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Rare diseases with oral components: care course and quality of life

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Aim: To describe links between the care course of individuals suffering from rare diseases and socio-behavioural risk factors and to ascertain the impact of dental conditions on the quality of life. ***Design:*** A cross–sectional comparative study involving self-reported questionnaire was performed. Care course was evaluated using Predisposing, Enabling and Needs factors. The impacts of dental conditions on quality of life were measured with the OHIP 14 questionnaire. Proportions were compared by Chi-square test. Logistic regression for multivariate analysis assessed statistical association between variables. ***Results****:* Responses were received from 355 subjects (mean age 36.9 years, 67.6% females). Thirty-three rare diseases were recorded. Respondents were classified as group A, individuals suffering from rare diseases with a dental component (n=207, 58.3%), and group B, without dental component. Group A reported earlier diagnosis, more positive attitude toward dentists, functional limitation and higher prosthetic treatment needs. Only 17.4% of subjects having fewer than 20 teeth wear prosthetics. A higher percentage of individuals claiming pain, physical disability, psychological discomfort and social disability, was found among group B ($p<0.001$). Logistic regression analysis retained two impact factors: psychological disability (Exp(B)=8.66; 95% CI 1.86-40.34) and social wellbeing (Exp(B)=0.06; 95% CI 0.02-0.215). ***Conclusion:*** Rare diseases with a dental component benefited from earlier identification of symptoms. Dentists could contribute to patients' quality of life by helping in early diagnosis, reducing functional limitation and improving social wellbeing.

Key words: *rare diseases, stomatognathic diseases, dental care, quality of life*

Introduction

The impact of chronic dental diseases on the quality of life of individuals and societies has been a topic investigated for decades. Poor oral health affects the most basic needs of human beings such as eating, drinking, smiling and communicating and can therefore potentially harm quality of life. Missing teeth, periodontal disease, untreated caries, social, behavioural, financial and environmental factors were found to be associated with a negative impact on the quality of life measured by the OHIP questionnaire (John *et al*., 2004; Leao and Sheiham, 1996; McGrath and Bedi, 2001).

However, studies measuring the impact of the health status of people suffering from rare diseases with an oral component on their access to treatment and quality of life are scarce. A large number of original articles describe distinct cases of rare diseases and their dental phenotypes. Indeed, numerous rare diseases affect the development of hard tissue around teeth and dental anomalies are known components of many syndromes (Bailleul-Forestier *et al*., 2008a; 2008b). Among 5,000 known genetic rare diseases, approximately 700 harbour dental, oral or craniofacial components (John Hopkins University, 2011). Since tooth germ development depends on epithelial-mesenchymal interactions, dental abnormalities such as tooth agenesis are prominent in ectodermal syndromes such as Ectodermal Dysplasias (Mikkola, 2009).

In their study, Locker and Matear (2001) supported the opinion that oral abnormalities can have impacts on the quality of life of patients, thereby affecting the well-being of individuals and society. Most studies of rare diseases are either studies of clinically identified cases or observational studies of populations of patients affected by a specific disease. The main explanation for this is the rarity of the cases and their diversity. Another reason is the limited medical knowledge on oral health in these specific conditions. Until now, little has been published on the situation of individuals affected by rare diseases with an oral component. More specifically, few epidemiological and socioeconomic data are available. A rare disease in the European Union is one that occurs in under 5 per 10,000 individuals, 27 to 36 million of European people are affected, which corresponds to a prevalence between 6 and 8% for all the rare diseases. In France, nearly 4 million people (5%) are affected (EURORDIS, 2005). Rare diseases are often complex, requiring multidisciplinary approaches for providing adequate care for patients. However, the care-course of patients with rare diseases is hampered by major problems: e.g. delays between the onset of the symptoms and diagnosis, the lack of standardised diagnostic procedures. The scarcity of clinical and natural history data due to the low prevalence of these diseases results from a lack of priority from the pharmaceutical industry and difficulty in establishing accurate diagnoses. Only ~300 of 3000 ORPHANET listed diseases benefit from disseminated knowledge, so most are insufficiently known by health professionals, a problem exacerbated by these diseases'

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characteristically wide variety of clinical symptoms (D'Amato Sizonenko, 2006). Despite their considerable diversity, rare diseases have several major common traits summarised as: diversity in severity, compromising of quality of life, very painful in terms of psychological burden, most often incurable and often difficult to identify treatments (EURORDIS, 2005). The French Ministry of Health has set up two reference centres for odontological rare diseases in France, since 2006, dedicated to the diagnosis, the treatment and the epidemiological statistics of these rare diseases.

In the last decade, Oral Health Impact Profile measures have been increasingly used for evaluating the care outcome of many diseases and genetic disorders (Stewart *et al*., 2008; Wong *et al*., 2006). This type of data for individuals with rare diseases may be valuable in informing oral health promotion and for integrating oral disease prevention in the national health plans for rare diseases.

The aim of this study was to describe how the oral care-course of individuals suffering from rare diseases is linked to socio-behavioural risk factors. Furthermore, the aim is to ascertain the impact of dental conditions on their quality of life and analyse the association of socio-demographic and behavioural factors with rare diseases.

Methods

The study had a cross-sectional design using a voluntary self-reported e-mailed survey. Information was gathered regarding socio-demographic criteria, and behavioural PEN factors (Predisposing, Enabling, Needs) as designed by Andersen (1995) for measuring care course. The short-form OHIP questionnaire (Slade, 1997) measured the impact of oral conditions on quality of life. The questionnaire has seven dimensions of impact (functional limitation, pain, psychological discomfort, physical disability, psychological disability, social disability and handicap). Subjects answered questions on how frequently they had experienced impacts in the preceding 12 months using a 4-point scale coded: 3, very often; 2, often; 1, rarely; and, 0, never. The survey was carried out in 2007 in close collaboration with different national associations for rare diseases in France. The target population was individuals affected by rare diseases. Heads of rare disease associations were briefed about the purpose and the procedure of the study before contacting their respective members. Non-members were reached via the Federation des Maladies Orphélines web site which explained arrangements for completing the questionnaire.

The minimum sample size needed has been calculated as 73 with a confidence level of 95% and taking in account the rare disease 5% prevalence in France. A stratified sampling frame was applied. For ethical purposes, participants had to give their consent to the project proposal before responding.

Analysis of the data was carried out using SPSS v.18. To better measure impacts, the study population was divided into two groups. Individuals who reported rare diseases with an oral component were assigned to group A, while those without an oral component were assigned to group B. This classification formed the basis for the comparative study. For the statistical evaluation, proportions were compared with the Chi-squared test.

Table 1. Rare diseases reported with or without oral component and numbers of cases.

Group A - Rare diseases <u>with</u> an oral component	*n*
Ostéogenèsis imperfecta	97
Incontinentia pigmenti	27
Oligodontia	27
Ectodermal dysplasia	17
Amelogenèsis imperfecta	9
Acromégaly	6
Dentinogenesis Imperfecta	6
Behçet's disease	4
Gougerot Sjögren Syndrome	4
Ehlers Danlos Syndrome	3
Costen Syndrome	2
Hypophosphatasia	1
Pachyonychia congénital	1
Tubérous sclerosis de Bourneville	1
Frazer Syndrome	1
Pierre Robin Syndrome	1
Total (58%)	207
Group B - Rare diseases <u>without</u> an oral component	*n*
Macrophagic Myofasciitis	92
Fibromyalgia	9
Sarcoidosis	4
Chromosomal abnormality	2
Takayasu disease	2
SAPHO	2
Alkaptonuria	1
Junctional epidermolysis bullosa	1
Charcot marie tooth disease	1
Obsteirq disease	1
Parry-Romberg disease	1
Verneuil disease	1
Auto immune Myasthénia	1
Pheochromocytoma	1
Scléroderma systémic	1
Marfan Syndrome	1
Cockayne Syndrome	1
Disease with no name assigned	18
Others	8
Total (42%)	148

A 5% level of significance was applied for all tests. In addition, a multinomial logistic regression model was performed to measure the impacts of dental conditions on individual quality of life of the following independent variables: functional limitation (chew correctly, tooth ache); psychological disability (feel different, belittled or lack of confidence); psychological discomfort and social handicap (emotional problems in your life with spouse). Goodness-off-fit table tests indicate how adequately the model fitted the data.

Results

Of 387 returned questionnaires only 355 were useable. Responses came from across the whole of France and from 5 respondents living in French overseas territories. Respondents' mean age was 37 years (sd 19) and 246 (68%) were female. Members of rare disease associations

Table 2. Care course risk factors according to rare diseases group

		Rare diseases	
		Group A (n=207)	*Group B (n=148)*
Factors	*Items*	*%*	*%*
Predisposing			
Time of diagnoses	Early	**49.7*****	**68.3*****
Dentist is flexible with appointments	Yes	**85.5*****	69.7
Dentist's works meet patient's expectations	Rather, Yes	40.4	38.1
Dentist takes into account aesthetic demands	Rather, Yes	**47.4****	29.3
Patient fearful of the dentist	Yes	79.1	74.2
Cost of treatments	Expensive	42.5	41.9
	Very expensive	28.4	37.6
Dentist offers deferred payment	Yes	**76.3****	58.2
Enabling			
Health insurance coverage and private insurance	Yes	90.8	88.7
Geographical access, travel time	>30mins	42.4	43.1
Having knowledge of reference centres	Yes	32.8	**62.4*****
Needs			
Having fewer than 20 teeth	Yes	**44.0*****	11.1
Has toothache all the time	Yes	9.2	**26.1*****
Prosthetic/implant treatment (n_A=155; n_B=99):			
Fixed Prosthetic (n_A=43, n_B=39)	Yes	27.7	39.4
Denture (n_A=34, n_B=25)	Yes	21.9	25.2
Implant (n_A=16, n_B=12)	Yes	10.3	12.1
Dental visit within the last 12 months	Yes	82.7	84.2
Frequency of dental visit	1-5 times	62.4	56.1

** p<0.01, *** p<0.001

Table 3. Quality of life related oral health status

	Rare diseases							
	Group A n=207				*Group B n=148*			
Measures of Quality of Life	*Never*	*Rarely*	*Often*	*V.often*	*Never*	*Rarely*	*Oftent*	*V.often*
Functional limitation								
Do you feel that you chew correctly?	7.2	31.9	30.4	**34.4***	6.7	47.9	30.2	15.1
Do you have problems eating ground steak?	53.7	26.9	14.2	5.2	45.2	29.6	16.5	8.7
Do you have trouble eating shredded carrot?	46.3	30.1	16.2	7.4	35.6	25.4	27.1	**11.9***
Physical pain and disability								
Do you have tooth ache?	25.7	45.6	21.3	7.4	17.1	35.0	**32.8*****	**13.6*****
Do you feel pain when eating steak?	72.9	14.6	8.3	4.2	74.1	17.2	5.2	4.2
Psychological disability								
Because of your disease do you feel:								
Different?	10.4	20.7	40.7	28.1	*7.1*	*15.0*	***44.2*****	*33.6*
Belittled, lack self-confidence?	17.2	24.2	36.7	21.9	*10.7*	*17.0*	***46.4*****	*25.9*
Psychological discomfort and social handicap								
Emotional problems living with spouse	40.4	23.4	25.5	10.6	*16.1*	*16.1*	***43.0******	***24.7******

* p<0.05, ** p<0.01, *** p<0.001

accounted for 254 (72%) of the 355 useable responses. Thirty-three kinds of rare diseases were reported, most commonly Ostegenesis Imperfecta (97 cases), Macrophagic Myofasciitis (92) and Oligodontia (27). Group A, those whose disease had an oral component, numbered 207 and were 58% of respondents (Table 1).

Table 2 summarises the care course PEN factors' distribution. Group A participants reported significantly earlier diagnosis ($p<0.001$; df=2; $\chi^2=128$) and more positive attitude toward dentists based on the overall rating for predisposing. Furthermore, they claimed greater satisfaction with their formulated aesthetic and deferred payment (85.5%, $p<0.001$) demands. The proportion of group A individuals having under 20 natural teeth was four times as many as in group B ($p<0.001$). The needs for prosthetic and implants treatment was large but satisfied for only 17.4% of those having under 20 teeth. Despite good public health insurance, the individuals of both groups A and B commonly complained about the high cost of the prosthetics treatment and implants. Indeed there was no significant difference in the number of prosthetic and implants treatments made between the groups A and B. Furthermore, twice as many in group B had knowledge of reference centres for their specific disease ($p<0.001$). Over half of both groups had visited the dentist 1 to 5 times in the last 12 months.

The proportion of participants claiming difficulties in terms of quality of life was high. The most prevalent oral health impact on quality of life was psychological discomfort followed by functional limitation, social disability and physical pain. There were differences were between the two groups. A higher proportion of subjects claiming functional limitation was found in the group A ($p<0.05$). But group B participants claiming toothache was twice that in group A ($p<0.001$). In addition, B participants claimed significantly more suffering from psychological discomfort and from social handicap expressed by emotional problems with one's spouse (both $p<0.001$). Furthermore, group B individuals were twice as often claiming they felt belittled and lacked confidence in themselves due to the disease ($p<0.001$) (Table 3).

The findings from logistic regression modelling predicted factors that are most related to quality of life. Psychological discomfort (feel different because of disease) was an impact of the diseases on poorer quality of life (Exp(B)=8.66; 95% CI 1.86-40.34). On the other hand, no social handicap (emotional problem in your life with spouses) seemed to be a protector (Exp(B)=0.06; 95% CI 0.02-0.21),.

Discussion

Dental anomalies have been found as significant diagnosis indicators in some cases of rare disease syndromes. The present study identified that more than half of rare diseases reported by participants included an oral component. The validity and accuracy of the responses to questionnaires were tested by comparing with medical knowledge on the specific concerned rare diseases. All the diseases reported were found in the list of rare diseases recently established by ORPHANET in 2010. Care course difficulties the patients faced were: the long time taken for reachng diagnosis, frequent changes of specialists and locations to access appropriate clinical assistance. The findings showed that the oral health care needs were extensive and greater in group A (those with a disease having an oral component) than in B due to a higher proportion of subjects having under 20 teeth. Difficulties in chewing or in eating some kind of food were often or very often reported, showing an almost daily functional limitation. The poor access to prosthetic rehabilitation due to the high cost of dental implants agreed with the commonly reported findings for rare diseases published by EURORDIS (2008). The study provided additional data on the functional, psychological and social impacts of rare diseases on quality of life. The psychological impact of poor dental appearance found in this study was also reported by Cushing *et al*. (1986).

The findings highlighted the importance of an early diagnosis. They also support the common characteristics of rare diseases reported by many authors as disabling, psychologically despairing and highly painful. Furthermore, the study pointed out the important role of dentists in early diagnosis of more than 50% of rare diseases and in dental treatment to improve the quality of life of these patients. The French national plan for rare diseases (2005-2008) prioritises the improvement of the health professional training and dissemination of knowledge of the epidemiology of rare diseases.

Conclusion

The findings support the recognition of oral health as a principal mediator of quality of life and showed that the daily quality of life of patients with rare diseases is compromised by pain and the inability to chew. Questions about the ease of access to implants for patients with rare diseases, such as oligodontia, should be seriously considered as it could help patients feel less different and improve their daily quality of life.

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