

Exploring pain interference and self-perceived health status in children with Osteogenesis Imperfecta - A cross-sectional study

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Research Article

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Abstract

Purpose

To explore presence of chronic pain, pain interference in daily life, and self-perceived health status in children with Osteogenesis Imperfecta (OI).

Methods

Children with OI, aged 6–18 years, were recruited consecutively to this cross-sectional study. Participants answered a standardised interview including five pre-structured questions, Numerical Rating Scale (NRS), the Pain Interference Index, and the PROMIS-25.

Results

Twenty-eight children (median: 11 years, IQR 6) with OI type I, III, or IV participated. Pain was present in 27 of 28 children, and interfered in their everyday life regardless of OI-type, sex, and age. The median NRS for average pain intensity was 4 (IQR 2), the median for pain frequency was 2–3 times/week, and the median frequency of school absence due to pain was 2–3 times per month. Pain in the feet was more frequently reported in children with type I ($p = 0.032$), and pain in the hip was more often reported in children ≥ 13 years ($p = 0.011$). Self-perceived health status for mobility was lower than the general population, and lowest for children with type III ($p = 0.016$). Pain interference was associated with children's self-perceived health status ($r_s=0.84$, $p < 0.001$).

Conclusion

Almost all children experienced pain, which interfered in children's everyday lives, affected participation in various activities and was associated with reduced self-perceived health status. If children avoid physical activities because of pain, it might cause a vicious circle of inactivity, which further decreases bone density and increase the risk of fractures. The results emphasize the importance to offer adequate pain reducing interventions.

What Is Known

- Chronic pain is common in children with severe OI
- Lower Health related Quality of Life is reported in children with OI

What is New

- Almost all children experienced pain, despite OI-type, sex, and age
- Pain interfered in children's everyday lives
- Pain affected participation in various activities and was associated with reduced self-perceived health status.

Introduction

Chronic pain has been reported to affect between 11–38% of children worldwide [1]. According to The World Health Organization (WHO), pain in children is a public health concern, causing unnecessary suffering, and is a multidimensional phenome with sensory, physiological, cognitive, affective, behavioural and spiritual components [2]. In the most recent definition, the International Association for the Study of Pain defines pain as, “An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage” [3]. Acute pain is classified as short-term pain, persisting less than three months, whereas chronic pain persists for longer than three months. Chronic pain is reported to be more frequent in girls and the prevalence increases with age [4].

Untreated pain may affect quality of life (QoL) negatively [2, 5]. WHO has defined QoL as “an individual’s perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns” [2]. QoL is a broad concept including physical health, psychological state, personal beliefs, and social relationships. Therefore, pain might negatively impact on all aspects of activities in children’s everyday lives [5, 6]. However, QoL and health-related quality of life (HRQoL) are concepts that have been debated and disputed, and the term “self-perceived health status” has sometimes been suggested as an alternative [7]. Thus, in relation to the present study, the term “self-perceived health status” will be used hereinafter.

In children with Osteogenesis Imperfecta (OI), both acute and chronic pain have been reported [8]. OI is a rare genetic disorder characterised by osteopenia and bone fractures, caused by mutations in collagen type I in up to 90% of affected individuals [9]. Common symptoms are skeletal deformities, multiple fractures, ligament laxity, muscle weakness, short stature, skeletal pain, dental and hearing problems, and sometimes cardiac and respiratory symptoms. The Sillence classification that has been used since 1979 identifies four types of OI based on clinical and radiographic criteria, combined with pattern of inheritance [10]. OI-type I is the mildest and most common form, with an absence of major bone deformities; type II is perinatally lethal; type III is severe, with short stature, severe limb and spine deformities, reduced muscle strength and multiple fractures; type IV is variable in severity, but often intermediate between type I and III [10]. This classification system has successively expanded and presently, the genome data base Online Mendelian Inheritance in Man (OMIM) includes 21 types of OI (Type I-XXI). There is still no cure for OI but treatment with intravenous bisphosphonate has been beneficial [11]. In addition, children may receive orthopaedic surgery with rodding, and physiotherapy aiming to support motor development and physical activity, increase opportunities for participation in everyday life, improve muscle strength, reduce fractures and chronic pain [12]. In OI, the most commonly reported pain is chronic pain, the musculoskeletal type, resulting from bone resorption or associated deformity [8]. Since chronic pain can affect and interfere in everyday life, pain assessment, including pain interference, is warranted [5]. It is, however, difficult to investigate pain in children with OI. Firstly, many children have adjusted their activities in order to avoid painful situations, and secondly many children have since an early age got used to pain and don’t report [13]. Thirdly, there is a lack of multidimensional pain assessment for children with OI [8]. It is, however, vital to investigate each child’s condition, in order to understand and treat the pain. The overall aims of this study were therefore to explore presence of chronic pain, pain interference in everyday life, and self-perceived health status in children with OI.

Materials And Methods

Design

The study was cross-sectional.

Participants

A consecutive recruitment of children with OI from six to 18 years old, with a regular visit to the hospital's physiotherapy department within the OI-team at Astrid Lindgren Children's Hospital in Stockholm, Sweden were invited to participate. Exclusion criteria was children that did not understand the Swedish language. The children and their parents were informed about the study after their scheduled appointment at the hospital. If they agreed to participate, informed consent forms were provided and signed. The study was approved by the Regional Ethical Review Board in Stockholm (Dnr 2017/1136-31/2) and conducted according to the ethical guidelines of the Declaration of Helsinki.

Assessments

A pre-structured interview

A pre-structured interview with five questions was used. The child was asked about: 1. absence or presence of pain, 2. number of days with pain (daily, 2–3 days per week, once a week, 2–3 times per month, or never), 3. absence from school as number of days that the child stayed at home or went home early due to presence of pain (daily, 2–3 days per week, once a week, 2–3 times per month, or never), 4. pain location/locations (head, neck, arm, hand, back, stomach, hip, knee, feet, and other), and 5. what the child believed to be the cause of the pain.

Numerical Rating Scale

Pain intensity was reported with the Numerical Rating Scale (NRS), a segmented numeric version scale (0–10) where "0" represents "no pain" and "10" is the worst pain imaginable. The child was also asked to rate the intensity when the pain was at its lowest, average, and at its highest. NRS is considered to be a well-established instrument in paediatric populations and for children ≥ 6 years of age with chronic pain [14].

Pain Interference Index

The Pain Interference Index (PII) was used to evaluate whether pain interfered with the child's functioning in everyday life (schoolwork, friends, mood, mobility, and sleep). PII was created to capture the interference of pain in children with longstanding pain syndrome and is a multidimensional instrument containing six statements where the child rates how well a statement describes his or her condition during the past two weeks, by using a numerical scale, ranging from 0 (not at all) to 6 (very much) [15]. The psychometric properties of PII have been evaluated and the results have shown that the instrument is suitable for children with chronic pain [15].

Patient Reported Outcome Measurement Information System Pediatric-25 Profile v1.1

The Patient Reported Outcome Measurement Information System Pediatric-25 Profile v1.1

(PROMIS-25) was used to assess self-perceived health status. PROMIS-25 is a multidimensional instrument for children that evaluates self-perceived health status during the preceding seven days [16]. The paediatric version 1.1 is composed of seven dimensions: mobility, anxiety, depressive symptoms, fatigue, peer relationships, pain interference, and intensity. The questions within the domain, pain interference, ask about pain interference during walking, running, concentration, and sleep. The instrument consists of a self-rating scale from 0 (never) to 4 (always) for all domains except pain intensity, in which the scale ranges from 0 (no pain) to 10 (worst pain). All domains, except pain intensity, are composed of four questions generating a total raw score within each domain, which can be summarised into a PROMIS-25 total raw score. The total raw score within each domain can then be converted to separate T-scores, and may be used to compare results with the general population [16]. The standardized T-score for the general population has a mean of 50 and a standard deviation of 10. A high T-score (≥ 60 points) for anxiety,

depressive symptoms, fatigue, and pain interference shows a poorer outcome, as compared with the general population. A low score (≤ 40 points) on mobility and peer relationships indicates a poorer outcome as compared with the general population. PROMIS-25 has been tested in children with chronic pain and showed support for validity and responsiveness [17].

Procedure

The interview was completed by the child and the same researcher (KL) and took around 30–50 minutes. The child could get help from the parent if necessary.

Statistical analysis

The SPSS version 26 was used for analysis. Nonparametric statistics was used. Descriptive data is presented as median, interquartile range (IQR), numbers and percentage. To compare groups, Mann-Whitney U test or Kruskal-Wallis were used accordingly. Age was categorised into three groups: ≤ 9 years, 10–13 and ≥ 13 years. The total raw score within PROMIS-25 was presented, and raw scores for the separate domains were converted into T-scores. The significance level was set at $p < 0.05$. Spearman's correlation coefficient (r_s) was calculated between the PII total score and the PROMIS-25 total raw score, and between the separate domains within PII and the T-cores within separate domains in PROMIS-25. The correlation was considered significant when $p < 0.05$ and $r_s > 0.37$. The following interpretation was used: r_s : 0.00–0.37 negligible correlation, 0.37–0.50 low correlation, 0.50–0.70 moderate correlation, 0.70–0.90 high correlation, and 0.90–1.00 very high correlation [18].

Results

In total 28 children, 17 boys and 11 girls, with a median age of 11 years (IQR: 6), participated in the study (Table 1). Due to time limitations, one child declined to participate. The children came from all over Sweden and had OI-type I, III or IV. The mobility was classified according to Wilson's Mobility scale (Table 1).

Table 1
Descriptive statistics of the participants.

Participants	n = 28
Age, mdn (IQR)	11 (6)
Sex, (n = 28) (%)	
Male	17 (61)
Female	11 (39)
Use of Bisphosphonate, (n = 28) (%)	
Yes	17 (61)
No	11 (39)
Type of OI, (n = 28) (%)	
Type I	18 (64)
Type III	7 (25)
Type IV	3 (11)
Fracture rate, mdn (IQR)	8 (13)
Wilson mobility scale, (n = 28) (%)	
1 Functional walking without aid in all surroundings	15 (54)
2 Functional walking without aid in secluded surroundings	11 (39)
3 Functional walking with crutches in all surroundings	0
4 Walking with crutches in secluded surroundings	0
5 Functional walking with key walker in all surroundings	0
6 Walking with key walker in secluded surroundings	0
7 Reciprocal crawling with arms and legs	0
8 Any other form of locomotion	1 (3.5)
9 Sitting with support and no mobility	1 (3.5)
Presence of pain, (n = 28) (%)	
Yes	27 (96)
No	1 (4)
Pain frequency, (n = 28) (%)	
Daily	11 (41)
2–3 days / week	5 (19)

Data is presented as number (n), percentage (%), median (mdn) and interquartile range (IQR). Mobility is classified according to Wilson mobility scale, a nine-level scale (1–9).

Participants	n = 28
Once a week	2 (7)
Less than 3 times / month	9 (33)
Never	1
Absence from school due to pain, (n = 27) (%)	
Daily	0
2–3 days / week	4 (14)
Once a week	1 (4)
Less than 3 times /month	15 (56)
Never	7 (26)
Data is presented as number (n), percentage (%), median (mdn) and interquartile range (IQR). Mobility is classified according to Wilson mobility scale, a nine-level scale (1–9).	

Please insert Table 1 about here

Pain was present in 27/28 (96%) of the participants. Of these 27 children with pain, 17 (63%) received intravenous bisphosphonate treatment. The median pain frequency was 2–3 times per week, and the median frequency of school absence due to pain was 2–3 times per month (Table 1). The most frequently reported locations of pain were the back (16/27) and feet (14/27), followed by the arm (5/27), head (4/27), hip (4/27), knee (4/27), stomach (2/27), neck (1/27) and hand (1/27). Pain in the feet was more frequently reported in children with type I ($p = 0.032$), and pain in the hip was more often reported in children ≥ 13 years ($p = 0.011$). Nine children reported pain in one location and 18 reported pain in multiple locations (≥ 2). There was no significant difference regarding presence of multiple pain between OI-types, sex, or age groups. The children were also asked about what they thought to be the cause of the pain ($n = 24$). The most frequent responses were “walking long distances” (7/24), followed by “any time” (4/24), “after injury” (3/24), “during activity” (2/24), and “all the time” (2/24). Many children additionally explained that remaining in prolonged sedentary positions caused pain. Pain intensity (NRS) was reported by 27 children, without significant differences between OI-types, sex, or age groups (table 2). The summarised median value for PII ($n = 27$) was 11 (IQR 16), without significant differences between OI-types, sex, or age groups (table 2).

Promis-25

The total median raw score for self-perceived health status in the total sample ($n = 28$) was 40 (IQR 27). Children with type III reported lower in the mobility domain as compared to type I and IV ($p = 0.016$). No differences regarding self-perceived health status were found between sex or age groups (table 2).

Table 2. Descriptive statistics for the Numerical Ratings Scale (NRS), the Pain Interference Index (PII) and the Patient Reported Outcome Measurement Information System Pediatric-25 Profile v1.1 (PROMIS-25).

Assessment	Median all children	IQR all children	Median Type I	Median Type III	Median Type IV	IQR Type I	IQR Type III
NRS¹ (n=27)							
NRS average	4	2	4	4	5	2	2
NRS worst	8	4	8	8	10	4	4
NRS little	1	2	1	1	1	2	3
PII² (n=27)							
Schoolwork	2	3	1	3	3	3	3
Leisure activity	2	3	2	2	1	4	3
Time with friends	1	3	1	1	0	3	3
Mood	2	4	1	2	1	4	5
Physical activities	3	5	3	3	1	4	5
Sleep	2	3	1	2	2	3	5
PROMIS-25³ (n=28)							
Mobility	40	12	41	27	41	13	18
Anxiety	50	11	49	55	44	7	21
Depressive symptoms †	52	11	52	59	44	6	11
Fatigue	51	15	54	50	41	10	17
Peer relationships †	47	18	48	39	61	17	16
Pain interference	50	14	48	57	49	13	14

¹ Numerical Ratings Scale, Self-rating from 0-10: 0 (no pain) and 10 (worst possible pain). ² Pain Interference Index, Self-rating from 0-6: 0 (not at all) and 6 (very high). ³ PROMIS-25, Self-rating from 0-4: 0 (never) and 4 (always). Median T-scores are presented for all children and each OI-type: I, III and IV. Interquartile range (IQR) for all children and type I and III (too few in type IV). † Two missing answers for depressive symptoms and one missing for peer relationships.

Please insert table 2 about here

Associations between PII and PROMIS-25

An association was observed between total median in PII and total median raw score in PROMIS-25 ($r_s=0.84$, $p < 0.001$). Separate domains within PII correlated with T-scores in separate domains within PROMIS-25 (table 3).

Table 3. Correlations between Pain Interference Index (PII) (n=27) and Patient Reported Outcome Measurement Information System Pediatric-25 Profile v1.1 (PROMIS-25) (n=28).

Variable	PROMIS-25 ²	Mobility	Anxiety	Depressive symptoms †	Fatigue	Peer relationships †	Pain interference
PII¹							
Schoolwork	$r_s=-0.20$ $p=0.310$	$r_s=0.50$ $p=0.003^{**}$	$r_s=0.49$ $p=0.012^*$	$r_s=0.43$ $p=0.023^*$	$r_s=-0.54$ $p=0.004^{**}$	$r_s=0.51$ $p=0.006^{**}$	
Leisure activities	$r_s=-0.51$ $p=0.006^{**}$	$r_s=0.43$ $p=0.024^*$	$r_s=0.54$ $p=0.005^{**}$	$r_s=0.39$ $p=0.043^*$	$r_s=-0.23$ $p=0.270$	$r_s=0.58$ $p=0.001^{**}$	
Time with friends	$r_s=-0.50$ $p=0.007^{**}$	$r_s=0.41$ $p=0.031^*$	$r_s=0.51$ $p=0.008^{**}$	$r_s=0.47$ $p=0.012^*$	$r_s=-0.37$ $p=0.060$	$r_s=0.58$ $p=0.001^{**}$	
Mood	$r_s=-0.43$ $p=0.025^*$	$r_s=0.77$ $p<0.001^{**}$	$r_s=0.72$ $p<0.001^{**}$	$r_s=0.36$ $p=0.058$	$r_s=-0.56$ $p=0.003^{**}$	$r_s=0.54$ $p=0.003^{**}$	
Physical activities	$r_s=-0.32$ $p=0.100$	$r_s=0.20$ $p=0.310$	$r_s=0.23$ $p=0.250$	$r_s=0.10$ $p=0.580$	$r_s=-0.077$ $p=0.70$	$r_s=0.52$ $p=0.005^{**}$	
Sleep	$r_s=-0.38$ $p=0.049^*$	$r_s=0.52$ $p=0.005^{**}$	$r_s=0.54$ $p=0.004^{**}$	$r_s=0.31$ $p=0.110$	$r_s=-0.41$ $p=0.038^*$	$r_s=0.60$ $p=0.001^{**}$	

Spearman's correlation coefficient (r_s) was calculated between PII (n=27) and PROMIS-25 (n=28). Significant at $p < 0.05$ and $r > 0.37$. ¹ PII consists of a self-rating from 0-6, where 0 means "not at all" and 6 "very high" pain interference during six activities: schoolwork, leisure activities, time with friends, mood, physical activities, and sleep. ² PROMIS-25 is a self-rating instrument with the domains mobility, anxiety, depressive symptoms, fatigue, peer relationships and pain interference. The rating is on a scale from 0-4 where 0 means never and 4 always. † Two missing answers for depressive symptoms and one for peer relationships.

Please insert table 3 about here

Discussion

The main finding was that pain was present in almost all children, regardless of OI-type, sex, and age group. In addition, pain interfered in children's everyday life, which was associated with children's self-perceived health status.

Almost all children reported presence of pain and the intensity was consistent with previous studies including children with OI [19, 20]. However, many children with OI have experienced pain from an early age and might have adjusted their life by avoiding activities in order to reduce pain or have adapted to a certain level of chronic pain, and therefore some children might have underestimated their level of pain [21]. Children reported presence of pain several times per week. The findings are in line with results from the UK, where a random sample of 35 children with OI, aged 5–18 years was included [6]. Concerning pain location, the present study showed that the back and feet were most common. Zack et al. also described the back as the most common location, together with the chin and front of the thighs [6]. In the present study children reported the probable causes of pain, of which the most frequent were walking long distances, followed by walking, exercise, football, jumping and after injuries. However, many children further explained that prolonged sedentary positions caused pain. Confirming results were reported by Zack and colleagues, where 43% of the participants described minor traumas, recent exercise, or prolonged poor positions as

painful situations [6]. In the present study, pain interfered in children's everyday lives, and affected participation in various activities. Since physical activity is a key factor for decreasing bone resorption and rebuilding bone mass, this information is essential. If children avoid physical activities because of fear of pain, or due to pain, it might cause a vicious circle of inactivity, which further decreases bone density and increase the risk of fractures, additional pain and further inactivity [13, 22].

Many children reported pain interference during sleep, which has been described earlier in an integrative review concerning pain experiences in children and adolescents with OI [8]. Zack et al. reported that the impact of pain was most frequent in participants when they were trying to fall sleep [6]. Altogether, these results indicate that sleep is a topic that should be further investigated, since sleep deprivation affects school performance, emotional status, relationships, and by increase the pain experience itself [5, 23, 24].

In our sample, pain interference during schoolwork was associated with anxiety, depressive symptoms, fatigue, and less social support from friends. Confirmatory results were described from the UK [6]. The frequency of children reporting school absence due to pain was high in our group of children. Many previous studies have used "school absence", to evaluate children's ability to participate in school-related activities, since they are considered to be the most important activities for children, due to social, cognitive, emotional, and physical aspects [25].

Self-perceived health status was investigated, and mobility was reduced in the total sample, and the lowest mobility was detected in children with type III, while a positive trend was that many children reported results similar to the general population in other domains, findings consistent with previous research [26, 27]. Confirming results were also presented in a review concerning QoL in children and adults with OI, where the authors concluded that physical QoL appeared to be lower than in the general population, while the mental and psychosocial QoL was equal or better [28]. Both low physical and social scores in HRQoL were detected in a Brazilian prospective cross-sectional study, including 52 children and adolescents with OI, aged 5–17 years; however, significant differences were detected between the OI types [26]. A lower HRQoL in children with OI than children in the general population, and especially those with severe OI-types, was reported in a Chinese cross-sectional study, including 138 children with OI, aged 2–18 years [27]. No difference between sexes was found in the present study, which could imply that the self-perceived health status might be similar for boys and girls within the Swedish OI population, a finding consistent with the Chinese study [27]. In our group of children, a high correlation was detected between children's self-perceived health status and pain interference in everyday life, a discovery emphasising the importance of finding optimal possibilities for treatments. The results are in line with previous research [26].

A limitation in this study was the small sample included, and a reason is that at our clinic a high number of children are below the age of six years, and in addition small sample is to be expected in single-site studies of children with rare diseases [28]. A further limitation was the use of the five structured questions in the interview, that had not previously undergone psychometric testing. A strength was that the representation of OI-types was consistent with the prevalence in the Swedish population [9]. Further strengths were that only one child declined to participate, that the response rate in the questionnaires was high, and that the same researcher (KL) conducted all interviews. The use of PII, a psychometric tested index, considered as an adequate tool to assess pain interference in children and adolescents, was a further strength [15]. Another strength was the use of PROMIS-25, since it offers possibilities for comparison with the general population.

In conclusion almost all children experienced pain, which interfered in children's everyday lives, affected participation in various activities and was associated with reduced self-perceived health status. If children avoid physical

activities because of pain, it might cause a vicious circle of inactivity, which further decreases bone density and increase the risk of fractures. The results emphasize the importance to offer adequate pain reducing interventions.

Abbreviations

HRQoL

Health-related quality of life

NRS

Numerical Rating Scale

OI

Osteogenesis Imperfecta

PII

Pain Interference Index

PROMIS-25

Patient Reported Outcome Measurement Information System Pediatric-25 Profile v1.1

QoL

Quality of Life

Declarations

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Conflicts of interest

The authors report no conflicts of interest.

Availability of data and material:

Not applicable. We do not have the ethical permission to make data available.

Code availability:

Not applicable.

Author Contributions

All authors contributed to the study conception and design. Kristina Löwing was responsible for data collection. Kristina Löwing and Anna Hallin were responsible for data analysis and the first draft of the manuscript. Kristina Löwing, Anna Hallin and Eva Åström revised it critically. All authors read and approved the final manuscript.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Regional Ethical Review Board in Stockholm (Dnr 2017/1136-31/2).

Consent for publication:

Consent for publication was signed by all parents, but no individual's data or image was published separately.

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