The Determinants of Quality of Life in Rett Syndrome: A Cross-sectional Study

İLAY ÇALIŞKAN, AYFER ARDUÇ AKÇAY

KOC UNIVERSITY FACULTY OF MEDICINE,
DEPARMENT OF PEDIATRICS DIVISION OF CHILD NEUROLOGY

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INTRODUCTION

Rett Syndrome (RTT) is a progressive neurodevelopmental disorder mostly affecting females with an estimated incidence of 1:10.000. An apparently normal development of 6-18 months is followed by multisystem manifestations including loss of speech, gait abnormalities, loss of purposeful hand skills and repetitive hand stereotypies. Additional multisystem comorbidities include sleep disorders, respiratory and autonomic dysfunction. Clinically, RTT is classified into classical and atypical forms. The mutated methyl-CpG binding protein-2 (MECP2) on X chromosome *Xq28* region, a modulator of the gene expression in neurons, is identified as the culprit in the majority of the cases. Specific variants of MECP2 have been correlated with clinical phenotypes. Given the disabilities caused by RTT, the experience of living with the disease is vastly more complex.

Quality of life (QoL) of RTT-inflicted families and children has been rarely investigated. This study aims to evaluate the clinical features in relation to QoL in genetically-confirmed RTT cases.

METHODS

The caregivers of children with RTT were reached via a social media announcement in 2019. Demographics, diagnostic challenges, developmental milestones, comorbidities (epilepsy, sleep-related problems, infectious diseases, hospital admissions and nutrition-related problems), genetic test results were collected by a web-based questionnaire filled out by caregivers on voluntary basis.

The assessment of health-related quality of life was made using the Pediatric Quality of Life Questionnaire (PedsQL)-Turkish Version, which assesses the domains of physical and psychosocial health (emotional, social and school functioning). This form was validated to measure the health-related quality of life of families and children between 0 and 18 years of age. Higher scores for each domain indicate higher quality of life.

Kruskal-Wallis test and Student's t-test were performed using IBM SPSS Statistics Version 26.

Table 1: Questionnaire sub-domains

Sub-domains	**Content**
Demographic information	Age, Sex, Parental age/educational status/occupation
Perinatal information	Uncomplicated pregnancy, Delivery route, Complicated labor rate, Birth weight, Birth height, Head circumference, Breastfeeding
Milestones and other domains of health	Verbal skills, motor skills, communication skills, stereotypical behaviors, infections and other diseases requiring admission, nutrition/gastrointestinal status, seizures
Diagnostic processes	First parental suspicion, First clinical suspicion, Time to diagnosis from first parental suspicion, Genetic testing, Conclusive genetic reporting
Quality of Life	Physical and psychosocial health (emotional, social and school functioning)

RESULTS

- A total of 76 caregivers filled out the questionnaire, with 36 diagnostic genetic test reports provided.
- The mean age was 7.1±3.9 years, the mean age at first parental or clinical suspicion was 12 months and the mean age at the time of genetic diagnosis was 24 months. The mean age at first seizure was 19 months (range 1.5-96).
- The mean ages at functional losses were 19 months (range 3-60) for hand function, 2 years (range 1-7) for speech and 6 years (range 2-15) for walking.
- Twenty children (%57.1) had sleep problems, 20 children (%57.1) drooling, 8 children (%21) swallowing problems.
- Among 26 children who experienced at least one seizure, 10 were seizure-free with anti-epileptic treatment.
- The mean QoL scores were similar for classical (48.1, SD=22), atypical (51.8, SD=18), and not certain (62.8, SD=17) phenotypes of MECP2 variants.
- The mean psychosocial health total score was 53.1±23.8 and the mean physical health total score was 42±31.1.
- The mean total QoL score was significantly greater in patients ≤12 years of age than in those >12 years of age (54.0 vs 38.4; p=0.047)
- There was an inverse correlation between the QoL score and children's swallowing problems (p=0.042) and chewing problems (p=0,002)
- The loss of communication predicted a lower total mean QoL score (OR=1.05, 95% CI 1.01,1.08).

DISCUSSION & CONCLUSION

- In children with RTT, other than swallowing and chewing problems, we found no significant association between QoL and epilepsy, breathing problems, drooling, sleep problems, and parental education. Older children had significantly lower QoL scores, as compared with younger children.
- Interventions targeting speech and language improvement and nutrition problems might be prioritized to increase the quality of life in children with RTT. However, these interventions should not only address the needs of children, but also those of the entire family.
- The experience of living with RTT substantially reduces QoL. Factors beyond physical manifestations of the disease, such as psychological well-being, coping, and disease perceptions are adversely affected, making them targets for intervention.

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