Diagnostic Delays and Socio-Demographic Factors Among Patients Referred to an Undiagnosed Rare Disease Clinic

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Background:
Rare diseases affect 25 million Americans, with average diagnostic delays of 6–7 years, 2–3 misdiagnoses, and approximately $29,000 in added annual costs. Patients with rare, undiagnosed conditions experience diagnostic delays influenced by social and demographic disparities. This study examined relationships between socio-demographic factors and diagnostic delay among patients at the Undiagnosed Rare Disease Clinic (URDC).

Methods:
This study retrospectively analyzed 149 patients at URDC (Jan 2020–Jun 2025), a rare disease program at Indiana University School of Medicine and clinical site for the NIH-funded Undiagnosed Diseases Network. Diagnostic delay was measured as: 1) time from symptom onset to first genetic testing (TSO-GT), and 2) time to first in-person URDC visit (TSO-UV). Independent variables included demographics and social determinants of health. Analysis included descriptive, bivariate (Mann–Whitney U, Kruskal–Wallis, Spearman's correlations), and multivariate (Multiple linear regression) analyses in SPSS v31.0 ($p<0.05$). This study was approved by Indiana University IRB (#2005902680).

Results:
Among 149 patients, 52.3% were female, 91.3% white, 57.7% publicly insured, and 57.4% urban. Median time from symptom onset to first genetic testing was 2.4 years (IQR: 6.2) and to URDC visit was 7.6 years (IQR: 9.4). Bivariate analysis revealed significant associations between TSO-GT and race ($p=.010$), number of Human Phenotype Ontology (HPO) terms ($p=.039$), and presence of constitutional HPO terms ($p=.014$). Having more HPO categories was associated with shorter TSO-UV. Following multivariate analysis, only constitutional HPO terms ($p=.027$) remained significantly associated with TSO-GT.

Conclusions:
Most factors were not significantly associated with diagnostic delays, reflecting limitations in sample size, diversity, and referral criteria. Findings highlight the importance of expanding rare disease programs and research to engage diverse and underserved urban populations. Findings will guide efforts to raise community and provider awareness, build larger multi-site cohorts, and identify socio-structural barriers to ensure timely, equitable rare disease care.