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# Assessment of health-related quality of life in children with osteogenesis imperfecta (OI).

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**ABSTRACT… Objective:** To assess the health-related quality of life (HRQoL) in children with different types of osteogenesis imperfecta (OI). **Study Design:** Cross-sectional study. **Setting:** Department of Endocrinology, National Institute of Child Health, Karachi, Pakistan. **Period:** July 2023 to December 2023. **Methods:** Children of either gender, aged 5-18 years and already diagnosed with clinical diagnoses of OI type I, III, IV, or V were analyzed. At the time of enrollment, demographic as well as clinical information were gathered. HRQoL was evaluated using Pediatric Quality of life Inventory (PEDSQL ™ 4.0 generic core). **Results:** In a total of 52 children, 27 (51.9%) were male. The mean age was 10.19±4.15 years (ranging between 5-18 years). The most common type of OI were Type-I, and Type-III, noted in 22 (42.3%), and 13 (25.0%) children respectively. It was found that total scores ($p<0.001$), psycho-social health ($p<0.001$), physical functioning ($p<0.001$), social functioning ($p<0.001$), and school functioning ($p=0.013$) were having distinct relationship with the types of OI. Bivariate analysis applying pearson correlation showed that there were no significant correlation that existed between age, weight, and PedsQL scores. **Conclusion:** Children with OI Type-III exhibited lower HRQoL across multiple domains, emphasizing the need for tailored interventions addressing the specific challenges associated with the severity of the condition.

**Key words:** HRQoL, Osteogenesis Imperfecta, PedsQL, Physical Functioning, Social Functioning.

## INTRODUCTION

Osteogenesis imperfecta (OI) is a genetic disorder marked by exaggerated bone fragility, reduced bone mass, and other manifestations in connective tissues. The diagnosis of OI primarily is dependent upon assessment of family history as well as clinical presentation, often indicated by reports of fractures occurring at prenatal phase, at the time of birth, or during younger pediatric age groups. Genetic testing is utilized for confirmation.[1] The dominant autosomal mutations affecting the "type I collagen coding genes (COL1A1 and COL1A2)" are the primary cause of OI, influencing the quantity or structure of collagen in around 85% of cases.[2,3] Phenotypic expressions of OI go beyond skeletal concerns, involving abnormalities in various organs. The widely used classification of OI relies on clinical and radiological criteria, categorizing it generally into five distinct types (I-V).[4-6]

Individuals with OI necessitate regular medical monitoring, corrective surgeries, drug therapies, physiotherapy, and adherence to special daily care patterns. Moreover, they face an elevated risk of fractures, particularly prevalent in children and adolescents, leading to the need for immobilization and causing significant suffering and short-term disability. The impact of OI on "quality of life (QoL)" is considered substantial.[7] The evaluation of "health-related quality of life (HRQoL)" in subjects with genetic abnormalities, specifically OI, are crucial for evaluating treatment outcomes and assessing patients' overall well-being. This approach not only aids professionals in altering factors that affect health outcomes but also addresses factors influencing patient's QoL.

Given that patients having genetic disorders often contend with a range of challenges associated with chronic conditions, OI patients

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significantly influence the QoL. The analysis of HRQoL in patients with genetic disorders becomes imperative for assessing not only treatment outcomes but also the overall well-being of patients. This comprehensive evaluation is essential in understanding and addressing the diverse impacts that genetic disorders, including OI, can have on patients' lives. There is paucity of local data exploring aspects of OI in Pakistan. This study was thought to add important insights in the impact of different types of OI on HRQoL. The objective of this study was to assess HRQoL in children with different types of OI.

## METHODS

This cross-sectional research was conducted at Endocrinology department of "National Institute of Child Health (NICH)", Karachi, Pakistan from July 2023 to December 2023 after approval (IERB-21/2023, 11.10.2023). OI is a rare disease therefore we enrolled all children fulfilling our inclusion criteria on their visit to Endocrinology department of NICH, Karachi, Pakistan adopting non-probability consecutive sampling technique. Approval from "Institutional Ethical Committee" was obtained (IERB-21/2023). Children between 5-18 years who were already diagnosed cases of OI types I, III, IV, or V were analyzed. Already diagnosed cases of anxiety and/or depression were excluded. Children or their parents/ guardians refusing to be part of this research were also not included. The classification of OI was determined using the clinical criteria outlined by "Van Dijk and Sillence".[5]

At the time of enrollment, demographic as well as clinical information were gathered. HRQoL was assessed utilizing the "Pediatric Quality of Life Inventory (PEDSQL TM 4.0 generic core)", a generic evaluation instrument. This tool comprises 23 items evaluating 4 domains: physical functioning (8 items), emotional functioning (5 items), and social functioning (5 items). Higher scores signify better QoL. For children aged between 5-7 years, the questionnaire was read and answers were recorded as per visual analog scoring according to PedsQL.

The data analysis was done using "IBM-SPSS Statistics", version 26.0. Quantitative variables such as age, height, and weight were summarized with mean and standard deviation (SD). Qualitative data were shown as frequencies and percentages. "Analysis of variance (ANOVA)" was employed to compare PedsQL scores across different types of OI. An independent sample t-test was applied to compare PedsQL scores between genders. Pearson correlation analysis was performed to examine the correlation between age, weight, and PedsQL scores. $P < 0.05$ was considered statistically significant.

## RESULTS

In a total of 52 children, 27 (51.9%) were male. The mean age was 10.19±4.15 years (ranging between 5-18 years). There were 32 (61.5%) children who were studying in the schools. There were 16 (30.8%) mothers who were illiterate. The most frequent types of OI were Type-I, and Type-III, noted in 22 (42.3%), and 13 (25.0%) children respectively (Table-I).

| Characteristics | | Frequency (%) |
|---|---|---|
| Gender | Male | 27 (51.9%) |
| | Female | 25 (48.1%) |
| Age (years) | 5-7 | 19 (36.5%) |
| | 8-12 | 17 (32.7%) |
| | 13-18 | 16 (30.8%) |
| Child's education | Studying school | 32 (61.5%) |
| | Not studying school | 20 (38.5%) |
| Mother's education | Illiterate | 16 (30.8%) |
| | Literate | 36 (69.2%) |
| Mother's occupation | Housewife | 48 (92.3%) |
| | Working | 4 (7.7%) |
| Father's education | Illiterate | 11 (21.2%) |
| | Literate | 41 (78.8%) |
| Osteogenesis imperfecta types | I | 22 (42.3%) |
| | III | 13 (25.0%) |
| | IV | 9 (17.3%) |
| | V | 8 (15.4%) |

**Table-I. Characteristics of children (n=52)**

It was found that total scores ($p<0.001$), psycho-social health ($p<0.001$), physical functioning ($p<0.001$), social functioning ($p<0.001$), and school functioning ($p=0.013$) were having distinct relationship with the types of OI. Table-II is showing comparison of PedsQL scores with respect to different types of OI. There were no

| PedsQL | Total (n=52) | Osteogenesis Imperfecta Types | | | | P-Value |
|---|---|---|---|---|---|---|
| | | I | III | IV | V | |
| Total | 39.2±19.1 | 49.7±15.6 | 22.4±13.2 | 45.7±17.3 | 31.8±17.2 | <0.001 |
| Psycho-social health | 19.4±11.9 | 25.9±11.4 | 10.5±7.7 | 22.9±10.1 | 12.9±8.9 | <0.001 |
| Physical functioning | 19.9±8.4 | 23.8±5.5 | 11.9±6.5 | 22.8±8.9 | 18.9±8.9 | <0.001 |
| Emotional functioning | 4.8±3.9 | 5.6±3.9 | 3.1±3.2 | 6.3±5.0 | 3.3±2.8 | 0.115 |
| Social functioning | 9.4±5.9 | 11.9±4.2 | 4.0±3.3 | 13.1±5.8 | 7.3±6.6 | <0.001 |
| School functioning | 5.4±6.1 | 8.5±7.1 | 3.4±4.7 | 3.4±3.8 | 2.4±2.8 | 0.013 |

**Table-II. PedsQL scoring according to osteogenesis imperfecta types (N=52)**

significant differences between PedsQL score across both genders (Table-III).

| PedsQL Scores | Gender | | P-Value |
|---|---|---|---|
| | Boys (n=27) | Girls (n=25) | |
| Total | 38.8±18.1 | 39.8±20.5 | 0.858 |
| Psycho-social health | 19.2±12.3 | 19.6±11.6 | 0.905 |
| Physical functioning | 19.6±7.1 | 20.3±9.7 | 0.759 |
| Emotional functioning | 4.6±3.7 | 5.0±4.2 | 0.688 |
| Social functioning | 8.9±5.2 | 9.9±6.6 | 0.523 |
| School functioning | 5.8±6.8 | 5.0±5.2 | 0.616 |

**Table-III. Comparison of PedsQL scores with respect to Gender (N=52)**

Bivariate analysis applying pearson correlation showed that there were no significant correlation that existed between age, weight, and PedsQL scores (Table-IV).

| PedsQL Scores | Age | | Weight | |
|---|---|---|---|---|
| | r | p | r | p |
| Total | 0.031 | 0.828 | 0.057 | 0.706 |
| Psycho-social health | 0.022 | 0.876 | 0.084 | 0.578 |
| Physical functioning | 0.026 | 0.855 | 0.001 | 0.994 |
| Emotional functioning | 0.219 | 0.118 | 0.268 | 0.068 |
| Social functioning | 0.030 | 0.832 | 0.016 | 0.914 |
| School functioning | -0.153 | 0.280 | -0.045 | 0.763 |

**Table-IV. Correlation between PedsQL scores, age, and weight (n=52)**

## DISCUSSION

The distribution of OI types in the study were type-I, III, IV, and V in 42.3%, 25.0%, 17.3%, and 15.4% children respectively. Study by Vanz AP et al from Brazil noted type-I OI to be identified in 50.0% children and adolescents with OI which correlates well with our findings.[8] Our findings also correlate well with a study by Najirad et al from Canada showed that OI type-I, III, IV, and other types were noted in 47.6%, 17.1%, 28.0%, and 7.3% children respectively.[9] Data from adult OI patients also exhibit type-1 to be the most common types noted in 57.3% patients.[10]

The present research was done to evaluate HRQoL applying PedsQL questionnaire among pediatric age groups with different types of OI and explored the potential associations between demographic factors and HRQoL scores. The results indicated significant variations in HRQoL across different types of OI, shedding light on the multifaceted impact of this rare genetic disorder on the psychosocial and physical well-being of affected children. Children with OI Type-III exhibited markedly lower total scores, psycho-social health, physical functioning, social functioning, and school functioning compared to those with OI Type-I, OI Type-IV, and OI Type-V. This finding underscores the importance of recognizing the clinical diversity within the spectrum of OI and tailoring interventions to address the unique challenges faced by individuals with different OI types. Vanz et al noted significant divergence in the physical and social functioning domains, based on the clinical presentation of OI, while the lowest scores were observed in the severe type, specifically OI type-III.[8] These findings suggest that patients with OI type-III undergo more pronounced challenges and limitations in both physical and social aspects of their lives compared to other OI types. n alignment with the study conducted by Fano et al, our findings similarly indicated that individuals with moderate and severe OI exhibit lower scores in the physical

functioning domain compared to those with mild OI.[11] The observed disparities in HRQoL could be attributed to the varying severity and clinical manifestations associated with different OI types. OI Type-III, characterized by progressively deforming bones and frequent fractures, might exert a more pronounced impact on physical functioning and psychosocial health, explaining the lower HRQoL scores in this subgroup. This aligns with prior studies that have highlighted the substantial physical and emotional burdens borne by individuals with more severe forms of OI.[8-11]

The present study contributes to the growing body of evidence by employing a comprehensive generic assessment instrument, PedsQL which encompasses multiple domains, providing a nuanced understanding of the diverse impacts of OI on children's lives.[12-14] Interestingly, our study did not reveal significant correlations between age, weight, and HRQoL scores, implying that the impact of OI on quality of life remains consistent across different age groups and weight. This contrasts with findings from Vanz et al where a positive correlation was ascertained with age and the social functioning domain score.[8] Further exploration of these differences in study methodologies, sample sizes, and cultural contexts could provide valuable insights into the complex interplay of factors influencing HRQoL outcomes in OI. HRQoL scores in relation to gender provided further insights into the nuanced experiences of boys and girls with OI. Our study correlates well with the findings of Najirad et al where they did not find any significant association of gender with HRQoL scores.[9]

This research contributes valuable insights into the nuanced associations between OI types and HRQoL in affected children. The findings underscore the need for tailored interventions that address the specific challenges posed by different OI types, with a focus on enhancing both physical and psychosocial well-being.[15,16] Future research endeavors should explore longitudinal aspects and incorporate broader demographic variables to deepen our understanding of the evolving impact of OI on HRQoL over time. The study's limitations included its single-center design and a relatively small sample size.

## CONCLUSION

Children with OI Type-III exhibited lower HRQoL across multiple domains, emphasizing the need for tailored interventions addressing the specific challenges associated with the severity of the condition. The observed significant variations in HRQoL scores among OI Type-I, Type-III, Type-IV, and Type-V highlighted the importance of recognizing the clinical heterogeneity within this rare genetic disorder.



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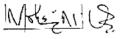
## AUTHORSHIP AND CONTRIBUTION DECLARATION

| No. | Author(s) Full Name | Contribution to the paper | Author(s) Signature |
|---|---|---|---|
| 1 | Sidra Mahmood | Data collection, Drafting. Responsible for data, Approval for publication. |  |
| 2 | Mohsina Noor Ibrahim | Study concept, Methodology, Proof reading, Approval for publication. |  |
| 3 | Maria Riaz | Critical revisions, Literature review, Discussion, Approval for publication. |  |
| 4 | Shahnila Hafeez | Data collection, Literature review, Approval for publication. |  |