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Examination of the Relation Between Periodontal Disease Parameters and Chronic Obstructive Pulmonary Disease: A Case-Control Study in Greek Adults

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Abstract

Aim: ***The aim of the present research was to investigate the association between Periodontal Disease (PD) indices and Chronic Obstructive Pulmonary Disease (COPD) risk in Greek adults.*** ***Methods:*** ***A sample of 392 individuals who suffered from COPD and 1,803 healthy individuals were participated in the study. COPD diagnosis was based on the Forced Expiratory Volume/1sec (FEV1)/ Forced Vital Capacity (FVC) ratio. The associations between Probing Pocket Depth (PPD), Clinical Attachment Loss (CAL) and Bleeding on Probing (BOP) as PD indices and risk for the development of COPD was assessed using univariate and multivariate logistic regression analysis models.*** ***Results:*** ***According to multivariate analysis lower socio-economic status (p= 0.000,OR =5.13, 95% CI= 2.53-8.39), smoking (p=0.000, OR= 15,78 95% CI=8,78-21,6), moderate / severe CAL (p=0.008, OR= 5.03, 95% CI=3.30-7.65), and the presence of BOP (p=0.012,OR= 4,33, 95% CI= 2,88-6,99) were statistically significantly associated with the risk for COPD. CAL and BOP remained to be significantly associated with the risk for COPD after adjusting for socio-economic status and smoking. Conclusion: CAL and BOP as PD indices were statistically significantly associated with the risk of developing COPD.***

Keywords: ***Periodontitis, Chronic Obstructive Pulmonary Disease, Adults***

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1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a major pathological condition and one of the main cause of mortality nowadays in industrialized societies as is the 4th leading cause of death worldwide, it is associated with an increasing economic cost and social burden, whereas it is predicted that by 2020 will be the 3rd leading cause of death and the 5th leading cause of overall disability worldwide [1]. COPD worldwide prevalence is 9-10% at the age of 40 years and older and a surprising increase of its prevalence has been detected in developing countries due to increased smoking rates, whereas COPD is deteriorated by exacerbations possibly due to viral or bacterial infections [2]. COPD can develop as a result of genetic, behavioral and environmental risk factors [3]. The genetic factor is a severe hereditary deficiency of a circulating serine proteases inhibitor, a1-antitrypsin [4,5]. According to previous studies various genes are implicated in COPD pathogenesis and it is possible that an interaction between genes and environment is responsible. However, the genetic factors that are involved in COPD pathogenesis except for the mentioned deficiency, have not been yet determined [6]. The environmental and behavioral risk factors are exposure to cigarette smoke and passive cigarette smoke [7,8]. However, not all smokers develop clinically significant COPD, observation that can lead to suggest that genetic factors may modify each individual's risk [9] and that passive smoking may also contribute to COPD development [8] by influencing the total burden of lungs of inhaled environmental gases and particles [10]. In addition, it remains unknown why individuals-never smokers develop COPD [11]. As has already mentioned the principal cause of COPD is smoking [12], however other environmental factors include occupational chemicals, such as organic and inorganic chemical fumes and agents [13], indoor and outdoor air and atmospheric pollution are implicated in COPD pathogenesis, despite the fact that the role of outdoor air pollution in COPD pathogenesis remains unclear [14,15]. Another environmental factor is socio-economic status (SES) as it has been recorded that the onset of COPD is inversely associated with SES [16] however, it is unclear whether SES is related to the mentioned pollutants or other unknown factors that are associated with low SES [17]. COPD consists a heterogeneous disorder that includes clinical conditions such as emphysema and chronic bronchitis [18] and is characterized by progressive airflow obstruction and airways inflammation, whereas the abnormal inflammatory respons of the lung to noxious gases or particles consists the main cause of airflow limitation [12]. However, as mentioned a rate of COPD cases cannot be explained by the known risk factors and chronic inflammation has been implicated etiologically in COPD pathogenesis as is characterized by an amplification of the respiratory system inflammatory response to chronic irritant agents such as cigarette smoke. Pathological alterations in COPD include chronic inflammation, increased levels of specific inflammatory cells at different regions of the lung, and tissue remodeling as a result of the repeated processes of lung tissues injury and repair. The possible mechanisms for that inflammatory response amplification have not been yet defined, however genetic factors may be implicated (19). Periodontal Disease (PD) and especially periodontitis consists a progressive inflammation, which leads to supporting tissue destruction and alveolar bone loss. Severe periodontitis and edentulism influence 743 and 158 million individuals worldwide, respectively [20,21]. The chronic infection of periodontal tissues can cause systemic effects and results in an increased plasma concentration of inflammatory cytokines and chemokines, that are linked to PD severity, such as C reactive protein (Crp), Interleukin (Il)-1 and -6. The possible implication of those inflammatory mediators in several systemic diseases development could be attributed to a general inflammatory reaction, a systemic immune response to periodontal pathogens or the entry of periodontal pathogens into the blood circulation [22,23]. Based on those suggestions in combination with the theory of 'focal infection' which was described at the beginning

of the 20th century, many studies have investigated a possible role for PD as a risk factor for systemic conditions over the past two decades [24], including diabetes mellitus (DM), cardiovascular disease (CVD), inflammatory bowel disease, respiratory diseases such as COPD [25-47], cancer [48], systemic infections [49,50], adverse pregnancy outcome [51], osteoporosis [52], rheumatoid arthritis [53], etc. Previous studies have linked several risk factors to PD including smoking, age, DM, gender and low SES [54]. In addition, PD is also associated with elevations of several mediators of chronic inflammation, as mentioned [55], and because of evidence implicating chronic inflammation in COPD pathogenesis, a possible link between PD and COPD could be hypothesized. Oral pathogens and inflammatory cytokines from periodontal lesions induce systemic inflammation, which may contribute to COPD pathogenesis [43]. Moreover, PD and COPD share common pathogenic pathways such as a chronic course, progressive and irreversible tissue destruction, gradual loss of normal organ function and risk factors such as tobacco smoking, age, SES, and living conditions [24]. Those observations strongly suggest that PD may be a risk factor for COPD and that periodontal pathogens may play a key role in COPD pathogenesis. A large amount of epidemiological surveys have investigated the association between PD and risk of COPD, and most of those recorded a positive outcome. However, those studies have used different population samples and PD indices and the outcomes were inconclusive and contradictory among them. Consequently, the possible role of PD in COPD pathogenesis remains an important issue. For these reasons there has been strong interest in evaluating whether PD is independently associated with COPD development. The aim of the present report was to assess the possible association between PD indices and the risk for COPD development in a sample of Greek adults.

2. Materials and Methods

2.1 Study sample

2,195 individuals, COPD patients-cases and healthy-controls, 1,450 males and 745 females, aged 40-78 years were recruited from 3 private practices and constituted the study sample. Cases and controls were responded to a medical and dental health questionnaire and their periodontal tissue status examined clinically by a well-trained and calibrated dentist. The study was conducted from December 2017 to September 2019. Participants selection criteria COPD-patients and controls included in the protocol in case they met the following selection criteria: they should not be received any type of periodontal therapy during the last ½ year, or systemic or antibiotic or anti-inflammatory medication during the last 1½ month, or a systematic treatment with glucocorticoids or immunosuppression agents. They also should not be suffered from diseases such as CVD, DM, rheumatoid arthritis, acute pulmonary diseases or any type of malignancies and should have at least 20 natural teeth. Those conditions could have potential effects on the periodontal tissues and excluded in an effort to minimize potential effects by known and unknown confounders which could lead to secondary biased associations.

The criteria of established periodontitis for assessing PD indices, Probing pocket depth (PPD) and Clinical attachment loss (CAL), were applied whereas gingival bleeding, (Bleeding on probing-BOP), was assessed as present or not within 30 seconds following probing with gentle pressure at four sites per tooth [56]. Cases group included individuals in which the diagnosis was set according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) spirometry guidelines. Lung function was examined and recorded using spirometry. The spirometric measurements had been assessed by the doctors of the cases and included to their medical files. During at least 5 forced expirations, the

doctor attempted to obtain three acceptable spirograms, at least two of which showed similar results for the Forced Expiratory Volume (FEV) /1sec (FEV1) and Forced Vital Capacity (FVC). The pulmonary function assessment was based on the FEV1/ FVC ratio and then used the percentage of predicted FEV1 to categorize severity. Air limitation was set using the fixed ratio post-bronchodilator FEV1/FVC<0.70 [3].

In an effort to avoid or eliminate as much as possible effects of potential confounders such as smoking and SES, the friendly and collegial environment of cases was the basis for controls selection and both groups were matched for gender and age. For the same reasons cases and controls were selected from the same city population in an effort to avoid or eliminate as much as possible selection biases which could lead to biased secondary associations and to select a representative study sample. According to that method, control group was drawn from individuals who were presented to routine health follow-up at the mentioned practices, between 2017 and 2019.

2.2 Dental and oral clinical examination

The oral and dental examination focused on periodontal health condition and included assessments of PPD, CAL and BOP as a measure of PD status. All PD indices were measured with a millimeter graduated probe (Hu-Friedy PCP 10-SE) at four sites per tooth (mesio-lingual, mesio-buccal, disto-lingual, and disto-buccal) in all quadrants and the worst values of the indices recorded to the nearest1.0 mm. Remaining roots and 3rd molars were excluded. PPD and CAL of missing tooth sites was set to the values of neighboring tooth sites. In a small number of individuals (n =12) who obviously had lost teeth due to PD the, PPD and CAL were set to the worst values of the indices recorded, according to their previous dental history. PPD index was dichotomously assessed as code 0: moderate periodontal pockets, 4-6.0 mm and code 1: advanced periodontal pockets, >6.0 mm [57]. Similarly CAL severity, was assessed as code 0: mild, 1-2.0 mm of attachment loss, and code 1: moderate / severe, ≥ 3.0 mm of attachment loss and BOP absence as code 0 and presence as code 1, respectively [58]. The same dentist re-examined a random sample of 440 (20.0%) cases and controls, after a period of 3 weeks for assessing the intra-examiner variance and no differences were found between both oral clinical examinations *(Cohen's Kappa= 0.96*), whereas during that time period no oral hygiene instructions were given to the participants.

2.3 Ethical consideration

The present study was a retrospective case-control study. Only experimental studies must be reviewed and approved by authorized committees (Ministry of Health, Dental Associations, etc.) in Greece. The individuals who agreed to participate in the present case-control study signed an informed consent form.

2.4 Statistical analysis

The worst values of PPD and CAL at four sites per tooth for each individual were estimated. Males, smokers, low socio-economic status, low educational level, absence of COPD family history and cases were coded as 1. Age groups distribution was coded as 0, 1, 2, and 3 for ages 40-49, 50-59, 60-69 and 70+, respectively. The univariate analysis model using chi-square test was performed to estimate the association between the independent indices examined and the COPD risk, separately. Multivariate logistic regression model was applied to assess the associations between the dependent variable, COPD, and independent ones using the Enter method. The final analysis was performed by

the application of Stepwise method which determined the significant associations among the indices examined. Unadjusted and Adjusted Odds Ratios (OR's) and 95% (Confidence Interval) CI were also assessed. The statistical method Cohran's and Mantel-Haenszel's was applied to control possible con-founders, such as smoking and SES. Statistical analysis was performed by SPSS statistical package (SPSS PC19.0, SPSS, Inc., Chicago, IL, USA), and a p value less than 5% ($p< 0.05$) was considered to be statistically significant.

3. Results

392 individuals of the study sample, 215 males and 177 females suffered from COPD and 1,803 individuals 1,235 males and 568 females consisted the control group. Cases and controls ranging in age from 40 to 77 years old and the mean age 62±5 years. Smoking, SES, CAL and BOP were found to be significantly associated with COPD risk after performing of univariate analysis (Table1)1. The same table shows unadjusted OR's and 95% CI.

According to regression model, the 1[a] step showed that SES (p= 0.004), smoking (p= 0.000), CAL (p=0.012) and BOP (p=0.038) were significantly associated with COPD risk (Table 2).

The same table presents adjusted OR's and 95% CI.The final model (step 3[a]), showed that lower SES (p= 0.000, OR= 5.13, 95% CI= 2.53-8.38), smoking (p= 0.000, OR= 15.78 95% CI= 8.78-21.6), moderate/severe CAL (p= 0.008, OR= 5.03, 95% CI=3.30-7.65), and the presence of BOP (p= 0.012, OR= 4.33, 95% CI=2.88-6.99) were statistically significantly associated, whereas age and PPD were statistically marginally associated with the risk for COPD (Table 3). CAL and BOP were also significantly associated with COPD risk after adjusting for smoking and SES (Table 4).

Table 1. Univariate Analysis of Cases and Controls Regarding each Independent Variable Examined.

Variables	Cases (no) (%)	Controls (no) (%)	p-value	Odds Ratio (OR)	95% Confidence Interval (CI)
Gender: Males Females	190 (48.5) 202 (51.5)	805 (44.5) 1003 (55.5)	0.155	1.17	0.94-1.46
Age (years): 40-49 50-59 60-69 70+	27 (6.9) 78 (19.9) 149 (38.0) 138 (35.2)	144 (8.0) 440 (24.4) 596 (33.1) 623 (34.5)	0.131	___	___
Socio-economic level: Low High	230 (58.7)	903 (50.1) 900 (49.9)	0.002*	1.42	1.13-1.77

	162 (41.3)				
Educational level: Low High	188 (48.0) 204 (52.0)	793 (44.0) 1010 (56.0)	0.151	1.17	0.94-1.47
Smoking: No Yes	157 (40.1) 235 (59.9)	1082 (60.0) 721 (40.0)	0.000*	0.45	0.36-0.56
COPD family history: No Yes	190 (48.5) 202 (51.5)	805 (44.6) 998 (55.4)	0.168	1.17	0.94-1.45
Periodontal pockets: Depth 4,0-6,0 mm Depth >6,0 mm	163 (41.6) 229 (58.4)	650 (36.1) 1153 (63.9)	0.040*	1.26	1.01-1.588
CAL: Mild 1-2,0mm Moderate/Severe≥ 3,0 mm	168 (42.9) 224 (57.1)	658 (36.5) 1145 (63.5)	0.018*	1.31	1.04-1.63
BOP: No Yes	137 (34.9) 255 (65.1)	811 (47.6) 892 (52.4)	0.000*	0.59	0.47-0.74
*p-value: statistically significant					

Table 2. Presentation of Association Between Independent Variables and COPD According to Enter (first step-1a) Method of Multivariate Logistic Regression Analysis Model.

Variables in the Equation								
							95% C.I.for EXP(B)	
	B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]								
gender	,364	,125	18,085	1	,123	1,372	0,858	2,427
age	,339	,140	5,883	1	,075	1,212	,542	1,537
s/econom. status	-,388	,176	11,209	1	,004	4,945	2,013	6,361
educat. level	,191	,253	3,605	1	,290	1,327	,421	1,874
smoking status	3,268	,139	32,317	1	,000	7,586	3,507	15,122
COPD fam. history	,112	,161	2,502	1	,548	,905	,106	1,193
prob. pock. depth	,384	,197	6,878	1	,067	1,832	,765	2,323
clin. attach. loss	1,102	,183	16,289	1	,012	3,011	2,103	4,309
bleed. on. prob	,201	,171	6,382	1	,038	3,818	1,585	4,143
Constant	1,714	,221	80,860	1	,000	,180		

a. Variable(s) entered on step 1: gender, age, s/economic status, educat. level, smoking status, COPD fam. history, prob. pock. depth, clin. attach. loss, bleed. on. prob.

Table 3. Presentation n of Association Between Independent Variables and COPD According to Wald (final step-3[a]) Method of Multivariate Logistic Regression Analysis Model.

x								
							95% C.I.for EXP(B)	
	B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 3[a]								
age	,383	,147	13,216	1	,058	2,278	1,205	3,677
s/econom. status	-,277	,171	12,630	1	,000	5,128	2,532	8,381
smok.status	4,933	,158	44,264	1	,000	15,779	8,777	21,596
prob. pock. depth	1,102	,187	25,632	1	,052	2,374	1,549	3,788
clin. attach. loss	1,615	,214	31,752	1	,008	5,026	3,302	7,651
bleed. on. prob	,281	,209	1,805	1	,012	4,325	2,879	6,996
Constant	3,996	,270	218,580	1	,000	,018		

a. Variable(s) entered on step 3: gender, age, s/economic status, educat. level, smoking status, COPD fam. history, prob. pock. depth, clin. attach. loss, bleed. on. prob.

Table 4. Application of Cohran's and Mantel-Haenszel's Statistical Method for Controlling Possible Confounders Possible Confounders.

Variables	Exp(B)	95% CI
Bleeding on probing		
Non - smokers	1.683	0.415-2.237
Smokers	4.512	2.519-10.443
Bleeding on probing		
Socioeconomic status: Low	5.144	2.833-11.242
High	1.746	0.737-3.044
Clinical attachment loss		
Non-smokers	1.387	0.263-1.821
Smokers	4.677	2.921-11.107
Clinical attachment loss		
Socioeconomic status: Low	4.708	2.037-9.478
High	1.424	0.615-2.637

4. Discussion

In recent years, there has been an essential interest in possible associations between PD and various systemic diseases and conditions [24]. However, many of those were based on variables such as number of missing teeth or gingivitis as direct or indirect PD indices, were retrospective and based on questionnaires and self-reported data. Periodontal tissue chronic infection by oral pathogens leads to systemic effects and an inflammatory reaction which is characterized by elevated plasma levels of inflammatory biomarkers, cytokines and chemokines such as Crp, Il-1-6, -10, -11, -18, Tumor necrosis factor-alpha (TNF-α), and Interferon- gamma (IFN-γ) [59]. Similarly, chronic inflammation is involved in COPD pathogenesis. Therefore, it could be hypothesized a possible association between PD and COPD as periodontal pathogens and inflammatory cytokines and chemokines derived from damaged periodontal tissues could induce a systemic inflammation which in turn may contribute to COPD pathogenesis [43].

According to previous researches, COPD was considered to be a disease that mainly affected elderly males, reflecting the high prevalence of smoking among them. However, smoking prevalence has increased among females and there is evidence that females may be more susceptible to the adverse pulmonary function effects of smoking than males. There may also be under- and misdiagnosis of COPD in both genders because unbiased measures of lung function are underused [60-64]. Similarly, Buist *et al.* [65] indicated that females may have a greater predisposition to COPD. In another study was recorded that COPD is commonly observed in females, as the prevalence of smoking in females has grown progressively [66]. Over the last few years, more recent studies indicated a growing health burden of COPD among females [67] and non-smokers [68], whereas exposure to biomass fuels is probably the leading cause of

COPD in younger females [68,69]. In the current study no association was recorded between both genders and COPD risk, whereas in general, gender is considered as a confounder.
Similarly, age is also considered as a confounder, although older individuals are at a higher risk for COPD development [26,70-77]. The association between age and COPD risk in the current report was statistically marginally significant.

Another crucial confounder is SES, and its possible role as a COPD risk factor has been proven. The risk of developing COPD is inversely related to SES [26,78-88], however it is unclear, whether this pattern reflects exposures to cigarette smoke, indoor and outdoor air pollutants, crowding, poor nutrition, or other factors that are related to low SES [17]. COPD is unevenly distributed in the population, as lowest SES individuals who suffer from COPD are more likely to experience poor health outcomes than those of the highest SES COPD patients [89]. Kim *et al.* [90] reported that COPD patients, irrespective of whether they suffered from PD or not, had higher age, less income, lower educational level, consumed more tobacco and alcohol. The current report showed a significant association between those variables examined. The possible role of educational level as a risk factor for COPD development has been investigated in a limited amount of previous reports. Those reports showed that low educated individuals were at a higher risk for COPD development [79,83,90,91], whereas it has been suggested that high-educated individuals take care of their own oral hygiene more than low-educated ones and could prevent diseases that are associated with PD [92]. No association was recorded between educational level and COPD risk in the present research.

Family history of specific diseases and disorders reflects the consequences of genetic susceptibilities, shared environment, and common behaviors. Under that precondition the genetic risk factor that is best documented in COPD pathogenesis is a severe hereditary deficiency of a circulating inhibitor of serine proteases, a 1-antitrypsin [4] and this abnormality most commonly has been observed in northern Europe [5]. Alfa-1 antitrypsin deficiency leads to COPD development at a much earlier age, regardless of smoking status. Genetic researches have implicated several genes in COPD pathogenesis and it is considered that all COPD risk factors result from a gene-environment interaction. However, the results of those genetic surveys have led to inconsistent out-comes, and functional genetic polymorphisms that influence COPD development, other than the mentioned deficiency have not been definitively identified [6,93,94]. The present survey recorded no association between COPD family history and its risk. A strong evidence has been suggested regarding the role of smoking in COPD pathogenesis. The current study recorded a statistically significant association between smoking and the risk for COPD, finding that was in accordance with those from previous reports [3,12,24,33,95,96].

Smoking and less commonly inhalation of other toxic agents leads to inflammation, which is characterized by the activation and release of elastase and other matrix-degrading proteinases [94,97]. Lung inflammation leads to recruitment of several inflammatory and immune cells which release proteinases and cause lung tissue destruction. Inflammatory cells such as macrophages, neutrophils and lung cells are stimulated by cigarette smoking and release chemokines and other inflammatory mediators such as IL-8, C5a, LTB4 [98]. Macrophages accumulation has been found, initially in respiratory bronchioles [94], however a gradual and progressive accumulation of macrophages concerns the lungs [99]. CD4 and CD8 cells are also increased in lung airways and alveoli, whereas epithelial cells in smokers with COPD showed an increased expression of CXCL10 [100]. Other cells such as dendritic cells, eosinophils and

mastcells have also been observed in COPD patients lung tissues, but their role is unclear. The inflammatory reaction leads to a significant oxidative burden to the lung due to oxidative substances present in smoke [98]. Oxidative stress also plays a role in cigarette smoke-induced lung cell destruction. Neutrophils, after its activation release matrix metalloproteinases, MMP1 and -9 which contribute to lung cell destruction [93]. It is clear that cigarette smoke initiates the inflammatory response and other factors maintain it in the absence of cigarette smoke [101,102].

In addition, smoking is an important risk factor for PD development and the association between the two conditions possibly reflects exposure to tobacco smoke [35]. However, it remains unclear whether the susceptibility to tissue destruction that is caused by smoke consists a general individual's characteristic or whether different individual's tissues show different reactions to the deleterious effects of smoking. If the sensitivity to smoking is not a general individual characteristic the destructive procedures in periodontal tissues will develop independently of changes in the lungs.

In case in which exists a general susceptibility to the deleterious effects of smoke the development of PD and COPD would be associated and there would be a co-variation between both pathological conditions.

According to the results of the current study deep periodontal pockets were significantly marginally associated with the risk of COPD, finding that was in agreement, in, with a large number of previous reports [40,44,103-109], whereas only in one study was not recorded such an association [36].

Similarly, moderate/severe CAL and presence of bleeding (BOP) were found to be significantly associated with risk of COPD after controlling for smoking and SES, observations that were in line with previous researches for CAL [33,36-38,40,47,104,109,110,111] and BOP, respectively [40,79].

The bleeding index (BOP) reflects the host's vascular inflammatory response, namely hyperemia, the capillaries expansion and increased blood flow at the inflammation location.PD and CAL refer to the long-term phases of chronic inflammation including destructive procedures signs of a chronic inflammatory response [112]. BOP is a widely used criterion for diagnosis of gingival inflammation, however it has been shown that periodontal pockets with a probing depth of greater than or equal to 5.0 mm showed a significantly higher incidence of BOP [113].

In general, a large amount of epidemiological studies [28-47] have investigated the association between PD and risk of COPD, and most recorded a positive association. The mentioned epidemiological studies included systematic reviews, case-control and cross-sectional ones, used different PD indices, such as the number of teeth lost or indices for assessing gingival inflammation and investigated different populations, and in some cases have led to contradictory out comes. In addition, in some of those studies the conventional risk factors, such as smoking, age, gender and SES were not adjusted in the statistical analysis, condition that can make the outcomes questionable.

Eventually, it remains unclear if PD is an independent COPD risk factor or a silent marker. Several limitations exist in the current retrospective study. Case-controls studies are subject to selection, recall, random, referral bias and the effect

of known and unknown con-founders which can to lead to biased secondary associations regarding the indices examined. The prospective cohort studies design can control confounding biases. An important limitation in the present survey is that PD and COPD share some common risk factors such as smoking and SES. Thus, an association between both diseases could be expected even if a causal association did not exist.

Another limitation was that questionnaire studies are susceptible to response bias as it is possible that the answer given is what the individuals consider the socially adequate response, not the real one. Moreover, individuals could forget or provide wrong information (recall bias).

Some strengths of the current study were the large and the representative study sample and that it was a matched case-control study, as was used randomly selected population based controls as were selected from non-COPD individuals derived from cases environment, methodology warrants interval validity. More studies, especially prospective are needed to confirm those findings to explore, potential biological associations and to define the mechanisms by which PD may influence COPD risk.

5. Conclusion

PD indices such as clinical attachment los and bleeding on probing were found to be statistically significantly associated with the risk of developing COPD after controlling for smoking and SES.

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