infants observed in our study may be explained by near-term changes, including a reduction in these tissues and the development of a more obvious lobular structure with tightly packed glandular components [16]. Follow-up ultrasound of premature infants and neonates showed isoechoic transformation of the pancreas in some premature infants who initially had hyperechogenicity. The study concluded that hyperechogenicity relative to the liver is common in premature infants and neonates [9].

The present study also identified a high occurrence of hypoechoic patterns in infants born to diabetic mothers, observed in 83.3% of IDM cases. While the reason for this predominant hypoechogenicity in these infants remains unclear, it may be attributed to intrauterine metabolic changes causing various structural alterations, and diabetic fetopathy, which is closely linked to the intensity and the time of onset of maternal hyperglycemia. According to J. Pedersen's hypothesis, elevated maternal blood glucose results in fetal hyperglycemia,

leading to beta cell hypertrophy and subsequent hyperinsulinemia [17]. An alternative explanation suggests that compromised placental blood flow affects fetal and pancreatic development, potentially resulting in long-term health issues such as diabetes mellitus, hypertension, or cardiovascular disease, as proposed by Barker et al [18].

Recent studies on fetal liver have demonstrated that venous circulation reflects the impact of maternal hyperglycemia. The umbilical return from the placenta is disproportionately directed to the fetal liver (exceeding that of normal fetuses). The fetal liver is solely responsible for initial fetal fat accumulation, regulated by the volume of umbilical liver perfusion [19–20]. Hepatic fat deposition causes the liver to appear hyperechoic in comparison to the pancreas. Additional factors contributing to a hypoechoic pancreas include edema, fluid accumulation, and exposure to intravenous fluids.

Ultrasound imaging provides a simple and safe method of examining abdominal organs in neonates, allowing measurement of the dimensions of the liver, pancreas, and spleen [21]. While research on the neonatal pancreas is limited, our investigation provides important insight into pancreatic disease in high-risk infants in the NICU. Study limitations include the impact of multiple risk factors and the lack of follow-up of the patients studied. Further research is needed that focuses on individual risk factors and includes follow-up assessments.

Conclusion

High-risk neonates have a predominantly hyperechoic pattern of the pancreas, whereas normal neonates have an isoechoic pancreas. There was no significant difference in pancreas size between the normal and high-risk neonates. Preterm infants, as well as those with perinatal asphyxia, premature rupture of membranes, and intrauterine growth retardation, presented with pancreatic hyperechogenicity, whereas infants of mothers with diabetes presented with pancreatic hypoechogenicity. It is important to evaluate the pancreas in high-risk neonates and monitor long-term outcomes, especially in the infants of diabetic mothers.

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Поступила 30.07.2024
Принята 27.08.2024