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Abstract Topic:- Prenatal, perinatal and developmental genetics

Abstract Title:- Newborn genetic screening: A promising technology and potential breakthroughs.

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Aims:-The aim is to design a comprehensive newborn genetic screening (NBGS) panel for the development of an extensive Indian database and the early detection of genetic and metabolic diseases, with the ultimate objective of advancing precision medicine, improving public health, reducing disease burden, and enhancing the overall well-being of the population.

Methods:- A cost effective NGS-based custom newborn genetic screening panel was designed to screen 47 genes associated with 35 congenital disorders. The panel was validated in 150 samples. The selection of disorders to be screened was based on Wilson and Jungner criteria as well as the Indian Academy of Pediatrics. A total of 800 heal-prick samples were screened by Ion ampliseq targeted sequencing. The raw data from the sequencing runs were processed using Torrent Suite Software. Variant calling was performed with the Torrent Variant Caller Plugin. Variant annotation was performed using ClinVar, Varsome, OMIM, GnomAD, etc.

Results:- In 800 newborns, a total of 10 newborns were detected with biallelic or hemizygous pathogenic mutations. We observed G6PD c.949G>A (p.Glu317Lys) as the most prevalent mutation followed by BTD c.1270G>C (p.Asp424His), GJB2 c.71G>A (p.Trp24Ter) and ACADM c.130C>T (p.Gln44Ter). A total of 230 newborns were found to be carriers with an overall carrier frequency of 28.7%. Significantly, a homozygous pathogenic variant in the ACADM gene responsible for causing medium-chain acyl-CoA dehydrogenase (MCAD) deficiency was identified in a newborn. This genetic anomaly is associated with a condition characterized by a disease onset typically manifesting between 1 to 3 years of age, displaying variable penetrance. Notably, conventional Newborn Screening (NBS) timeframes may not capture the onset of this condition. Failure to detect this pathogenic variant in a timely manner can result in developmental challenges and, in severe cases, failure to thrive, underscoring the importance of early detection and intervention.

Conclusions:- Newborn genetic screening plays a multifaceted role in neonatal healthcare. Beyond its immediate function in early disease detection and management, it serves as a valuable tool for elucidating hereditary predispositions within the Indian population. This data will contribute significantly to the establishment and enrichment of an Indian genetic database, addressing an existing knowledge gap. Furthermore, this information lays the groundwork for tailored healthcare strategies, public health planning, and the development of precision medicine approaches, ultimately enhancing the quality of healthcare and fostering a healthier future for our population.

Keywords:- Newborn Genetic Screening, Early Detection, Hereditary Predispositions, Genetic Database, Carrier Frequency