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Prevalence of Periodontitis in Erectile Dysfunction Patients

Hirzi Kamaludin^{a*}, Jamie Chin Kok Kwong^b, Lili Zuryani Marmuji^c,
Khamiza Zainol Abidin^a

^aPeriodontic Specialty Clinic, Gunung Rapat Dental Clinic,
Ministry of Health Malaysia, 31350 Ipoh, Perak, Malaysia

^bUrology Clinic, Department of Surgery, Raja Permaisuri Bainun
Hospital, 30450 Ipoh, Perak, Malaysia

^cFamily Medicine Specialty Clinic, Gunung Rapat Health Clinic,
Ministry of Health Malaysia, 31350 Ipoh, Perak, Malaysia

*Corresponding author: hirzi.bkam@gmail.com

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ABSTRACT

Erectile dysfunction (ED) and periodontitis have common risk factors, such as diabetes mellitus and tobacco smoking. Multiple reports are available in regard to the association between ED and chronic periodontitis (CP). The study aimed to determine the association of ED and CP in selected Malaysian population. In this study, 74 patients (mean age = 52.4 ± 10.9 years old) diagnosed with ED, from scores via the International Index of Erectile Function (IIEF-5) questionnaire, were included. ED severity was classified as mild, mild to moderate, moderate, and severe. Periodontal condition was recorded using basic periodontal examination (BPE) method, of which scores of 0, 1, 2, and 3 were associated with having no periodontitis while a score of 4 was considered to have periodontitis. There are 40 (54.1%) subjects found to have periodontitis and the association of ED and periodontitis showed a moderate positive degree of correlation, $\rho = 0.487$ ($p < 0.001$). The percentage of subjects having periodontitis indicated an increasing trend with the severity of ED; from 19.0% (mild ED), 54.2% (mild to moderate ED), 75.0% (moderate ED), to 84.6% (severe ED). A greater degree of correlation was noted between dental scaling experience and ED, $\rho = 0.635$ ($p < 0.001$). Binomial logistic regression had shown no other co-morbidities and factors were affecting this relation. There seemed to be an association between ED and periodontitis existing in these selected Malaysian populations.

Keywords: Basic periodontal examination (BPE); chronic periodontitis; dental scaling; erectile dysfunction; International Index of Erectile Function (IIEF-5)

INTRODUCTION

Periodontitis is defined as the inflammation of the gingiva extending to the adjacent attachment apparatus, which can be described by the destruction of both the periodontal ligaments and the supporting alveolar bone and may cause the loss of

functioning dentition if left untreated. Oral health-related quality of life (OHRQoL) in patients suffering from periodontitis are low when compared to periodontally healthy subjects (Durham *et al.*, 2013). In Malaysia, the burden of periodontal diseases is high, as 94% of adults are experiencing some form of the disease while 18.2% of the population

is suffering from severe form of chronic periodontitis (CP) (Mohd Dom *et al.*, 2016).

Erectile dysfunction (ED) is defined as the persistent inability to achieve or maintain a penile erection sufficient for satisfactory sexual performance. ED patients are having significantly diminished health-related quality of life (HRQoL) (Litwin *et al.*, 1998). Most men who develop ED have underlying vascular changes usually from complications of atherosclerosis, giving rise to vasculogenic ED due to impairment of smooth muscle relaxation, occlusion of cavernosal arteries, or both (Carneiro *et al.*, 2010). CP is proposed to contribute to the aetiology of ED via an increase of serum C-reactive protein (CRP) and tumour necrosis factor- α (TNF- α) (Zuo *et al.*, 2011). CRP and TNF- α inhibit the expression of endothelial nitric oxide synthase (eNOS) in endothelial cells and reducing its biological activity (Venugopal *et al.*, 2002; Carneiro *et al.*, 2010) sequentially decreasing the production of nitric oxide (NO) and in turn decreasing cyclic guanosine monophosphate (cGMP) levels, resulting in the inhibition of endothelial dependent corpus cavernosum smooth muscle relaxation (Burnett, 2006).

There are studies done all over the world positively linking CP as the causal factor for ED, either done as a population-based study or as a more focused single centre study (Kellesarian *et al.*, 2018). Thus, the prevalence of CP in severe ED subjects varies but can be up to 81.8% (Sharma *et al.*, 2011). Other related research showed that subjects with ED are more likely to have CP, with an OR of up to 2.28 (Liu *et al.*, 2017).

To the best of our knowledge, no study had been done in Malaysia which relates the link of periodontitis to ED. Thus, the aim of this study was to find out whether the positive association between ED and periodontitis applies to the Malaysian population. Meanwhile, the objectives were to quantify the prevalence of periodontitis in patients diagnosed with ED, and to assess the correlation between the severities of periodontitis with the severity of ED.

MATERIALS AND METHODS

Study Population

This study was designed as a cross-sectional observational study, measuring the number of patients having periodontitis while having ED at the same point of time without any future review. In this study, 74 male patients were included; 36 subjects were obtained from the outpatient of the Urology Clinic, Department of Surgery in a government hospital and 38 subjects were acquired from screenings done at the Family Medicine Specialty Clinic in a government health clinic. Both centres are located in Malaysia.

Ethical approval was attained from the Medical Research and Ethics Committee (MREC), Ministry of Health (MOH), Malaysia [Reference no.: KKM/NIHSEC/P20-406(12)] and the study was registered with the National Medical Research Register (NMRR), Malaysia (Registration no.: NMRR-19-3936-52463). The study was conducted from July 2020 to December 2020. Each subject was ensured to be informed verbally, and consequently written informed consent was taken for participation in this study.

The inclusion criteria were ED-diagnosed patients presenting to the Urology Unit and Family Medicine Specialty Clinic, aged between 30 years old to 70 years old, and had 10 teeth or more in the mouth. Whereas the exclusion criteria were patients currently taking nitroglycerin for myocardial infarction, taking calcium channel blockers medications for hypertension, taking systemic antibiotics within the last six months, as well as having undergone non-invasive and invasive periodontal therapy within the last 12 months.

Sample Size Calculation

The sample size calculation using the Cochran formula when the finite population size and the estimated population proportion were known had determined that 74 subjects

were required to estimate a large population with a 95% confidence interval ($\alpha = 0.05$) based on the accumulative annual attendance of ED patients in the primary and tertiary settings, of which only 99 patients had attended both units annually complaining of ED symptoms (Uakarn *et al.*, 2021). Meanwhile, the population proportion of 74% of ED patients suffering from periodontitis was shown by the latest case-control study in a European population (Martín *et al.*, 2018). Afterwards, patients were selected by consecutive sampling method to allow for some refusal in participation.

International Index of Erectile Function (IIEF-5) Questionnaire

International Index of Erectile Function (IIEF-5) questionnaire was chosen because it was easy to administer, simple and short while requiring only 10 min to 15 min to be filled by respondents. It contained five questions rated on a 5-point scale from 1 to 5. The total score was calculated by adding all the answer scores together, and patients would be categorised as having ED if their IIEF-5 score was 21 points and below. Patients would not have ED if their IIEF-5 score was 22 points and above (Rosen *et al.*, 2002). Patients that scored between 22 and 25 points would be excluded from this study. The scores are represented in Table 1.

Table 1 IIEF-5 questionnaire scores in relation to ED severity

IIEF-5 scores	ED severity
≥ 22	No
17 to 21	Mild
12 to 16	Mild to moderate
8 to 11	Moderate
1 to 7	Severe

The IIEF-5 questionnaire had been validated for the local Malaysian population (Quek *et al.*, 2002). This questionnaire is useful to evaluate ED symptoms, and to examine prevalence and incidence as well. It is also

useful as an initial screening instrument in general practice settings, and in epidemiological studies where many people are assessed (Rhoden *et al.*, 2002).

Study Procedure

ED-diagnosed subjects were screened for their periodontal health on site using the basic periodontal examination (BPE), following the community periodontal index (CPI) protocol (Cutress *et al.*, 1987). BPE is a method for periodontal screening and recording, using Ivoclar Vivadent Community Periodontal Index of Treatment Needs C (CPITN C) round handle probe (product number #718283) that has a 0.5 mm ball tip and is colour-coded black from 3.5 mm to 5.5 mm and 7.5 mm to 9.5 mm. The patient's mouth was divided into six sextants (maxillary right, anterior and left; mandibular left, anterior and right). Each tooth was probed by moving the CPITN C probe inside the gingiva around the entire circumference of the tooth to examine at least six sites (mesiolabial, midlabial, distolabial, and the corresponding lingual or palatal areas). The highest score was then recorded in each sextant, and out of the six readings, only the single highest score was considered as the BPE score, as shown in Table 2. Measures of gingival recession, tooth mobility, the intensity of inflammation, and precise identification of pocket depths or differentiation between supra- and sub-gingival calculus were not included in this procedure.

BPE scores of 0, 1, 2, and 3 were considered as having no periodontitis and 4 was considered as having periodontitis, as defined by the Global Burden of Disease (GBD) 2010 Study (Marcenes *et al.*, 2013).

Statistical Analysis

The results were analysed using a statistical programme (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA). A descriptive analysis was conducted for the gathered data. Shapiro-Wilk tests

Table 2 The BPE coding

Code	Findings
0	In the deepest sulcus of the sextant, the probe's coloured band remains completely visible. Gingival tissue is healthy and does not bleed on gentle probing. No calculus or defective margins are found.
1	The coloured band of the probe remains completely visible in the deepest sulcus of the sextant. No calculus or defective margins are found, but some bleeding after gentle probing is detected.
2	The probe's coloured band is still completely visible, but there is bleeding on probing, and supragingival and subgingival calculus and/or defective margins are found.
3	The coloured band is partially submerged.
4	The coloured band completely disappears in the pocket, indicating a depth of greater than 5.5 mm.

were performed to assess whether they were distributed normally. As it was found that the variables were not normally distributed, a non-parametric test (Fisher's exact test) was used with a p -value of < 0.05 considered to be statistically significant. Ordinal or nominal variables were analysed for frequency and percentage. The association between the severity of periodontitis and the severity of ED was presented as percentages in a bar chart, to allow greater appreciation of its trend. Correlations were tested using Spearman's rho (ρ). Logistic regression tests were also performed on the dependent variable against all the other independent variables collected in this study.

RESULTS

Demographic Data

The demographic characteristics are presented in Table 3. There were 74 male subjects with a mean age of 52.4 ± 10.9 years old, ranging from 30 years old to 70 years old, selected from 85 patients that were approached. Six subjects were excluded due to the exclusion criteria, while the remaining were edentulous. The largest number of subjects belong to the 51 years old to 60 years old group of Malay ethnicities, suffering from hypertension, and smoke 1 pack or less cigarette. Majority of the subjects had never done dental scaling before in their life and out of these, some did not know anything in regard to the nature of dental scaling. Meanwhile, the highest

percentage of ED subjects belong to the mild to moderate ED group.

The percentage of subjects having periodontitis against their ED severity are presented in Table 4 and Fig. 1.

The percentage of subjects having periodontitis indicated an increasing trend with the severity of ED; from 19.0% (mild ED), 54.2% (mild to moderate ED), 75.0% (moderate ED), to 84.6% (severe ED). Fisher's exact test was $p < 0.001$ and Spearman's correlation (ρ) was 0.487 ($p < 0.001$) indicating that there is a positive and moderate correlation. This signifies that as the ED progresses in severity, periodontitis also becomes more severe in form.

Fig. 2 shows a graph of the percentage of subjects' dental scaling experience against their ED severity. There is an increasing trend noted in the percentage of subjects that had never done dental scaling with the severity of ED. Spearman's correlation (ρ) was 0.635 ($p < 0.001$) indicating that there is a positive and moderate correlation signifying that as the ED progresses in severity, there are increased likelihood that the subjects never had any dental scaling treatment performed on them.

Logistics regression tests were conducted on the variables of study site, age groups, race, smoking status as well as pre-existing co-morbidities namely diabetes mellitus, hypertension, ischaemic heart disease, and benign prostatic hyperplasia. Of note, ED subjects in the age group of 51 years

Table 3 Demographic characteristics of subjects

Group	Sub-group	Total <i>n</i> (100%)
<i>n</i>		74
Age (years old)		52.4±10.9
30–40		13 (17.6%)
41–50		16 (21.6%)
51–60		25 (33.8%)
61–70		20 (27.0%)
Age range (years old)		30–70
Race	Malay	41 (55.4%)
	Chinese	16 (21.6%)
	Indian	16 (21.6%)
	Others	1 (1.4%)
Medical history	Diabetes	27 (36.5%)
	Hypertension	35 (47.3%)
	IHD	7 (9.5%)
	BPH	15 (20.3%)
	Others	10 (13.5%)
Smoking history	Never	20 (27.0%)
	Stopped	22 (29.7%)
	Smoke ≤ 1 pack	30 (40.5%)
	Smoke > 1 to 2 packs	2 (2.7%)
Last dental visit for scaling	≤ 1 year	9 (12.2%)
	> 1 year	30 (40.5%)
	Never	35 (47.3%)
ED severity	Mild	21 (28.4%)
	Mild to moderate	24 (32.4%)
	Moderate	16 (21.6%)
	Severe	13 (17.6%)

Note: IHD = Ischaemic heart disease; BPH = Benign prostatic hyperplasia

Table 4 Percentage of subjects having periodontitis against ED severity

IIEF-5 severity	Presence of CP				Total	
	Yes		No		<i>n</i>	%
	<i>n</i>	%	<i>n</i>	%		
Mild ED	4	5.4	17	23.0	21	28.4
Mild to moderate ED	13	17.6	11	14.9	24	32.4
Moderate ED	12	30.0	4	11.8	16	21.6
Severe ED	11	14.9	2	2.7	13	17.6
Total	40	54.1	34	45.9	74	100.0

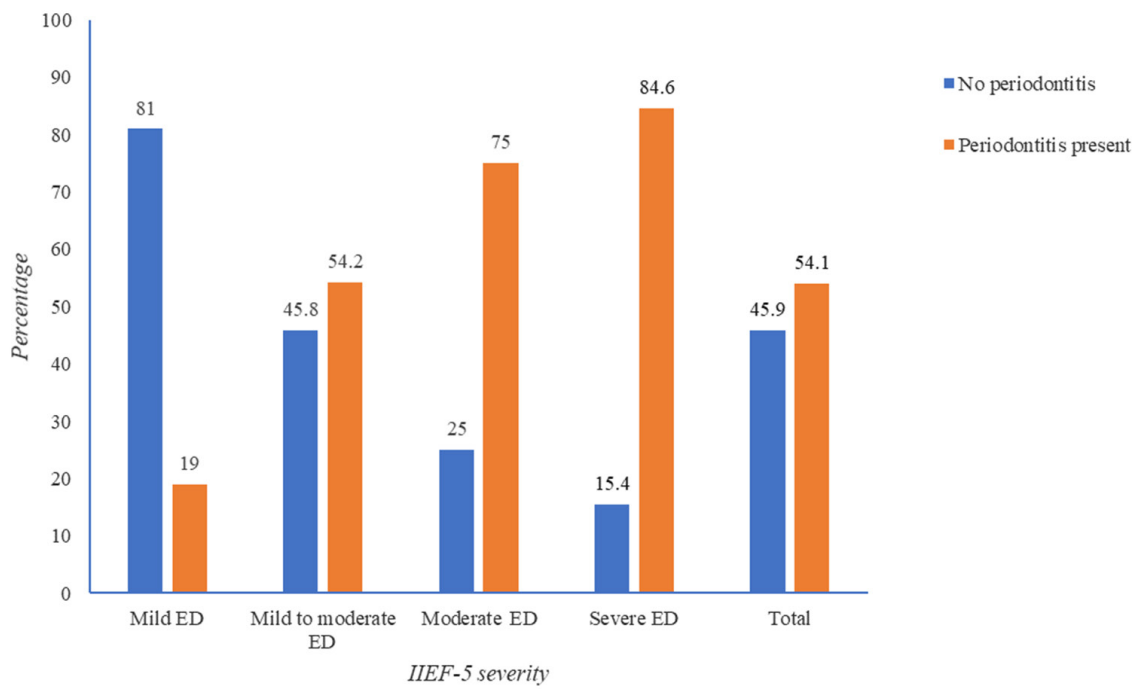


Fig. 1 Percentage of subjects having periodontitis against ED severity.

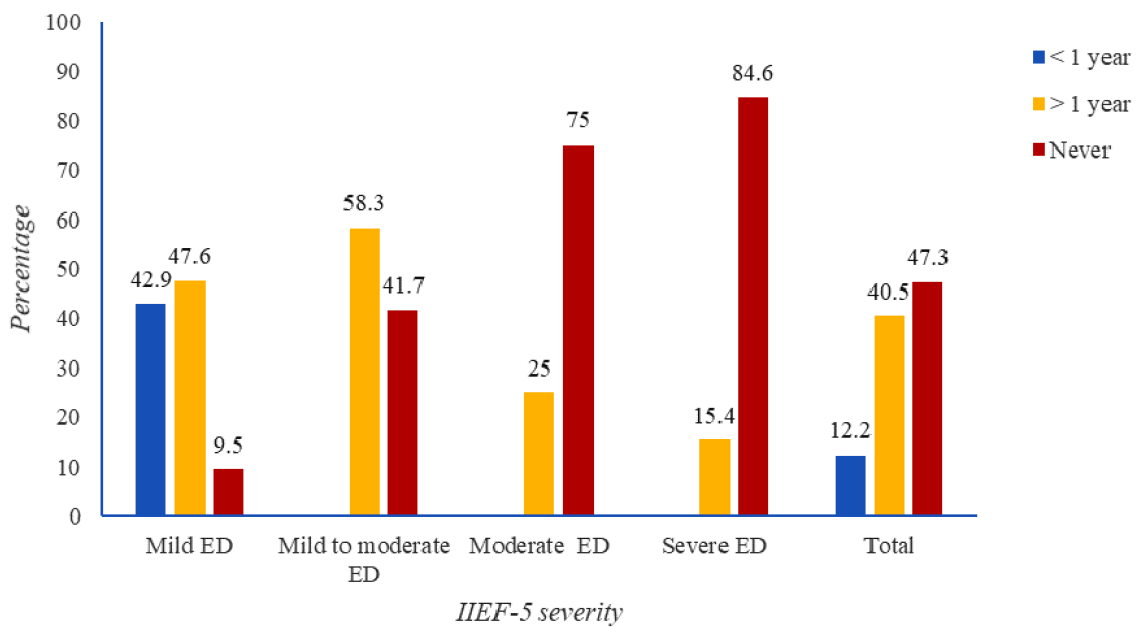


Fig. 2 Percentage of subjects' dental scaling experience against ED severity.

old to 60 years old had an odds ratio of 2.5 of having periodontitis and then the odds ratio declined to 1.5 in the 61 years old to 70 years old ED subjects. Nevertheless, none of these results are statistically significant. It is worthy to note that ED subjects with diabetes mellitus and whom currently smoke in this study have a low odds ratio to suffer periodontitis.

DISCUSSION

To the best of our knowledge, the present study was the first conducted on the Malaysian population and had presented an apparent link between periodontitis and ED, and between dental scaling experience and ED. The mean age in this study is 52.4 ± 10.9 years old, concurring with a study that found age above 50 years old is the single most significant risk factor for ED (Tan *et al.*, 2003) with its OR for the 50 years old to 60 years old age groups being similar to this study.

The percentage distribution of the subjects in this study by race were almost similar to the general population distribution in Malaysia as a whole, according to a 2010 census (DOSM, 2011). There were 20.3% Indians subjects in this study as compared to 7.3% in the general population. This notable increase may be explained by the tendency of the Indian population to have ED, having an adjusted odds ratio of 1.93 as compared to the Malay, Chinese and others in the population (Tan *et al.*, 2003). Furthermore, previous studies have found that the prevalence of ED in the Malaysian population based on race were similar (Nordin *et al.*, 2019), closely resembling the prevalence of ED based on race of the present study. Therefore, the results of this study could be generalised to the whole Malaysian population if there was an increase in the sample size and greater number of sites were recruited. A previous cross-sectional study of CP in ED (Sharma *et al.*, 2011) which had similar methodology as ours except that it had verified the ED with

penile coloured Doppler ultrasound, also had similar observations.

This study had included diabetics, hypertensive, ischaemic heart disease and smoking subjects, plus patients with benign prostatic hyperplasia. In order to detect a difference with a higher precision, which is 95% confidence interval, a larger sample size was required and therefore to omit these diseases' known risk factors would result in the inability of this study to be completed. As there were only 99 ED patients seen annually, the calculated sample size of 74 patients is already a huge sum as it is.

Common established risk factors of periodontal disease and ED are diabetes, and tobacco smoking. Poorly controlled diabetes mellitus type 1 or type 2 is a risk factor for periodontal disease, associated with an increase in susceptibility to oral infections including periodontal diseases, as well as its more rapid progression (Meng, 2007). Likewise, diabetic men have an increased risk of developing ED with a high prevalence rate, of up to 90% (Sasaki *et al.*, 2005). However, many well-controlled diabetics can maintain periodontal health and respond well to periodontal therapy (Pucher & Stewart, 2004), which may result in a lower rate of ED prevalence (Wessells *et al.*, 2011). Conversely, tobacco smoking has a destructive effect on periodontal tissues and increases the rate of periodontal disease progression (Zini *et al.*, 2011) via the modification of host response to the challenge of bacterial plaque (Ozçaka *et al.*, 2011). Similarly, smoking causes oxidative stress and is accepted as a risk factor in the development of ED (Peluffo *et al.*, 2009), with smokers being at an increased risk of ED at all points of time compared to those who have never smoked (Bacon *et al.*, 2006). Despite this, improvements in erections after smoking cessation were reported to happen albeit in a different time frame depending on the previous smoking duration (Pourmand *et al.*, 2004). On the other hand, this study did not find any correlation between diabetes and smoking with ED or periodontitis, which

may be explained by the small number of subjects participating in this study causing a loss of sensitivity and may be rectified by increasing the number of subjects in future studies.

The overall prevalence of ED in this study differs from a previous study which had seen a larger proportion of ED subjects having the severe form of ED (Nordin *et al.*, 2019), whereas the bulk of the subjects in this study were found to have mild and mild to moderate ED. This may be explained by the fact that the previous study was conducted in a larger urban centre with a higher cost of living, thus possibly translating to the higher stress experienced by subjects.

Evidence had shown that chronic periodontal disease can be associated with ED (Zadik *et al.*, 2009), via the impairment of nitric oxide (NO) production by vascular endothelium. A study demonstrated this relationship by experimentally inducing periodontitis in rats, which led to impaired penile erection and reduced endothelial nitric oxide synthase (eNOS) expression (Zuo *et al.*, 2011). In essence, C-reactive protein (CRP) and tumour necrosis factor- α (TNF- α) are two important cytokines and inflammatory markers, inhibiting the endothelial cells' production of eNOS, in turn causing its biological activity to be diminished (Venugopal *et al.*, 2002). Superoxide resulting from the oxidative stress may interact with NO ensuing the reduction of its activity (Jeremy *et al.*, 1999). All of this denotes that there is a chronic and low intensity inflammation arising from systemic response initiated by periodontitis, subsequently causing a deterioration in endothelium-dependent vascular dilatation (Villar *et al.*, 2006).

This may explain the stronger degree of correlation between previous scaling experience and IIEF-5 severity ($\rho = 0.635$) in contrast with the correlation of the severity of CP against the severity of ED ($\rho = 0.487$). Bacterial load inside the periodontal pockets as a result of failure in obtaining regular

professional dental treatments such as scaling may have caused the worsening of ED symptoms in a linear progression. Whereas studies had shown that the amount of dental plaque and calculus may not result in periodontal disease progression in a linear fashion, as it also depends on the variability of microbe-induced host immune response (Pan *et al.*, 2019). Proper immune response will dominate if local tissue stimulation and host immune response are balanced (Moutsopoulos & Konkel, 2018). Periodontal tissue destruction is initiated if the pathogenicity of the local microbial population is elevated by the colonisation of keystone pathogens causing over-activation of the host immune response via pro-inflammatory cytokines, such as interleukins families and tumour necrosis factors (Pan *et al.*, 2019), affecting its homeostatic balance.

Moreover, periodontal treatment has been suggested to improve endothelial dysfunction (Tonetti *et al.*, 2007), but evidence had suggested that this may be confined to the population with severe CP (Amar *et al.*, 2003). Periodontal bacteria, *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*, with their lipopolysaccharides (LPS)-mediated effects have been shown to cause endothelial dysfunction (Kebschull *et al.*, 2010) via penetration into the vascular endothelium.

On the other hand, it is imperative to note that there is a high number of subjects (47.3%) that had never sought dental treatment, especially routine maintenance such as dental scaling. A substantial number of subjects also did not seek dental scaling treatment annually. It is generally accepted that females displayed lower periodontal disease prevalence and severity than males (Furuta *et al.*, 2011), crediting to the fact that the female gender has a better oral health behaviour and hygiene status, even though dental fear is more prevalent and more severe amongst them. Thus, it was suggested that males' attitude is to be blamed for their shortfall in dental care

utilisation, as attitude affects behaviour directly (Skaret *et al.*, 2003). Consequently, it can be hypothesised that with routine dental treatment such as scaling, the association between periodontitis and ED would be weakened, as periodontal disease is eliminated.

During the duration of this study, there were notable instances of five ED patients that were excluded as they were edentulous, while at the same time were reported to be unresponsive to the prescribed oral phosphodiesterase-5 (PDE-5) inhibitors. All five patients were informed of having extracted all of their teeth due to mobility in a short period of time (within a few years) when they were relatively young (around their late 30s and early 40s). These appeared to be classic signs and symptoms of a severe form of periodontitis. Hence, it can be postulated that some sort of unknown causative pathways is responsible, whether it be their own hosts' uncontrolled pro-inflammatory immune responses or because of the virulence characteristics of existing periodontal pathogens present, which had possibly damaged their endothelial cells permanently. A possible link is via genetic predisposition to overexpression of reduced nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NOX) enzymes causing excessive reactive oxygen species (ROS) production, consequently initiating endothelial cells damage with fibrosis (Joshiyura *et al.*, 2015). Increased NOX can also cause decreased NADPH (reduced NADP⁺) availability, lessening NO production, as NADPH acts as one of the many co-enzymes in the conversion of L-arginine into NO.

Study Limitations

One of the limitations in this study was the use of BPE scoring to determine the presence of periodontitis. It was done to simplify the method of data collection due to logistics constraints and the limited availability of funds. Even so, many epidemiological studies in this field employ this particular

method. The preferable method would be a full periodontal charting of each subject as well as radiological examinations. In this study, there was no information regarding subjects' household income level, educational level, activity level, employment status as well as mental health status being recorded and analysed, as it was suggested that these factors may contribute to the occurrence of ED as well. Thus, it would be ideal if these factors were included in future research so that a holistic analysis may be performed. Future research should be directed to the outcomes of the severity of vasculogenic ED when periodontal therapy is performed in a randomised controlled trial set-up. This can establish a causative link between these two diseases.

CONCLUSION

There seemed to be an association between periodontitis and ED in the selected Malaysian population, as evident by the high prevalence, the rising trend of periodontitis incidence plus never having dental scaling done, with the severity of ED. Thus, it is advisable to enquire periodontitis patients regarding the possibility of having ED by utilising the validated and simple IIEF-5 questionnaire, and vice versa, and then to refer accordingly for the benefit of patients.

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