Archives of Oral Biology 116 (2020) 104745

Contents lists available at ScienceDirect

Archives of Oral Biology

journal homepage: www.elsevier.com/locate/archoralbio

Oral health in patients with Marfan syndrome

Gabriele Cervino[a], Marco Cicciù[a], Rosa De Stefano[b], Domenico Falcomatà[a], Alberto Bianchi[c], Salvatore Crimi[c], Luigi Laino[d], Alan Scott Herford[e], Michele Gaeta[b], Luca Fiorillo[a,*]

[a] Department of Biomedical and Dental Sciences, Morphological and Functional Images, School of Dentistry, University of Messina, ME, Italy
[b] Department of Biomedical and Dental Sciences, Morphological and Functional Images, University of Messina, ME, Italy
[c] Department of General Surgery and Medical-Surgery Specialities, University of Catania, 95100 Catania CT, Italy
[d] Department of Biomedical and Surgical, Biomedical Sciences Naples University, Naples, NA, Italy
[e] Department of Maxillofacial Surgery, Loma Linda University, Loma Linda, CA 92354, USA

ARTICLE INFO

Keywords:
Marfan syndrome
Oral health
Syndromic patients
Oral syndroms
Oral abnormalities
Semeiotics
Periodontitis

ABSTRACT

Introduction: The role of this study is to highlight a correlation between patients with Marfan syndrome and oral health status by evaluating and reviewing the relevant scientific literature. The syndrome is characterized by an abnormal production of the fibrillin1 protein. The manifestations of Marfan syndrome affect organs that contain connective tissue such as the skeletal system, the eyes, the heart and the blood vessels, the lungs and the fibrous membranes that cover the brain and the spine. The facial bony and soft structures can therefore be affected, influencing the stage of tooth formation and the structure of the teeth, we also want to analyze in this study, the periodontal complications and the management of the latter, with the use of surgical techniques that include the use of biomaterials.

Materials and methods: A comprehensive review of the literature was conducted according to PRISMA guidelines. After a careful analysis of the work obtained by two independent academics, there have been 18. All data from the studies were compared and many of these highlighted the presence of abnormalities in the oral district.

Results: The studies taken into consideration a whole series of oral manifestations related to the Marfan syndrome. Oral mucosa, periodontal, dental abnormalities, bone abnormalities or joint dysfunction are frequently involved in patients affected by this disease.

Conclusions: All the research have given positive results in terms of dental or oral anomalies. This information may be essential to limit and intervene early improving the oral health of syndromic patients.

1. Introduction

Marfan syndrome (MFS) is an autosomal dominant genetic disorder of connective tissue described for the first time in 1896, which can involve different organs. MFS is caused by a mutation of fibrillin-1 located at chromosome 15q-21.1 (Dietz et al., 1991; Gray & Davies, 1996; McKusick, 1955). FBN1 gene is translated into fibrillin-1, an extracellular matrix protein important in both elastic and non-elastic connective tissues and elastic fibrillogenesis. Mutations commonly lead to deficiency in fibrillin-1, an increased susceptibility of fibrillin-1 to proteolysis and/or disruption to cell-cell signalling.

The prevalence is estimated to be one to two affected individuals per 10 000 live births (Gray & Davies, 1996; Gray, Bridges, & Faed, 1994) with no gender or ethnic prevalence. The diagnosis is purely clinical with the classical triad of MFS: Ocular, Cardiovascular and musculoskeletal disorders (De Paepe, Devereux, & Dietz, 1996; Loeys, Dietz, & Braveman, 2010). This pathology is characterized by individuals with tall stature, elongated extremities, protruded breastbone, and other manifestations that could interest central nervous system, respiratory system and skin. Regarding the maxillo-facial district could be found dolichocephalism, enophthalmos, downward slanting palpebral fissures, deep palatal vault, maxillary constriction, maxillary retrognathism (SNA < 80°), mandibular retrognathia (SNB < 78°), temporomandibular joint hypermobility, and enamel and dentine defects (De Coster, Martens, & De Paepe, 2002). About teeth, could be highlighted, long narrow teeth, large positive overjet, posterior crossbites, general malocclusion and periodontal disease. Normally affected patients present normal intelligence and cognitive development (De

Abbreviations: MFS, Marfan syndrome; SNA, sella–nasion–A point angle (cephalometric analysis); SNB, sella–nasion–B point angle (cephalometric analysis); CNS, central nervous system; DMFT, decayed missed fillet teeth

* Corresponding author.
E-mail addresses: lucafiorillo@live.it, lfiorillo@unime.it (L. Fiorillo).

https://doi.org/10.1016/j.archoralbio.2020.104745
Received 18 December 2019; Received in revised form 3 April 2020; Accepted 30 April 2020

Coster et al., 2002; De Paepe et al., 1996; Dietz et al., 1991; Gray & Davies, 1996).

The purpose of this article was to perform a systematic review of the literature on patients affected by MFS, with the aim of evaluating the most common problems and the correct dental management.

2. Material and methods

2.1. Protocol and registration

This review was registered on PROSPERO with 120208 ID protocol. PROSPERO includes protocol details for systematic reviews relevant to health and social care, welfare, public health, education, crime, justice, and international development, where there is a health related outcome. Systematic review protocols on PROSPERO can include any type of any study design. Reviews of reviews and reviews of methodological issues that contain at least one outcome of direct patient or clinical relevance are also accepted.

2.2. Focus question

The following focus question was: developed according to the population, intervention, comparison, and outcome (PICO) study design:

- There is a correlation between patients with Marfan syndrome and oral health status?
- What are the dental and oral anomalies in Marfan patients?

2.3. Information sources

The search strategy incorporated examinations of electronic databases, supplemented by hand searches. A search of four electronic databases, including Ovid MEDLINE, PubMed, EMBASE, and Dentistry and Oral Sciences Source, Human syndrome for relevant studies published in the English language to 2018 was carried out. A hand search was also performed in other medical journals. The search was limited to English language articles. Furthermore, a search of the reference lists in the articles retrieved was carried out to source additional relevant publications and to improve the sensitivity of the search.

2.4. Search

The following key-words were used: “Marfan syndrome”AND “dental" OR “Oral manifestation”. The choice of keywords was intended to collect and to record as much relevant data as possible without relying on electronic means alone to refine the search results. The research was also limited to medical journal and only to articles written in English.

2.5. Selection of studies

Two independent reviewers, of University of Messina singularly analysed the obtaining papers in order to select inclusion and exclusion criteria as follows. Reviewers compared decisions and resolved differences through comparing the manuscripts. For the stage of reviewing of full-text articles, a complete independent dual revision was performed. The results have been compared at the end of the research. A possible disagreement regarding the inclusion of the studies was discussed among the authors. The first phase of the research consisted of the selection of titles, which allowed us to make a first screening of the manuscript eliminating those not concerning our research. Finally, the full text of all studies was obtained and according to the expected inclusion/exclusion criteria articles were selected and included in the present review. 36 results were obtained after the first electronic and manual search with keyword used. Only 26 full text english articles and subsequently, 20 studies of these on human were evaluated. After reviewers screening only 18 articles were included.

2.6. Types of selected manuscripts

The review included studies on humans published in the English language. Letters and editorials were excluded.

2.7. Types of studies

The review included all human use studies and literature review published on Marfan syndrome patients with focus on oral anomalies.

2.8. Inclusion and exclusion criteria

The full text of all studies of possible relevance was obtained for assessment against the following inclusion criteria:

- Study of patients with Marfan syndrome.
- Study of patients with dental anomalies and Marfan syndrome

The applied exclusion criteria for studies were as follows:

- Studies involving patients with other specific diseases, immunologic disorders, uncontrolled diabetes mellitus, osteoporosis.
- Not enough information regarding the selected topic, no information about oral status and oral health.
- No access to the title and abstract in English language or letters and editorials
- Animal studies
- Not full text articles

2.9. Sequential search strategy

After the first literature analysis, all article titles were screened to exclude irrelevant publications, case reports and the no English language publications. Then, researches were not selected based on data obtained from screening the abstracts. The final stage of screening involved reading the full texts to confirm each study’s eligibility, based on the inclusion and exclusion criteria.

2.10. Data extraction

The data were independently extracted from studies in the form of variables, according to the aims and themes of the present review, as listed onwards.

2.11. Data collections

Data were collected from the included articles and arranged in the following fields as seen in Table 1:

“Author (Year)” – revealed the author and
“Title” – title of study
“Year” – year of pubblication
“Type of study” - indicated the type of the study

2.12. Risk of bias assessment

This type of work brings together all the studies in the literature in the last eighteen years presenting a review of recent data about dento-musculoskeletal anomalies in MFS. The risk of bias is minimal as the work is intended to be a collection of works carried out about these patients and about only dental anomalies, but we can only consider full text and abstract accessible articles in English language. Regardless of the results of the studies taken into consideration, the evaluation was carried out on the field of action of the analyzes carried out by the studies. A Risk of bias analysis according to Cochrane guidelines has

Table 1
Analysis of obtained study.

Author	Title	Year	Type of Study
(Nally (1966)	The Marfan syndrome. Report of two cases.	1966	Case report
(Kamen (1966)	Oral manifestations of Marfan's syndrome in twins.	1966	Case report
(Parker (1973)	Marfan's syndrome. A review of literature and case report.	1973	Review
Hirota et al. (Sugiyama et al., 1988)	Systemic management of Marfan's syndrome during dental treatment: a case repor	1993	Case report
(Westling et al. (1998)	Craniofacial manifestations in the Marfan syndrome: palatal dimensions and a comparative cephalometric analysis	1998	??
(Straub et al. (2002)	Severe periodontitis in Marfan's syndrome: a case report.	2002	Case report
De coster et al. (De Coster et al., 2002)	Oral manifestations of patients with Marfan syndrome: a case-control study.	2002	Case-control
(Bauss et al. (2004)	Temporomandibular joint dysfunction in Marfan syndrome.	2004	??
(Bauss et al. (2008)	Prevalence of pulp calcifications in patients with Marfan syndrome	2008	Case report
Utreja et al. (Utreja & Evans, 2009)	Marfan syndrome-an orthodontic perspective.	2009	Case report
Morales-Chavez et al. (Morales-Chávez & Rodríguez-López, 2010)	Dental treatment of Marfan syndrome. With regard to a case	2010	Case report
Bilodeau et al. (Bilodeau, 2010)	Retreatment of a patient with Marfan syndrome and severe root resorption.	2010	Case report
(Raja et al. (2008)	Rutherfurd syndrome associated with Marfan syndrome.	2012	Case report
(Ganesh et al. (2020)	Marfan syndrome: a case report	2012	Case report
(Mallineni et al. (2012)	Concomitant occurrence of hypohyperdontia in a patient with Marfan syndrome: a review of the literature and report of a case	2012	Review
Bain et al. (Bain & Schafer, 2013)	Physical signs for the general dental practitioner. Case: Marfan's syndrome	2013	Case report
Stufenbiel et al. (Staufenbiel, Hauschild et al., 2013)	Periodontal conditions in patients with Marfan syndrome - a multicenter case control study	2013	Case control
(Tsang et al. (2013)	Marfan syndrome: a review of the literature and case report.	2013	Review
(Shiga et al. (2015)	Orthodontic Treatment and Long-Term Management of a Patient With Marfan Syndrome.	2015	??
Franca et al. (França et al., 2016)	Oral management of Marfan syndrome: an overview and case report	2016	Case report

been conducted.

2.13. Marfan syndrome

Marfan syndrome is an autosomal dominant genetic disorder of connective tissue. The spectrum of the manifestations of the syndrome is broad and diversified: while for some patients the diagnosis is immediate and early, for those subjects for whom only some of the symptoms are present the diagnosis is difficult. Only a genetic investigation could ultimately guarantee a precise diagnosis for these people who, paradoxically, are those at risk. The ocular manifestations are fundamentally characterized by the displacement of the crystalline lens and by the sferofachia. In musculoskeletal manifestations, what is most striking is the height of patients, who are higher than the average, and often develop signs of excessive thinness (understood not only as a simple underweight) (Kamen, 1966; Nally, 1966). Hands are often afflicted by arachnodactyly, a characteristic linked to Marfan's syndrome. This is recognizable by the length and tapered shape of the fingers, and by the sign of the thumb. Hypermobility of the fingers, is linked to the generalized laxity of the ligaments. In the oral field there are typical anomalies affecting connective tissues. Therefore anomalies that concern both the functions of the salivary glands, dental anomalies and musculoskeletal abnormalities, like mandibula or maxillary retrognathia (Parker, 1973). The cardiovascular system includes sometimes very serious alterations: the occurrence of an aortic dissection is not uncommon. While a diagnosed patient will be followed throughout the course of the disease and then monitored with an echocardiogram for possible changes in aortic measures.

3. Results

3.1. Study selection

Article review and data extraction were performed according to PRISMA flow diagram (Fig. 1). The initial electronic and hand search retrieved 36 citations. 10 papers were excluded because were not identified as free full text. On 26, 20 of which were included because are about human. At last only 18 studies were included because of topic reasons (Tables 1–4).

3.2. Study characteristics

In this systematic review different oral alterations in MFS patients have been evaluated as: MFS and endodontics, periodontology, orthodontic or oral abnormalities as showed in Tables 1 and 2 (Bain & Schafer, 2013; Bauss et al., 2004, 2008; Bilodeau, 2010; França, Abreu, Paiva, Drummond, & Cortes, 2016; Ganesh, Vijayakumar, & Selvakumar, 2020; Kamen, 1966; Mallineni, Jayaraman, Yiu, & King, 2012; Morales-Chávez & Rodríguez-López, 2010; Nally, 1966; Parker, 1973; Raja, Albadri, & Hood, 2008; Shiga, Ogawa, Ekprachayakoon, & Moriyama, 2015; Staufenbiel, Hauschild et al., 2013; Straub et al., 2002; Sugiyama et al., 1988; Tsang, Taverne, & Holcombe, 2013; Utreja & Evans, 2009; Westling, Mohlin, & Bresin, 1998). Hypermobility of the fingers, is linked to the generalized laxity of the ligaments. In the oral field there are typical anomalies affecting connective tissues. Therefore, anomalies that concern both the functions of the salivary glands, dental anomalies and musculoskeletal abnormalities, like mandibula or maxillary retrognathia (Parker, 1973). After the study selection a new division related to the oral alteration has been performed:

- MFS and endodontics or periodontology (Bauss et al., 2008; Bilodeau, 2010; Staufenbiel, Hauschild et al., 2013)
- MFS and orthodontic alteration (Bauss et al., 2004; Shiga et al., 2015; Utreja & Evans, 2009; Westling et al., 1998)
- MFS and oral abnormalities (Bain & Schafer, 2013; França et al., 2016; Ganesh et al., 2020; Kamen, 1966; Mallineni et al., 2012; Morales-Chávez & Rodríguez-López, 2010; Nally, 1966; Parker, 1973; Raja et al., 2008; Straub et al., 2002; Sugiyama et al., 1988; Tsang et al., 2013).

3.3. Studies results

The results were analyzed by the authors independently and were evaluated according to their dental interest field. The review aims to evaluate Marfan Syndrome patients symptoms in the medical field and precisely in odontology, all studies have therefore led to satisfactory results. Studies evaluating all type of abnormalities in maxillo-facial district reported. The purpose of this work is to index oral abnormalities and give a rapid diagnostic method proposal for Marfan syndromic patients, and for other syndroms early diagnosys.

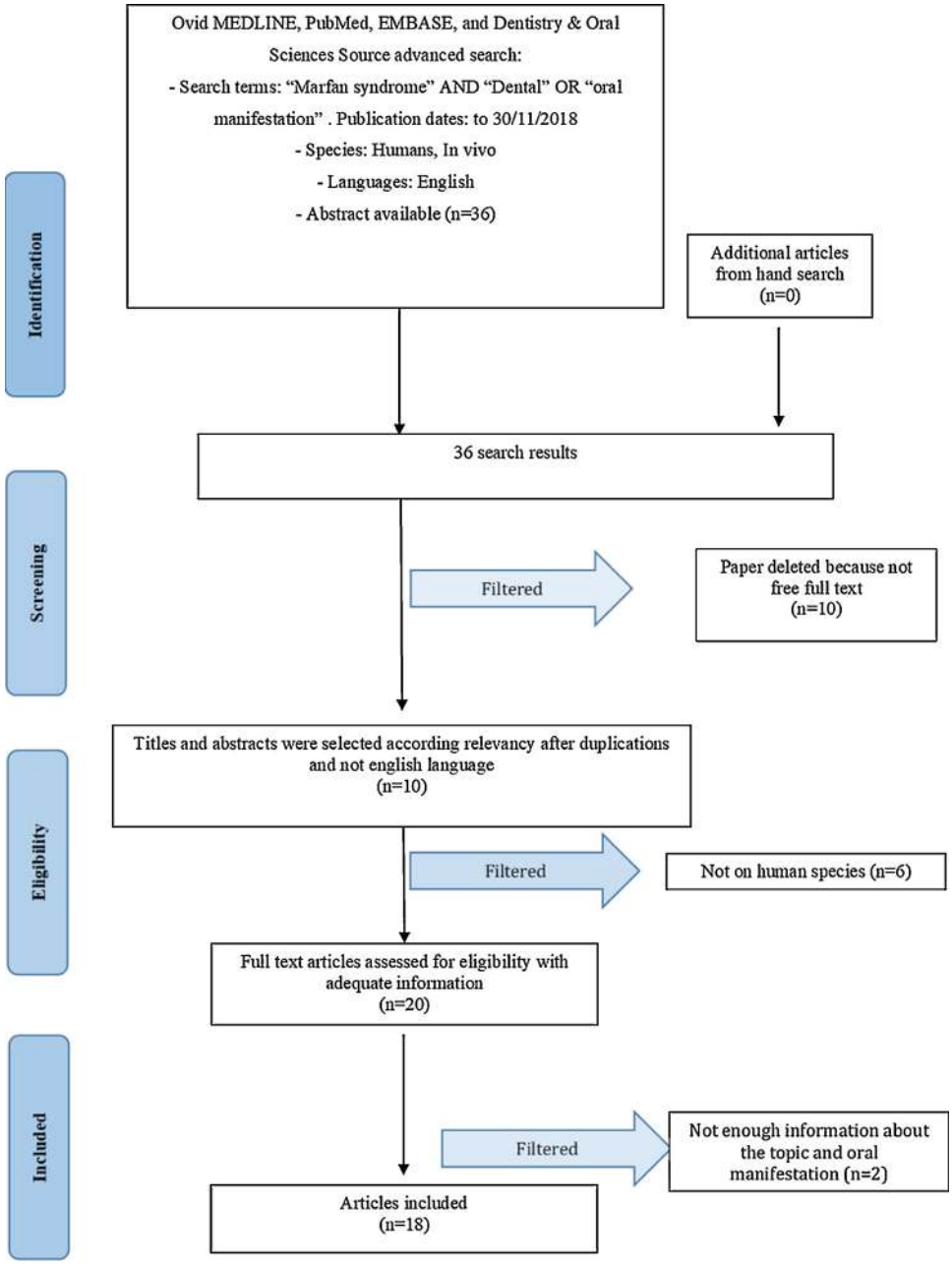

Fig. 1. PRISMA flow diagram.

4. Discussion

Several authors have studied the relationship between alterations of the TMJ and MFS, (Westling et al. (1998) studied in 76 patients how the craniofacial morphology, evaluated from dental casts and lateral cephalograms, differs in subject affected by MFS. They highlighted how high and narrow palatal vault and maxillary/mandibular retrognathy were strongly correlated to the syndrome. Westling et al. also studied TMJ complaint but without differentiating the type of problem and the kind of treatment.

Table 2
Most common signs and symptoms of patients with MFS.

RESPIRATORY SYSTEM	MUSCOLOSKELETAL DISORDERS	SKIN
• Wrist AND thumb signs • Pectus carenatum deformity • Hindfoot deformity • Penumothorax • Dural ectasia • Wrist OR thumb sign • Pectus excavatum or chest asymmetry	• Reduced upper segment / lower segment ratio AND increased arm span / height AND no severe scoliosis • Scoliosis or thoracolumbar kyphosis • Reduced elbow extension ≤170 degrees with full extension • Facial features (at least 3 of 5: dolicocephaly, enophthalmos, downslanting palpebral fissures, malar hypoplasia, mandibular retrognathia)	• Skin striae / striae atrophicase

Table 3
Studies and number of specimens.

Author	Title	Number of patients	Age and Sex
(Nally (1966)	The Marfan syndrome. Report of two cases.	2	18 M ; 17 F
(Kamen (1966)	Oral manifestations of Marfan's syndrome in twins.	2	8 F ;8 F
(Parker (1973)	Marfan's syndrome. A review of literature and case report.		
Hirota et al. (Sugiyama et al., 1988)	Systemic management of Marfan's syndrome during dental treatment: a case repor	1	26 M
(Westling et al. (1998)	Craniofacial manifestations in the Marfan syndrome: palatal dimensions and a comparative cephalometric analysis	76	–
(Straub et al. (2002)	Severe periodontitis in Marfan's syndrome: a case report.	1	M 41
De coster et al. (De Coster et al., 2002)	Oral manifestations of patients with Marfan syndrome: a case-control study.	23	9 – 53 years old 39.1 % F; 60.8 % M
(Bauss et al. (2004)	Temporomandibular joint dysfunction in Marfan syndrome.	350	225 F 125 M Mean age 41.3
(Bauss et al. (2008)	Prevalence of pulp calcifications in patients with Marfan syndrome	21	10 M 11 F Mean 38 yo (range17 – 57)
Utreja et al. (Utreja & Evans, 2009)	Marfan syndrome-an orthodontic perspective.	3	12 F ;13 M ;20 F
Morales-Chavez et al. (Morales-Chávez & Rodríguez-López, 2010)	Dental treatment of Marfan syndrome. With regard to a case	1	M 14
Bilodeau et al. (Bilodeau, 2010)	Retreatment of a patient with Marfan syndrome and severe root resorption.	1	28 F
(Raja et al. (2008)	Rutherfurd syndrome associated with Marfan syndrome.	–	–
(Ganesh et al. (2020)	Marfan syndrome: a case report	1	F 6
(Mallineni et al. (2012)	Concomitant occurrence of hypohyperdontia in a patient with Marfan syndrome: a review of the literature and report of a case	–	–
Bain et al. (Bain & Schafer, 2013)	Physical signs for the general dental practitioner. Case: Marfan's syndrome	–	–
Stufenbiel et al. (Staufenbiel, Hauschild et al., 2013)	Periodontal conditions in patients with Marfan syndrome - a multicenter case control study	51	30 F 21 M 40 ± 15 yo
(Tsang et al. (2013))	Marfan syndrome: a review of the literature and case report.	–	–
(Shiga et al. (2015)	Orthodontic Treatment and Long-Term Management of a Patient With Marfan Syndrome.	1	F 12
Franca et al. (França et al., 2016)	Oral management of Marfan syndrome: an overview and case report	1	M 11

Table 4
Typical oral manifestation reported in literature.

Dolichocephaly	Susceptibility to periodontal diseases (Image 1)
Oral calculus (Image 2 a, Image 2b)	Root deformities
Pulp anomalies	Mandibular retrognathia
Skeletal class II malocclusion	Maxilla retrognathia
Posterior crossbite	Abnormal dentine formation
Large positive overjet	Hypermobility at the temporomandiular joints
Malar hypoplasia	Severe maxillary crowding
Downslanting palpebral fissures	Enophthalmos
Maxillary constriction	High/deep arched palate

(Bauss et al. (2008) showed how the 56 % indicated dysfunctions and pain in the TMJ, and 25 % of patients were undergoing medical treatment for these manifestations. Furthermore, more than 10 % of the respondents in the study had undergone surgery for TMJ complaints. The reason for the increase in TMJ problems can be explained by hypermobility of the disc caused by the connective tissue disorder in MFS. Other studies have determined a high prevalence of symptoms of TMJ dysfunction in the population. For example, in a study conducted in Canada, 48.8 % of 1002 respondents gave at least one positive answer to the nine questions regarding dysfunction symptoms, whereas 13 % of respondents even indicated that they experienced pain in action or at rest (França et al., 2016). A research conducted in Germany reveals a frequency of TMJ complaints of about 35 % (Zwijnenburg, John, & Reiber, 1999). In different epidemiological studies, the frequency of symptoms is given in a range from 12 % to 59 %.

Barr et al. (Barr, 1979) showed a case of osteoarthrosis of the TMJ in a Marfan patient before the age of 30, bilateral TMJ clicking and capsular tenderness in other patients. While Nally et al. (Nally, 1966) observed unilateral TMJ subluxation in 1 case with MFS. It is therefore evident that TMJ dysfunction might represent an important aspect in MFS.

Few studies in the literature focus on the correlation between MFS and endodontic alterations. (De Coster et al. (2002) reported a prevalence of pulp stones equal to 21.7 % with a mean age of patients of 26 years, while the percentage reported by (Bauss et al. (2008) is 71.4 % with a mean age of 38 years. Both searches revealed an important correlation between prevalence of pulp stones and age, the discrepancy of data is probably attributable to the differences in age distribution between the two samples. Furthermore, Bauss et al. evaluated the presence of pulp stones by the use of radiographs.

Possible interpretation could be a genetically induced formation of pulp calcifications or a link with the vascular defects in MFS. It cannot be excluded that a genetic predisposition may also exist in MFS and that this syndrome might be associated with abnormal dentin formation, and so dental adhesion lack during restorative dentistry (De Stefano, 2019), resulting in an increased frequency of pulp calcifications. Additionally, a possible association with the vascular defects in MFS cannot be excluded. The connective tissue dysplasia underlying MFS leads to a weakened tunica media, which can cause dilatation or even dissection of the blood vessels, especially of the ascending aorta. Similar results were reported in a histological research of pulpal biopsies from subjects with MFS. The authors observed a separation of the tunica media of the arteries, a dilatation of blood vessels, and an augmentation in abnormal elastic fibers (Mommertz et al., 2008) this phenomenon could prevent pulpal blood supply. Avery (1981) has supposed that a decreased vascular flow in the pulp could result in pulpal respiratory depression leading to pathological mineralization of the the pulp. Moreover, these vascular deficiently might even lead to endothelial ruptures in pulp arterioles, causing haemorrhagic areas in the pulp (Cicciù, Beretta, Risitano, & Maiorana, 2008; De Coster et al., 2002; Temtamy, Nassar, Ismail, & Aboul-Ezz, 1989).

As regard Periodontal aspect despite in the literature many authors have reported severe periodontitis in patients with other heritable disease of connective tissue (for example Ehlers-Danlos syndrome) few researchers have studied the relationship between MFS and periodontal problems.

Straub et al. (2002) showed a case of MFS with severe periodontitis and evaluated this aspect. The study suggests that an abnormal constitution of the periodontal connective tissue could be the key factor that causes damage and degradation of the periodontal tissue, exposing to post-rehabilitative diseases, such as peri-implantitis (Staufenbiel et al., 2013b). In these studies, an increase in the mobility of dental elements is reported. Since the patient presented a severe form of periodontitis and therefore the destruction of the tooth support device, it is not possible to state that the increase in mobility is due to the structural alterations caused by Marfan but simply a sign of advanced periodontitis. Another consideration is that periodontitis has a multifactorial origin. In fact, it is necessary to consider the patient's specific risk factors such as obesity, diabetes or smoking. For this reason, it may be concluded that genetic predisposition, patient-specific periodontal risk factors independent from MFS may have been responsible for the severe periodontitis in the patient showed by Straub et al.

De Coster et al. (2002) in a case control study compared the dental and gingival health status of 23 patients with MFS and 69 controls. The researchers obtained a gingival index in the Marfan group: 1.9 vs. 1.0 in the control group. The gingival index used by De Coster et al. is not a reliable and reproducible method for the evaluation of the degree of inflammation; in fact, the evaluation is done only through the inspection. Furthermore, people with Marfan have a degree of crowding that is clearly superior to healthy subjects. This leads to greater difficulty in oral hygiene, a greater accumulation of bacteria and consequently to a greater degree of inflammation and presence of plaque. In conclusion, the degree of inflammation evaluated by De Coster et al. could be due to the overcrowding of dental elements and not to alteration caused by MFS.

Staufenbiel et al. (2013) in a case-control study selected 81 patients (51 with MFS and 31 control cases), performed a periodontal evaluation evaluating gingival recession, clinical attachment level, bleeding on probing, probing pocket depth. Finally, he evaluated DMFT (Decayed/Missed/Filled/Teeth) index. The conclusions of the study were that patients suffering from MFS do not show greater periodontal damage. The mutation associated with MFS does not predispose the periodontal ligament to a higher susceptibility to periodontitis (Ammash, Sundt, & Connolly, 2008). The MFS-associated mutation does not predispose to greater susceptibility to periodontitis.

Regarding the dental treatment of these patients, it is important to keep in mind the cardiac abnormalities typical of these patients. Ammash et al. (2008) and Dean et al. (Dean, 2002) report the dilatation of the ascending aorta as the most frequent. Therefore, in these patients, it is necessary to perform an antibiotic prophylaxis by means of the intake of 2 g of Amoxicillin one hour prior to the procedure or 600 mg of Clindamycin in case of allergic patients has to be carried out (Tornos, 2002). The use of local anaesthetics containing adrenaline should be reduced, because its use increases the cardiac output. The use of anaesthetics with no adrenaline are more suitable in patients with Marfan. Finally, constant monitoring of the patient is recommended by measuring blood pressure and aortic wave velocity (Hirota, Sugiyama, & Joh, 1986; Hirota, Sugiyama, Niwa, & Matsuura, 1993).

Patients with MFS have morphological features of the craniofacial district, widely reported in the literature (Images 1–3) (Docimo et al., 2013; Poole, 1989). These patients show dolichocephaly, retrognathia, long face, and a high and narrow palatal arch. Another characteristic initially associated with patients with MFS was mandibular prognathism, but recent studies do not confirm this association (Docimo et al., 2013; Poole, 1989). Poole et al. report how patients with MFS also have a short mandibular plane height and obtuse gonial height. Furthermore, De Coster et al. states that the growth of the cranial base sutures decreases their growth potential, thus increasing the anterior facial height. Thus, the elongated face characteristic typical of MFS patients is a product of this exceeding facial growth. As regard the periodontal ligament, no significant differences were found between affected and not affected patients (Cervino et al., 2019; Shiga, Ogawa,

Image 1. Periodontal disease in syndromic patient, complicated with benign neoformation. With permission from Dr. L. Fiorillo, 2018.

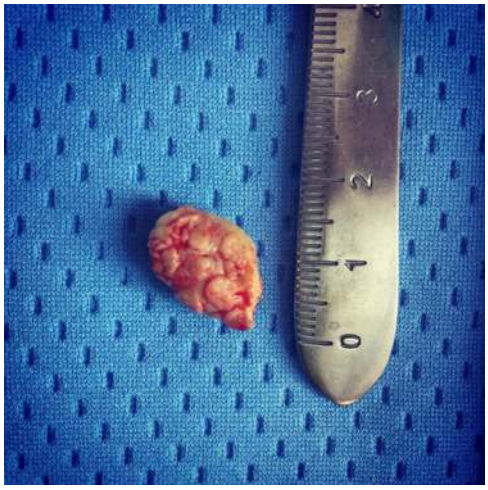

Image 2. Excision of sublingual salivary calculus in syndromic patient, excised calculus. Adapted from private practice. With permission from Prof. M. Cicciù, 2018.

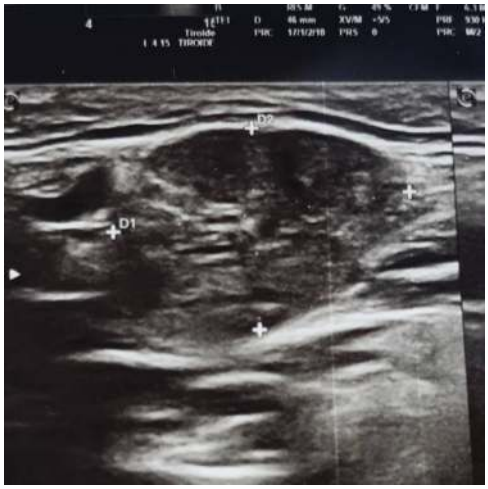

Image 3. Excision of sublingual salivary calculus in syndromic patient, ultrasound examination. Adapted from private practice. With permission from Prof. M. Cicciù, 2018.

Ekprachayakoon, & Moriyama, 2017). The approach by the medical staff to these patients is also important, and they could often go against social problems (Pingani et al., 2013).

5. Limitation

The main limitation of this review is represented by the fact that it has collected many clinical data, signs and symptoms, while equally

uneven among them. Not having obtained raw data or measurements, it does not make it possible to carry out a statistical analysis or a further analysis of the data. Further studies, and especially measurements on these patients, are needed to perform a statistical analysis and understand all the anomalies present in MFS patients. Knowing the measurements, it would also be possible to carry out a clinical diagnosis, once an anomaly confidence interval has been carried out and defined.

6. Conclusion

It has been possible to highlight and bring to light oral manifestations, which could also go unnoticed in front of an unskilled doctor in dentistry field. These oral manifestations could guide the clinician in a quicker diagnosis, even before performing instrumental diagnostic tests. Early diagnosis in syndromic patients is very important to immediately set up pharmacological therapy or other type of therapy. Sensitizing the audience towards the symptoms and signs present at the oral level is the ultimate goal of this study. The oral manifestations often show alterations that reflect the health status of the organism. Mucous, skin, lips, bone structures, or abnormalities affecting the teeth may be clear signs of a more complex medical situation. In the review, the authors have collected all the useful literature to date, which highlights anomalies in the dental field with this syndrome, the promotion of study and research for syndromes and rare diseases is a wish that the authors themselves propose. Returning to the semeiotics, therefore, with rapid and inexpensive exams, especially in countries where some diagnostic investigations may be impossible is essential.

Declaration of Competing Interest

The authors declare that there are no conflicts of interest.

Acknowledgments

We acknowledge Prof. M. Cicciù for the support in writing this work, and for providing useful material (such as images) to complete the review.

References

Ammash, N. M., Sundt, T. M., & Connolly, H. M. (2008). Marfan syndrome-diagnosis and management. *Current Problems in Cardiology, 33*, 7–39.
Avery, J. (1981). Repair potential of the pulp. *Journal of Endodontics, 7*, 205–212.
Bain, S. C., & Schafer, E. (2013). Physical signs for the general dental practitioner. Case: Marfan's syndrome. *Dental Update, 40*(9), 781.
Barr, M. (1979). Temporomandibular joint dysfunction and oro-facial pain. *Australian Dental Journal, 24*, 190–191.
Bauss, O., et al. (2004). Temporomandibular joint dysfunction in Marfan syndrome. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*.
Bauss, O., et al. (2008). Prevalence of pulp calcifications in patients with Marfan syndrome. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*.
Bilodeau, J. E. (2010). Retreatment of a patient with Marfan syndrome and severe root resorption. *American Journal of Orthodontics and Dentofacial Orthopedics, 137*(1).
Cervino, G., Terranova, A., Briguglio, F., De Stefano, R., Famà, F., D'Amico, C., et al. (2019). Diabetes oral health related quality of life and oral alterations. *BioMed Research International, 14* March.
Cicciù, M., Beretta, M., Risitano, G., & Maiorana, C. (2008). *Cemented-retained vs screw-retained implant restorations: An investigation on 1939 dental implants, 57*, 167–179 4.
De Coster, P. J., Martens, L. C., & De Paepe, A. (2002). Oral manifestations of patients with Marfan syndrome: A case-control study. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics, 93*, 564–572.
De Paepe, A., Devereux, R. B., Dietz, H. C., et al. (1996). Revised diagnostic criteria for the Marfan syndrome. *American Journal of Medical Genetics, 62*, 417–426.
De Stefano, R. (2019). Psychological factors in dental patient care: Odontophobia. *Medicina, 55*(10), 678.
Dean, J. C. (2002). Management of Marfan syndrome. *Heart, 88*, 97–103.
Dietz, H. C., Cutting, G. R., Pyeritz, R. E., et al. (1991). Marfan syndrome caused by a recurrent de novo missense mutation in the fibrillin gene. *Nature, 352*, 337–339.
Docimo, R. M. P., D'Auria, F., Grego, S., Costacurta, M., Perugia, C., & Chiariello, L. (2013). Association between oro-facial defects and systemic alterations in children affected by Marfan syndrome. *Journal of Clinical and Diagnostic Research: JCDR, 7*, 700–703.
França, E. C., Abreu, L. G., Paiva, S. M., Drummond, A. F., & Cortes, M. E. (2016). Oral management of Marfan syndrome: An overview and case report. *General Dentistry* November/December.
Ganesh, R., Vijayakumar, R., & Selvakumar, H. (2020). Marfan syndrome: A case report. *Case Reports in Dentistry, 2012*. https://doi.org/10.1155/2012/595343 Article ID 595343, 4 pages.
Gray, J. R., & Davies, S. J. (1996). Marfan syndrome. *Journal of Medical Genetics, 33*, 403–408.
Gray, J. R., Bridges, A. B., Faed, M. J., et al. (1994). Ascertainment and severity of Marfan syndrome in a Scottish population. *Journal of Medical Genetics, 31*, 51–54.
Hirota, Y., Sugiyama, K., & Joh, S. (1986). An echocardiographic study of patients with cardiovascular disease during dental treatment using local anesthesia. *Journal of Oral and Maxillofacial Surgery: Official Journal of the American Association of Oral and Maxillofacial Surgeons, 44*, 116–121.
Hirota, Y., Sugiyama, K., Niwa, H., & Matsuura, H. (1993). Systemic management of Marfan's syndrome during dental treatment: A case report. *Anesthesia & Pain Control in Dentistry, 2*, 162–170.
Kamen, S. (1966). Oral manifestations of Marfan's syndrome in twins. *Oral Surgery, Oral Medicine, and Oral Pathology, 21*(1), 19–26.
Loeys, B. L., Dietz, H. C., Braveman, A. C., et al. (2010). The revised ghent nosology for the Marfan syndrome. *Journal of Medical Genetics, 47*(7), 476–485.
Mallineni, S. K., Jayaraman, J., Yiu, C. K., & King, N. M. (2012). Concomitant occurrence of hypohyperdontia in a patient with Marfan syndrome: A review of the literature and report of a case. *Journal of Investigative and Clinical Dentistry, 3*(4), 253–257. https://doi.org/10.1111/j.2041-1626.2012.00148.x.
McKusick, V. A. (1955). Heritable disorders of connective tissue. III. The Marfan syndrome. *Journal of Chronic Diseases, 2*(6), 609–644.
Mommertz, G., Sigala, F., Langer, S., Koeppel, T. A., Mess, W. H., Schurink, G. W., et al. (2008). Thoracoabdominal aortic aneurysm repair in patients with Marfan syndrome. *European Journal of Vascular and Endovascular Surgery: the Official Journal of the European Society for Vascular Surgery, 35*, 181–186.
Morales-Chávez, M. C., & Rodríguez-López, M. V. (2010). Dental treatment of Marfan syndrome. With regard to a case. *Medicina Oral, Patologia Oral Y Cirugia Bucal, 15*(6), e859–e862.
Nally, F. F. (1966). The Marfan syndrome. *Oral Surgery, Oral Medicine, and Oral Pathology, 22*, 715–724.
Parker, S. (1973). Marfan's syndrome. A review of literature and case report. *Journal - Oklahoma State Dental Association, 64*(2), 15–16 No abstract available.
Pingani, L., Fiorillo, A., Luciano, M., Catellani, S., Vinci, V., Ferrari, S., et al. (2013). Who cares for it? How to provide psychosocial interventions in the community. *The International Journal of Social Psychiatry, 59*(7), 701–705.
Poole, A. E. (1989). Craniofacial aspects of the Marfan syndrome. *Birth Defects Original Article Series, 25*(4), 73–81.
Raja, T. A., Albadri, S., & Hood, C. (2008). Rutherfurd syndrome associated with Marfan syndrome. *European Archives of Paediatric Dentistry: Official Journal of the European Academy of Paediatric Dentistry, 9*(3), 138–141.
Shiga, M., Ogawa, T., Ekprachayakoon, I., & Moriyama, K. (2015). Orthodontic treatment and long-term management of a patient with Marfan syndrome. *The Cleft Palate-Craniofacial Journal*.
Shiga, M., Ogawa, T., Ekprachayakoon, I., & Moriyama, K. (2017). Orthodontic treatment and long-term management of a patient with Marfan syndrome. *The Cleft Palate-craniofacial Journal: Official Publication of the American Cleft Palate-Craniofacial Association, 54*(3), 358–367.
Staufenbiel, I., et al. (2013). Periodontal conditions in patients with Marfan syndrome - a multicenter case control study. *BMC Oral Health*.
Staufenbiel, I., Hauschild, C., Kahl-Nieke, B., Vahle-Hinz, E., von Kodolitsch, Y., Berner, M., et al. (2013). Periodontal conditions in patients with Marfan syndrome—A multicenter case control study. *BMC Oral Health, 13*, 59. http://www.biomedcentral.com/1472-6831/13/592013.
Straub, A. M., et al. (2002). Severe periodontitis in Marfan's syndrome: A case report. *Journal of Periodontology*.
Sugiyama, K., Hirota, Y., Shibutani, T., Niwa, H., Idoji, Y., & Matsuura, H. (1988). Systemic management of a patient with Marfan's syndrome during dental treatment. *Osaka Daigaku Shigaku Zasshi] the Journal of Osaka University Dental Society, 33*(2), 496–504 Japanese.
Temtamy, S. A., Nassar, A. M., Ismail, S. R., & Aboul-Ezz, E. H. A. (1989). Orodental and ultrastructural studies of pulp and gingiva in Marfan syndrome. *American Journal of Medical Genetics, 32*, 242.
Tornos, P. (2002). Infective endocarditis: Are we managing our patients well? *Revista Espanola de Cardiologia, 55*, 789–790.
Tsang, A. K., Taverne, A., & Holcombe, T. (2013). Marfan syndrome: A review of the literature and case report. *Special Care in Dentistry: Official Publication of the American Association of Hospital Dentists, the Academy of Dentistry for the Handicapped, and the American Society for Geriatric Dentistry, 33*(5), 248–254. https://doi.org/10.1111/scd.12018 Epub 2013 Feb 28. Review.
Utreja, A., & Evans, C. A. (2009). Marfan syndrome-an orthodontic perspective. *The Angle Orthodontist, 79*(2), https://doi.org/10.2319/112707-558.1.
Westling, L., Mohlin, B., & Bresin, A. (1998). Craniofacial manifestations in the Marfan syndrome: Palatal dimensions and a comparative cephalometric analysis. *Journal of Craniofacial Genetics and Developmental Biology, 18*, 211–218.
Zwijnenburg, A. J., John, M., & Reiber, T. (1999). Funktioneller Behandlungsbedarf in Leipzig und Halle—erste Ergebnisse. *Deutsche Zahnarztliche Zeitschrift, 54*, 409–411.