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Identification of Genetic Disorders based on Phenotype and Subsequent Medical Management

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Background

- Genetic disorders often present in the neonatal period and contribute to significant morbidity and mortality.
- Symptom-driven exome sequencing (ES) has emerged as a cost effective and relatively rapid means of identifying single gene disorders.
- This tool has been shown to help guide management of critically ill infants.

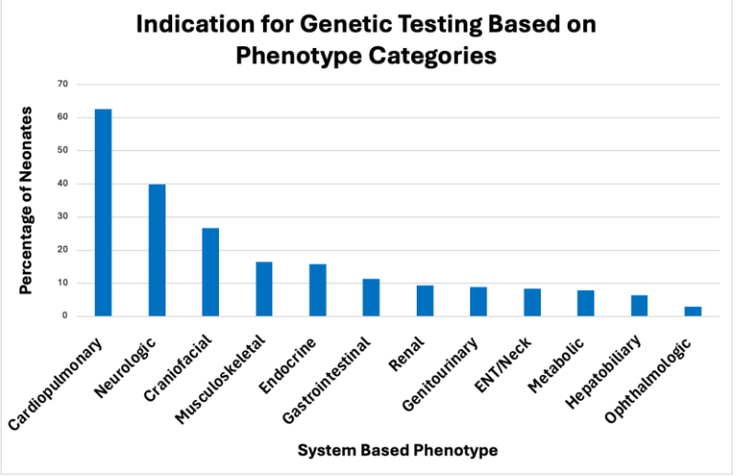
Objective

- Evaluate the indications for genetic testing based on phenotype and compare these with the diagnostic yield of symptom-driven exome sequencing (ES) in the NICU.

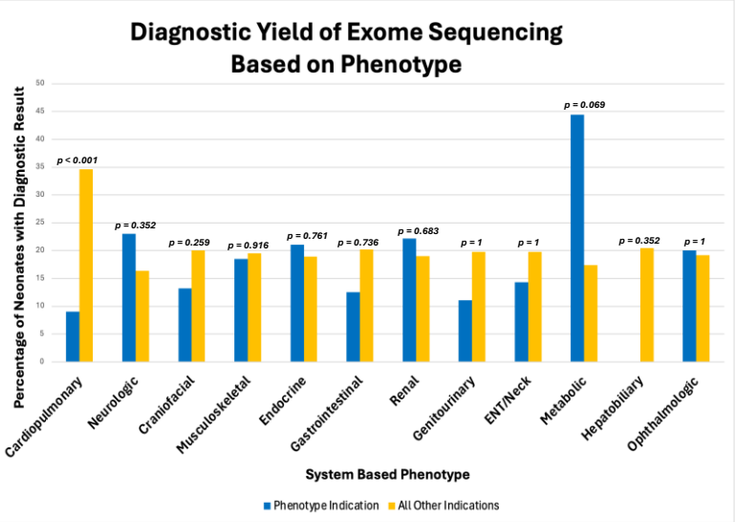
Methods

- Retrospective chart review of neonates admitted to the Children's Mercy Kansas City level IV NICU between 1/1/22-12/31/22.
- 203 neonates underwent genetic testing: ES (rapid and non-rapid), microarray, gene panels, and FISH.
- Patients with well-defined chromosomal anomalies (trisomy 13, 18, and 21) were not included
- Chi-square and Fisher's exact tests were used to evaluate relationships between the phenotypes and the diagnostic yield of ES.

Methods



Results



Results

- The median gestational age of patients was 37.8 weeks [IQR: 23.57-39.0].
- Most common admission diagnosis was congenital anomalies (65.5%).
- Cardiopulmonary phenotype (65.6%) was the most common indication for genetic testing.
- 130 out of 203 (64%) neonates underwent ES.
- ES identified 25 single gene disorders (diagnostic yield of 19.2%).
- Cardiopulmonary concerns had a significantly lower diagnostic yield of ES compared to other phenotypes (9% vs. 34.6%, p<0.001).
- Management changes occurred in 48 of the 203 (23.6%) infants.

Conclusions

- This study demonstrates that genetic testing is an important adjunct, but not the only determining factor, for the clinical care of critically ill neonates.
- Continued development of new technology for diagnosis of genetic diseases remains relevant.
- Limitations of this study include a small sample size, short timeframe, confounding factors, and low yield indications.

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