Periodontal and Oral Health Status of People with Cystic Fibrosis: A Systematic Review

Abstract

Introduction and Objectives

People with Cystic Fibrosis (PWCF) may be presumed to be at lower risk of periodontal disease due to long term antibiotic use but this has not been comprehensively investigated. The oral hygiene and periodontal status of individuals with Cystic Fibrosis in comparison to the general population has not been well established.

The objective of this systematic review was to critically evaluate the literature on periodontal and oral hygiene status in people with cystic fibrosis (CF), to see if this group are at increased risk of periodontal disease (gingivitis or periodontitis).

Data Sources

5 databases were searched: Scopus, MEDLINE via Ebsco, Embase, Cochrane and Web of Science.

Study Selection

The search resulted in 614 publications from databases. One more publication was identified by searching bibliographies. 13 studies were included in the qualitative analysis.

Conclusions

The majority of studies showed better oral hygiene, with lower levels of gingivitis and plaque among people with Cystic Fibrosis (PWCF) than controls. Interestingly, despite this, many studies showed that individuals with Cystic Fibrosis had higher levels of dental calculus. Three studies found there was no difference in Oral Hygiene between people with CF and controls. One study found that people with CF aged between 6 and 9.5 years had increased levels of clinical gingivitis, and one study showed that people with CF with gingivitis had more bleeding on probing than people without CF. The vast majority of people with CF examined were children- only five studies included people over the age of 18, and only one of these looked exclusively at adults. There is a need for further study into the periodontal health of individuals with Cystic Fibrosis- particularly those over the age of 18.

Clinical Significance

Neither the NICE pathway on CF (2017) or the CF Trust's "Standards for the Clinical Care" (2011) make any reference to the oral health of PWCF, despite their increasing life expectancy. Studies have suggested that the oral cavity, and specifically the subgingival region, may act as a reservoir of bacteria (e.g. *pseudomonas* aeruginosa) which may colonise or recolonise the lungs [1, 2]. Therefore, it may be prudent to recommend regular periodontal disease screening for PWCF to facilitate early detection, especially if they are found to be at an increased risk.

Introduction

Cystic fibrosis (CF) is the most common lethal genetic disease in white populations [3]. It was first recognised as a separate disease entity in 1938 when Dorothy Andersen's study distinguished a disease of mucus plugging of the glandular ducts from that of coeliac disease [4]. The genetic basis for this disease is a well-characterized, severe monogenic recessive disorder, found mainly in Caucasian populations of European ancestry, which arises from mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene on chromosome 7 [5]. More than 1500 CFTR mutations have been identified, but the functional importance of only a small number is known [3]. ΔF508 is the most common CF mutation worldwide, accounting for approximately 66% of the cases of CF [6]. The mutations of the CFTR epithelial chloride channel dehydrates secretions in the airways, the pancreatic ducts, and in other organ systems which results in progressive organ damage. The main impact can be seen in the Respiratory/Pulmonary System (e.g. repeated infective pulmonary exacerbations, bronchiectasis, pneumothorax, haemoptysis), Pancreatic Disease (e.g. pancreatic insufficiency, Cystic Fibrosis Related Diabetes), Hepatobiliary Disease (e.g. Liver disease, Cirrhosis) , Gastrointestinal Tract (e.g. GORD, malabsorption of fat), Kidney Disease (including chronic renal insufficiency), Genitourinary (including male infertility), Bone Disease (e.g. osteopenia, osteoporosis) and Cutaneous Diseases (including urticaria and vasculitis) [7-9]. The manifestations of CF can impact significantly on quality of life, which tends to deteriorate as the severity of the disease increases [10].

Epidemiology

As of 2018, over 10,500 people in the UK have cystic fibrosis; it is estimated that 1 in every 2,500 babies are born with CF [11]. The Republic of Ireland has the highest incidence of CF worldwide, with approximately 1478 people with CF living in Ireland [12].

Life expectancy

CF was previously seen as a disease of childhood with many individuals dying before their teen years. However, due to pharmaceutical therapy advances in recent decades, there has been a great improvement in survival of individuals with CF [13, 14].

In 2018, 4314 people on the UK registry were under 18 (43.8%) and 5544 (56.2%) were aged 18 and over, i.e. the majority of people with CF today are adults. Keogh's analysis of UK CF

Registry data in 2018 concluded that over 50% of babies born with CF can expect to survive into at least their fifth decade [14]. Similarly, in the U.S. the median predicted survival age of those born in 2016 was 47.7 years (95 percent confidence interval: 45.6-51.1 years) as compared to 41.2 in 2015 (95 percent confidence interval: 38.2-43.9) [15]. This is comparable to the Republic of Ireland, where median age of survival is 44.4 years, an increase from 36.6 years in 2008 [12].

Oral manifestations

Oral manifestations of cystic fibrosis were studied at least as far back as 1960 when Zegarelli discussed the tooth discolouration seen in children with cystic fibrosis secondary to tetracycline staining [16]. Other reviews [17-19] have investigated the literature regarding dental caries prevalence, enamel defects, and gingival health status amongst people with CF. Of these, Pawlaczyk-Kamienska carried out the most thorough investigation of the periodontium. However, the review looked at the literature from 1997 to 2018 and so only focused on six studies [20-26] Some of the co-morbidities mentioned earlier can put patients at higher risk of dental disease – e.g. GORD can lead to dental erosion [27], uncontrolled diabetes is a risk factor for periodontal disease [28, 29], osteoporosis is also considered a risk factor for periodontal disease [30, 31]. However, the link between CF as a separate disease entity and it's link with oral health has not been studied in great depth. It has also been suggested that the oral cavity could be a reservoir for *pseudomonas aeruginosa,* chronic colonisation of which can cause lung destruction leading to death [1].

Due to the increasing life expectancy of individuals with CF, it is timely to review the evidence regarding the oral manifestations of CF. The aim of this paper was to carry out a systematic review investigating the literature surrounding oral hygiene status, specifically levels of plaque and calculus present, and periodontal health in people with CF.

Review:

Material and methods

Protocol and registration

This study was conducted following the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines adapted by Liberati [32] (see Appendix 1).

The primary aim of this systematic review was to answer the following PICO question: Are PWCF at higher risk of gingivitis and periodontitis?

Population: Adults (aged 18 years and above) and children (aged under 18 years)
Intervention: Diagnosed with Cystic Fibrosis
Comparison: People without Cystic Fibrosis
Outcome: Increased risk of having periodontal diseases (gingivitis or periodontitis)

The secondary aims were to establish if PWCF have higher levels of plaque or calculus than people without CF.

Eligibility Criteria

The results obtained from the literature search were filtered, according to these inclusion and exclusion criteria:

Inclusion criteria

- Individuals had a diagnosis of cystic fibrosis
- Studies that were of case–control or cohort or cross-sectional designs. Studies were included if they directly compared the association between cystic fibrosis and periodontal disease (gingivitis or periodontitis)
- Studies on human subjects published in English language
- Studies from 1960 to the present day

Exclusion criteria

- Studies on animal subjects
- Studies not in English
- Review articles and case series were excluded
- Studies based on self-reported diagnosis of periodontal conditions were also excluded

Information Sources

The searches were conducted in the following electronic databases: Scopus, MEDLINE via Ebsco, Embase, Cochrane and Web of Science. The bibliographies of relevant articles were hand- searched to identify any additional studies that may have not been captured by the digital searches.

Search Strategy and Selection Criteria

The following search terms were used "Cystic Fibrosis" [MeSH] AND "periodontal disease"[MeSH] or "periodontitis"[MeSH] OR "periodont*" OR "gingivitis"[MeSH] OR "gingiv*" OR "oral health"[MeSH] OR "oral hygiene '[MeSH] OR "dental plaque" [MeSH] . The last search was run on the 21st April 2020. An example of a search strategy in included in appendix 2.

Two investigators (N.C., F.O'L.) independently reviewed titles and abstracts to determine eligibility for inclusion. Full articles were obtained for the identified titles and those which met the selection criteria were included. Differences of opinion of the two investigators about study eligibility were resolved by discussion with the third author (M.H.).

Results

Study Selection

The search resulted in 614 publications from Scopus, MEDLINE via Ebsco, Embase, Cochrane and Web of Science databases. One more publication was identified by searching bibliographies. Based on information provided in the study title and abstract, 533 publications were excluded from the review (Figure 1). Fourteen publications met the eligibility criteria and were included in the qualitative systematic review. *Note: 2 of these*

publications[22, 33] referred to the same study and are therefore considered together, i.e. there are thirteen studies included in the qualitative analysis.

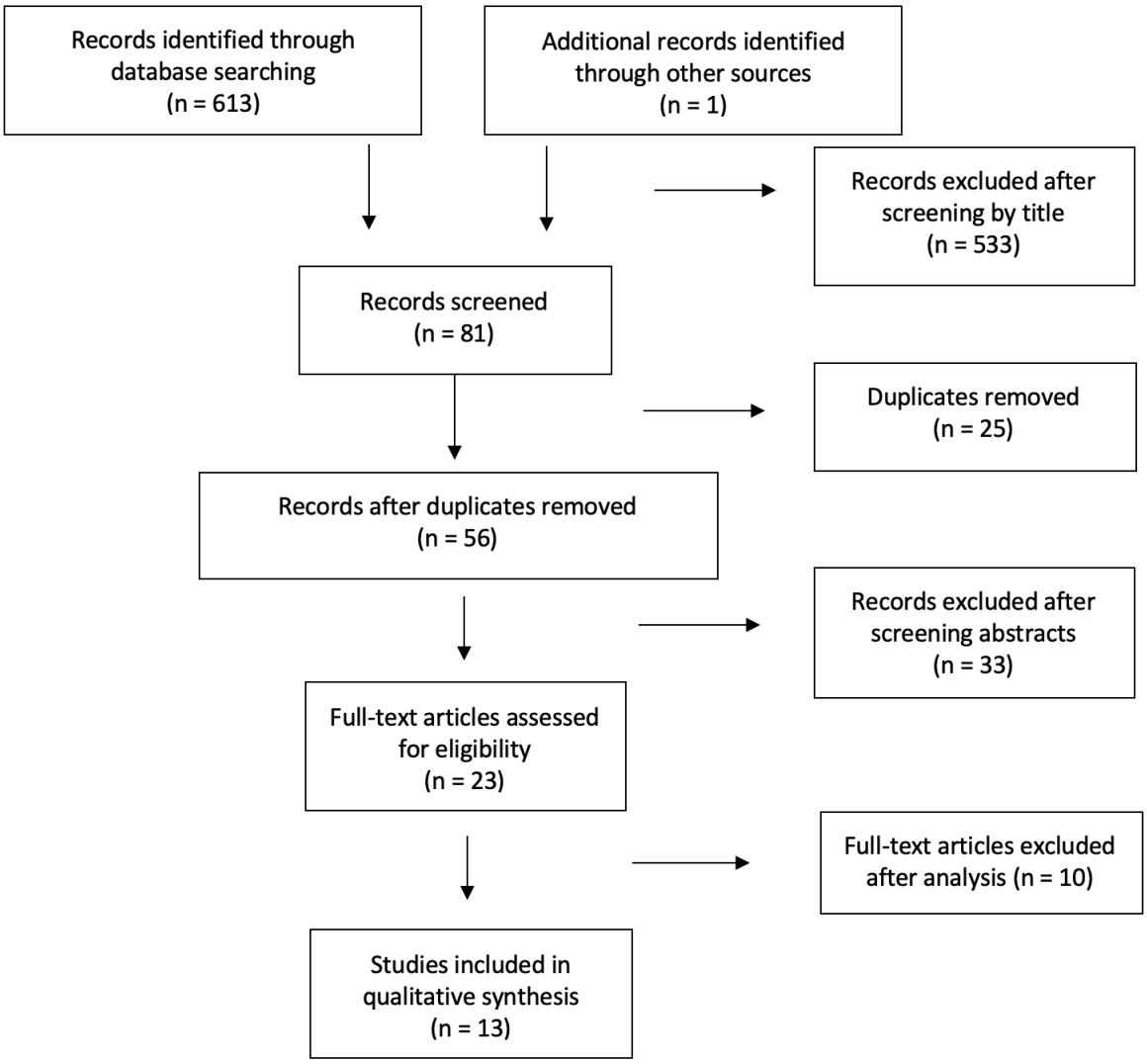

Figure 1: Flow Chart Indicating the Number of Records Identified and Included in Systematic Review on Oral Hygiene and Periodontal Status in People with Cystic Fibrosis

Study Characteristics

Data was abstracted from each publication (Table 1). The majority of studies were carried out in Europe- in Belgium, Poland, Italy, Turkey and the United Kingdom. 2 studies were carried out in the United States of America[34, 35] . The earliest study considered was from

1976 [36] and the most recent was published in 2020 [37] Figure 2 shows the number of publications per year.

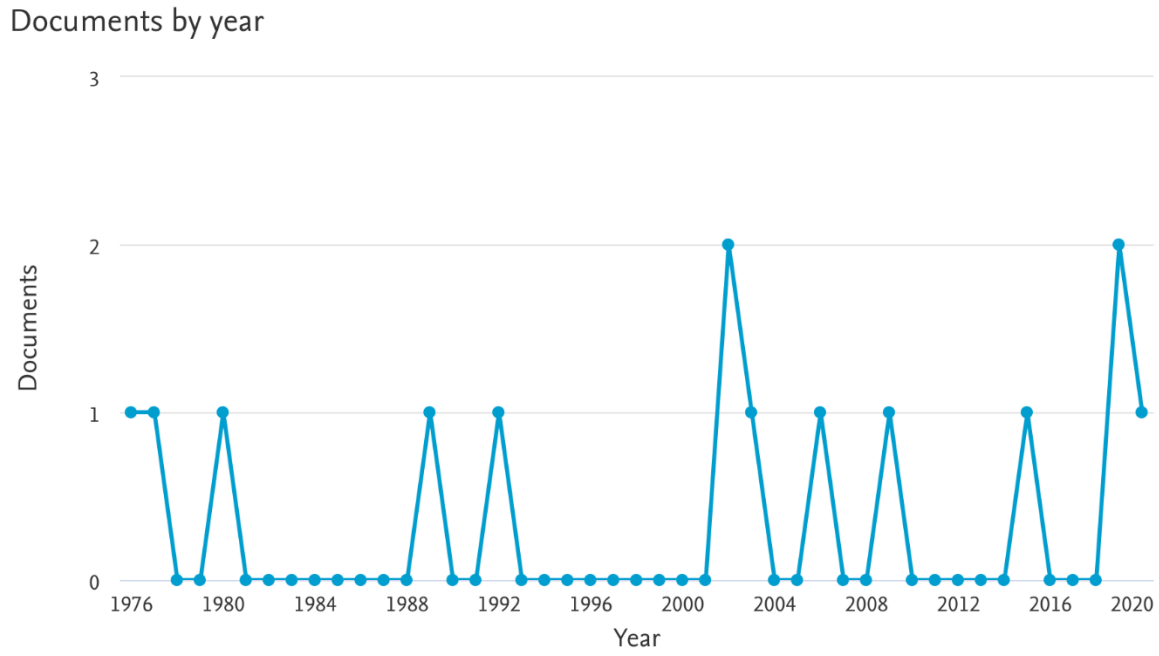

Figure 2: The relevant articles by year. Note there was maximum 2 per year since 1976. Note: The 2 articles in 2002 related to 1 study and so are considered as one in the review below[22, 33]

A total of 792 people with CF were examined. Seven studies considered people both over and under the age of 18 [20-23, 25, 35, 38].The remaining seven studies concentrated exclusively on children under the age of 18. No study considered adults exclusively. Sample sizes of the CF group ranged from 20 [25, 34] to 163[39]. Eleven of the studies were case-control studies, and the remaining two were cross-sectional.

Twelve of the studies measured Oral Hygiene; of these, ten used a WHO recommended index such as the Simplified Greene-Vermillion Index or Oral Hygiene Index of Silness Loe [20-23, 25, 34, 36, 38-40]. Eleven assessed the gingival status of the study subjects; of these – three used the CPI/CPITN index [24, 26, 34], four used the Gingival Index of Loe and Silness [37, 39, 40], four measured the presence of absence of gingival bleeding on probing [21-23, 41]and one noted subjective gingival inflammation based on clinical photographs and gingival attachment levels by millimeter probing [35]. Pawlaczyk-Kamienska et al. and Duruel et al. also measured the periodontal pocketing depth of the

individuals examined. The type of study, population, age of individuals examined and methodology used in each study is tabulated in Table 1.

Author	Type of Study	Study Population	Age group	Oral Hygiene Assessment	Gingival Assessment
Jagels and Sweeney 1976	Case-Control Study	Case: 63 Control: 56	5 – 12 years	Simplified Oral Hygiene Index/Greene-Vermillion Index	No data recorded
Blacharsh, C., 1977	Case-Control Study	Case: 42 Control: 10	Case: 4 – 25 years	Presence of plaque assessed after chewing disclosing tablet. Calculus noted as none, mild, or moderate	Gingival inflammation noted "by observing photos" Gingival attachment levels measured using "calibrated millimetre probe"
Kinirons, M. J. (1989)	Case-Control Study	Case: 131 Control: 131	3 – 17 years	Loe plaque Index Presence of absence of dental calculus	Gingival Index of Loe and Silness
Kinirons, M.J. (1992)	Case-Control Study	Case: 163 Control: 163	4 – 18 years	Loe plaque Index	Gingival Index of Loe and Silness

Martens, Luc & Aps, Johan & Maele, Georges. (2001)	Case-Control Study	Case: 37 Control: 37	6 – 38 years	Dental plaque recorded when visible - for every tooth and every surface	Bleeding of the gingiva on “gentle probing”
Aps, J.K.M. et al (2002a) **Aps, J.K.M. et al (2002b)**	Case-Control Study	Case: 42 (homozygotes) 48 (heterozygotes) Control: 62	Case: 16.2 ± 8.1 years (homozygotes) 29.5 ± 15.9 (heterozygotes) Control: 19.9 ± 11.5 years	Simplified Loe Index (dental plaque, dental calculus)	Presence or absence of gingival bleeding
Narang, A. et al (2003)	Case-Control Study	Case: 74 Control: 106	Case: 2.5 – 16.5 years Control: 3.0 – 16.5 years	No Oral Hygiene Index used	CPI – only checked either healthy, probing of calculus, no pocketing
Dabrowska E., et al. (2006)	Case-Control Study	Case: 20 Control:20	2.5 – 24 years	Greene-Vermillion Index	No data recorded
Ferrazzano, G.F., et al. (2009)	Case-Control Study	Case: 54 Control: 101	7 – 12 years	No data recorded	CPITN on index teeth

Peker, S. et al, 2015	Case-Control Study	Case: 35 Control: 12	Case: 3 – 12 years Control: 3 – 12	Oral Hygiene Index of Silness Loe	No data recorded
Pawlaczyk-Kamienska, T., et al, 2019	Cross-sectional Study	22	29.43±6.78 years	Plaque Index of Silness Loe	Gingival Index of Loe and Silness Periodontal Pocketing Depth
Abu-Zahra et al (2019)	Cross sectional	20	6 – 18 years	Simplified Greene-Vermillion Index	CPITN
Duruel et al, 2020	Case-control study	Case: 41 Control: 39	Case: 10.09 ± 3.18 Control: 9.41 ± 2.20	Plaque Index of Silness Loe	Gingival index of Loe Probing depth Bleeding on Probing

Table 1: Tabulated Results showing the Author, Year of Study, Number of Individuals Examined, Age Group, Oral Hygiene and gingival assessment technique used (if any)

Of the thirteen studies, four demonstrated lower levels of plaque in the CF group compared to the control group [25, 35, 39, 40]. Four studies concluded that there were lower levels of gingivitis in the CF group compared to the control group [26, 35, 39, 40]. Similarly, Abu-Zahra et al. concluded that individuals with CF demonstrated less gingivitis than the national average. Five studies found there was no significant difference in Oral Hygiene between people with CF and controls [20-23, 37]. Despite this, some studies showed that individuals with Cystic Fibrosis had higher levels of dental calculus compared to a control group [24, 35, 40].

One study found that people with CF aged between 6 and 9.5 years had increased levels of clinical gingivitis compared with a control group [24]and another study found that there was

more bleeding on probing in people with CF who had gingivitis compared to people without CF who had gingivitis [41] . One study [38] found that although there was moderate to severe plaque accumulation on the dentition of 63% of the subjects with CF, there was no patient with severe gingivitis or periodontal pocketing depths greater than 4mm. Jagels and Sweeney found there was “no significant difference” in Oral Hygiene Index between 2 groups but that there was a “pronounced trend” toward lower scores for the patients with CF. These results are summarised in Table 2 .

Study	**Oral Hygiene Status**	**Gingival Status**	**Conclusion**
Jagels and Sweeney, (1976)	“Extremely low” levels of calculus in 2 groups “no significant difference” in Oral Hygiene Index between 2 groups “pronounced trend” toward lower scores for the patients with CF.	No data recorded	Better Oral Hygiene in Cystic Fibrosis Group

Blacharsh, C., (1977)	Plaque accumulation: CF group: 74% Control group: 100% "Several patients with cystic fibrosis had a slight amount of calculus, primarily about the mandibular anterior teeth. Calculus was not evident in the siblings in the control group."	Mild gingivitis-periodontitis, CF group: 83.33% Control group: 100%	CF group had lower levels of plaque and gingivitis/periodontitis but higher levels of calculus
Kinirons, M. J. (1989)	Mean Plaque score: CF group: 0.53 Control: 0.77 CF group: 40.5% had calculus Control group: 9.2% had calculus	Mean Gingival score: CF group: 0.44 Control: 0.70	CF group has significantly less plaque and gingivitis CF group had significantly more calculus

Kinirons, M.J. (1992)	Median plaque index scores: CF group: 0.58 - 0.77 Control group: 0.80-0.82 These differences were largest in individuals with a “high” percentage of antibiotic usage	Median gingival index scores: CF group: 0.42 - 0.67 Control group: 0.64 – 0.74	CF subjects had better gingival health and less plaque than the control group. This was particularly notable in children who received antibiotic therapy in the previous month
Martens, Luc & Aps, Johan & Maele, Georges. (2001)	Plaque Levels: No significant difference between CF patients and controls	Gingival bleeding: CF patients had less gingival bleeding than controls; (this was, however, not significantly different)	No significant difference in oral hygiene levels or gingival bleeding between CF group and controls

Aps, J.K.M. et al (2002a) **Aps, J.K.M. et al (2002b)**	Plaque Levels: CF homozygotes: 3.62±5.6 CF heterozygotes: 2.63 ± 4.44 Control group: 2.85±3.87 Calculus levels *CF homozygotes:* 1.93±3.05 CF heterozygotes: 2.77±3.82 Control group: 2.10±3.46	Gingival bleeding: CF homozygotes:0.24±0.79 CF heterozygotes: 2.35±5.15 Control group: 1.15±2.38	CF groups had higher levels of dental plaque, CF homozygotes had the lowest levels of plaque. However, there was no significant difference in levels of plaque or calculus. CF homozygotes had less gingival bleeding, CF heterozygotes had highest levels of gingival bleeding
Narang, A. et al (2003)	No data recorded	No difference between case and control group in <6years, or greater than 9.5 years 6-9.5 years : Slightly higher levels of calculus and slightly lower numbers of healthy sextants (not statistically significant)	Periodontal health of CF patients aged 6 – 9.5 years was worse than the periodontal health of the non-CF group with the CF group In all other age groups, there was no statistical difference between them

Dabrowska E., et al. (2006)	Plaque score CF group: 1.83 Control Group: 3.11	No data recorded	Control groups had slightly higher levels of plaque when compared to the CF groups
Ferrazzano, G.F., et al. (2009)	No data recorded	<u>"Good periodontal status"</u> 62.4% of CF patients 48.6% of control group. <u>BOP</u> 27.1% of CF patients 41.4% of control group. <u>Calculus</u> 10.5% of CF group and 10% of control group had calculus.	Healthier periodontium in CF patients compared to control group, similar levels of calculus
Peker, S. et al, (2015)	Plaque index CF: 1.43 ± 0.22 Control: 1.44 ± 0.22	No data recorded	Similar Oral Hygiene Levels in case and control group

Abu-Zahra, R., et al, (2019)	Plaque score was 1.02 ± 0.42, which is considered fair oral hygiene	75% of CF patients had gingivitis, lower than national mean of 85%	CF children had fair oral hygiene that did not differ from the national mean of 1.42. There was lower levels of gingivitis in the CF patients compared to the national mean
Pawlaczyk-Kamienska, T., et al. (2019)	Plaque Index Mild dental plaque accumulation (PLI=0.1–1.0): 36% Moderate (PLI=1.1–2.0): 45% Severe (PLI=2.1–3.0): 18%	GI index No gingivitis (GI <0.1): 27% Mild inflammation (GI 0.1 - 1.0): 68% Moderate inflammation (GI=1.0–2.0): 45%. No patient showed severe gingivitis (GI≥2.1). No patient with periodontal pocket >4 mm was recorded	"Despite the widespread presence of bacterial dental deposits in cystic fibrosis patients, none of them had clinical symptoms of periodontal disease"

Duruel et al, 2020	Gingivitis: 46% of CF group 58% of non-CF group Groups were subdivided into people who had gingivitis (GI³1) or were "periodontally healthy" (GI<1) Plaque Index: CF with gingivitis: 1.53 ± 0.56 CF who were "periodontally healthy": 0.83 ± 0.32 Non-CF with gingivitis: 1.71 ± 0.18 Non-CF who were "periodontally healthy": 0.91 ± 0.34	GI Index: CF with gingivitis: 1.39 ± 0.36 CF who were "periodontally healthy": 0.70 ± 0.14 Non-CF with gingivitis: 1.22 ± 0.26 Non-CF who were "periodontally healthy": 0.49 ± 0.29 Pocketing depth (mm): CF with gingivitis: 1.69 ± 0.29 CF who were "periodontally healthy": 1.41 ± 0.25 Non-CF with gingivitis: 1.71 ± 0.18 Non-CF who were "periodontally healthy": 1.44 ± 0.16 BOP: CF with gingivitis: 83.36%	No significant difference (*p>0.05)* between mean values of pocketing depths between CF and non-CF subjects. GI values of subjects without gingivitis were higher in CF group than non-CF subjects (*p* = 0.035) BOP percentages of CF subjects with gingivitis were significantly higher than non-CF subjects with gingivitis (*p*=0.017*)*

	CF who were “periodontally healthy”: 5.27% Non-CF with gingivitis: 57.23% Non-CF who were “periodontally healthy”: 9.93%

Table 2: Data abstracted from studies regarding Oral Hygiene and Periodontal Status in People with Cystic Fibrosis

Risk of bias

The risk of bias was assessed by a number of headings (see Table 3). These were adapted from previous reviews by Chi et al, Pawlacyzk-Kamienska et al and the Cochrane Collaboration guideline adapted by Higgins et al [17, 19, 42]. No study was deemed to be at low risk of bias. Studies were not blinded but this could be impractical/unreasonable due to People with Cystic Fibrosis 'complex medical history and physical appearance, as mentioned by Jagels and Sweeney (1976). The majority of studies only had one examiner. All bar two of the studies adopted a validated OH/periodontal status measure. Most of the studies age and sex-matched their cases with controls, however there was differentiation in further criteria- e.g. Jagels and Sweeney (1976) and Blacharsh (1977) employed siblings as controls and Narang et al. (2003) employed other individuals with respiratory diseases as controls. As siblings could be carriers of CF, and people with respiratory diseases may have a similar therapeutic history in terms of antibiotics and inhalers etc., there is potentially a limitation compared to if healthy controls were used.

Study	Included a control group (Selection bias)	Justified selection of control group	Use a valid statistical approach	Validated OH/Periodontal Assessment Measure	Examiner Number	Examiner(s) B (Performance
Jagels and Sweeney, (1976)	Yes	Yes-but controls were sibling, therefore may have been carriers of CF gene	No	Yes	1	Yes but admit tell if people h not

Blacharsh, C., (1977)	Yes	Yes-but controls were siblings, therefore may have been carriers of CF gene	No	No	Unknown	No
Kinirons, M. J. (1989)	Yes	Yes	Yes	Yes	1	Unknown
Kinirons, M.J. (1992)	Yes	Yes	Yes	Yes	1	Unknown
Martens, Luc & Aps, Johan & Maele, Georges. (2001)	Yes	Yes- but just age matched	Yes	No	1	No

Aps, J.K.M. et al (2002a) **Aps, J.K.M. et al (2002b)**	Yes	No	Yes	Yes	1	No
Narang, A. et al (2003)	Yes	Yes-but control group included individuals with other respiratory conditions	Yes	Yes	1	No
Dabrowska E., et al. (2006)	Yes	Yes	No	Yes	Unknown	Unknown
Ferrazzano, G.F., et al. (2009)	Yes	Yes	No	Yes	2	Unknown
Peker, S. et al, (2015)	Yes	No	Yes	Yes	1	No

Abu-Zahra, R., et al, (2019)	No	N/A	Yes	Yes	2	No
Pawlaczyk-Kamienska, T., et al. (2019)	No	N/A	Yes	Yes	2	No
Duruel et al (2020)	Yes	No	Yes	Yes	1	No

Table 3: Risk of bias assessment

Discussion

The above results show that there is lack of agreement regarding the oral hygiene levels and periodontal status of people with Cystic Fibrosis compared to a healthy control. Some studies indicate that they are at reduced risk of gingivitis, whereas others have not found any such link. As periodontitis is much more common in adults than in children [43, 44], it is impossible to extrapolate the adult with CF's risk of periodontal disease based on these results alone.

Some studies have shown an increased accumulation of dental calculus and it has been hypothesised that this is due to increased calcium and phosphate levels in the saliva of these individuals[40, 45]. Three studies showed that PWCF had higher levels of dental calculus compared to a control group [24, 35, 40] and, as calculus can sometimes promote gingival recession and also periodontal attachment loss[46], its increased presence could be seen as a potential risk factor for the progression of periodontal disease. Although dental plaque is well known to induce gingivitis, which can sometimes lead to periodontitis [47], it is interesting to note that in the most recent study of Pawlacyzk-Kamienska (2019), that although there was a significant amount of plaque accumulated, none of the subjects demonstrated clinical signs of periodontitis (defined in this study as periodontal pocket depths greater than 4mm).

None of the studies looked exclusively at adults with Cystic Fibrosis, although this is a group that is increasing in size due to the increased life expectancy. Currently, neither the NICE pathway on Cystic Fibrosis [48] or the Cystic Fibrosis Trust's "Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK (Second Edition)" [49] make any reference to the oral health of individuals with Cystic Fibrosis. Therefore, it may be prudent to carry out a study into the oral health of adults with CF.

There are new treatment modalities for people with Cystic Fibrosis, including CFTR regulator modulators such as ivacaftor, lumacaftor/ivacaftor (Orkambi®, Vertex Pharmaceuticals, Boston, Massachusetts, USA), and tezacaftor-ivacaftor (Symdeko®, Vertex Pharmaceuticals, Boston, Massachusetts, USA) [50]. The first of these, Ivacaftor (Kalydeco, ®, Vertex Pharmaceuticals, Boston, Massachusetts, USA) was only introduced in 2012 but the use of CFTR modulators is now widespread. The vast majority of studies on oral health in CF were

carried out prior to this. It would be interesting to see what effect, if any, these drugs would have on the periodontium.

In terms of study design, the majority of the studies used WHO recommended indices of measurement and this would be recommended in order to make studies reproducible in future. It is important that examiner/s are calibrated to reduce the risk of introducing bias and that this is noted in the study.

The small sample size of some of these studies could potentially reduce the power of the study and increase the margin of error; therefore it would be recommended to carry out a power calculation before carrying out any clinical studies in future. All of the studies were carried out in one geographical area and this may skew the results, therefore, it may be wise to consider a multi-site study in future.

Limitations

Studies not written in English were excluded, and there may be studies done in other languages that are relevant.

Conclusion

There is lack of data available as to whether an individual with Cystic Fibrosis is at higher risk of periodontal disease.

There is a need for high quality reproducible studies to investigate the oral hygiene levels and periodontal status of people with CF, especially adults, in order to ascertain their risk of periodontal disease.

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