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Abstract Topic: - Clinical Genetics

Abstract Title: - Cystic Fibrosis in Infants: Missing the Boat?

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Aims: - The aim of this study is to describe the various clinical and laboratory features of cystic fibrosis cases and analyse their genetic mutations.

Methods: - Cases were sourced from Vidharbha region during October 2022- September 2023. Genetically confirmed four cases of cystic fibrosis were studied, including comprehensive records of medical history, disease progression, various clinical investigations and their whole exome sequencing (WES) reports.

Results: - In this study, all cases exhibited symptoms within 1st month of life, with a confirmed genetic diagnosis established before the age of 6 months. Consanguinity was prevalent in 75% (3/4) cases, without any discernible family history. The mothers of Case-1 and 2, experienced distinct maternal complications, with pregnancy induced hypertension and polyhydramnios, respectively. Consequently, Case 2 was delivered via cesarean section at 36 weeks. Case-3 necessitated admission to Neonatal Intensive Care Unit for brachial palsy and respiratory distress (RD) due to obstructed labour. None of the infants underwent newborn screening at birth, underscoring a critical gap in early diagnosis. In all cases, 1st symptom was seen from birth to 25th day of life which included vomiting, loose motions (LM), convulsions, and RD. At the time of diagnosis, failure to thrive (FTT) was a prevailing feature in all, other symptoms being, LM, convulsions, RD, fever, skin lesions etc. Blood gases revealed different metabolic abnormalities not limited to metabolic alkalosis. Notably, Hypochloraemia was seen in all while hyponatremia was seen in 75%. Cases 1 and 3 also exhibited increased creatinine without a proportionate increase in blood urea. Both Case 2 and 3 experienced severe anemia necessitating blood transfusion but only in Case 3, sickle-thalassemia was detected. Interestingly, in Case 2, the investigation divulged distinct features, including white coloured stool, fat globules in stool, hypoproteinaemia, and pigmentary changes in the retina. The abdominal ultrasound showed renal issues in 75% of babies. The genetic analysis, conducted through WES exposed six different mutations with 2 in the Homozygous and the remaining 4 in the heterozygous state. It is notable that there is only one delta 508 mutation and every case had different mutations. All mutations except 1, are either pathogenic or likely pathogenic according to ACMG classification. Unfortunately, the outcome of this study reveals a grim reality, with two babies succumbing to the illness within months of diagnosis.

Conclusions: - Cystic fibrosis should be suspected in any baby with FTT before 6 months. Along with common other symptoms may be seen with CF. NBS testing is helpful for earlier diagnosis. WES scores over common mutation panel of cystic fibrosis

Keywords: - In this study, all cases exhibited symptoms within 1st month of life, with a confirmed genetic diagnosis established before the age of 6 months. Consanguinity was prevalent in 75% (3/4) cases, without any discernible family history. The mothers of Case-1 and 2, experienced distinct maternal complications, with pregnancy induced hypertension and polyhydramnios, respectively. Consequently, Case 2 was delivered via cesarean section at 36 weeks. Case-3 necessitated admission to Neonatal Intensive Care Unit for brachial palsy and respiratory distress (RD) due to obstructed labour. None of the infants underwent newborn screening at birth, underscoring a critical gap in early diagnosis. In all cases, 1st symptom was seen from birth to 25th day of life which included vomiting, loose motions (LM), convulsions, and RD. At the time of diagnosis, failure to thrive (FTT) was a prevailing feature in all, other symptoms being, LM, convulsions, RD, fever, skin lesions etc. Blood gases revealed different metabolic abnormalities not limited to metabolic alkalosis. Notably, Hypochloraemia was seen in all while hyponatremia was seen in 75%. Cases 1 and 3 also exhibited increased creatinine without a proportionate increase in blood urea. Both Case 2 and 3 experienced severe anemia necessitating blood transfusion but only in Case 3, sickle-thalassemia was detected. Interestingly, in Case 2, the investigation divulged distinct features, including white coloured stool, fat globules in stool, hypoproteinaemia, and pigmentary changes in the retina. The abdominal ultrasound showed renal issues in 75% of babies. The genetic analysis, conducted through WES exposed six different mutations with 2 in the Homozygous and the remaining 4 in the heterozygous state. It is notable that there is only one delta 508 mutation and every case had different mutations. All mutations except 1, are either pathogenic or likely pathogenic according to ACMG classification. Unfortunately, the outcome of this study reveals a grim reality, with two babies succumbing to the illness within months of diagnosis.