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Navigating Life with Rare Syndromes and Congenital Heart Disease: The Unseen Link

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INTRODUCTION

- ✓ **Congenital heart disease (CHD) is the *4th leading cause of global infant mortality*, with complex etiology involving *genetic, environmental factors, or an interactive effect*, and prevalence of ~4 to 50 per 1000 livebirths.[1]**

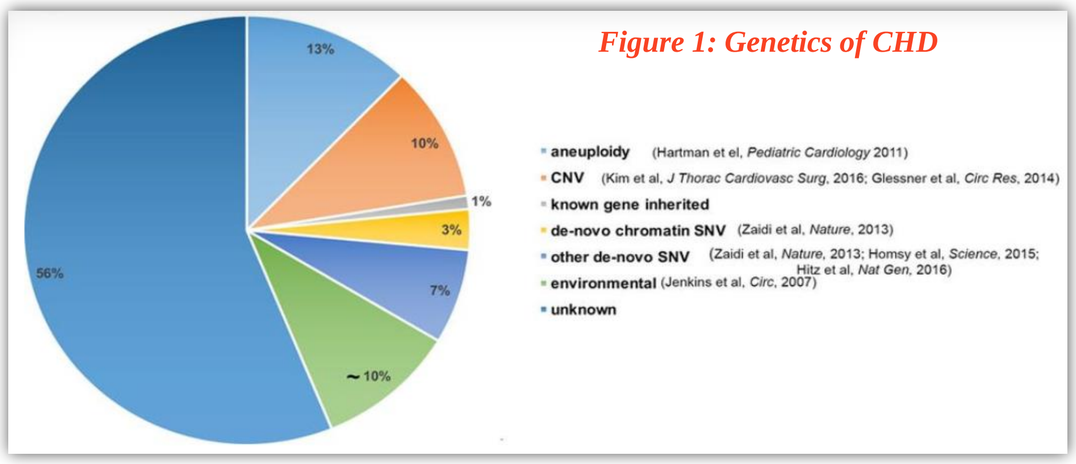


Figure 1: Genetics of CHD

- ✓ **As per WHO, rare diseases affect ~1 in 2000 individual globally and ~1 in 5000 in India, with around 7000 types reported so far.[2,3]**
- ✓ **Notable, ~ *30 % of CHD cases are associated with genetic syndromes*, which often present with extra-cardiac anomalies.[4]**

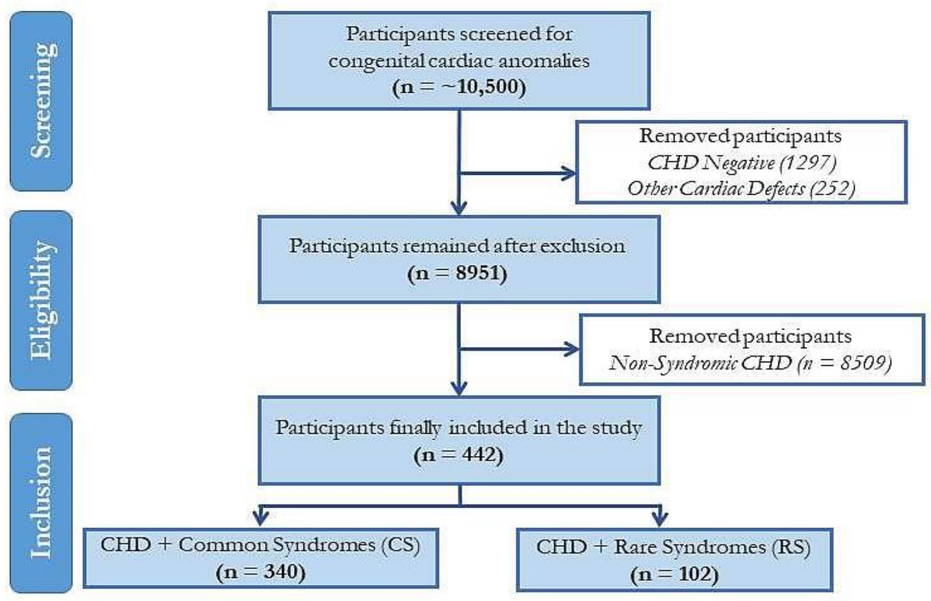
OBJECTIVE

To explore rare genetic syndromes linked to CHD, focusing on the socio-demographic & socio-economic profile of family, and associated risk factors

METHODOLOGY

- ✓ **Study Design: *Retrospective Observational Study***
- ✓ **Study Participants: Families of patients of Indian ethnicity who underwent echo-cardiography during 2022 to 2024 at *Sri Sathya Sai Sanjeevani Hospital- A Totally free of cost tertiary cardiac care centre***
- ✓ **IEC Approved with waiver in consent**

Figure 2: Recruitment of Participants & Study Design



CHD, congenital heart disease

**** Statistical Tests (SPSS): χ2 /Fisher's Exact Test, Multivariate Regression***

RESULTS & DISCUSSION

Table 1: Spectrum of Cases Reported at our Centre & Their Global Prevalence

Types	Prevalence per 1000	Congenital Conditions/Syndromes Based on Clinical Examination and Availability of Genetic Reports (Cases)
Rarest	**< 0.01**	*Ellis-van Creveld Syndrome* (8), *Pentalogy of Cantrell* (3), *Premature Ageing Syndrome* (1), *Spondylocostal Dysostotis* (1), *Thrombocytopenia-Absent Radius Syndrome* (2), *WAGR Syndrome* (1)
Rarer	**0.01-0.10**	*Achondroplasia* (1), *Anotia & Aural Atresia* (2), *Alagille Syndrome* (1), *Anorectal Malformation* (2), *Cornelia deLange Syndrome* (1), *Heterotaxy Syndrome* (1), *Holt Oram Syndrome* (1), *Klippel-Feil Syndrome* (3), *Microcephaly* (1), *Microtia* (11), *Pierre Robin Syndrome* (1), *Pompe Disease (GSD)* (2), *Scimitar Syndrome* (1), *Congenital Thumb Hypoplasia* (5), *Treacher Collin Syndrome* (3), *Williams Syndrome* (6)
Rare	**> 0.1 – 0.5**	*Congenital Facial Nerve Palsy* (2), *Congenital Renal Dysplasia* (1), *Congenital Rubella Syndrome* (1), *DiGeorge Syndrome* (6), *Esophageal Atresia* (1), *Goldenhar Syndrome* (2), *Marfan Syndrome* (11), *MicroCornea* (1), *MRKH Syndrome* (2), *Noonan Syndrome* (17)
Common	**> 0.5**	*Downs Syndrome* (274), *Cleft Lip/Palate* (16), *Congenital Hearing Loss* (1), *Lutembacher Syndrome* (1), *Pectus Carinatum* (1), *Penile Hypospadias* (1), *Polydactyly* (6), *Raghib Syndrome* (1), *Single Palmar Crease* (1), *Syndactyl* (2)
Misc.	**NR**	*Connective Tissue Disorder* (1), *Delayed Milestone* (4), *Dysmorphic Body* (1), *Dysmorphic Face* (30)

Figure 3: Socio-economic & Socio-demographic Profile of Patients[5]

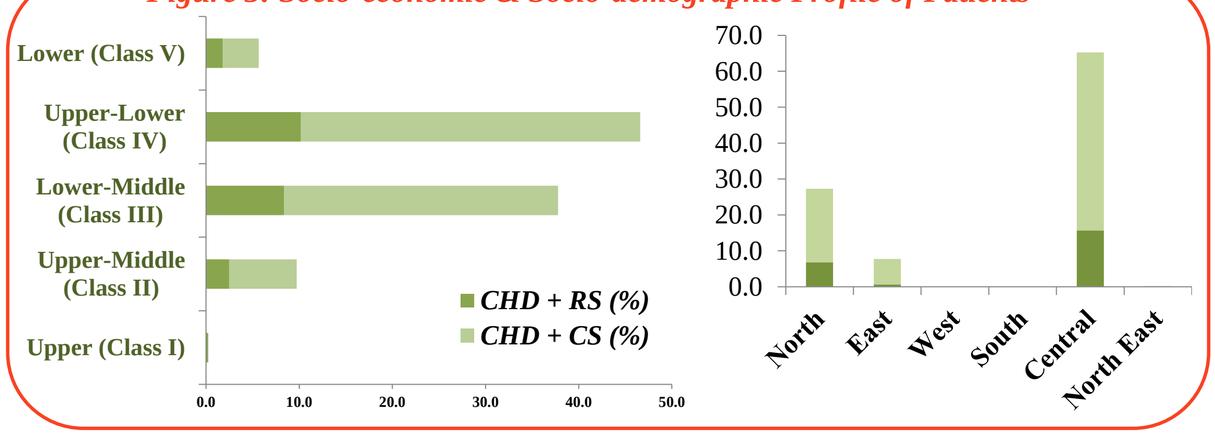


Table 2: Characteristics of Patients &Associated Risk Factors for Rare Syndromes

Factors (RS vs CS)	*P* value
Prenatal	
Paternal Addiction (44.1 vs 33.5%)	**0.050**
Maternal Addiction (1.9 vs 1.8%)	0.896
Exposure to Radiation (24.5 vs 30.3%)	0.259
Exposure to Pollution Source (1.9 vs 2.1%)	0.951
Primipara (47 vs 37.6%)	0.089
Primigravida (14.7 vs 25%)	**0.031**
Artificial Reproduction (1.9 vs 2.6%)	0.698
Teenage Pregnancy (<17Y) (1.9 vs 1.5%)	0.729
Delayed Pregnancy (>35Y) (2.9 vs 8.5%)	0.069
Consanguinity (1 vs 1.5%)	0.709
Bad Obstetric History (30.4 vs 23.5%)	0.162
Nuclear Family (20.6 vs 13.8%)	0.099
Familial CHD History (6.8 vs 0.3%)	**0.003**

Factors (RS vs CS)	*P* value
Antenatal	
Sonography (83.3 vs 90%)	0.067
Supplementation	
Iron + Folic Acid (60.8 vs 73.8%)	**0.012**
Calcium (66.7 vs 74.7%)	0.111
Multivitamins (33.3 vs 27.3%)	0.243
Tetanus Vaccination (81.4 vs 91.2%)	**0.007**
Underweight (99 vs 99%)	0.927
Postnatal	
NICU Stay at Birth (24.5 vs 30.9%)	0.217
Preterm Birth (5.9 vs 15%)	**0.020**
Cesarean Delivery (25.5 vs 31.5%)	0.249
Low Birth Wt. (<2.5Kg) (22.5 vs 34.1%)	**0.029**

P value ≤ 0.05 is considered statistically significant

Table 3: Risk of Specific CHDs in Patients with Rare Syndromes

Factors	CHD + RS (%)	CHD + CS (%)	*P value*	RR (95 % CIs)
Males	69 (67.7%)	205 (60.3%)	0.16	-
Age at Diagnosis (Days)	1812.5 (30-12147)	289 (18-14442)	< 0.05	-
Cyanotic CHD	26 (25.5%)	55 (16.2%)	0.03	1.58 (1.05-2.38)
Complex CHD	36 (35.3%)	117 (34.4%)	0.87	1.03 (0.76-1.39)

REFERENCES

[1] Pierpont ME, *et al*. *Circulation*. **2018**; 138 (21): e653-e711.
[2] The Lancet. *Lancet Glob Health*. **2024**; 12 (3): e341.
[3] The Organization for Rare Diseases India.
[4] Ko JN. *Korean Circulation*. **2015**; 45 (5): 357-361.
[5] Mohanty M, *et al*. *Preventive Medicine Research & Reviews*. **2024**; 1(3): 166-167.

CONCLUSION

- ✓ **Identifying *clinical variability in syndromes associated with CHD aids early diagnosis*, while understanding *genetics can help reduce mortality and morbidity*.**
- ✓ **It also highlights *regional risk factors* and *socio-economic disparities*, underscoring the need for targeted prevention in underserved areas.**