Inflammatory Bowel Disease and Periodontitis – A Retrospective Chart Analysis

by

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Abstract

Background & Objective: Periodontitis has been an increasingly common finding in patients who have been diagnosed with Inflammatory Bowel Disease (IBD). Several studies have investigated the association between the two diseases and have confirmed that these two disease entities have a common pathogenesis. However, data regarding the prevalence of periodontal disease, age variation and, the effect of other risk factors such as smoking on these two conditions have not yet been explored. This study intends to estimate the variation in prevalence of periodontitis occurrence among different sexes, age groups, smoking status, oral hygiene adherence in patients affected by either Crohn's Disease (CD) or Ulcerative Colitis (UC).

Methodology: This retrospective chart analysis collected data from Kaye Edmonton Clinic (dental hospital setting at University of Alberta, Edmonton, Canada) patients' electronic health records who attended the clinic between the years of 2013 to 2019. Patient records were searched for multiple keywords and selected records from the search were then analyzed further. The inclusion and exclusion criteria were applied to filter the records. A total of 80 patient charts reported IBD or CD or UC in their medical history and were included in the study. The patient charts were thoroughly screened to gather information such as age, sex, smoking status, and a variety of periodontal parameters. Collected data were analyzed using SPSS software by using Pearson's Chi-square, Fischer's Exact, Pearson correlation, and Mann-Whitney U test.

Results: Data from the study shows that the age group 50-64 years is most affected by periodontitis in patients having IBD. There is no sex preference for periodontitis in patients presenting with IBD. IBD patients with a history of smoking do not have higher odds of developing periodontitis derived from the records in the present study. Oral hygiene adherence did not seem to increase the

prevalence of periodontitis in patients presenting with IBD; however, this was based on a small sample. Also, periodontitis did not differ between UC and CD.

Conclusion: The data from this study shows that age has a significant effect on IBD-affected individuals in developing periodontitis; thus, it is advised to keep patients above 50 years of age under closer watch for early diagnosis and preventive care. Hence, periodontists can work closely with gastroenterologists to maintain periodontal health in IBD-affected individuals.

Preface

This thesis is an original work by Dr. Nazia Abrol. This project is aimed to create awareness of periodontal health amongst those suffering from Inflammatory Bowel Disease. Special thanks to NCOHR (Network for Canadian Oral Health Research) for funding my research project.

He is in the idols at the temples,
in our surroundings
as well as in ourselves too.
Not here, not there,
but everywhere he is present,
the ultimate god of the supreme being.

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Abbreviations

CAL- Clinical Attachment Loss

FI- Furcation Involvement

PD- Probing Depth

RBL- Radiographic Bone Loss

IBD- Inflammatory Bowel Disease

CD- Crohn's Disease

UC- Ulcerative Colitis

CCHS- Canadian Community Health Survey

QC- Quebec

NS- Nova Scotia

NF- Newfoundland

NHANES- National Health and Nutritional Examination Survey

CHMS- Canadian Health Measure Survey

NCOHR- Network for Canadian Oral Health Research

GBD- Global Burden of Disease

DALY- Disability-Adjusted Life Years

HIPAA- Health Insurance Portability and Accountability Act

ONC-ATCB- Office of the National Coordinator Authorized Testing Certification Body

HER- Electronic Health Record

KEC- Kaye Edmonton Clinic

PHI- Protected Health Information

SPSS -Statistical Package for the Social Sciences

OR- Odds Ratio

CI- Confidence Intervals

TNF-α - Tumour Necrosis Factor-alpha

CRPs - C-Reactive Proteins

Chapter 1: Introduction

1.1: Introduction to Periodontium & Periodontitis

The periodontium is a multilayered tissue structure essential in maintaining oral health and preventing inflammatory disease in tooth-supporting structures.[1] It is comprised of four structures: gingiva, alveolar bone, periodontal ligament, and cementum.[1] Together, these tissues act as a barrier to inflammatory processes that occur as a response to microbial insult.[2] They also provide support against masticatory forces and act as a rich source of macro and micronutrients.[2] These tissues are also essential for providing cells and cytokines essential for wound healing and act as an attachment apparatus for the dentition.[2] These tissues can adapt to changes in the external environment and wear associated with aging through the continuous process of remodeling and regeneration.[2] They also offer an internal defense mechanism that protects against noxious stimuli present in the oral cavity.[3] Thus, a healthy periodontium is crucial in supporting the teeth in function.[3]

Periodontitis involves the inflammation and degeneration of tissues surrounding and supporting the teeth. It is generally chronic in nature. It begins as gingivitis and, in some cases, progresses to periodontitis in a susceptible host as a result of exposure to dental plaque and biofilms that accumulate on the tooth surfaces.[2] The dental plaque and biofilm usually consist of several colonies of gram-negative bacteria.[4] While the role of bacteria in the initiation of periodontitis is primary, an array of host-related factors impacts the disease susceptibility, host modulation, clinical presentation, and rate of progression of the disease.[5,6] This implies considerable variation among individuals in their risk for disease progression and severity.[7]

Several studies have identified tobacco and/or cigarette smoking as one of the major risk factors for the development and progression of periodontitis.[8-13] Likewise, a bi-directional relationship has been explored between diabetes mellitus and periodontitis.[14-20] Obesity has also been reported as a significant risk factor that affects the progression of periodontitis.[21-23] Other factors like Vitamin D deficiency, rheumatoid arthritis, stress, etc., have also been associated with periodontitis.[24-26] Another disease entity called inflammatory bowel disease (IBD) has also emerged as a possible risk factor influencing the prevalence of the periodontitis. Newer studies have endeavored to explore its association with periodontitis. [5,27-33]

Diagnosis of periodontitis is a complex decision-making process.[34] Several clinical parameters need to be considered for appropriate diagnosis, including probing depths, clinical attachment loss (CAL), mobility, furcation involvement (FI), and radiographic bone loss.[35] Probing depth is the distance from the gingival margin to the base of the gingival sulcus (Figure 1).[36] CAL is the distance from the cementoenamel junction to the bottom of the pocket.[37] It is measured by subtracting the length from the cementoenamel junction and free gingival margin from the probing depth (Figure 1).[38] Furcation involvement refers to bone loss that occurs in between the tooth roots of multirooted tooth (Figure 2).[39]

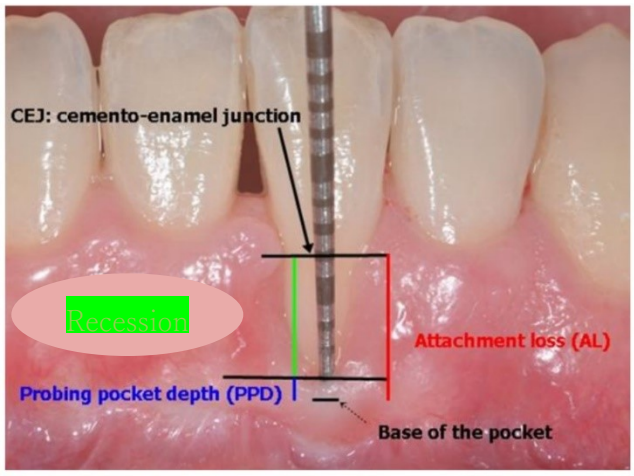

Figure 1: Clinical Parameters to Determine Periodontitis[40]
(Adapted from Handbook of dental hygienist by Valyi)

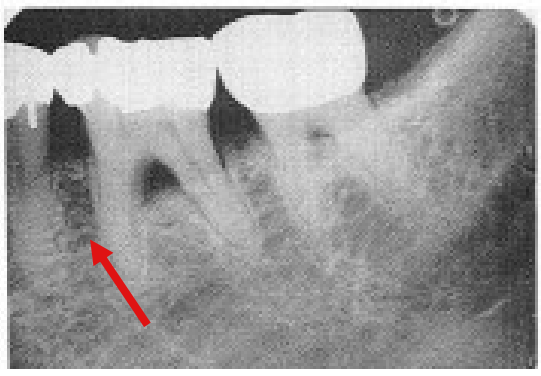

Figure 2: Furcation Involvement[39]
(Adapted from Furcation Involvement in Maxillary and Mandibular molars by Ross IF & Thompson RH)

Considering these parameters, World Workshop 2017 have classified periodontitis into four different stages to classify severity and extent of disease and to assess complexity.[34]

Stage 1 Periodontitis: This stage describes the patient who reveals minimal clinical attachment loss (1-2mm) and radiographic bone loss of less than 15%, with no tooth loss due to periodontitis and maximum probing depth ≤ 4mm, mainly presenting with horizontal bone loss (Table 1).[34]

Stage II Periodontitis: This stage presents with interdental clinical attachment loss of 3-4mm, radiographic bone loss of 15-33%, with no tooth loss due to periodontitis and maximum probing depth ≤ of 5mm, primarily horizontal bone loss (Table 1).[34]

Stage III Periodontitis: This stage presents with interdental clinical attachment loss of ≥ 5mm, radiographic bone loss extending to mid-third of the root and beyond, with tooth loss due to periodontitis of ≤ 4 teeth and probing depth ≥ 6mm, vertical bone loss ≥ 3mm, furcation involvement class II or III, moderate ridge defects (Table 1).[34]

Stage IV Periodontitis: This stage is advanced of all stages with interdental clinical attachment loss of ≥ 5mm, radiographic bone loss extending to mid-third of the root and beyond, with tooth loss due to periodontitis of ≥ 5 teeth and probing depth ≥ 6mm, vertical bone loss ≥ 3mm, furcation involvement class II or III, secondary occlusal trauma, mobility ≥ 2, bite collapse, drifting, flaring, less than ten opposing pairs of teeth, masticatory dysfunction, severe ridge defects (Table 1).[34]

Stage I	Stage II	Stage III	Stage IV
CAL 1-2mm	CAL 3-4mm	CAL > = 5mm	CAL > = 5mm
RBL < 15%	RBL 15-33%	RBL Extending to mid-third of root	RBL Extending to mid-third of root
PD < = 4mm	PD > = 5mm	PD > = 6mm	PD > = 6mm
No tooth loss	No tooth loss	Tooth loss < = 4	Tooth loss > = 5

Table 1: Stages of Periodontitis (where CAL presents the clinical attachment loss in mm, RBL presents the radiographic bone loss in percentage, and PD presents the pocket depth in mm).

In addition to staging, periodontitis is further graded into three categories referred to as Grade A, B or C to assess the future risk of periodontitis progression and assess periodontitis' potential health impact on systemic disease and vice versa.[34]

Grade A- evidence of no bone loss over five years, with bone loss versus age ratio < 0.25, heavy biofilm deposits with low levels of destruction, nonsmoker, and no diagnosis of diabetes (Table 2).[34]

Grade B- < 2mm bone loss over 5 years, with bone loss versus age ratio- 0.25-1.0, destruction commensurate with biofilm deposits, smoker < 10 cigarettes/day and HbA1c < 7.0% in diabetes patient (Table 2).[34]

Grade C- ≥ 2mm bone loss over five years, with bone loss versus age ratio- > 1.0, destruction disproportionate to biofilm deposits, evidence of periods of rapid progression and early-onset disease, expected inadequate response to therapy, smoker ≥ ten cigarettes/day, and HbA1c ≥ 7.0% in diabetes patient (Table 2).[34]

The bone loss versus age ratio is crucial and helps determine the rate of periodontitis progression. If this ratio is higher (>1) at a younger age, that would imply that more destruction of periodontal tissues has occurred in young age and would be considered a rapid rate of disease progression. However, if the ratio is lower (<0.25), a slow progression of disease is considered. The ratio ranging from 0.25-1mm would imply moderate rate of progression. Assigning a grade helps strategize and devise the treatment plan accordingly. It is also very useful to decide the maintenance schedule of the patients.

Grade A	Grade B	Grade C
No bone loss over five years	< 2mm bone loss over five years	>= 2mm bone loss over five years
% bone loss/age < 0.25	% bone loss/age 0.25-1.0	% bone loss/age > 1
Nonsmoker	Smoker < 10 cigarettes/day	Smoker >= 10 cigarettes/day
Non-Diabetic	HbA1C < 7	HbA1C >= 7

Table 2: Grades of Periodontitis

1.2: Epidemiology of Periodontitis& Disease Burden on the Population

National Health and Nutrition Examination Survey (NHANES) 2009 to 2012 estimated about 46% of US dentate adults aged ≥ 30 years presented with periodontitis.[41] Another report, conducted in Canada by the Canadian Health Measure Survey (CHMS) revealed that 21% of adults across Canada presented with periodontitis.[42] Other studies in the literature have shown that untreated periodontal patients had compromised function of the periodontium, which ultimately led to increased probing pocket depths, more alveolar bone loss, and eventually, loss of teeth, thus increasing severity and extent of disease .[43,44]

Global burden of disease study provided comparable worldwide information on disability-adjusted life years (DALYs). The Disability-Adjusted Life-Year (DALY) is a metric that combines the burden of mortality and morbidity (non-fatal health problems) into a single number. It is the primary metric used by the World Health Organization to assess the global burden of disease. It showed that oral conditions affected 3.9 billion people worldwide, where caries was the most prevalent condition followed by severe periodontitis.[45] It also reported the direct and indirect costs involved and estimated productivity losses >$1 billion yearly for Canada alone.[45]

1.3: Perio-Systemic Link

Periodontitis occurs because of microbial attacks on a susceptible host. However, several risk factors affect the host immunity, making individuals more prone to periodontitis and increasing the severity of the disease in susceptible populations. Periodontitis and certain systemic disorders share genetic and environmental etiological factors and, therefore, affected individuals have predisposition to both diseases.[46] Several studies have established the bi-directional association between diabetes mellitus and periodontitis and have established that glycaemic control improves periodontal status and vice-versa.[14-20,47] Studies by several researchers trying to explore the perio-systemic link are currently being conducted to study the association of periodontitis in individuals with Chronic Obstructive Pulmonary Disease (COPD), chronic kidney disease, cardiovascular disease, and cognitive impairment; however, a causal relationship hasn't yet been established.[48-55]

The relationship between the gastrointestinal tract and oral cavity has gained much attention recently. Some studies have reported a positive association between the two diseases, but the association of IBD with the severity of the periodontitis taking into consideration of the effect of various factors like sexes, smoking status, age etc. hasn't been explored.[29,31,33] Periodontitis and IBD have been linked as they are known to share common etiological factors and pathogenesis.[56] To better understand the co-existence of these two conditions, studies emphasizing other aspects such as their immune-inflammatory profiles or variation in the presence of several risk factors or genetics would be helpful.[28,33,57,58]

1.4: Inflammatory Bowel Disease Background

Inflammatory bowel disease (IBD) is a broad term used to define a group of disorders affecting the gastrointestinal tract.[59] Crohn's disease (CD) and ulcerative colitis (UC) are two specific forms of inflammatory bowel disease (IBD). They present with chronic intestinal and systemic inflammation, resulting from an aberrant mucosal immune response to the bacteria of the gastrointestinal tract in genetically susceptible individuals.[59] A majority of the IBD cases fall under CD or UC types, with only 10% of cases falling under the IBD-type of unclassified category.[60]

CD is a chronic condition that results in inflammation in any area of the gastrointestinal tract from the mouth to the anus, most frequently affecting the small intestine and colon. It varies in terms of symptoms and complications.[30] It has been classified as mild, moderate, or severe based on several factors like the age at diagnosis, the location in the gastrointestinal tract, and the disease pattern.[30]

UC is also a chronic condition, most commonly affecting the colon. It presents as inflammation and ulceration of the colon mucosa associated with cramping in the abdomen.[30] The symptoms and complications fluctuate, and that solely depends on the extent of inflammation.[30]

A clear distinction does not exist between the two forms of IBD, Crohn's disease (CD) and ulcerative colitis (UC), and thus an overlap exists. Listed below (Table 3) is the comparative table to understand these IBD forms better.

	Crohn's Disease	Ulcerative Colitis
Occurrence	F>M, All ages, peak 25-34 yrs, 2nd peak 55-64 yrs	F=M, All ages, peak 25-34 yrs, 2nd peak 55-64 yrs
Distribution	Patchy	Continuous
Colon & rectum involvement	Often	Always
Depth of inflammation	Transmural affecting the entire thickness of the wall	Shallow, mucosal
Oral Cavity Involvement	Pyostomatitis vegetans, gingival hyperplasia, papillomatosis of the oral mucosa, cheilitis granulomatosa, orofacial granulomatosis, pemphigus vegetans, periodontitis, and caries	Less frequent involvement Aphthous ulcers, angular cheilitis seen sometimes.

Table 3: Comparative table for characteristics of CD and UC (where F- Females, M-Males)

In addition to intestinal inflammation, some additional extraintestinal symptoms can be observed in many patients, including the joints, eyes, skin, mouth, nerve system, and liver.[30] Roughly 16.7%–40% of IBD patients have at least one extraintestinal manifestation, and the oral cavity is one of the most commonly affected areas.[61] The most common oral signs and symptoms in patients with CD are pyostomatitis vegetans, gingival hyperplasia, papillomatosis of the oral mucosa, vesicular eruptions such as in pemphigus vegetans, periodontitis, and caries.[30]

1.5: Epidemiology of IBD & Burden on The Population.

Inflammatory bowel disease can be diagnosed at any age, peaking at 20-30 years.[62] It is a global disease, and thus several statistical studies have been conducted to the same.[62] The Canadian

Community Health Survey (CCHS) conducted by Statistics Canada completed a cross-sectional estimate of the prevalence of UC and CD for each province. It was reported that approximately 206,000 Canadians reported having CD or UC out of the 27 million sampled for the survey which translated to 758 cases per 100,000, or 0.76% of the population.[60]

Canada has been recorded as having among the highest incidence rates of IBD in the World.[62] Increased incidence and prevalence of IBD in Canada tend to affect the quality of life of the affected indiviuals.[60,62] An epidemiological report conducted in 2018 reported that the highest incidence of IBD is reported in Nova Scotia at 54.6 per 100,000 people (1996 to 2009). However, the incidence of IBD in Alberta, British Columbia, Manitoba, Ontario, Quebec, and Saskatchewan were almost similar, ranging from 18.7 to 28.3 per 100,000. The report also stated that the ratio of Crohn's disease to ulcerative colitis was equal in all provinces except for Quebec, where the incidence of Crohn's disease was higher.[62] It was suggested that the prevalence is expected to climb with the highest estimation in Nova Scotia, followed by Ontario and Alberta amongst all the provinces across Canada.[60,62]

It has been estimated that prescription drugs in Canada for IBD cost about $521 million in 2012 and hospitalizations related to IBD cost $395 million per year.[60] A report stated that for those people who will have an IBD hospitalization, 58% of these hospitalizations occur within the first two years of diagnosis, and 36% of surgeries also occur within the first two years.[60]

1.6: Pathogenesis of IBD and Periodontitis

The pathophysiology of IBD is multifactorial. It results from an intricate association among genetic, immunological, and environmental factors.[61] Its pathogenesis is the result of an atypical immune response in a susceptible host, which is influenced by environmental factors (Figure 3).[61]

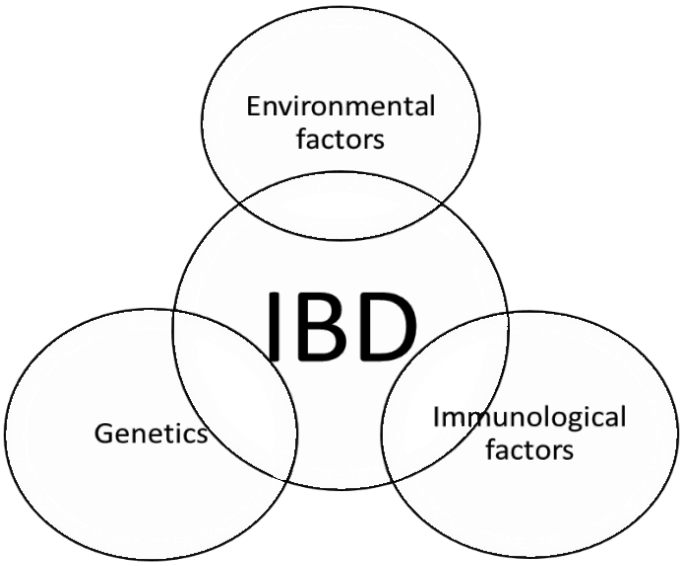

Figure 3: Pathogenesis of IBD

Initially, IBD was considered autoimmune-related or due to a nonspecific inflammatory response. But presently, it is believed that IBD occurs because of the interaction of factors including genetic predisposition, an altered immune response, the microbial flora of the gut, and environmental factors that may act as a prompt of the disease manifestations.[61]The genetic studies conducted to understand the pathogenesis of IBD stated higher risk in populations with positive family history of IBD.[61,63] According to a studies in the literature that explored various environmental factors in the pathogenesis of IBD, smoking was stated as a well established risk factor for CD development, however a lower incidence of UC was reported in smokers.[61,65]

Similar to IBD, a combination of genetic predisposition with suitable environmental factors, in the presence of pathogenic microflora in particular host response, are primary factors involved in the pathogenesis of periodontitis (Figure 4).[61]

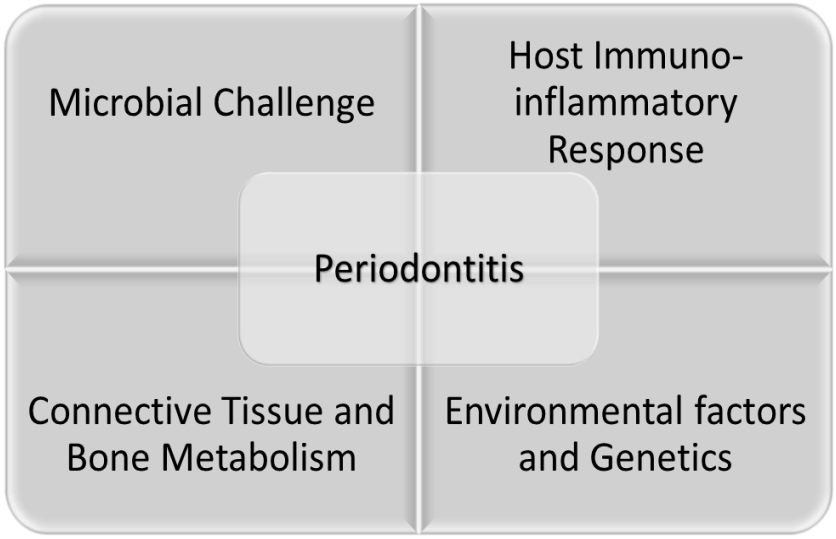

Figure 4: Pathogenesis of Periodontitis

Considering the pathogenesis of IBD and periodontitis individually, some common factors like immune-inflammatory responses, microbial components, cytokine array, genetic predisposition, environmental factors etc. can explain the co-existence of these two inflammatory diseases. Periodontitis has been reported as a manifestation in patients with IBD, but there are no longitudinal studies that could establish a causative link between IBD and periodontitis.[63]

A pathogenesis model of periodontitis and IBD has thus been proposed (Figure 5).[63] This model demonstrates the possible connection, either microbial composition, environmental factors, or genetic factors. These factors result in an immune-inflammatory pathway in an individual that might result in one of these conditions.

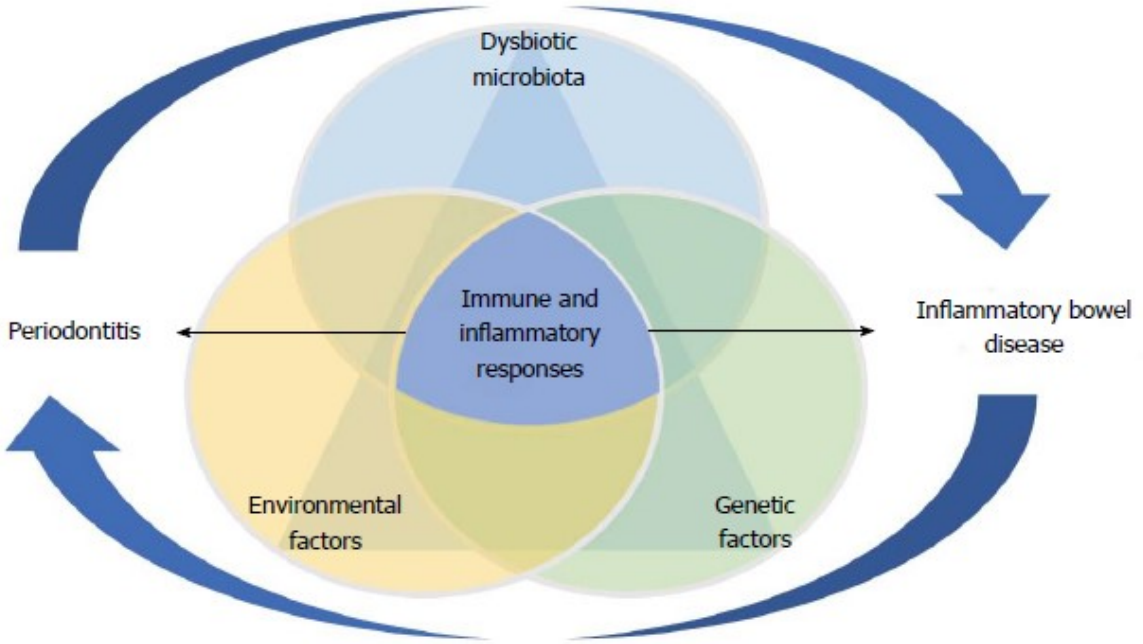

Figure 5: A Model of the Pathogenesis of Periodontitis and IBD

(Adapted by Lira-Junior R & Figueredo CM)[63]

Considering the complexity of both periodontitis and IBD, it is quite challenging to understand the possible pathways that might be involved in their coexistence. Few attempts have been made in the past to explore the microbial link between the two entities.[56,63] A study inspected the periodontal tissues in IBD affected individuals and showed the existence of gram negative small motile rods.[56] Another study used salivary compositions in IBD individuals and assessed variations in microbial composition as opposed to salivary microbiota in a healthy individual.[63]

Another aspect i.e., the immunological aspect that might link these two conditions have also been explored in the past.[33,56,57,63] Expression of various interleukins were evaluated in gingival crevicular fluid and serum from patients with untreated periodontitis and IBD was evaluated. There were no significant differences in the expression of an array of cytokines (like IL-1β, IL-4, IL-6, IL-10, TNF-α etc) between CD and UC when gingival tissue of patients was assessed.[33] Studies also explored defects in neutrophil chemotaxis in IBD patients with periodontitis.[56] Genetic

condition like single nucleotide polymorphisms, gene mutations and allele variations have been explored to investigate the genetic association.[63]

Even though the literature in the past explored the common pathways to associate these two inflammatory diseases, yet few other domains remain unexplored. So, to further contribute to the existing knowledge, a new direction of investigation is aimed in the present study. It has been stated that people living with IBD must cope with a lifelong condition that sometimes requires significant lifestyle adjustments that might influence oral hygiene behaviors and dietary habits. Thus, it is recommended to inform patients with IBD about the relationship between their disease and oral health. The significant impact of IBD on the oral health remains a matter of concern and several aspects that might explain the correlation between these two conditions remains unexplored. The present study is an attempt to explore this relationship taking into considerations the newer and unexplored aspects like variations amongst sexes, age groups, smoking status, type of IBD and oral hygiene adherence. Considering perio-systemic link, an early diagnosis of periodontitis is important for the overall health of an individual. These patients must be informed about the consequences of a higher risk of periodontitis incidence and prevalence, as well as the importance of its early diagnosis Thus, it is necessary to conduct further studies to explore the relationship between these two inflammatory conditions.

Chapter 2: Aims

Few studies have provided limited insight of periodontal status in patients with IBD and most studies examined clinical and microbiological levels while considering one or two parameters at a time.[57,61,63] To date, an ongoing attempt by researchers inspecting the gastrointestinal and oral health suggests an interaction between IBD and periodontitis. It has been hypothesized that interaction of these two conditions might alter the nature of the microbiota and increase the inflammatory response related to the other.[29] Still, more evidence is needed to confirm the effect of risk factors in the association between these two inflammatory conditions.

More studies are needed to study the effect of risk factors on the association between IBD patients and susceptibility to periodontitis. This will result in greater awareness amongst medical/dental practitioners and patients. There is an urgent need for investigation to understand the potential association between IBD and periodontitis and work in harmony to help vulnerable patients. It can help educate IBD patients on their periodontitis risk and the importance of maintaining dental health and adequate oral hygiene.

To help fill these gaps in the literature, we designed a retrospective study to estimate the risk of developing periodontitis considering variables like sex, age, smoking status, oral hygiene adherence in a population affected by different forms of IBD, i.e., CD or UC. If we consider the prevalence of periodontitis amongst sexes, NHANES reported an increased prevalence of periodontitis in males compared to females.[41] However, no data is available regarding this variable in IBD patients with periodontitis. Another factor that plays a crucial role in the variance of periodontitis amongst different populations is age. As shown in other studies, the prevalence of periodontitis is positively associated with increasing age.[41,64] We would like to determine if individuals suffering from IBD also show similar patterns of increasing periodontitis prevalence in different age groups.

Smoking is considered a significant risk factor in the development and progression of periodontitis.[8,9,12,13] When periodontal status was compared amongst smokers and nonsmokers, it was clearly shown that smoking significantly impacted the severity of the periodontitis.[10] The role of smoking in inflammatory bowel disease has been studied in the past, and it has been seen that

smoking has a negative association with UC but a positive association with CD which means it presents with benefits in UC patients but is detrimental in CD patients.[65]

This study also aimed to explore the effect of smoking on the severity of periodontitis in patients suffering from IBD; both UC and CD. We anticipate an increased burden of pathogens with an additional risk factor (smoking) leading to a more severe form of periodontitis manifestation in IBD patients.

Considering the etiological factors, the presence of bacterial plaque is one of the essential factors in the development of gingivitis which, sometimes can further progress into periodontitis.[66] Presence and amount of plaque on the tooth surface are used to determine the effectiveness of oral hygiene and patient compliance with their oral hygiene home-care regime, which is also one factor used to assess periodontitis risk in an individual. We want to explore if oral hygiene adherence would affect the severity of periodontitis amongst individuals with IBD. Also, it would be interesting to explore variation in prevalence of periodontitis between the two forms of IBD, i.e., CD and UC. It is important to estimate the prevalence of periodontitis in IBD-affected individuals, which will be completed by reviewing patient charts in a dental school clinical facility.

Thus, the aims of this study have been listed as follows (Table 4):

Specific Aim 1: To determine sex predilection for periodontitis in patients presenting with inflammatory bowel disease (IBD).

Specific Aim 2: To assess age-related changes in periodontitis prevalence in patients having IBD.

Specific Aim 3: To evaluate the odds of periodontitis in IBD patients with a smoking history.

Specific Aim 4: To assess the effect of oral hygiene adherence on the prevalence of periodontitis in patients presenting with IBD.

Specific Aim 5: To determine if the prevalence of the periodontitis varies between two forms of IBD, specifically, CD and UC.

Sex Predilection: Males v/s Females
Age Groups: 20-34 v/s 35-49 v/s 50-64 v/s 65-74 v/s >75[67]
Smoking Status: Smokers v/s Nonsmokers
Oral Hygiene Adherence: in terms of Plaque Percentage
Type of IBD: UC v/s CD

Table 4: Variables used to determine IBD and Periodontitis Association

Chapter 3: Materials & Methods

3.1: Ethics Approval

This study is a retrospective study that received ethical approval from Research Ethics and Management Online (REMO) ID#Pro00090612. Eight custodians of the Kaye Edmonton Dental Clinic signed research agreements for disclosure of patient records to conduct retrospective data mining.

3.2: Study Design and Data Collection

This study evaluated patient records from Kaye Edmonton Dental Clinic consisting of a history of IBD (Inflammatory Bowel Disease, IBD, Inflammatory bowel syndrome, Crohn's disease, Ulcerative Colitis, Indeterminate Colitis) between January 2013 and December 2019. All data for this study was obtained from the existing AxiUm clinic records.

AxiUm Dental is a HIPAA-compliant (Health Insurance Portability and Accountability Act), ONC-ATCB (Office of the National Coordinator- Authorized Testing and Certification Body) certified system. It involves applications such as electronic health records (EHR), billing, and practice management designed to address the needs of dental institutions. AxiUm also consists of modules for specialty practices, like orthodontics and periodontics.[68]

No PHI (Protected Health Information) was collected for this study. Patient records were retrieved and evaluated only by their AxiUm chart number. No personal data, including name, that could reveal the patient identity was accessed. Only individuals who have complied with the School of Dentistry patient privacy training (Privacy & Security Awareness Training and Acknowledgement) and were authorized to use AxiUm had any access to patient records.

Since we had access to the complete pool of patients who visited Kaye Edmonton Clinic from Jan 2013 to Dec 2019, we used unique keywords to define the search in the records. Therefore, the initial investigation aimed to identify patients that reported the presence of IBD, CD, or UC in their medical history.

For accuracy of data retrieval, AxiUm experts (technical staff dealing with AxiUm in the university setting) helped conduct a unique search of patients with IBD, CD, or UC by using specialized keywords. Thus, for the initial screening, a variety of keywords were used to widen the search. The keywords were also used to account for different spellings as spelling errors were noted in the free text data reporting. Therefore, the keywords for searching the AxiUm patient records resulted in an extensive list.

Specific keywords used to search AxiUm charts are listed as follows: (Table 5)

Inflammatory Bowel disease	Ulcerative colitis	Crohn's disease
Inflammatory bowel disease	Ulcrative colitis	Crohns disease
Inflammatory bowel disease	Alcerative colitis	crohn
Inflammatory bowel disease	Ullcerativ collitus	Chron disease
Inflamatry bowel disease	Ulcrative colittis	Chrons disease
Inflamtry boul disease	Elcertive colitis	Crohon disease
Bowel dsease	Ullcerative colitis	Cron disease
IBD	UC	CD
Inflammation bowel disease	Allcrativ colitis	Crohns disiase
Inflammatory bovel disease	Ulcer colitis	Cronss disease
Inflammatory boul disease	colitis	Craun disease
Bowel disease	collitis	Crauhn disease

Table 5: Keywords for Screening Charts.

A total of **239** patient records were retrieved in the initial screening that was done by using special keywords. From these 239 records that got listed in the initial search, 46 were obtained from reporting medical history; however, 193 were obtained from free texts in patient charts, which implies the variability of data recording amongst different operators who might have screened these patients in the past like undergraduate students, dental hygiene students, graduate periodontics residents.

After the initial screening, each patient chart was reviewed in detail. Each chart was assessed for the inclusion and exclusion criteria set in the study, which resulted in further elimination of charts. Duplicate records were removed. The patient charts selected in the initial search which did not fall into inclusion criteria, i.e., presence of IBD, CD, or UC were excluded.

Thus, the second search screening in AxiUm resulted in the retrieval of **132** patient records. Finally, a third screening was conducted to exclude any patient records, which were incomplete (did not present with complete recording of all the parameters used in the study listed in Table 9) and not useful for the study. Therefore, after three rounds of screening, the final number of patients' charts that were included in the study was **80**. The screening process has been displayed below (Table 6):

Records identified through database searching (n=239)
Records after duplicate removal (n=132)
Records screened (n=132)
Records excluded (n=52)
Records eligible (n=80)
Final charts reviewed (n=80)

Table 6: Flow Diagram presenting the Screening Process.

Inclusion Criteria: Patient records with a diagnosis of IBD, CD or UC, age > = 20 years, patient chart with complete periodontal assessment records.

Exclusion Criteria: Incomplete periodontal assessment charts, if selected patient records did not indicate IBD, CD, or UC or like terms (Table 6). Patients with a history or ongoing use of recreational drugs like cannabis, cocaine etc., and bisphosphonates were excluded from the study (as it masks the bone loss). Pregnant and lactating patients and immunocompromised individuals were excluded. And patients with age < 20 years were excluded from the study (to rule out the aggressive periodontitis).

Data collection: After the intensive search, the patient charts that fulfilled the inclusion criteria were each comprehensively studied. Information on the type of disease they were diagnosed with, i.e., IBD, CD, or UC was collected. It was essential to fulfill the specific aim five, which wanted to determine the variation in prevalence of periodontitis in both types of IBD. Sex and age were recorded to fulfill specific aims 1 and 2.

Other parameters, such as the number of missing teeth (n), maximum probing depths (PD), percentage of bone loss (expressed in percentage), clinical attachment loss (expressed in millimeters), mobility of tooth (grade 1,2,3), furcation involvement (grade1,2,3) were recorded to assign a diagnosis to each patient chart.[69-71] Bone loss was determined by subtracting 2mm from the cementoenamel junction (CEJ) and measuring up to the alveolar bone crest (X). Further percentage bone loss was calculated by dividing X with length from CEJ to the apex of the tooth multiplied by 100.[69] All calculations were done in AxiUm software using the radiographs available in patient records.

Thus, these variables were used to determine whether periodontitis was present or not. If present, it was recorded as Y; if not, it was denoted as N. Furthermore, if periodontitis was present, the patient charts were further categorized into four stages of periodontitis (Stage I-IV).[34] This was done to simplify when reporting variation among different variables as listed in the specific aims regarding the severity of the periodontitis.

Oral hygiene adherence was recorded in terms of plaque scores as the study design did not permit contacting patients to collect information about their oral hygiene adherence. Plaque scores (using O' Leary Plaque Scoring method) were recorded on four tooth surfaces, three on buccal (mesial, mid, distal) and one on palatal/lingual. The scores range from 0-1; 0 means no plaque, and 1 represents the presence of plaque. The percentage of plaque is calculated by dividing the total surfaces with score one by the total number of surfaces recorded multiplied by 100.[72]

Lastly, the patients' smoking status was recorded in terms of smokers if they were currently smoking or had a history of smoking, and nonsmokers if they had never smoked.

Parameters recorded from each patient chart are listed as follows (Table 7):

Type of Disease: IBD, CD, UC
Age of the patient
Sex of the patient
Number of missing teeth
Maximum probing depth
Maximum bone loss
Maximum CAL
Mobility with 3 grades, 1,2,3
Furcation Involvement with 3 grades 1,2,3
Plaque percentage
Smoking status: Nonsmoker, Past smoker, Current smoker

Table 7: Patient Chart Parameters.

3.3: Data Analysis

Once we retrieved all the data, grouping was done to conduct statistical analysis. For the specific aim one, which compares both sexes, we divided into two groups: males denoted as M and females denoted as F.

Another grouping was done in terms of age groups to fulfill the specific aim 2. Patient records were divided into five groups, as per the NHANES criteria for age, namely: Group 1: included patients from 20-34yrs of age, Group 2: 35-49yrs, Group 3: 50-64yrs, Group 4: 65-74yrs and Group 5: equal to or greater than 75yrs of age.[67]

Patient records were grouped according to their smoking status, and the data included 39 smokers and 41 nonsmokers. Another grouping was done in terms of the type of IBD, i.e., UC or CD.
IBM SPSS 21 (Statistical Package for the Social Sciences) statistical package was used to conduct all the statistical analyses performed in this study. Odds Ratio (OR) and 95% confidence intervals (CI) was used to present the risk of periodontitis. CI indicates that if this experiment were to be done multiple times, 95% of the values from this experiment would contain the actual value. A two-sided p-value < 0.05 was considered statistically significant.

2x2 contingency tables were drawn, and the odds ratio was calculated to determine the sex preference for periodontitis in patients presenting with IBD. 3x2 contingency tables were drawn, and the odds ratio was determined if smoking had any effect on the development of periodontitis in IBD patients.

To analyze which age group was most affected, 5x2 contingency tables were drawn and the odds ratio calculated. Pearson's correlation was calculated to ascertain if oral hygiene adherence affected the severity of periodontitis in IBD patients. Mann-Whitney U test was conducted to verify the effect of disease type, i.e., UC or CD, on the development of periodontitis. All tests of significance were evaluated at a 0.05 error level.

Chapter 4: Results

4.1: Sex differences

In the present study, the patient records comprised 43 females and 37 males (Figure 6). About 74.4% of females presented with periodontitis and 75.7% of males presented with periodontitis (Table 8, Figure 7).

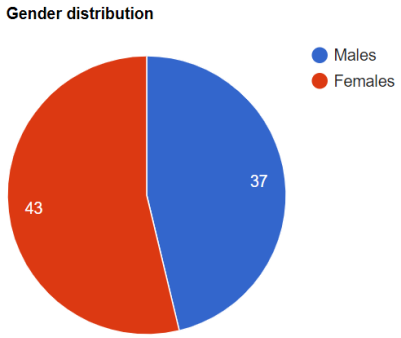

Figure 6: Sex distribution

Sex * Perio Disease Crosstabulation

			Perio Disease		
			N	Y	Total
Sex	F	Count	11	32	43
		Expected Count	10.8	32.3	43.0
		% within Sex	25.6%	74.4%	100.0%
		% within Perio Disease	55.0%	53.3%	53.8%
		% of Total	13.8%	40.0%	53.8%
	M	Count	9	28	37
		Expected Count	9.3	27.8	37.0
		% within Sex	24.3%	75.7%	100.0%
		% within Perio Disease	45.0%	46.7%	46.3%
		% of Total	11.3%	35.0%	46.3%
Total		Count	20	60	80
		Expected Count	20.0	60.0	80.0
		% within Sex	25.0%	75.0%	100.0%
		% within Perio Disease	100.0%	100.0%	100.0%
		% of Total	25.0%	75.0%	100.0%

Table 8: CrossTabulation for Sex Distribution

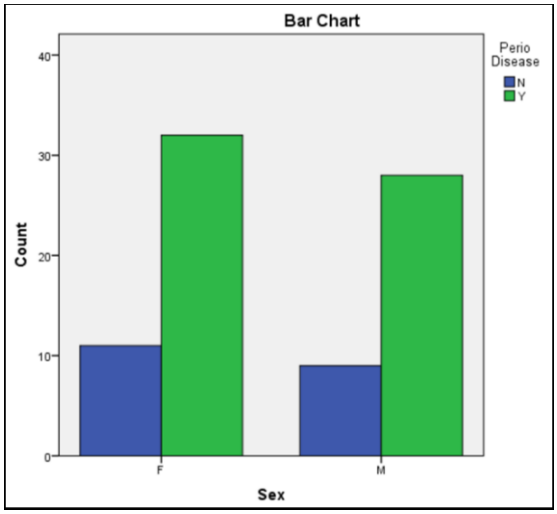

Figure 7: Periodontitis v/s Sexes.

Expected counts are the projected frequencies in each cell if the null hypothesis is true, i.e., if we consider that there is no association between sex and periodontitis in IBD individuals. Pearson's

Chi-square Test of Association was used for two independent variables, i.e., sexes (M-Males, F-Females) and periodontitis. This statistical test was used to determine if there was any relationship between two these two independent variables. A p-value of 0.897 was obtained, which implies that the difference in males and females presenting periodontitis in IBD patients is not significant (Table 9).

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.017[a]	1	.897		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.017	1	.897		
Fisher's Exact Test				1.000	.553
N of Valid Cases	80				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 9.25.

b. Computed only for a 2x2 table

Table 9: Pearson's Chi-square Test to Determine Sex Differences.

The odds ratio was calculated via cross tabulations to compare periodontitis in each sex. Typically, an odds ratio of 1 would indicate that there is no sex difference. If the odds ratio is much higher than 1, the odds are greatly increased for women than men. If the odds ratio is much lower than 1, the odds are much lower for women. The results depicted an OR=1.069 for females with IBD to present with periodontitis compared to males (Table 10).

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for Sex (F / M)	1.069	.387	2.955
For cohort Perio Disease = N	1.052	.490	2.257
For cohort Perio Disease = Y	.983	.763	1.267
N of Valid Cases	80		

Table 10: Odds Ratio b/w Females v/s Males

Another analysis was conducted to determine if there was any variation in severity of periodontitis amongst males and females, (Table 11). The absence of periodontitis was marked as stage 0 for statistical analysis. And stage 1-4 represented the severity of the periodontitis, Stage 4 being the most severe.

Sex * Severity Crosstabulation

			Severity					Total
			0	1	2	3	4	
Sex	F	Count	11	2	7	22	1	43
		% within Sex	25.6%	4.7%	16.3%	51.2%	2.3%	100.0%
		% within Severity	55.0%	100.0%	87.5%	50.0%	16.7%	53.8%
		% of Total	13.8%	2.5%	8.8%	27.5%	1.3%	53.8%
	M	Count	9	0	1	22	5	37
		% within Sex	24.3%	0.0%	2.7%	59.5%	13.5%	100.0%
		% within Severity	45.0%	0.0%	12.5%	50.0%	83.3%	46.3%
		% of Total	11.3%	0.0%	1.3%	27.5%	6.3%	46.3%
Total		Count	20	2	8	44	6	80
		% within Sex	25.0%	2.5%	10.0%	55.0%	7.5%	100.0%
		% within Severity	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
		% of Total	25.0%	2.5%	10.0%	55.0%	7.5%	100.0%

Table 11: Severity of Periodontitis in Sexes

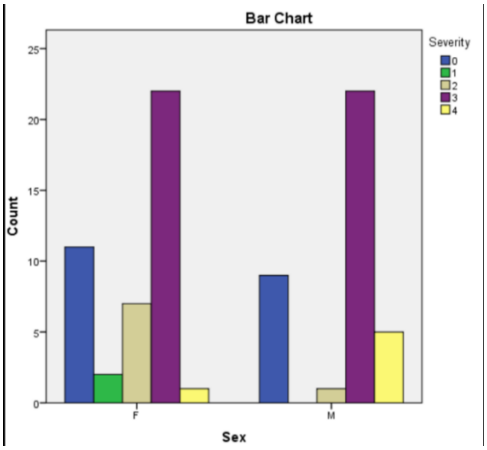

Figure 8: Severity of Periodontitis in Sexes.

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.967[a]	4	.062
Likelihood Ratio	10.496	4	.033
N of Valid Cases	80		

a. 6 cells (60.0%) have expected count less than 5. The minimum expected count is .93.

Table 12: Pearson's Chi-square Test to Determine Sex Differences and Severity of Periodontitis.

The crosstabulations revealed a higher percentage of Stage 3 periodontitis in both groups. In this study, 59.5% of the males and 51.2% of females presented with Stage 3 periodontitis (Table 11, Figure 8). Pearson's Chi-square Test was applied to determine the statistical difference in each sex in terms of disease severity, p-value=0.062, which implies the difference in males and females in terms of severity of periodontitis in IBD patients was not statistically significant (Table 12).

4.2: Age variation

To verify the variation in age groups, the patient records were divided into five groups, as per the NHANES (National Health and Nutritional Examination Survey) criteria, namely[67]:

- Group 1: patients from 20-34yrs of age,
- Group 2: patients from 35-49yrs,
- Group 3: patients from 50-64yrs,
- Group 4: patients from 65-74yrs
- Group 5: patients equal to or greater than 75yrs of age.

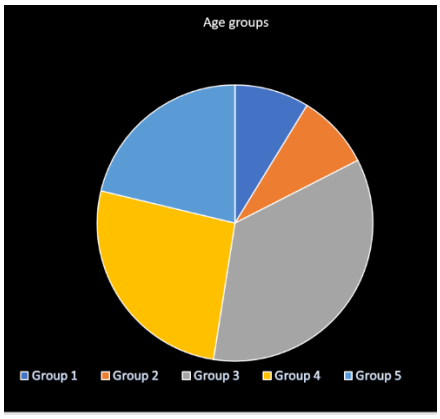

Figure 9: Patient records in each Age Group.

		Perio Disease		
		N	Y	Total
Age group	1	4	3	7
	2	4	3	7
	3	3	25	28
	4	3	18	21
	5	6	11	17
Total		20	60	80

Table 13: Periodontitis in Different Age Groups.

The data resulted in retrieving 7 patient records for groups 1& 2 each, 28 patient records in group 3, 21 in group 4 and 17 in group 5 (Figure 9, Table 13). Age Group 3 (50-64yrs) presented with the highest number of patient charts depicting the presence of periodontitis (Table 14, Figure 10).

			Perio Disease		
			N	Y	Total
Age group	1	Count	4	3	7
		Expected Count	1.8	5.3	7.0
		% within Age group	57.1%	42.9%	100.0%
		% within Perio Disease	20.0%	5.0%	8.8%
		% of Total	5.0%	3.8%	8.8%
	2	Count	4	3	7
		Expected Count	1.8	5.3	7.0
		% within Age group	57.1%	42.9%	100.0%
		% within Perio Disease	20.0%	5.0%	8.8%
		% of Total	5.0%	3.8%	8.8%
	3	Count	3	25	28
		Expected Count	7.0	21.0	28.0
		% within Age group	10.7%	89.3%	100.0%
		% within Perio Disease	15.0%	41.7%	35.0%
		% of Total	3.8%	31.3%	35.0%
	4	Count	3	18	21
		Expected Count	5.3	15.8	21.0
		% within Age group	14.3%	85.7%	100.0%
		% within Perio Disease	15.0%	30.0%	26.3%
		% of Total	3.8%	22.5%	26.3%
	5	Count	6	11	17
		Expected Count	4.3	12.8	17.0
		% within Age group	35.3%	64.7%	100.0%
		% within Perio Disease	30.0%	18.3%	21.3%
		% of Total	7.5%	13.8%	21.3%
Total		Count	20	60	80

Table 14: Crosstabulation Presenting the Periodontitis v/s Age.

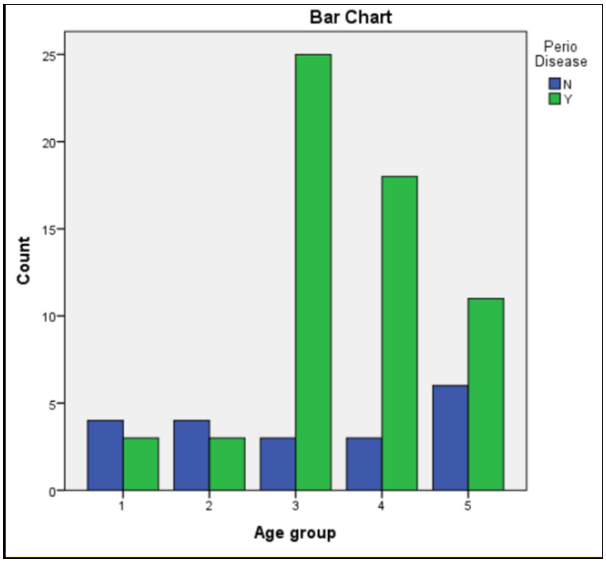

Figure 10: Periodontitis v/s Age.

The recorded data presented with variation in the number of patient records in each age group; thus, the data was not uniformly distributed. Therefore, to determine significant differences between 5 different age groups, Fischer's Exact Test was the chosen statistical method. This test was selected because of the smaller sample size, and in this case, the p-value is exact and is not an approximation. The Pearson's Chi-square test is not appropriate when the expected values in one of the contingency table cells are less than 5, and in this case, Fisher's Exact Test is preferred. The Fischer's Exact Test computed the p-value of 0.010, which implies a significant difference in age groups in presenting periodontitis in IBD patients (Table 15).

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	13.008[a]	4	.011	.009
Likelihood Ratio	12.485	4	.014	.021
Fisher's Exact Test	12.400			.010
N of Valid Cases	80			

a. 3 cells (30.0%) have expected count less than 5. The minimum expected count is 1.75.

Table 15: Fischer's Exact Test for Periodontitis v/s Age.

Odds ratios were calculated amongst different age groups (Table 16). The odds of having the periodontitis in Group 2 v/s Group 1 was 1, which implies similar periodontitis rates in both

groups. Thus, ages 20-49 years have identical odds of developing periodontitis. However, the odds of having the periodontitis in Group 3 v/s one was calculated to be 11.1. Thus, depicting greater odds of periodontitis as age increases over 50 years. Similarly, when odds were calculated for Group 4 v/s Group 1, OR of 8 was found. Also, an OR of 2.44 was seen when Group 5 was compared with Group 1.

Group 2 v/s Group 1= 1
Group 3 v/s Group 1= 11.1
Group 4 v/s Group 1= 8
Group 5 v/s Group 1= 2.44

Table 16: Odds Ratio in Different Age Groups.

Thus, consistent higher odds of periodontitis were seen with ages equal to and above 50 years compared to those less than 50 years of age.

4.3: Smoking status

Analysis was conducted to determine the effect of smoking status on the development of periodontitis in IBD patients. To conduct statistical analysis, the data were divided into two groups according to their smoking status:

- Smokers (Y): patient records that reported current smoking or the patient records indicated a history of smoking, but the patients had quit smoking (regardless of the time of quitting).
- Nonsmokers (N): patient records that did not report smoking.

The data presented with 41 nonsmokers and 39 smokers (Figure 11, Table 17). The patient records could not be categorized into current and former smokers because of the lack of data reporting their smoking history.

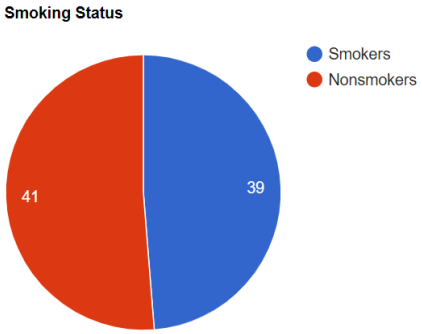

Figure 11: Smoking Status.

Smoking * Perio Disease Crosstabulation

Count

		Perio Disease		
		N	Y	Total
Smoking	No	11	30	41
	Yes	9	30	39
Total		20	60	80

Table 17: Smoking Status Distribution

A total of 73.2% of nonsmokers and 76.92% of smokers presented with periodontitis (Table 18, Figure 12).

Smoking * Perio Disease Crosstabulation

			Perio Disease		
			N	Y	Total
Smoking	No	Count	11	30	41
		Expected Count	10.3	30.8	41.0
	Yes	Count	9	30	39
		Expected Count	9.8	29.3	39.0
Total		Count	20	60	80
		Expected Count	20.0	60.0	80.0

Table 18: Periodontitis Amongst Smokers & Nonsmokers.

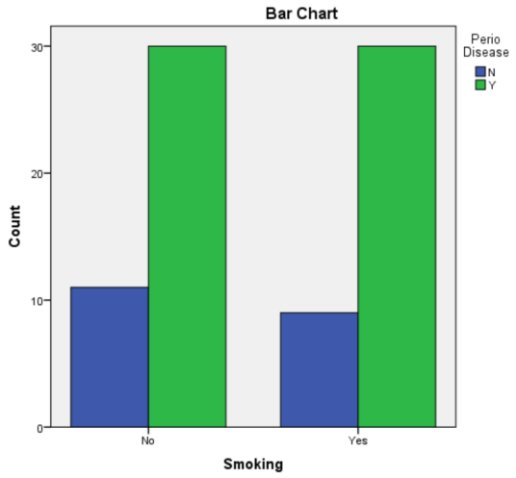

Figure 12: Periodontitis Status in Smokers& Nonsmokers.

The odds ratio was calculated amongst smokers and nonsmokers (Table 19). Data derived from the included patient records reported was not statistically significant.

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for Newsmoking (No / Yes)	1.222	.443	3.376
For cohort Perio Disease = N	1.163	.541	2.496
For cohort Perio Disease = Y	.951	.739	1.225
N of Valid Cases	80		

Table 19: Odds Ratio Calculations for Periodontitis v/s Smoking Status

Nonsmokers were considered a control group, and statistical analyses were conducted among smokers and nonsmokers. Pearson's Chi-square Test was applied to determine a significant difference between 2 groups divided based on their smoking status. A p-value=0.698 was determined, which implies no significant difference in these groups in presenting periodontitis in IBD patients (Table 20).

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.150[a]	1	.698		
Continuity Correction[b]	.017	1	.897		
Likelihood Ratio	.150	1	.698		
Fisher's Exact Test				.798	.449
N of Valid Cases	80				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 9.75.

b. Computed only for a 2x2 table

Table 20: Pearson’s Chi-square Test for Periodontitis in Different Smoking Statuses.

4.4: Oral hygiene adherence

Oral hygiene adherence is another factor which has an essential role in developing periodontitis and was assessed in the present study. The study to evaluate if oral hygiene adherence was related to the severity of periodontitis in patients presenting with IBD. Since the nature of the study was retrospective, the oral hygiene adherence was determined based on plaque percentage recorded in the patient charts. AxiUm software provides plaque percentage (recorded using O’ Leary plaque scoring method) in the summary tab against the periodontal charts. Those percentages were used in the study. The percentage is determined based on all existing teeth. Plaque percentage was

corelated against severity of periodontitis (Stage 1-4), considering that as the plaque score increases, the severity of periodontitis is expected to increase.

Pearson's correlation test was conducted to evaluate the variation in severity of the periodontitis based on plaque percentage. The statistical analysis revealed a p-value of 0.339, which was not statistically significant, thus reflecting that there was no effect of plaque on the prevalence of periodontitis in IBD-affected individuals (Table 21).

Correlations

		Plaque %age	Severity
Plaque %age	Pearson Correlation	1	.121
	Sig. (2-tailed)		.339
	N	64	64
Severity	Pearson Correlation	.121	1
	Sig. (2-tailed)	.339	
	N	64	80

Table 21: Pearson's correlation Test for Oral Hygiene Adherence v/s Periodontitis.

Another analysis was done taking 50% plaque score as a cut off and then corelated with severity of periodontitis (Table 22). It was tested based on assumption that once certain amount of plaque is present, the severity of periodontitis should not vary. Pearson Chi-Square test applied and a p-value of 0.636 was obtained, which was not significant.

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.223[a]	1	.636		
Continuity Correction[b]	.029	1	.865		
Likelihood Ratio	.224	1	.636		
Fisher's Exact Test				.765	.433
N of Valid Cases	64				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 6.78.

Table 22: Pearson Chi-Square Test for Oral Hygiene Adherence v/s Periodontitis

4.5: Disease type

This study aimed to consider the variation of periodontitis amongst two different forms of IBD, i.e., UC and CD. Thus, the data were grouped according to the type of IBD as follows:

UC: Patients presenting with Ulcerative Colitis.

CD: Patients presenting with Crohn's Disease.

The data revealed 25 patients with CD and 24 patients with UC (Table 22, Figure 13).

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	Disease	N	Percent	N	Percent	N	Percent
Severity	CD	25	100.0%	0	0.0%	25	100.0%
	UC	24	100.0%	0	0.0%	24	100.0%

Table 23: Data presenting UC & CD cases

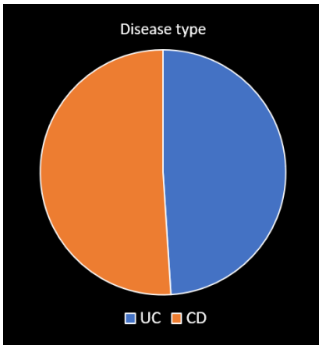

Figure 13: CD and UC Cases.

A total of 17/24 patients in the UC group and 20/25 in CD group presented with periodontitis (Table 23, Figure 14).

Count

		Perio Disease		
		N	Y	Total
Diseasegroup	UC	7	17	24
	CD	5	20	25
Total		12	37	49

Table 24: Data with UC and CD Group v/s Periodontitis.

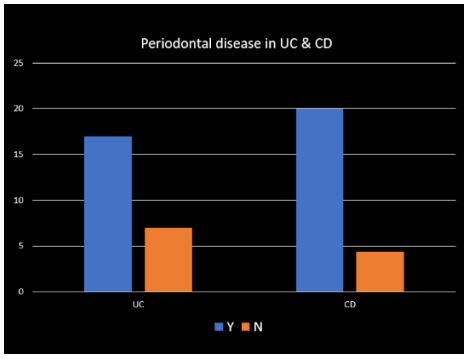

Figure 14: Periodontitis in 2 Types of IBD.

Mann-Whitney U test (a nonparametric test for small sample sizes <30) was conducted to analyse the difference of periodontitis presentation in the two forms of IBD (UC and CD). A p-value of

0.420 was obtained, hence reporting no significant difference in periodontitis in UC or CD (Table 24).

Ranks

	Diseasegroup	N	Mean Rank	Sum of Ranks
Severity	UC	24	23.50	564.00
	CD	25	26.44	661.00
	Total	49		

Test Statistics[a]

	Severity
Mann-Whitney U	264.000
Wilcoxon W	564.000
Z	-.806
Asymp. Sig. (2-tailed)	.420

Table 25: Mann-Whitney U Test for Periodontitis in 2 Types of IBD.

4.6: Summary of results

Summary of results, with limitation due to retrospective nature of the present study, has been noted as follows:

1. There is no sex predilection for periodontitis in patients presenting with IBD, the odds ratio for females with IBD presenting with periodontitis compared to males was not statistically significant.
2. NHANES (National Health and Nutritional Examination Survey) criteria were used for grouping the data according to age into five groups.[67] Patients in the age range of 50-64 years and who had IBD were most affected by periodontitis. Stage 3 periodontitis was most prevalent in this age group.
3. Smoking in IBD patients did not increase the odds of developing periodontitis.
4. Oral hygiene adherence did not affect the prevalence of periodontitis in patients presenting with IBD.
5. The prevalence of periodontitis did not differ between patients who had UC or CD.

Chapter 5: Discussion

The retrospective chart analysis revealed that in most patient records, periodontitis co-existed in patients with inflammatory bowel disease. Out of 80 IBD patient charts reviewed, 60 (75%) patients were recorded as having periodontitis. Thus, most patients presented with periodontitis. Previous literature has indicated an association of periodontitis in IBD patients.[30,59] A previous study reported that prevalence of periodontitis in IBD patients was 37.5% in the Chinese population.[30] The objective of the present study was to delve into the periodontitis variation amongst sexes, different age groups, smoking status, oral hygiene adherence, and the two types of IBD. Data from this study shows that patients presenting with IBD, falling in the age range of 50-64 years, were most affected by periodontitis, and Stage 3 periodontitis was most prevalent.

Due to the retrospective study design of the present study, it could not be confirmed which of the two conditions occurred first because of which a causal relationship cannot be established between the two diseases. More studies considering different time points before and after periodontal therapy are needed to determine a causal relationship, if any. Alternatively, time lapse since the patients were diagnosed with IBD (1 year, 2 years, 5 years etc.) can also be taken into consideration. Also, it would be interesting to include IBD patients with healthy periodontium as control and their assessment over the years to find out the change in their periodontal status. In the present study, only 25% of the data comprises patients devoid of periodontitis; thus, due to the very small sample size, it was not possible to use this group as a control group to complete any further analysis.

The study looked at the variation in periodontitis in IBD individuals in both the sexes i.e males and females. Out of 43 females, 32 (74.4%) presented with periodontitis. From the 37 male patients, 28 (75.7%) had periodontitis (Table 8). Chi-square tests did not reveal any significant difference between males and females in terms of periodontitis (p-value=0.897) (Table 9). The odds ratio for females with IBD to present with periodontitis compared to males was 1.069, which was not statistically significant (Table 10). Studies in the past have demonstrated males as a risk determinant in periodontitis; thus, a sex predilection has been determined to be associated with periodontitis.[5,41] Literature shows that sex distribution is variable in patients with IBD depending on the type of IBD (UC and CD).[82] No sex variation was noticed in this study. This might be

possible because of the smaller sample size, that sex predilection could not be determined in the present study. Similar studies with larger sample sizes are needed to justify a predilection in sexes, if any.

A study that looked at sex variation in IBD stated that in patients with CD, a greater prevalence of females with the disease was noticed, while in patients with UC, no significant differences between prevalence of the disease in females or males was observed.[74] It was also stated that the sex ratios in CD varied with age and geographic region.[74] In spite of the male predilection for periodontitis and female predilection for CD, our study failed to establish any sex predilection for the two diseases. A larger study with more patients in each age group of both the sexes is needed to explore this further.

The literature to date supports that periodontitis has a higher incidence in the elderly group.[41,64]. However, the results of this study showed higher odds of presenting with periodontitis in the age range of 50-64. This contrasted with NHANES study in which age groups over 65 and 75 presented with higher prevalence of periodontitis. The third age group (50-64yrs) in the present study that had higher risk of presenting with periodontitis showed an OR 11.1 when compared to ages 20-34 years (Table 16). NHANES data established that the prevalence of periodontitis was positively associated with age.[41,64] However, in the present study there was no linear relationship between the patient's age and these two disease conditions. It can be explained that periodontitis tends to peak in the elderly group, i.e.,>50 yrs.[64] Also, it has been found that IBD has a bimodal incidence pattern, with the main peak of occurrence being found between 15-25 years of age and a second, smaller rise in IBD occurrence during the fifth to seventh decades of life.[75] Thus, there is a possibility that patient records included in the data were in the 2nd peak of their IBD presentation and thus formed most of the data. In the present study Group 3 comprised of ages 50-64 which presented with increased odds of periodontitis which could be attributed to the occurrence of peak in the IBD symptoms in this age group. Or another explanation for this finding could be cumulative effect of age-related periodontal changes and peak occurrence of IBD. However, the patient distribution was not equal for all groups; a future prospective study with equal group distribution of patients in each age group could address this shortcoming.

Fischer's Exact test was applied to determine significant difference between the five age groups and a considerable difference was found in age groups for those patients presenting with periodontitis and IBD (p-value=0.010) (Table 15).

Another factor assessed in the present study was to examine the effect of smoking status on the presentation of periodontitis in IBD-affected individuals. Smoking is an established risk factor for periodontitis and tends to increase the prevalence and severity of the disease.[8-13] For the present study, the patient records were divided into two categories: smokers and nonsmokers. A percentage of 73.2% of nonsmokers and 76.92% of smokers presented with periodontitis. The odds ratio was calculated amongst smokers and nonsmokers (Table 19). It was seen that nonsmokers had higher odds of having periodontitis when compared to smokers, but the result was not statistically significant (p-value= 0.698) (Table 20). The results of the study could be because the group who smoked comprised of past smokers and current smokers. The periodontal literature emphasizes that years of smoking and years of cessation are crucial elements in determining the effects of smoking on developing periodontitis. Due to the nature of the study, years of cessation and years of smoking could not be taken into consideration. Thus, there was expected variability in periodontal disease presentation. Also, there is an established dose-response in smokers, and the present study could not collect information about how many cigarettes per day were being consumed.[10] It could have been possible that the past smokers might have quit long back, and the effects of smoking, as shown in literature, stay for up to 11 years.[10] Usually, smoking is considered a risk factor in IBD, but a contrasting evidence was cited in literature. An observational study was conducted to explore the risk of developing IBD with smoking.[76] They used mendelian randomization and showed that smoking does not causally increase the risk of IBD.[76] The findings of this study can be supported by previous research where they defined smoking to be an effective modifier since there was no difference in the prevalence of periodontitis among non-smoking control patients and non-smoking patients with IBD.[77]

The effect of oral hygiene adherence on the severity of periodontitis in patients presenting with IBD was analyzed in the present study. The oral hygiene adherence was assessed in terms of plaque percentage recorded in the patient charts. This correlation was investigated because it has been

seen that poor oral hygiene is one of the main etiological factors in developing periodontitis, and the study was designed to explore it in IBD-affected individuals. A systematic review reported the increased association of poor oral health with IBD.[78] In the present study, Pearson's correlation was used to evaluate patients with IBD and the variation in severity of periodontitis when assessed based on plaque percentage. A p-value of 0.339 resulted, which was not statistically significant, thus reflecting that there was no effect of plaque on the rates of periodontitis in IBD-affected individuals. The data was only derived from a plaque score, but if oral hygiene adherence were to be recorded in person using standardized established questionnaires, it would have been assessed differently, but this was out of the scope of the present study given this was a retrospective chart review.[79]

Lastly, the study was aimed to assess if the prevalence of periodontitis differs in patients who have UC versus CD. Since it has been seen that these two forms of IBD vary in their clinical presentation and symptoms, and the study was designed to explore the varying effect, if any, on periodontitis presentation.[30,59,60] The data revealed 24 UC and 25 CD cases. Mann-Whitney U test revealed a p-value of 0.420; hence there was no significant difference in periodontitis in patients with UC versus CD. Therefore, it can be derived that although the clinical presentation of CD and UC vary in terms of periodontitis, there is no variation between these two forms. This could be explained by the fact that both forms of IBD share the common pathogenesis with periodontitis and thus no difference in prevalence of periodontitis was seen in the present analysis.

This study focused mainly on the clinical features to determine periodontitis in IBD patients. A few studies have evaluated the gingival and intestinal tissues to inspect the cytokines thus to accommodate for their co-existence but failed to report any association and rather evidenced different clustering patterns of cytokines in the gingival tissues and gut tissues.[33]

Tumour necrosis factor-alpha (TNF-α) is a cytokine of high importance in IBD.[80] It has been established that TNF-α disrupts the intestinal epithelial barrier resulting in intestinal inflammation.[81] The scientific advancement in medicine has advised anti- TNF-α antibodies for treating IBD-affected individuals.[81] Similarly, TNF-α has been proven to be a suitable indicator of existing periodontitis, and elevated levels have been recorded in the gingival crevicular fluid in

periodontitis.[82] It would be informative to correlate the levels of TNF-α with the severity of periodontitis in IBD patients. Another element that can be explored is the level of C-Reactive Proteins (CRPs). Studies have seen that CRP levels are increased in both IBD and periodontitis.[83-87] Thus, it would add insight to the literature to compare levels of CRPs in their co-existence v/s in individual diseases. Also, immunological evidence correlated with clinical findings would be of immense value.

It would be helpful for future studies to compare IBD activity and variation of periodontitis. Validated questionnaires like Harvey Bradshaw Index for Crohn's disease and Partial Mayo Score for Ulcerative colitis have been used to determine the activity of these diseases.[88] It would be beneficial to see if the activity of IBD had a variation in presentation of periodontitis. A carefully designed clinical study with questionnaires to determine the activity of IBD and corelating the periodontitis severity to the activity/remission of IBD individuals could be useful for further understanding of the association of these two diseases.

Chapter 6: Conclusions

The findings of this study showed reported that patients having IBD in the age range of 50-64 years have greater odds of periodontitis. Since age has a significant effect on IBD-affected individuals in developing periodontitis and its severity, it is advised to keep them under regular recall for early diagnosis and maintenance. No sex predilection for periodontitis in patients presenting with inflammatory bowel disease was seen. The present study did not state increased odds of periodontitis in patients with IBD with a smoking history.

When oral hygiene adherence was assessed in the present study, it did not affect the occurrence of periodontitis in patients presenting with IBD. But since plaque is an etiological factor in periodontitis, plaque control regimes should be encouraged. Although there is a variation in the clinical presentation of UC and CD, the prevalence of periodontitis did not differ between UC and CD. Patients who have either UC or CD should be examined with the same assessment measures for determining their regime for periodontal care. Since the increased prevalence of periodontitis was seen in IBD, it is advised for gastroenterologists to collaborate with periodontists and possibly other dental professionals to ensure periodontal health is maintained in IBD-affected individuals.

Chapter 7: Limitations & Future Directions

7.1: Limitations of the study

Some of the limitations of this study have been listed as follows:

1. Retrospective study design: The nature of the study being retrospective, lack of exact parallel study design, incomplete standardization, and missing detailed baseline data were amongst the biggest limitations of the present study. As the study was conducted using past patient records, this limited the data collection, and the researcher had no control of increasing the sample size. The study design restricted the usage of available patient records only. The data once collected after the screening consisted of incomplete patient chart recording, missing baseline information. Thus, a good number of patient records could not be included hence decreasing the overall sample size. Also, a variation in data recording was seen since patient records were not collected by one examiner at one time point**.** Thus, data collection was tedious.
2. Another limitation was that a control group could not be selected, and thus statistical analysis was conducted by strategic grouping of data from the study.

7.2: Recommendations for data entry when recording health and dental history

Considering the challenges faced throughout this study, following recommendations are proposed:

- Consistent measures to educate and calibrate dental students to collect patient information and comprehensive periodontal assessment.
- Specific AxiUm recommendations for data collection like recording complete medical history with special emphasis on the IBD section, recording the disease onset, flare ups, activity/ remission status, and current medications.
- Patients who present with IBD should be set up with regular periodontal examinations annually.
- Record of previously missing teeth should be documented, stating the reason being periodontal or others, if patient is aware of the same.

- Along with the periodontal charting, although plaque scores are recorded in the periodontal charts, it should be made sure that plaque is recorded for every patient who has been diagnosed with IBD at each appointment to assess oral hygiene adherence.
- Although there is a defined space to record the oral hygiene regimen, stating the frequency of brushing and flossing, an additional column to record the use of interdental aids, if any is recommended.

  The medical history forms should be filled with tobacco use information that should be more detailed and should include years of smoking, smoking frequency, and added pack years column. Other forms of smoke, like vaping, cannabis, etc., should also be recorded. For every past smoker, a cessation history should be complete. Since smoking is an established risk factor in periodontitis, it is highly recommended that there should be a prompt or warning generated on patient record if the smoking history is not recorded. This could create a habit in dental practitioners to be thorough while data recording especially smoking.
- It is recommended that recall intervals for each patient should be set up using Periodontal Risk Assessment tool.[89]
- The study found out that there was a considerable variation in terms of spellings used during the data screening; specifically, with the use of several keywords provided in materials and methods in this study. It would be of great value if a spell check function can be added to the AxiUm software to eliminate spelling errors for future data screening for similar studies.

7.3: Future Directions

- A case-control prospective study is recommended using patients with healthy periodontium as a control group. It is also recommended to design a clinical study correlating with immunological markers such as TNF-α, CRP. It would also be helpful to compare the periodontal status of IBD patients in active disease v/s in remission. Since IBD has a bimodal peak, study groups can be used from the peak ranges, and their periodontal status can be compared. Collaboration with gastrointestinal clinic is recommended to corelate the

IBD activity with severity of periodontitis. More studies are needed to explore the relationship between these two disease entities.

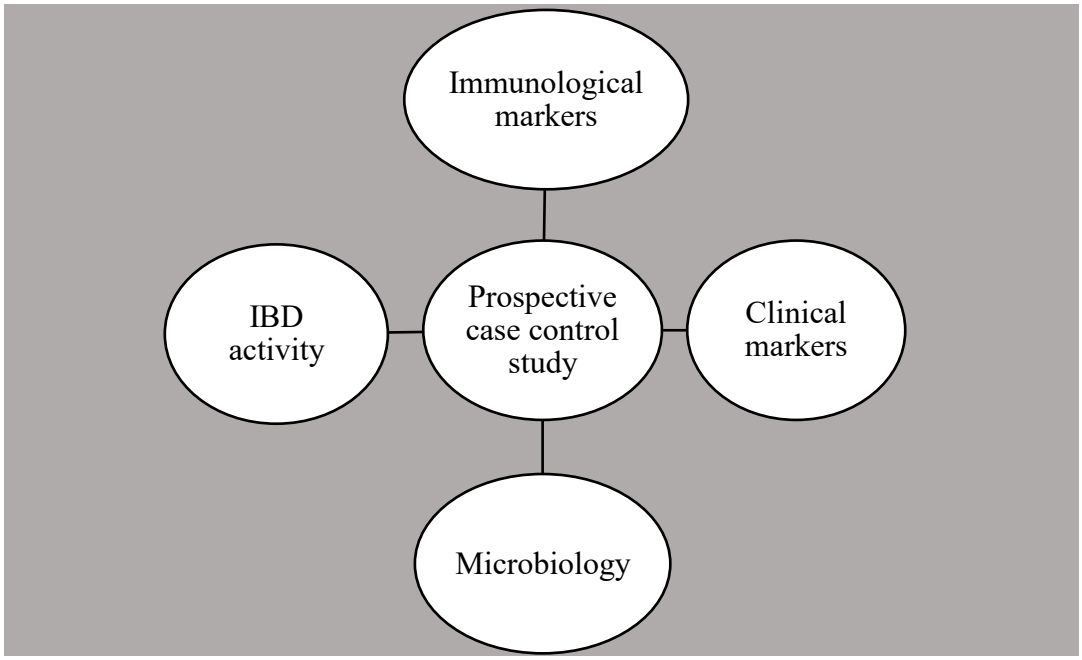

Figure 15: Future study design

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