Volume 2 | Issue 12 |2023

SMART PEDI UPDATE

Pedismart Newsletter
Vol 2 | Issue 12 | 2023

Pedi smart News Letter
Vol 2| Issue 12 |2023

Dear Doctor,
Greetings from Micro Labs Limited. We are happy to bring you **"PEDI SMART"** which contain latest and interesting news in the field of Paediatrics.

This issue contains:

1. **Incidence of hypoglycemia and related comorbidities among newborns of mothers with diabetes.**
2. **Assessment of Troponin-I, creatine-kinase myocardial band (CK-MB), and inotropic score (IS) in hypoxic ischemia encephalopathy (HIE) and associated mortality.**
3. **Relationship between headache characteristics and serum ferritin, vitamin B12 and vitamin D levels.**
4. **Case report on rhabdomyomas in a neonatal patient with tuberous sclerosis complex.**

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

Volume 2 | Issue 12 |2023

SMART PEDi UPDATE

Incidence of hypoglycemia and related comorbidities among newborns of mothers with diabetes

Introduction

Pre-gestational diabetes is significantly associated with an increased risk of emergency cesarean section among women with pre-gestational diabetes

Hypoglycemia a common metabolic abnormality in newborns which usually occurs in babies whose mother is diabetic or having hormonal imbalance. On the other hand, low blood glucose levels (<47 mg/dl) in the first few hours or days following delivery is known as hypoglycemia in newborns.[1] GDM is a metabolic condition that affects 7.5% of mothers and increases the risk of hypoglycemia in their newborns by up to 27% when compared to newborns of mothers without this condition. Studies has demonstrated a substantial correlation between chronic pre-gestational diabetes mellitus (PGDM) and adverse fetal and neonatal comorbidities, including neurological issues, congenital malformations, pulmonary disease, and feeding difficulties.[2] Therefore, postnatal glucose monitoring and control should be provided to newborns whose mothers have diabetes mellitus (DM) until metabolic stability is ensured. This study aimed to assess the incidence of hypoglycemia in newborns of diabetic mothers and to evaluate which comorbidities are associated with newborns of mothers with pre-gestational diabetes mellitus (PGDM) and mothers with gestational diabetes (GD)

Methods

A retrospective cohort study was carried out among diabetic mothers, with gestational or pre-gestational diabetes mellitus. Study included newborns of mothers with diabetes mellitus. A total of 1,036 individuals were eligible for the study and classified into one of two groups: Gestational diabetes mellitus (GDM) or pre-gestational diabetes mellitus (PGDM). Maternal characteristics included Type of diabetes (pre-gestational or gestational), the method of diabetic control (diet or drug), and the presence of medical comorbidities, such as hypertension and thyroid disease, were also recorded. New-borns characteristics such as gender, birth weight (in grams), and Apgar scores, were assessed at 5 min after delivery.

Results

Mothers with GDM experienced spontaneous labour 53% greater than that of mothers with PGDM. In this study group, prevalence of hypoglycemia was 13% and hypoglycemia in babies born to mothers with gestational diabetes was 12% and in those with chronic diabetes it was 22% (Figure 1). Pregnant women who had pre-gestational diabetes had a

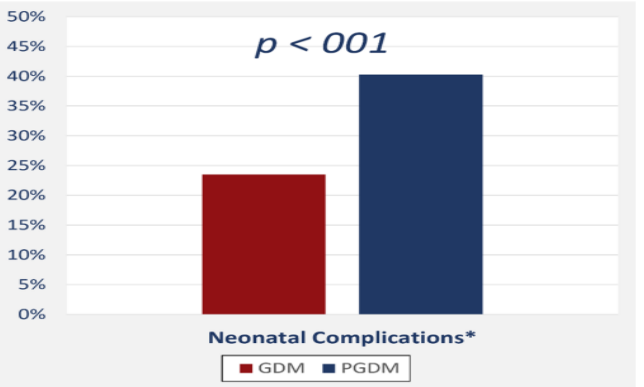

Figure 1. Neonatal complications

significantly higher risk of requiring an emergency caesarean surgery and have a baby who is large for its gestational age, must be admitted to NICU (22%), respiratory distress syndrome (15%) and needs gavage feeding (13%). Average hospital stay was significantly longer with newborns of mothers with PGD (4.5 days) than newborns of mothers with GD (2.4 days).

Discussion

Infants born to diabetic mother's experience neonatal hypoglycemia as a result of an impaired gluconeogenesis pathway. When the two forms of maternal diabetes were examined, it was found that 21% of newborns of mothers with PGDM and 12% of newborns of mothers with GDM had been diagnosed with hypoglycemia. According to this study, there was a significant association between maternal PGDM and the infant's need for gavage feeding. According to this study, infants born to women with PGDM had an average hospital stay that was significantly longer than that of infants born to mothers with GDM. The results of the current study also indicated that there is a significant risk of respiratory distress syndrome in infants born to women with PGDM.[1] In Arimitsu et al., 200 (45%) of the 443 full-term singleton newborns born to mothers with GDM experienced hypoglycemia. The neonatal hypoglycemia group had significantly higher incidences of insulin therapy, gestational weight gain (GWG), HbA1c at the first trimester, and HbA1c at the diagnosis of GDM than the non-neonatal hypoglycemia group.[3]

Conclusion

13% of newborns of mothers with diabetes experience hypoglycemia. Of these, hypoglycemia was identified in 12% of infants of mothers with GDM and 21% in those with PGDM. But, newborns of mother with PGDM are more likely to experience high birth weight; neurological problems, like sucking difficulty, extended hospital stays, NICU admissions and RDS.

References

1. Bamehrez M. Hypoglycemia and associated comorbidities among newborns of mothers with diabetes in an academic tertiary care center. Frontiers in Pediatrics. 2023;11:1267248.
2. Sharma A, Davis A, Shekhawat PS. Hypoglycemia in the preterm neonate: etiopathogenesis, diagnosis, management and long-term outcomes. Transl Pediatr. 2017;6(4):335–48..
3. Arimitsu T, Kasuga Y, Ikenoue S, Saisho Y, Hida M, Yoshino J, Itoh H, Tanaka M, Ochiai D. Risk factors of neonatal hypoglycemia in neonates born to mothers with gestational diabetes. Endocrine Journal. 2023;70(5):511-7.

Assessment of Troponin-I, creatine-kinase myocardial band (CK-MB), and inotropic score (IS) in hypoxic ischemia encephalopathy (HIE) and associated mortality

Volume 2 | Issue 12 |2023

SMART PEDI UPDATE

Introduction

Troponin I and inotropic score are important indicators of infant mortality with Hypoxic-ischemic encephalopathy

Hypoxic-ischemic encephalopathy (HIE), the most common cause of neonatal encephalopathy which is defined as impaired cerebral function due to lack of oxygen to the brain following antenatal/perinatal adverse events. Neonatal encephalopathy is characterised by abnormal neurological function, difficulty in maintaining respiration, decreased activity and level of consciousness, reduced motor tone, persistence of primitive reflexes, and seizures.[1] Hypoxic-ischemic encephalopathy (HIE), one of the main causes of multi-organ failure in newborns, frequently involves cardiovascular dysfunction.[2] The purpose of this study was to evaluate the relationships between the levels of troponin I, creatine-kinase myocardial band (CK-MB), and inotropic score (IS) as well as HIE staging and mortality, in HIE patients.

Methods

Retrospective study included infants born at a gestational age of >34 weeks diagnosed with HIE. A total of 195 HIE patients were included in the study analysis. Demographic characteristics of the infants, seizures, anticonvulsive therapies, maximum inotrope doses, and the derived IS and CK-MB and troponin-I levels obtained in the first six hours of life were compared according to HIE staging. Comparisons were made between survivors and non-survivors.

Results

Out of 195 patients, 25 patients (12.8%) were classified as stage 3, 116 patients (59.4%) to stage 2, and 54 patients (27.6%) to stage 1 HIE. The mean birth weight and gestational age were similar between the HIE stage groups. Every patient with stages 2 and 3 of HIE underwent therapeutic hypothermia (TH). 13 (46.4%) infants had stage 2 HIE, 15 (53.6%) had stage 3 HIE, and 28 (14.3%) infants needed inotrope treatment. Maximum IS, CK-MB levels, and troponin I were all significantly increased by the severity of the HIE illness. When survivors and non-survivors were compared, it was found that the deceased infants had significantly higher median IS and median troponin I level, but the mean CK-MB values were similar in both groups. Median CKMB and Troponin I, was significantly higher in infants who underwent therapeutic hypothermia compared to infants who were not received. An examination of the receiver operating characteristic (ROC) curve was done to find potential mortality predictors in newborns with HIE. It was discovered that IS and Troponin I, with area under the curves (AUC) of 0.968 and 0.81, respectively, were both

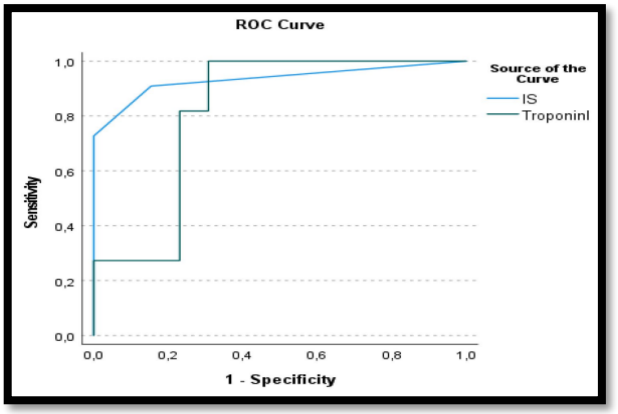

Figure 1. ROC curve analysis showing the effect of IS and Troponin I to predict mortality

sensitive predictors of death. Troponin I's ideal cut-off value for estimating mortality was 0.249 ng/ml (Figure 1).

Discussion

The results of this retrospective investigation showed that the inotropic score and troponin I are important indicators of infant mortality with HIE. Moreover, the severity of HIE is similarly associated with CKMB and Troponin. Within the first few hours of life, levels of CK-MB started to rise and are significantly higher in moderate and severe grades of new-born hypoxia ischemia compared to mild grades and normal controls. In this study, the level of troponin I increased with the HIE stage, and a mortality cut-off value of 0.249 ng/mL was determined.[2] Doucette et al. reported 8.1 mg/ml was the troponin I cut-off value for predicting mortality.[3]

Conclusion

Overall, mortality due to circulatory failure was notably higher. In HIE, troponin I, CK-MB, and IS could be effectively used as indicators of disease severity. Moreover, IS and troponin I are accurate predictors of mortality.

References

1. Lee BL, Glass HC. Cognitive outcomes in late childhood and adolescence of neonatal hypoxic-ischemic encephalopathy. Clinical and experimental pediatrics. 2021 Dec;64(12):608.
2. Gözde Kanmaz Kutman H, et al. Troponin I, CK-MB, and inotropic score in hypoxic-ischemic encephalopathy and associated infant mortality. BMC pediatrics. 2023 Oct 16;23(1):511.
3. Doucette SM, Kelly EN, Church PT, et al. Canadian Neonatal Network (CNN) Investigators and CNFUN Investigators and Steering Committee. Association of inotrope use with neurodevelopmental outcomes in infants < 29 week's gestation: a retrospective cohort study. J Matern Fetal Neonatal Med. 2022;35(25):6044–52.

Relationship between headache characteristics and serum ferritin, vitamin B12 and vitamin D levels

Introduction

Low vitamin D and low ferritin levels were associated with disease prolongation and an increase in the frequency of attacks.

Headache in children and adolescents is one of the most common neurological symptoms affecting 88% of this age group. Migraine and tension-type headaches (TTH) are the most prevalent types of primary headaches. Most widely accepted hypothesis involved in pathogenesis of migraine is neurogenic inflammation.[1] Increase in frequency of childhood migraine and recurrent headache was seen due to changes in children's lifestyle. The frequency of headaches in childhood age ranges from 26.6% to 93.3%.[2] This study aimed to compare headache components and scores,

including the number of attacks, duration of attacks, frequency, severity and accompanying symptoms, between the two groups, and to reveal their effects on daily life in pediatric patients with migraine and TTH. It also aimed to investigate the association between headache characteristics and serum ferritin, vitamin B12 and vitamin D levels.

Methods

A single-center, cross-sectional, clinical-based and retrospective study was conducted on patients with headache complaints. Study included patients who were diagnosed with migraine and TTH. Demographic data such as age, gender, neurological examinations, headache characteristics, laboratory findings (hematological parameters, routine biochemistry, serum ferritin, vitamin B12 and vitamin D), neuroimaging results were recorded. The PedMIDAS score system is used to determine the effects of headaches, determine options for prophylaxis, and evaluate the chronicity process. PedMİDAS scores were used to categorise people, those with a score of 1-10 were classified as none, between 11-30 as mild, 31-50 as moderate, and above 50 as severe.

Results

A total of 264 patients were included, out of which 100 had migraine, 64 had TTH and 100 were controls. According to ICHD-3 beta classification 80 (80%) patients were diagnosed as migraine without aura, 11 (10%) migraine with aura, 9 (9%) chronic migraine. Family history of migraine was found in 49 (49%) migraine group and 16 (25%) in TTH group. In patients diagnosed with migraine the duration of attacks was significantly longer and the severity of headache was higher. In migraine group, unilateral, throbbing, nausea, vomiting, and discomfort from light and sound were significantly higher. Positive and significant association was found between prolongation of the disease duration and an increase in the frequency of attacks and an increase in the duration of attacks in migraine group. Low vitamin D and ferritin levels were significantly associated with longer disease duration in patients with migraine group. There was an increase in migraine headache attacks in children with iron deficiency anemia (IDA) and vitamin D deficiency. Simultaneously, a reduction in serum iron levels was associated with an increase in the intensity of headaches and a decrease in vitamin D levels with a longer attack duration. A significant association was found between a decrease in serum ferritin level and an increase in the frequency of attacks (Figure 1). In children with TTH, there was no statistically significant correlation found between headache characteristics and other laboratory parameters. 52% of cranial magnetic resonance imaging (MRI) were normal and 48% of them had benign changes

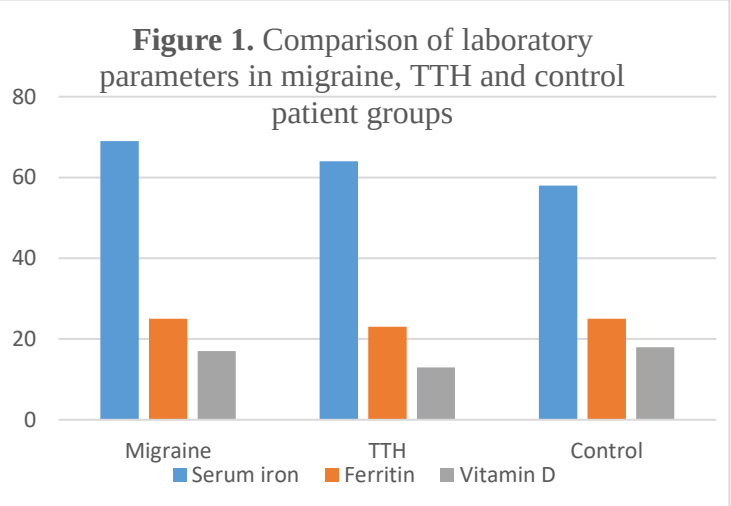

Figure 1. Comparison of laboratory parameters in migraine, TTH and control patient groups

in migraine patients. In patients with TTH, 33 (51.5%) of the cranial MRIs were normal and 31 (48.4%) had benign changes.

Discussion

According to this study, children with migraines who have low serum ferritin and vitamin D levels have longer disease durations and more frequent attacks. A reduction in vitamin D levels has been associated to increased attack durations, but a decrease in serum iron levels was associated to more severe headaches. It was discovered that in children diagnosed with TTH, a low ferritin level was linked to a higher frequency of attacks.[2] A study evaluating 300 children with migraine found that vitamin D deficiency was common in children and the children with vitamin D deficiency had a higher prevalence of recurring headaches than children in the control group.[3]

Conclusion

Vitamin B12, vitamin D, and iron deficiency anaemia should be periodically screened and treated in patients with primary headache.

References

1. Çelik E, Anık A, Ayanoğlu M. Neutrophil-lymphocyte Ratio and Serum Ferritin, Folate, Vitamin B12 and 25-hydroxyvitamin D Levels in Children and Adolescents with Primary Headaches. Meandros Medical and Dental Journal. 2021 Aug 1;22(2):203.
2. Yücel G. The role of serum ferritin, vitamin B12 and vitamin D levels in childhood primary headaches. Çukurova Anestezi ve Cerrahi Bilimler Dergisi. 2023;6(3):411-5.
3. Pisarda L, et al. Relationship between severity of migraine and vitamin D deficiency: a case-control study. Neurol Sci. 2018; 39(Suppl 1): 167-8

Case report on rhabdomyomas in a neonatal patient with tuberous sclerosis complex

Introduction

Tuberous sclerosis complex and related rhabdomyomas result from mutations in the tumor suppressor genes TSC1 or TSC2.

Tuberous sclerosis complex (TSC) is caused by mutations in the TSC1 or TSC2 genes which is rare and complex genetic disorder. As a result of genetic changes, continuous hyperactivation of the mechanistic target of rapamycin (mTOR) pathway occurs, which cause uncontrolled cell growth and proliferation. TSC occurs as benign growths called hamartomas in a number of organs, including the heart, where they are known as cardiac rhabdomyomas.[1] Cardiac rhabdomyoma is a benign mesenchymal tumor of striated muscle origin and is usually the most common paediatric heart tumour which develops before the child reaches 1 year of age. The majority of cardiac rhabdomyomas occur in the ventricular myocardium, atria, cavoatrial junction, or epicardial surface and are associated with tuberous sclerosis (TS).[2] This case report

describes a 15 days old neonate who was hospitalized due to intracardiac masses and brain lesions in the absence of TSC gene mutations.

Case presentation

A 15 days old male neonate on physical examination observed a pale solid plaque measuring 2 × 2 cm on the posterior lateral side of the neonate's right lower leg. Facial angiofibromas on both malar prominences and in the nasolabial folds was seen in patient's mother. Transthoracic echocardiography confirmed the presence of multiple neoplasms within the interatrial septum, interventricular septum, right ventricular outflow tract, and left ventricle posterior wall. The largest nodule, measuring 31 × 14 mm, which was located in the inferolateral wall of the left ventricle, which extends from the level of the mitral valve to the papillary muscle, with unclear borders and protrusion towards the pericardium. Presence of multiple tumorous masses in the heart was confirmed by three-dimensional echocardiography and three-dimensional cardiac computed tomography angiography (Figure 1). Three dimensional cerebral computed tomography angiography showed multiple nodular, high-density shadows with distinct borders in various regions, including the left fronto-parietal lobe, right frontotemporal lobe, and bilateral subependyma of the lateral ventricles. Adjacent to the frontal horn of the right lateral ventricle, a 1.2 × 1.4 cm prominent lesion was observed (Figure 2). Despite the absence of mutations in both the TSC1 and TSC2 genes, an accurate diagnosis of TSC was obtained for this case based on the shagreen patche (Major Criteria 4), cardiac rhabdomyomas (Major Criteria 9), and multiple cortical tubers (Major Criteria 6). Close monitoring was recommended instead of open-heart surgery as there was no significant effect in hemodynamics. Patient was followed up for a period of 2 years during which the cardiac masses remained undetected, and the patient remained asymptomatic.

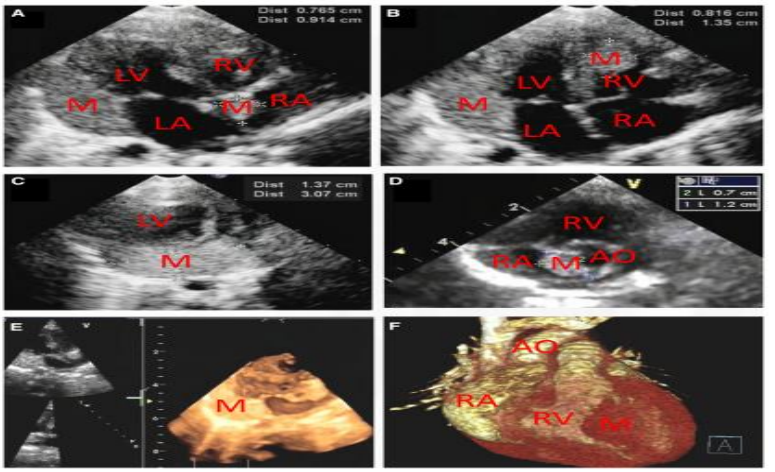

Figure 1. Transthoracic echocardiography (A–D), Three dimensional echocardiography (E) and Three-dimensional cardiac computed tomography angiography (F)

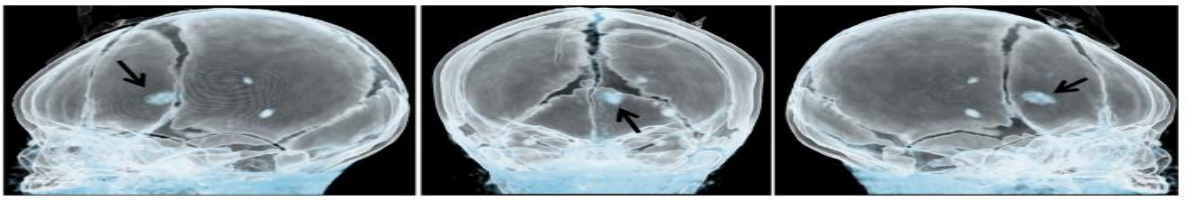

Figure 2. Three-dimensional cerebral computed tomography angiography showing multiple nodular high-density shadows.

Discussion

The most prevalent types of primary paediatric cardiac tumours are rhabdomyoma, teratoma, and fibroma. These tumours are usually benign. A deficiency of hamartin or tuberin proteins is caused by mutations in the tumour suppressor genes TSC1 or TSC2, which results in TSC and associated rhabdomyomas. The mTOR pathway is dysregulated when these proteins are eliminated, which promotes uncontrolled division of cells which results in the development of hamartomatous growth in a multiple organ. Asymptomatic rhabdomyomas requires a close monitoring and clinical intervention is required only in cases of hemodynamic impairment and intractable arrhythmia.[1] Since TSC1 or TSC2 mutations are not detectable in 10%–15% of clinically identified TSC cases, as demonstrated in this case report, genetic testing is not required for TSC diagnosis.[3]

Conclusion

This case highlights that surgical intervention is not always necessary in case of cardiac rhabdomyomas. Close monitoring is recommended in case of asymptomatic cardiac rhabdomyomas because of spontaneous regression.

References

1. Zhou H, Zheng Z, Tu Z, Li Y, Yang J, Fan C. Cardiac self-limiting rhabdomyomas in a neonatal patient with tuberous sclerosis complex: a case report with negative genetic testing. Frontiers in Pediatrics. 2023;11:1263631.
2. Sarkar S, Siddiqui WJ. Cardiac Rhabdomyoma. 2022 Nov 14. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 32809444..
3. Curatolo P, Specchio N, Aronica E. Advances in the genetics and neuropathology of tuberous sclerosis complex: edging closer to targeted therapy. Lancet Neurol. 2022;21(9):843–856.