

Dental care course and oral quality of life in patients with X-linked hypophosphatemia: a qualitative exploration

Lisa Friedlander (✉ lisa.friedlander@inserm.fr)

INSERM UMR 1123 <https://orcid.org/0000-0003-3056-3624>

Caroline Nguyen

Université Paris 7 Diderot: Université de Paris

Elisabeth Celestin

APHP: Assistance Publique - Hopitaux de Paris

Delphine Chambolle

association of people with vitamin-resistant hypophosphatemic rickets, France

Agnès Linglart

APHP: Assistance Publique - Hopitaux de Paris

Martin Biosse Duplan

APHP: Assistance Publique - Hopitaux de Paris

Catherine Chaussain

APHP: Assistance Publique - Hopitaux de Paris

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Abstract

Background. X-linked hypophosphatemia (XLH) is a rare, hereditary, progressive, and lifelong phosphate wasting disorder characterized by pathological elevations in fibroblast growth factor (FGF) 23 serum concentration and activity. In the oral cavity, spontaneous abscesses can occur often without any clinical signs of alteration of the causal tooth. The objective of our study was to evaluate the readability of the oral care pathway and the oral quality of life of patients followed in an expert oral medicine department located within a Parisian hospital and working in close collaboration with an endocrinology department expert in this pathology.

Methods. This study employed a qualitative descriptive design including semi-structured interviews using guiding themes.

Results. Twenty-one patients were included in the study, with an average age of 28 years. The topics discussed exceeded the initial objectives as the patients largely addressed the alteration of their oral and general quality of life, a very chaotic oral health care pathway with oral health professionals not aware of their pathology, consequences on their social, professional, and school integration and access to care complicated by financial factors. Patients reported the importance of having a multidisciplinary team around them, including medical and dental professionals.

Conclusions. The variety of manifestations in patients with XLH necessitates a high coordination of multidisciplinary patient care to optimize quality of life and reduce disease burden. Education of oral health professionals on this disease is essential to enable patients to receive the best possible care as early as possible.

Background

In the European Union, a disease is considered rare when it affects less than one person in 2000 (1). Awareness of rare diseases has increased in the European Union since 2009, when the Council of the European Union asked Member States to develop plans and strategies in this regard. X-linked hypophosphatemia (XLH) is a rare, hereditary, progressive, and lifelong phosphate wasting disorder characterized by pathological elevations in fibroblast growth factor (FGF) 23 concentration and activity; XLH has an incidence of approximately 1 in 20–25,000 individuals. Excess FGF23 activity leads to increased phosphate excretion in the kidneys – mediated by downregulation of renal tubular phosphate transporters – and reduced phosphate absorption in the intestines – due to impaired vitamin D activation (2). Signs of XLH typically manifest in the first two years of life when leg bowing becomes apparent with the onset of weight bearing. Other signs/symptoms include impaired growth, bone tenderness, muscle weakness, dental abscesses, muscle spasms, and wrist widening. Adults with XLH may develop additional complications such as hearing loss, hyperparathyroidism, obesity, renal damages, kidney stones, periodontitis, osteoarthritis and enthesopathy (3).

In France, management of patients with X-linked hypophosphatemia (XLH) (X-linked hypophosphatemia rickets) is coordinated by an expertise center for calcium and phosphate metabolism, whose coordinating center is located at the Bicêtre Paris Saclay hospital in Kremlin-Bicêtre, near Paris. Dental care and follow-up are carried out at the Bretonneau Hospital (Paris). The expertise center belongs to the OSCAR national network of healthcare providers for rare diseases of bone, calcium, and cartilage. A national diagnosis and care guideline protocol (PNDS) was set up by the expertise center in 2018 (4) (5). Many French experts together with the French patient advocacy group also participated to the European guidelines in 2019 (6).

Some rare disease, such as the one discussed in this work, are chronic, both in terms of their impact on the lives of patients and their duration. If a chronic disease is, according to the WHO definition, “a health problem that requires management over a period of years or decades”, then orofacial diseases are an appropriate example. Despite differences in disease etiology and symptoms, many rare diseases are therefore chronic, involve multi-systemic dysfunction, have no curative treatment and require complex care (7).

It is well established today that chronic diseases pose a problem for health-related quality of life, physical and mental well-being perceived by patients. However, they can create additional barriers to a good quality of life due to insufficient access to information, treatment and support, as well as high stigma (8).

In X-linked hypophosphatemia, the complexity of management for professionals in terms of oral health is multiple. Rarity of the disease makes it difficult for patients to organize high quality oral care. Not only are there few competent professionals in the management of this disease but also, professionals who are not trained in the phenotypic specificity of this disease may steer patients in unsatisfactory therapeutic directions.

Many rare diseases have severe direct or indirect consequences on tooth formation (number, shape, structure anomalies) or craniofacial bone (9). However, in the case of XLH, these abnormalities are not secondary effects of the condition but a direct consequence of XLH on the tooth structure. The dental manifestations of patients with XLH appear as soon as the teeth erupt and will persist throughout their lives resulting in severe functional, aesthetic, and nutritional problems (4)(10). One of the main oral findings in patients with XLH is the occurrence of “spontaneous” dental abscesses in the primary and permanent dentition, not associated with decay or trauma. Other dentition-related findings are delays in tooth eruption in both the primary and permanent dentition, impacted teeth and, in adults, periodontitis and increased dental implant loss ((11). Affected teeth are characterized by a thin enamel layer and dentinal and cementum mineralization defects. In addition, short roots and root resorptions in the primary dentition, a poorly defined lamina dura and a hypoplastic alveolar ridge are common findings(12).

Inappropriate management will necessarily have negative consequences on the patients' oral and general quality of life. These oral manifestations seem to be particularly unknown to private dentists who sometimes refuse to manage patients due to lack of information and training. Health insurance coverage

of dental cares and transportation to referral centers is not always accepted, which increase the difficulty for patients to access care when health professionals are geographically distant.

In this work, where we performed qualitative method with face-to-face semi-structured interviews, our objective was to evaluate the readability of the oral care pathways and the oral quality of life of patients with XLH followed in an expert oral medicine department located within a Parisian hospital and working in close collaboration with a rheumatology department also expert in this pathology.

Methods

Design

This study employed a qualitative descriptive design including semi-structured interviews using guiding themes.

Participants

Given the active file of patients with this pathology in the department studied, it was agreed to recruit around 10 children and 10 adult patients over a 6-month period.

Recruitment of patients

In collaboration with the medical team, a sample has been selected according to the inclusion criteria following one of their regular follow-up consultations. Then, according to the usual consultations of the center, and the appointments made for the care of these patients, they were included progressively.

At the beginning of the planned care consultation, the usual practitioner and the researcher briefly but clearly explained the study and collected the non-opposition of the person taking part in the research or that of his legal representative.

Eligibility criteria

Eligibility criteria were to have X-linked hypophosphatemia and to be a patient of the center aged over 6 years.

Procedure

A semi-structured interview guide was developed by the research group and discussed with researchers and clinicians in our department beforehand.

Interview

Data collection

Face-to-face, semi-structured interviews were held by the first and second author (L.F. and C.N.), trained in qualitative sociological and anthropological interview methods. All interviews took place in the Dental Medicine Department of the Bretonneau Hospital in a dedicated room after a standard dental consultation. We used an interview guide, structured by the following six themes: “care course,” “quality of life”, “feelings,” “impact of handicap disabilities,” “school and work integration and daily life” and “renouncement to dental care”. During these interviews, themes were discussed with the patients who were encouraged to talk freely about their care pathway and their quality of life as well as their experiences and the repercussions on daily life.

Interviews with a duration between 30 and 60 min were conducted and recorded in the period of October 2020 until March 2021. Transcripts and other sensitive data were stored at Research Clinical Unit in Robert Debré Hospital, Paris.

Qualitative thematic analysis

For the analysis of the qualitative data, the recorded interviews were manually transcribed and then analyzed using a thematic data analysis software (NVIVO 10 on PC). The thematic analysis of the questionnaires was carried out according to the following process (13):

1. Key themes, or big ideas, were identified by reading and re-reading the interview transcripts.
2. Phrases or blocks of words that correspond directly to the research question were highlighted.
3. These phrases were categorized so that they can be grouped together thematically.
4. These categories gave rise to sub-themes which were examined and analyzed.

The transcripts were reviewed to identify key themes and coded by a single researcher. Interviews were performed until the data was saturated and no further themes emerged, as is the current standard for qualitative data analysis in health settings.

Ten percent of the interviews were analyzed by a second coder to ensure consistency and quality assurance of the data.

Key themes were organized in a table and those mentioned by three or more patients were considered common.

Common key themes were converted into questions and grouped into general themes.

Results

Patient characteristic

Twenty-one patients participate to the study. Of these, 6 were under 18 years of age and 15 were 18 years and older. The average age is 28 years, and the median is 23.

Of these patients, 85% are female and 15% are male.

Of the adult patients of working age, 2 are on invalidity (Table 1).

| Participant | Gender | Age (Y) | Occupation |
|-----------------------|---------------|----------------|----------------------|
| <i>Participant 1</i> | F | 61 | Invalidity |
| <i>Participant 2</i> | F | 10 | School |
| <i>Participant 3</i> | F | 15 | School |
| <i>Participant 4</i> | F | 51 | Medical secretary |
| <i>Participant 5</i> | F | 39 | Administrative agent |
| <i>Participant 6</i> | F | 29 | Assistant |
| <i>Participant 7</i> | F | 18 | School |
| <i>Participant 8</i> | F | 53 | Invalidity |
| <i>Participant 9</i> | F | 9 | School |
| <i>Participant 10</i> | M | 19 | Unemployed |
| <i>Participant 11</i> | F | 37 | Military |
| <i>Participant 12</i> | F | 9 | School |
| <i>Participant 13</i> | F | 18 | School |
| <i>Participant 14</i> | F | 11 | School |
| <i>Participant 15</i> | F | 36 | Employed |
| <i>Participant 16</i> | F | 52 | Employed |
| <i>Participant 17</i> | F | 11 | School |
| <i>Participant 18</i> | M | 47 | Nurse |
| <i>Participant 19</i> | F | 9 | School |
| <i>Participant 20</i> | F | 48 | Academic |
| <i>Participant 21</i> | M | 14 | School |
| Mean age | 28 | | |
| Median age | 23 | | |

Table 1 Patient's characteristics

The exploration of themes

The different themes and sub-themes discussed by the patients during the interviews are shown in table 2 with the number of references per theme and the number of interviews in which the theme was present and in table 3 with examples of patients' verbatims per theme and sub-themes.

| Themes and sub-themes | Number of interviews where the notion is present | Number of references to the themes |
|---|--|------------------------------------|
| Feelings about oneself and others | | |
| Recognition and gratitude | 14 | 29 |
| Self-esteem | 12 | 30 |
| Expressed feelings | | |
| Sadness | 5 | 18 |
| Resentment | 8 | 25 |
| Regrets | 2 | 6 |
| Fear | 11 | 22 |
| Anger | 8 | 33 |
| Access to care | | |
| Technical aspects | 5 | 6 |
| Financial aspects | 13 | 27 |
| Quality of life | | |
| General quality of life | 9 | 31 |
| Oral quality of life | 7 | 22 |
| Care course | | |
| General care course | 14 | 23 |
| Oral care course | 16 | 43 |
| Limitations | | |
| Due to disabilities | 13 | 43 |
| Due to tiredness | 2 | 9 |
| Social insertion | | |
| School life | 9 | 18 |
| Professional life | 8 | 20 |
| Attitude and behavior towards the disease | 12 | 62 |

Table 2 Themes and sub-themes and number of references per theme

Care course

Oral health care course

One of the particularities of this oral disease is the occurrence of spontaneous dental abscesses at any age. Teeth can have a completely intact external appearance, which can sometimes be a source of misdiagnosis for a dentist not trained in this disease. Many patients describe a lack of awareness by dentists of the clinical signs of the condition. At the oral level, the care pathway is therefore felt to be very chaotic, with a lot of therapeutic wandering.

The patients interviewed raise the complexity, at the local level where they live, of finding competent professionals who know the disease. This led in most adults to a worsening of the situation due to a lack of appropriate care. All of them acknowledge the improvement of their oral condition when they were treated in this expertized dental service, where medical professionals know perfectly well their pathology. The patients interviewed described the weariness of having to repeat the history of their disease and its oral particularities to all the dentists they had seen. They describe that dentists do not see the clinical link with the disease.

For children, parents describe that if they are taken care of early during childhood, it is much easier for them both.

The patients interviewed described multiple extractions, which they considered to be over-treatment, because according to them no one had been able to treat their teeth correctly until they arrived in the Parisian service.

The patients reproached the practitioners for not candidly saying when they did not know and for misdirecting them.

General disease care course

In this department, interviewed patients described living sometimes far from the hospital. Adult patients and parents of young patients described meandering care pathways and diagnostic wanderings, going from doctor to doctor to get an accurate diagnosis.

One patient even described how a surgeon wanted to remove her hips and put plastic hips on her. Some patients described feeling like guinea pigs as children.

The interviewed patients described that finding a team in a hospital department that could take care of their condition and direct them to this Parisian oral medicine department significantly improved their care pathway. Team cohesion and communication were a major source of improvement in their care pathway.

The patients interviewed described again, at times, a lack of knowledge of this rare disease on the part of general practitioners and doctors.

Quality of life

General quality of life

The quality of life of the patients was described by them in terms of the psychological and physical consequences of their pathology on their daily life. Overall, the disease had consequences on physical abilities, impacting the participants' general quality of life. Indeed, they reported a decrease in their physical abilities: leg pain, both in adults and children, of varying degrees, including difficulty walking, occurred during major physical efforts (long walks, runs, etc.). Patients refrained from playing certain sports they would have liked to play, such as football for example, or even taking part in physical education and sports classes at school, as they could not keep up. The patients described a general quality of life altered by the daily limitations due to the disability generated by the disease.

Oral health related quality of life

About the quality of life related to oral health, more specifically, the patients interviewed described, in addition to the lack of knowledge of health professionals concerning the oral aspects of the pathology, episodes, for most of the patients, of intense pain, infection, extracted teeth not replaced given the financial costs, an altered smile and problematic chewing. The patients described an impaired oral quality of life.

Spontaneous abscesses were not consistently observed in patients. The impact of the disease on oral quality of life was therefore very variable among patients, but more impact was noted in adult participants than in child participants.

The pain, caused by abscesses and/or necrosis of the teeth, might have had no consequences - especially in children - or it may have affected patient's daily life: sleeplessness, physical suffering and fatigue, as well as mental fatigue affecting their professional activity. Edentulism affected the patients' chewing ability; indeed, patients could not chew properly and had to avoid certain foods.

In terms of the function and appearance of their teeth, patients reported difficulties in eating, biting into bread or a sandwich since they were young. One of the main point described by the patients interviewed was the spontaneity and speed of the infectious crisis, without prior signs. The patients described that since their care was assured in this specialized hospital service, constant attention was paid to both functional and aesthetic rehabilitation.

Renouncement to oral health care

For financial reasons/aspects

Whenever a patient described access to financial care in relation to oral rehabilitation, they described high fees, too expensive for them, given the amount of care involved. Additionally, patients felt that practitioners expressed that they were not 'profitable' patients.

For technical reasons/aspects

In addition, as already mentioned, the patients interviewed described the ineptitude of many of the dentists they met in their care, unable to recognize the clinical features of their condition.

Feelings expressed:

Sadness

The first feeling patients express is sadness, due to the announcement of an incurable progressive genetic disease. The diagnosis was made rather young, sometimes without much phenotypic expression, forcing the patients, according to them, to project themselves into the future. This projection into the future was described by many of the patients as being able to arouse a great deal of fear and apprehension as to the physical handicap that may have occurred during their lives.

The patients interviewed mentioned the moral and psychological suffering linked to the disease and the gradual onset of limitations in their daily performance. The psychological impact of the physical alteration, even for the patients interviewed who were not in a wheelchair, was widely reported.

Fear

Many patients expressed their feelings of fear about the future, their own and that of their children when they were also carriers of the pathology. The fear of the future focused on the deterioration of their physical conditions, on ageing with significant joint pain and an even greater deterioration of their oral health.

Their anger was also expressed in the slowness of the administrative processes to have their disability recognized.

Resentment

Furthermore, the patients interviewed expressed resentment, against doctors who, in their opinion, had not been sufficiently attentive to their needs, even though they had a good reputation.

In addition, the patients interviewed have a lot of resentment and anger about the urban infrastructure, which they felt was not sufficiently adapted to physical disabilities and wheelchairs.

The patients' feelings of resentment and anger were quite focused on the lack of knowledge of the professionals about their disease and the lack of infrastructures compatible in their daily life with the disability.

Feelings about oneself and others

Gratefulness/ reconnaissance

When patients explained the difficulty of their oral health care pathway, they expressed great recognition and gratitude towards the department where the interview were conducted. Thanks to the expertise of the practitioners, appropriate care and long sought-after answers could be provided, to the great relief of patients.

The availability and attentiveness of the practitioners were elements that were often mentioned by the patients interviewed.

The joint, interdisciplinary care within an oral medicine department but also within the rheumatology department, taking care of their pathology, was, according to the patients' feelings, a source of appeasement, and of regained confidence towards the medical profession.

Self-esteem

The patients interviewed report many elements that echo their self-esteem. The disease has a huge impact on patients' growth and many report complexes about their height. These complexes also affect the description of the shape of their bowed legs.

The patients interviewed all described being teased at school as children. In addition, many of the patients spoke of the inconvenience of taking their medication orally, which they had taken since childhood and which tasted bad, at different times of the day, particularly at school, where some had to hide to take it so that they would not be asked questions.

The loss of self-confidence, increased by the limitations of their body due to the disability generated by the disease, is also reported by the patients interviewed. Furthermore, the patients interviewed reported that when, because of their disability, they needed help to do simple things such as their daily toilet, the psychological impact was significant.

Social integration

Professional integration

The patients interviewed reported limitations in their career progression, feeling that they had been mostly confined to jobs below their competence due to repeated absences from medical consultations and interventions, or limitations of their body. The reported interruptions due to examinations and medical interventions were also reported to be obstacles to a normal school career for many of the patients in the study.

School integration

The child patients interviewed report fear of being teased at school by their peers and questions about their treatment. Many of the children interviewed said that they had to take their treatment in secret from others.

Patients described that school absences due to frequent medical appointments and surgeries had a significant impact on their academic performance.

Daily limitations

The fact that they can no longer walk for long periods, dance, do housework, look after the house, or drive, are elements that are often reported by the patients interviewed. In this respect, they describe the lack of facilities, which excludes them from many activities, such as getting a haircut.

The patients interviewed also described that pain and physical discomfort are sources of impairment of their general quality of life. In this sense, the patients interviewed describe limitations in access to certain jobs and thus give up their professional careers.

Attitude to disease

The comments reported in this study by the patients interviewed on how they perceive life in general and their daily life in particular were quite variable. Some patients were quite resigned and accept the limitations in their daily lives on a day-to-day basis. Others were truly angry about the lack of facilities for people with disabilities, they were worried for themselves but also for their children when they were also carriers of the same pathology. The patients interviewed whose children were also affected by the same pathology reported a feeling of guilt and of having transmitted the genetic disease but also a form of appeasement to put them early, unlike sometimes themselves, in an effective and adapted oral and general care pathway.

Overall, patients were more concerned about their general health than their oral health. Despite the feeling of being well followed in their care, patients were worried about the worsening of their symptoms, particularly their pain. Also, seeing the evolution of the disease in older people in their family is a source of concern but allowed them to realize that their care had changed for the better following an accurate diagnosis.

As XLH is a genetic and hereditary disease, some patients also expressed fears about the transmission of the disease to their offspring, leading them to think about whether to have children or not. But the feeling of good follow-up from birth reassured them. Regarding the future of their oral health, the main concerns of patients were the weakening of their teeth due to dental necrosis and that it may lead to edentulism. Similarly, the feeling of being well monitored and informed about the consequences of XLH on their oral health decreased the patients' worries: parents of XLH children were reassured to observe an oral monitoring adapted to the oral conditions in their child.

Discussion

X-linked hypophosphatemia is an inherited condition with an X-linked dominant mode of transmission. Affected men pass the condition on to all their daughters and none of their sons. Affected mothers have a 50% risk of passing on the condition with each pregnancy(14). This condition is X-linked dominant, but

men and women are equally likely to be affected and with the same degree of severity. Indeed, the "healthy X" does not compensate for the "sick X". The gene responsible has been identified as the phosphate-regulating endopeptidase homolog X-linked (*PHEX*), which plays an important role in preserving phosphate balance in the body (3) (15).

In this study, out of 21 patients interviewed, 18 were female and 3 were male. This difference may be explained by the fact that women may place more importance on their oral health than men (16)(17).

The average age of the patients is 28 years. This is a relatively young population with a dense dental and general health care history.

The aim of this study was to analyze the oral health-related quality of life of patients with this condition and their oral health care pathway. During the interviews with the patients, many other themes were raised by both adults and children. The richness of this type of study is that the information collected goes beyond the initial objectives. Even though the study focused on the oral health care pathway, the patients were able to express themselves freely on the limitations due to their disability, especially about their social integration, their relationship with others and their place in society. One of the strengths of this study is that it goes beyond the usual methods of analyzing quality of life in a quantitative way, which misses many aspects reported by the patients in their daily lives and feelings.

Few studies have investigated oral quality of life of these patients, both children and adults. These studies use quantitative methods whose main measure is standardized questionnaires (18)(19). These questionnaires, although particularly useful for orienting and highlighting certain aspects of the impact of the disease on oral quality of life, are nevertheless limited in their precision concerning the feelings and experiences expressed by the patients. For this disease, there is no data in the literature from qualitative studies based on interviews or focus groups.

Qualitative research provides a detailed understanding of patients' perspectives and expectations and can be an essential first step in the development of future patient-centered measures. Qualitative research and its methods provide opportunities for a systemic and holistic understanding of the challenges faced by patients (20).

Qualitative methods are increasingly used in the medical literature to understand issues in patients' daily lives and care pathways (21).

In the case of this disease, the oral care pathways are intricately linked to the general care pathway of the disease (22). The lack of knowledge by oral health professionals of the disease in general is a burden for patients. Spontaneous abscesses, without visible signs of tooth destruction, is a phenotypic sign that is not well known to practitioners (6). Therefore, in addition to the physical, dental pain, there is the frustration of not being listened to and understood. The patients describe in a global and detailed way their numerous difficulties before arriving in this specialized center, where the disease is very well known, to find suitable professionals who know the pathology. This aspect of therapeutic wandering is a major

element, according to the patient's statements, in the alteration of the quality of life linked to oral health. In the general, physical aspects of this pathology have been well described in the literature, this therapeutic wandering for their oral health has been little described. One of the interests of this study is that it is carried out in a center of expertise working in close collaboration with a rheumatology and endocrinology service specialized in this pathology. This transdisciplinary approach is one of the major keys to good patient care especially in case of rare diseases. All the patients interviewed described that their arrival in this department, with a multidisciplinary team working with practitioners dealing with their disease, not only on a dental level, is a major element in the improvement of their care pathway and therefore their quality of life.

When XLH is diagnosed, the aim of treatment is to reduce the functional handicap, restore the axis of the lower limbs, improve bone and dental mineralization and muscle strength. Social and family aspects and therapeutic education must be an integral part of the care. Finally, follow-up should focus on the prevention of endocrine, rheumatological and renal complications. The patient must be managed by a multidisciplinary team including an expert in metabolic bone pathology from the expertise center, a radiologist, an orthopedic surgeon, a rheumatologist, an endocrinologist, a physiotherapist, a neurosurgeon, a dentist, an orthodontist, a periodontal specialist, a psychologist and a social worker (23).

Limitations and Strengths

XLH is a disease whose phenotypic variability, and the weight of the disease, differ from patient to patient, making patients not comparable with each other. Therefore, in this study, the patients have various disabilities, which do not limit them in the same way in their daily lives. This aspect may appear as a limitation in the comparison of what is reported between patients. Indeed, we did not report the different treatments taken by the patients, nor did we quantify their body damage precisely. This was not the purpose of the study and it does not seem to alter the interpretation of the results. Moreover, patients were interviewed in a department with a high level of expertise in this pathology. Patients therefore probably have a more severely affected oral health than other patients with the same pathology but in a less severe form. This pitfall was already expressed in a quality-of-life study in 2015, carried out in a center of the same network and this is why we cannot generalize these results to all patients with this pathology (3).

Our study has clearly shown the complexity of the oral care course for patients with XLH, despite the establishment in recent years of a territorial network and a political will, both French and European, to facilitate the care pathway for patients with rare diseases (22)(24)(25). The results of this study provide information on the quality of life related to oral health, but also on the place of patients with disabilities in society, both in terms of professional integration and daily lives.

Conclusion

Patients have largely reported the improvement of their care conditions since their arrival in this specialized service where their pathology is very well known. Their oral care pathway has been very

chaotic, and has contributed as much to their poor oral quality of life as the disease itself.

XLH is a rare disease, which implies specific care for patients at different levels. To facilitate their access to care, several organizations are implicated: the rare disease health network, the centers of reference and the patient associations. The calcium and phosphorus metabolism reference center facilitates access to diagnosis and care for patients while avoiding multiple medical consultations. It brings together in one location (Bicêtre University Hospital, Paris Sud) many specialists such as orthopedic surgeons, endocrinologists, neurosurgeons, ENT specialists, radiologists, dieticians, and dental surgeons to ensure comprehensive patient care. Since 2016, the reference center has been part of the European BOND (bone rare disease network), a collaboration that will improve knowledge of the natural history of the disease by facilitating data sharing. In addition, the health network for rare bone, calcium and cartilage diseases, created in 2014, coordinates various actors: reference centers and competence centers (which allow patients to be monitored close to home), patient associations, professionals from the medico-social sector, analysis and molecular diagnosis laboratories, research units and learned societies. This makes possible to improve patient care at a higher level, but also to develop research and train various health professionals.

The variety of symptoms in patients with XLH necessitates a high coordination of multidisciplinary patient care to optimize quality of life and reduce disease burden (26). Education of oral health professionals on this disease is essential to enable patients to receive the best possible care as early as possible.

Declarations

Ethics approval and consent to participate

Ethical and scientific approval was gained according to local guidelines (CPP 2020-A02631-38) for the conduct of qualitative study involving patient interviews. Informed, written consent was gained and recorded. Data were handled in accordance to national data regulation guidelines.

Consent for publication

All the patients or their parents gave written informed consent for participation in the study and the publication of the study results.

Availability of data and materials

The datasets during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

No funding was received for the study.

Authors' contributions

All the authors were involved in the design of the study. MBD, and CC treated the study patients and aided data collection. LF and CN collected the data. LF and CN analyzed the data. All the authors drafted the first and further versions of the manuscript. All the authors reviewed and revised the manuscript and approved its final version. Overall responsibility: LF.

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Table 3

| Themes | Subthemes | Quotations |
|--------------------|------------|--|
| Expressed feelings | Sadness | <p>"I could no longer do my passion because I used to dance a lot, I could no longer dance. " (Female, 61 y.o., invalidity)</p> <p>"It affects life, the quality of life, not to mention the moral suffering."(Female, 52 y.o., employed)</p> <p>"I cry but... well it's fine, it's over but it's still painful and it's a real choice... it has an impact on psychological suffering, physically, we're not in a wheelchair, physically, we're normal, it still has an impact on daily life. "(Male, 47 y.o., nurse)</p> |
| | Resentment | <p>"When you are outside in a wheelchair ... when you see France behind on the problems, the pavements, the doors that have to be pulled up! You can't go to the toilet because it's not provided. Now they are obliged in the new structures. " (Female, 61 y.o., invalidity)</p> <p>"You need to get a haircut; how do you do it? You take your hair and then you put a bowl on your head and then you cut what's sticking out. I swear you have to see it to believe it. " (Female, 61 y.o., invalidity)</p> <p>"Where I work, in a research centre, there are many areas where I could work, but the situation means that the qualifications are lower. And then, with secretarial diplomas, what do you do with that? You don't do anything. » (Male, 47 y.o., nurse)</p> |
| | Regrets | <p>"Afterwards, yes, I think I could have done more, been less of a failure than I was and done studies that would have taken me further maybe but it's sure that if I had been less absent in secondary school and high school... "(Female, 51 y.o., medical secretary)</p> <p>"I would have been perhaps less lost, less drowned in school. " (Female, 51 y.o., medical secretary)</p> <p>"It's more afterwards, as I'm getting older, that I say to myself that maybe I should have been more careful, and now I'm careful about my son. "(Female, 53 y.o., invalidity)</p> |
| | Fear | <p>"I'm worried that I'm losing all my teeth, they're dying as I go along... "(Female, 37 y.o., military)</p> <p>"I'm worried that the implants won't work, and I'll have a total brace. And then I'm afraid I'll have hip replacements soon enough and then the pain I have is not getting better, on the contrary, it's getting worse. So, I'm not very optimistic about old age."(Male, 47 y.o., nurse)</p> <p>"what's really difficult is the transmission of the disease knowingly, like all genetic diseases I think. "(Female, 29 y.o., assistant)</p> <p>"I'm afraid that as the years go by it will get worse, because right now I'm young, I'm a bit energetic but I'm afraid it will have consequences later on. "(Female, 18 y.o., School)</p> |
| | Anger | <p>"They don't want to keep crippled people at work. "(Female, 61 y.o., invalidity)</p> <p>"You need a haircut; how do you do it? You take your hair and then you put a bowl on your head and then you cut what's sticking out. I swear you have to see it to believe it. "(Female, 61 y.o., invalidity)</p> |

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| | | <p><i>"To be less blindfolded and say, well, I've learned that A+B=C and well, that will never make D, there will never be any brackets for a little C or I don't know what. But then, whether it's a dentist or a doctor, it's the same thing. You realise that it's books, books, books... lawyer, article 1, article 2. It's impressive how dentists and doctors are trained not to be curious, not to learn anything other than what they've learned in books, I don't understand, maybe it's a trick or I don't know... that's the biggest criteria I would say. But be curious, look elsewhere, listen to the patient. "(Female, 52 y.o., employed)</i></p> |
| Access to care | Financial aspects | <p><i>"I even have a certificate that I have a dentist who told me that I was not profitable for him and that he could not treat me." (Female, 52 y.o., employed)</i></p> <p><i>"But if you don't have a full wallet, nobody will treat you. "(Female, 52 y.o., employed)</i></p> |
| | Technical aspects | <p><i>"The dentists didn't believe me, X-rays, healthy teeth, healthy exteriors, no cavities... And no matter how hard I tried to explain to them that I had spontaneous dental necrosis. Once, I went to 15 dentists but uh... I couldn't work anymore; it's really disabling because you can't have a life anymore." (Female, 52 y.o., employed)</i></p> <p><i>"They don't want to hear, especially in my area, I think they are not specialized at all. And then, there is still a lack of information in my area and so they don't want to hear that rickets can be the cause of many oral problems. "(Female, 29 y.o., assistant)</i></p> |
| Quality of life | Oral quality of life | <p><i>"You can't eat croutons, you can't eat things that hurt because I have a lot of bones sticking out, I have exostoses everywhere." (Female, 61 y.o., invalidity)</i></p> <p><i>"So, crunching on a sandwich, it's always been since I got my bridge in the 85s, you can't crunch on apples. There are things you can't do but that's okay. "(Female, 48 y.o., academic)</i></p> <p><i>"I can't chew left and right anymore, I tried to take a piece of meat out and it was the tooth I took out."(Female, 53 y.o., invalidity)</i></p> <p><i>"It prevents me from sleeping, it prevents me from eating well. Instead of painkillers, sometimes I drink alcohol to knock myself out, which makes me very tired, but at least I recover more quickly in the morning to go to work." (Female, 36 y.o., employed)</i></p> <p><i>"Since I have a black tooth, I avoid smiling too much, but we keep smiling anyway, that's life. "(Female, 53 y.o., invalidity)</i></p> <p><i>"It wasn't cavities, so ... it was pain that came on suddenly ... it was abscesses, so there you go and obviously it came on a Saturday night at 2 o'clock. "(Female, 36 y.o., employed)</i></p> |

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| | | <p><i>"It's not very aesthetic, it's always, in terms of seduction, it's true that it's not fabulous but, well, it's not just the smile. "</i> <i>(Female, 39 y.o., administrative agent)</i></p> |
| | General quality of life | <p><i>"There are many things in everyday life that make life difficult, and I use my electric wheelchair to do my shopping. "</i> <i>(Female, 61 y.o., invalidity)</i></p> <p><i>"And morally, I suffer enormously, I have a lot of physical pain, especially in my leg, sciatica, because it's the lumbar, and I would have to undergo an operation, but I don't want to because it has already weakened me so much in terms of walking. "</i> <i>(Female, 61 y.o., invalidity)</i></p> <p><i>"There was a time when I had to take all my treatment, all the time in front of others, I had to hide so that no one would ask me questions. No, I had a bad time of it, I had a really bad time of it. "</i> <i>(Female, 36 y.o., employed)</i></p> <p><i>"With my wife, we decided not to have children for example. Since it's a disease that is on the X dominant gene and therefore, we have a one in two chance of having a sick child and I don't want a sick child. »</i> <i>(Male, 47 y.o., nurse)</i></p> |
| Limitations | Due to disabilities | <p><i>"I had to get my ears fitted because, the disease affected my ears too. "</i> <i>(Female, 61 y.o., invalidity)</i></p> <p><i>"And even to cook, I can't do it because I can't stand up, because I walk with a walker at home, I have one downstairs and one upstairs, because walking with canes how do you want to hold a pan".</i> <i>(Male, 19, unemployed)</i></p> |
| | Due to tiredness | <p><i>"It's a complicated time to be tired all the time and then of course the others don't understand, the mockery. (</i> <i>Female, 37 y.o., military)</i></p> <p><i>"But it's a lot of suffering and a lot of fatigue. It's especially the fatigue of not sleeping for months on end. I have a tooth that needs to be treated, which has been treated, but it's still there. "</i> <i>(Female, 52 y.o., employed)</i></p> <p><i>"Fatigue has affected my studies. It's affected my work, it's created a lot of work stoppages and brain fatigue which means that I'm really weakened intellectually some days, with a lowered morale. "</i> <i>(Femle, 52 y.o., employed)</i></p> |
| Social insertion | Professional life | <p><i>"the disease has affected my work; it creates a lot of downtime and brain fatigue, so I'm really weakened intellectually some days"</i> <i>(Female, 61 y.o., invalidity)</i></p> <p><i>"I can't take a full-time job for example so... it's complicated. "</i> <i>(Female, 37 y.o., military)</i></p> <p><i>"You're a girl, you're disabled, you'll be a secretary, that's it. I did not have a choice. It wasn't what I wanted to do at all. "</i> <i>(Female, 52 y.o., employed)</i></p> <p><i>"I was stopped after my hip replacement and... they put me on disability and so now I realize that I couldn't really work at a job all day, it's becoming difficult. "</i> <i>(Female, 39 y.o., administrative agent)</i></p> |

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| | School life | <p><i>"I often missed school and as the disease was not very well known until the age of... I knew my first class; I was 9 years old. "(Female, 52 y.o., employed)</i></p> <p><i>"It caused me to have absences, so I managed... the school level it was but I found myself in a wheelchair regularly, I had to change schools. I was in a school where there was no lift. So, there was no wheelchair access, so I had to change schools. And then, I shut myself up in a shell."(Female, 11 y.o., School)</i></p> <p><i>"I had to redo my school year because I had a follow-up in the rehabilitation Centre, so I was a year late."(Female, 18 y.o. School)</i></p> |
| Care course | Oral care course | <p><i>"They didn't understand why the gums recede, why my teeth die quite often... we have to re-explain each time."</i></p> <p><i>"It's months and months of suffering, months of not believing, months of trying to explain a disease they didn't know about with supposedly healthy teeth."</i></p> <p><i>"The dentists didn't believe me.... And no matter how much I explained to them that I had spontaneous dental necrosis pff. Once, I went to 15 dentists... I couldn't work anymore; it's really disabling because you can't have a life anymore". (Female, 61 y.o., invalidity)</i></p> <p><i>"They started pulling my teeth and they realized that it wasn't a good principle and I... I've been to a lot of dentists in my life. Apart from offering me treatment or treating the cavity or... they didn't understand. I could explain that I had a genetic disease, but dentists don't look at it like doctors do, they don't look at the disease at all."(Female, 36 y.o., Employed)</i></p> |
| | General care course | <p><i>"my mother had taken me to all the hospitals, no one knew about the disease and so they said they had to come back when I was finished growing and operate on me. "(Female, 11 y.o., School)</i></p> <p><i>"I was dragged from Lyon, Marseille, Paris, I went to a lot of places and they put me in a centre, they spread my legs, they put me in plaster casts, they did a lot of tests. There was even a surgeon who wanted to remove my hips and put on plastic hips. It was all and then nothing. Everyone wanted to get my case to say "yes, I discovered a case".(Female, 52 y.o., employed)"The doctor treating me doesn't know about this disease, in fact, there are many doctors... it's a rare disease so they don't know about it".(Female, 11 y.o., School)</i></p> |
| Feelings about oneself and others | Recognition and gratitude | <p><i>"Thanks to this doctor who defended my case in commission, and I was able to continue working. "(Female, 53 y.o., invalidity)</i></p> <p><i>"I am happy to be followed by a dentist who knows a little bit about pathology, and he is super careful, he doesn't hurt compared to other dentists, no, no... I prefer to take 1 hour to come here and have a good dentist. " (Female, 61 y.o., invalidity)</i></p> <p><i>"The service is very good, we have the direct mobile numbers of the doctors, it's not everywhere. We're great, we're really lucky. And even, during the holidays, I needed to call because</i></p> |

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| | | <p><i>she had toothache, she made sure to find us a doctor, it's great, it's rare, we are really lucky to be here."</i>(Female, 11 y.o., School)</p> <p><i>"Here I feel really listened to and above all, I am informed about the consequences of the disease and this allows me to adapt my lifestyle."</i>(Female, 11 y.o., School)</p> <p><i>"Here I feel like I'm on another planet. I come here, they tell me about rickets normally, they tell me that there are solutions, they know what it can produce in my mouth and everything, I've never heard that. I don't feel like I'm crazy. "</i> (Female, 48 y.o., academic)</p> |
| | Self esteem | <p><i>"I was always very self-conscious about my size so I was all dressed up when I went to work and anywhere else for that matter. "</i>(Female, 61 y.o., invalidity)</p> <p><i>"If I don't have anyone coming to see me, I don't open my shutters all day, I cry, I just do it. "</i>(Man, 19 y.o., Unemployed)</p> <p><i>"If you ask for someone to do your washing, then already psychologically it's very hard and well, everything goes with what".</i>(Female, 37 y.o., military)</p> <p><i>"But before, I had to turn around to see if there was anyone behind me, so that no one could see how I was walking".</i> (Female, 18 y.o. School)</p> <p><i>"Well, when I was at school, people didn't necessarily understand. So... especially because you could see it because I had bowed legs, unlike my sister, you can't really see it, but I could really see it and I was teased. »</i> (Female, 18 y.o. School)</p> |
| Attitude and behavior towards the disease | | <p><i>"I never accepted the disease. Morally, it destroyed me. "</i> (Female, 61 y.o., invalidity)</p> <p><i>"Morally, you are... I have never accepted the disease. Morally, it destroyed me."</i> (Female, 61 y.o., invalidity)</p> <p><i>"But as I grew up, even before I had the operation, I understood that it's something you can't choose, and I grew up with it and I ended up accepting it on my own. ".</i> (Man, 19 y.o., Unemployed)</p> <p><i>"I've always loved humans, so I've never really had any... I've always loved humans, so I've never really hated them, but it's true that I've often put myself in the background to avoid talking and smiling stupidly when you know very well that things aren't going well, that all you want to do is go out the window. "</i>(Female, 37 y.o., military)</p> <p><i>"Teeth are a drag on your life. When you fight tooth pain, you can't fight it, because I've got two broken femoral necks, I've got fractured neck bones, you can't fight pain anywhere else and like dogs biting you everywhere."</i> (Female, 52 y.o., employed)</p> <p><i>"I've always lived with pain, so I've dealt with it".</i>(Male, 47 y.o., nurse)</p> |

Table 3 Examples of extracted codes, subcategories, and categories