TREATMENT MODALITIES AND ANTIBIOTIC PRESCRIPTION PATTERN OF AGGRESSIVE PERIODONTITIS IN A TEACHING DENTAL CLINIC SETTING.

A Thesis
Submitted to
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MASTER OF SCIENCE

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by
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ABSTRACT:

Periodontal infection can manifest itself in many different clinical presentations. The aggressive form of this disease is frequently seen in the younger patient population referred for treatment to the Temple University Kornberg School of Dentistry (TUKSD). This study was done to assess the demographics of aggressive periodontitis cases and the types of periodontal treatment methods provided to these patients, antibiotic prescription patterns and compliance with treatment. A chart review was conducted to identify cases of aggressive periodontitis in patients <30 years of age referred for treatment at the Graduate Periodontology and Oral Implantology Clinic, TUKSD. The diagnosis of aggressive periodontitis was validated by presence of characteristic radiographic bone loss at permanent incisors and molars. Exclusion criteria were deficient radiographs, and a medical history of systemic diseases that compromise the immune response. Twenty-two aggressive periodontitis cases were identified among 300 charts surveyed. All patients were 12-26 years old. The patient sample was comprised mainly of African American race-ethnicity, with no predominance of a sex group. Initial treatment with scaling and root planing, was done in 64% of cases with 36% dropout before treatment. Microbial plaque testing was done in 46% of cases, and 59% received systemic antibiotics. A combination antibiotic therapy regimen was often used in combination with nonsurgical periodontal therapy. Most patients did not present for treatment beyond the non-surgical phase, and some even before the treatment started. Because periodontal non-surgical treatment of aggressive periodontitis cases in the pre-doctoral clinic takes relatively long time, it is recommended that the treatment of these cases be expedited by

referring the patients to the graduate clinic for all periodontal treatment including the initial phase.

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CHAPTER 1

INTRODUCTION

Periodontal infection can manifest itself in many different clinical presentations. The International Workshop for a Classification of Periodontal Diseases and Conditions was held in 1999 to categorize and create a new classification system of periodontal diseases. [(1)] The new classifications revised and modified the 1989 World Workshop in Clinical Periodontics classifications of various forms of periodontitis. Some of the key changes were the addition of a section on gingival diseases [(2)], removing the category of ”early onset periodontitis” and its replacement with “aggressive periodontitis”. The new classifications were created to help clinicians differentiate and identify various forms of gingival and periodontal diseases including chronic, aggressive and necrotizing forms. Each periodontal condition that follows a certain clinical presentation with associated symptoms is now recognized as having individual clinical syndromes.

Aggressive periodontitis has been described in the dental literature as juvenile, localized juvenile, generalized juvenile, rapidly progressive, severe and pre-pubertal periodontitis. The AAP World Workshop in Clinical Periodontics, 1989, characterized early onset periodontitis as being associated with specific microflora, seen in those with defects in host defenses. This disease entity was recognized as having a rapid progression of periodontal attachment loss, with an age of onset <35 years old. The 1993 European Workshop on Periodontology, altered the definition to include individuals < 40 years of age at the time of onset. In 1999, the AAP International Workshop for the Classification of Periodontal Diseases changed the name of early onset periodontitis to aggressive periodontitis. This classification was further subdivided into a localized form with an age

of onset around puberty, and a generalized form, usually affecting individuals under 30 years of age. The new classifications replaced the previously classified the localized juvenile periodontitis (LJP) with localized aggressive periodontitis (LAP), and the generalized juvenile periodontitis (GJP) with generalized aggressive periodontitis (GAP).[3]

There are shared commonalities between individuals diagnosed with aggressive periodontitis. Many patients are of good systemic health, yet experience a rapid loss of attachment and bone destruction. Microbial cultures of affected sites often reveal an infection with *Aggregatibacter Actinomycetemcomitans*. Some individuals may have abnormalities in phagocyte function or hyper-responsive macrophages producing increased levels of inflammatory cytokines such as PGE_2 and IL-1β.

It has not been consistently shown that specific pathogens are exclusively involved in the chronic and aggressive forms of periodontal disease. Some of the difficulty in analyzing various research findings is due to much variability in study designs, materials and methods and differences of case definitions.[4]

Socransky delineated certain criteria to determine which microorganisms play an etiological role in periodontal infections. He proposed that there should be proof of microbial association with disease. The microorganisms should be present in high numbers in the sites of infection and their elimination or suppression should arrest the progression of disease. Also, the microorganisms should be capable of producing an inflammatory or aberrant host response, elicit infection when inoculated into an animal model and have identifiable mechanisms of pathogenicity. Studies applying these criteria

have shown that certain microorganisms are pathogens in chronic and aggressive forms of periodontitis.[5,6]

Research to identify the microbial profiles of patients with generalized aggressive or chronic forms of periodontitis has shown prevalence of cultures for red and orange complex species, as well as, *A. actinomycetemcomitans*. A systematic review by Mombelli, to answer the question *"Can presence or absence of periodontal pathogens distinguish between subjects with chronic and aggressive periodontitis?"* did not find any definitive differences in the presence of *P. gingivalis, A. actinomycetemcomitans, P. intermedia, T. forsythia and Campylobacter rectus* that can be used to distinguish between the generalized aggressive and chronic forms of periodontitis. Today, there is still incomplete knowledge base of the putative periodontal pathogens responsible for initiation and propagation of various forms of periodontal disease. Much research has focused on the pathogenicity of *A. actinomycetemcomitans*.[7]

Early studies of microbial cultures in localized aggressive periodontitis (LAP) subjects revealed an association with *A. actinomycetemcomitans*. Large amounts of this microorganism were present in periodontal breakdown sites of these patients. One study comparing the amount of *A. actinomycetemcomitans* culture from patients with LAP, chronic periodontitis and healthy controls showed presence of this microorganism in 97% of LAP patients, 21% of chronic periodontitis (CP) and 7% of healthy controls.[8] A recent study analyzed subgingival microbial composition of healthy subjects, those with LAG, GAP and CP using checkerboard DNA-DNA hybridization. In subjects with LAP, the majority of microbial species identified were members of the red and orange complex. A higher proportion of *A. actinomycetemcomitans* was present in shallow and

intermediate pockets of LAP patients in comparison to those with GAP, CP, and healthy controls.[9]

Differences in clinical presentations of LAP and GAP, prompted research to identify whether these clinical differences are due to differences in *A. actinomycetemcomitans* pathogenicity. The rapid onset and severe destruction in the incisor and molar areas of subjects with LAP in comparison to the slower rate of breakdown in those with GAP is associated with more virulent strains of *A. actinomycetemcomitans*. present in LAP lesions. *A. actinomycetemcomitans* JP2 strain isolated from LAP subjects was described to be 10 – 20 times more leukotoxic. The role of highly leukotoxic isolates of *A. actinomycetemcomitans* in the pathogenesis of localized juvenile (LJP) and other forms of early-onset periodontitis (EOP) has been shown in more recent studies. A study where cultures were taken of 146 subjects including those with periodontally healthy status revealed *A. actinomycetemcomitans* present in 55% of those diagnosed with LJP and EOP where 73% of the *A. actinomycetemcomitan*s cultures were highly leukotoxic strains.[10]

A. actinomycetemcomitans is a fastidious, facultatively anaerobic, non-motile, non-sporing, small gram-negative rod, 0.4–0.5 μm x 1.0–1.5 μm in size. The cells may appear coccobacillary microscopically. This microbe has developed various ways of interfering with host defenses such as inhibition of PMN chemotaxis. *A. actinomycetemcomitans* has shown resistance to killing by PMNs' defensins is also able to diminish PMN production of perioxide. The ability of *A. actinomycetemcomitans* to bind Fc region on opsonizing IgG antibodies prevents its killing by inhibiting PMN opsonization. The leukotoxin produced by *A. actinomycetemcomitans* is able to lyse

human neutrophils, monocytes and some lymphocytes. It has been shown in vitro that *A. actinomycetemcomitans* is able to cleave IgG, serum IgA and IgM. This would prevent the antibodies from inducing the complement-mediated cytolysis, neutralizing toxins, agglutination and opsonization of microorganisms. In a mouse model, injection with A.a was observed to have an immunosuppressive. *A. actinomycetemcomitans* is able to overcome host defenses in many ways as shown by human immunologic studies, in vivo and in vitro observations. [(11)]

A study of early onset periodontitis in the U.S., by Löe and Brown estimated the prevalence of localized and generalized aggressive periodontitis to be approximately 0.53% and 0.13%. These seemingly insignificant percentages represented almost 300,000 U.S. adolescents at the time of this study. The demographics of the study patient population were evaluated and showed that aggressive periodontitis is more prevalent in African-Americans than whites. There was insufficient evidence to definitively show sex predilection, although when the distribution was evaluated by race, African-American males showed 2.9 times higher prevalence of localized disease than females, but this ratio was reversed in whites.[(12)]

There are various recommendations and treatment protocols for aggressive periodontitis. The first phase of treatment in clinical practice usually involves antimicrobial therapy.[(13)] Studies have shown that systemic antimicrobial therapy used without subgingival debridement can be beneficial. When systemic antibiotics were given after the completion of scaling and root planing, especially patients with deeper pockets, the need for surgical therapy was reduced.[(14)] Combination therapy using amoxicillin and metronidazole as adjuncts to mechanical debridement has shown to improve pocket depth

and clinical attachment level gain in chronic and aggressive periodontitis patients. Our study was performed to evaluate the demographics of aggressive periodontitis cases, the types of periodontal treatment methods provided to these patients, antibiotic prescription patterns and compliance with treatment at TUKSD department of graduate periodontology and oral implantology.

CHAPER 2.

MATERIALS AND METHODS.

A chart review was conducted to identify cases of aggressive periodontitis. General population of patients in the Graduate Periodontology and Oral Implantology Clinic at Temple University Kornberg School of Dentistry was surveyed to identify patients who would fit into the appropriate age range to be diagnosed with aggressive periodontitis. Patients less than 30 years of age at the time of referral for treatment to the graduate clinic were selected. The charts reviewed to identify those diagnosed with aggressive periodontitis. The diagnosis was validated by the presence of characteristic radiographic bone loss at permanent incisors and molars. Patients were excluded from the sample identified as having aggressive periodontitis if their records had deficient radiographs, and there were positive medical history findings of systemic diseases that compromise the immune response. Data on patient demographics such as age at the time of presentation for treatment, sex and race, medical diagnosis, microbial testing, systemic antibiotic administration, number of appointments in the graduate clinic and the type of treatment provided was compiled and analyzed.

CHAPTER 3.

RESULTS.

Three hundred records of patients under the age of 30 were reviewed to identify possible patients with aggressive periodontitis. Twenty-two cases of aggressive periodontitis cases were identified. Radiographs in Figure 1 show a typical case of aggressive periodontitis. Figure 2 shows radiographs of several patients presenting with localized aggressive periodontitis, and radiographs in Figure 3 are representative of patients with generalized aggressive form of periodontitis. The range of ages in the sample population was 12-26 years. The sex distribution was 59% males, and 41% females.

Figure 4 shows the distribution of cases by race-ethnicity. 82% (18 cases) were African American, 9% (2 cases) were Hispanic, 5% (1 case) Asian, and in 1 case the race-ethnicity was unknown.

Figure 5 represents the cases with a medical diagnosis. Fifty five percent of the cases had medical diagnosis, though not among the exclusion criteria of aggressive periodontitis. The diagnoses included 4 patients with asthma, 3 had iron deficiency, 2 patients with allergies, 2 autistic patients, and 1 with glucose-6 phosphatase deficiency. Only 1 case had a systemic immune-related disease (Common Variable Immune Deficiency). However, the patient was included in the study because they were maintained on an immunoglobulin G infusion and the lab studies in the patient's record showed no evidence of systemic immune deficiency.

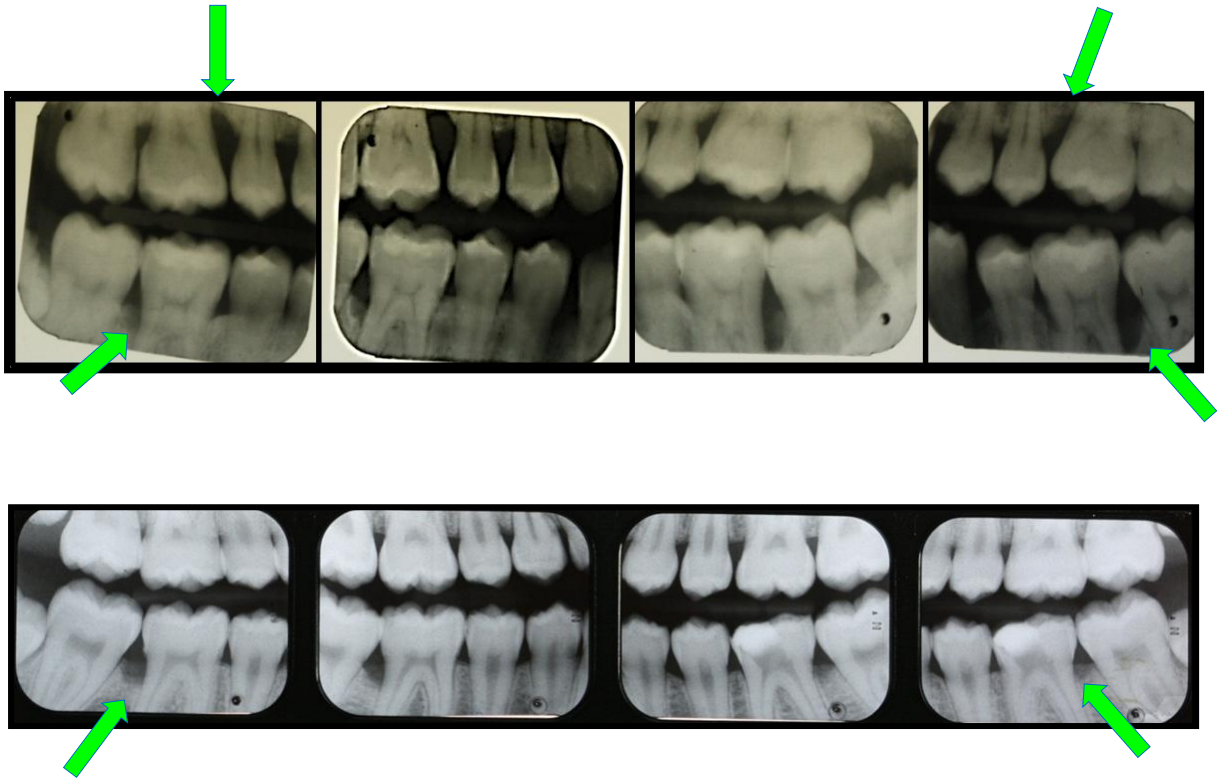

Figure 1. Typical presentation of aggressive periodontitis.

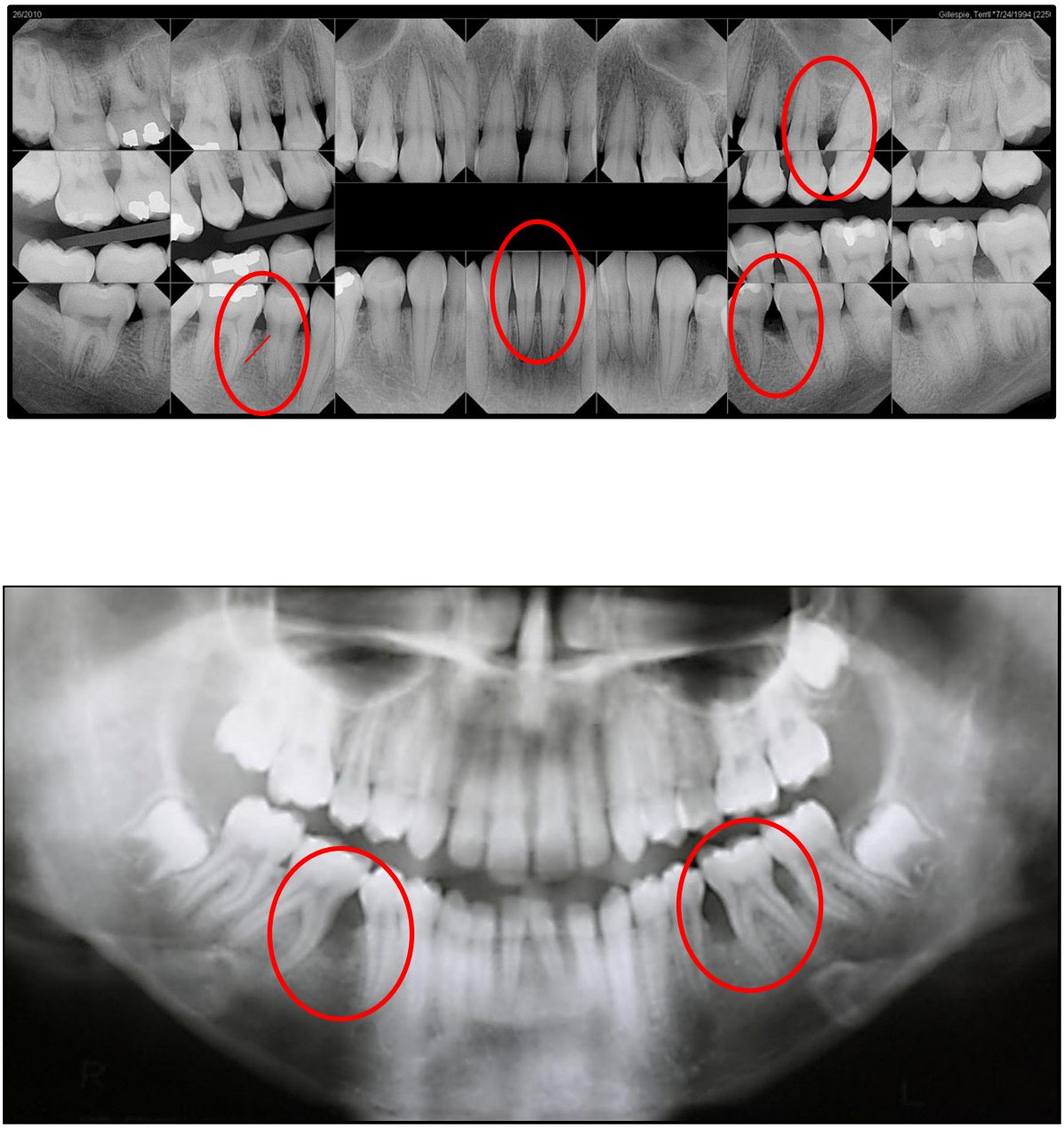

Figure 2. Typical presentation of localized aggressive periodontitis.

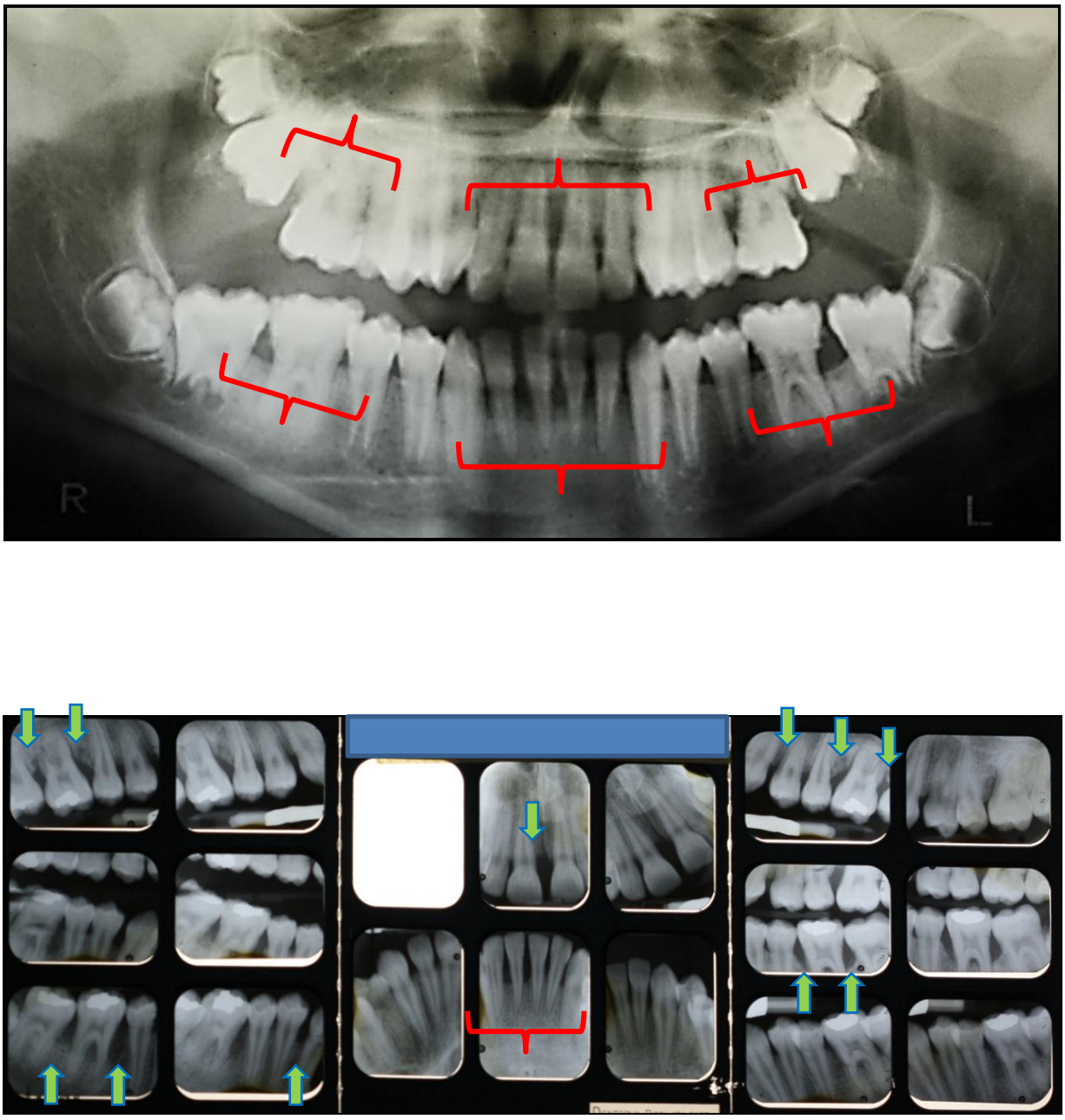

Figure 3. Typical presentation of generalized aggressive periodontitis

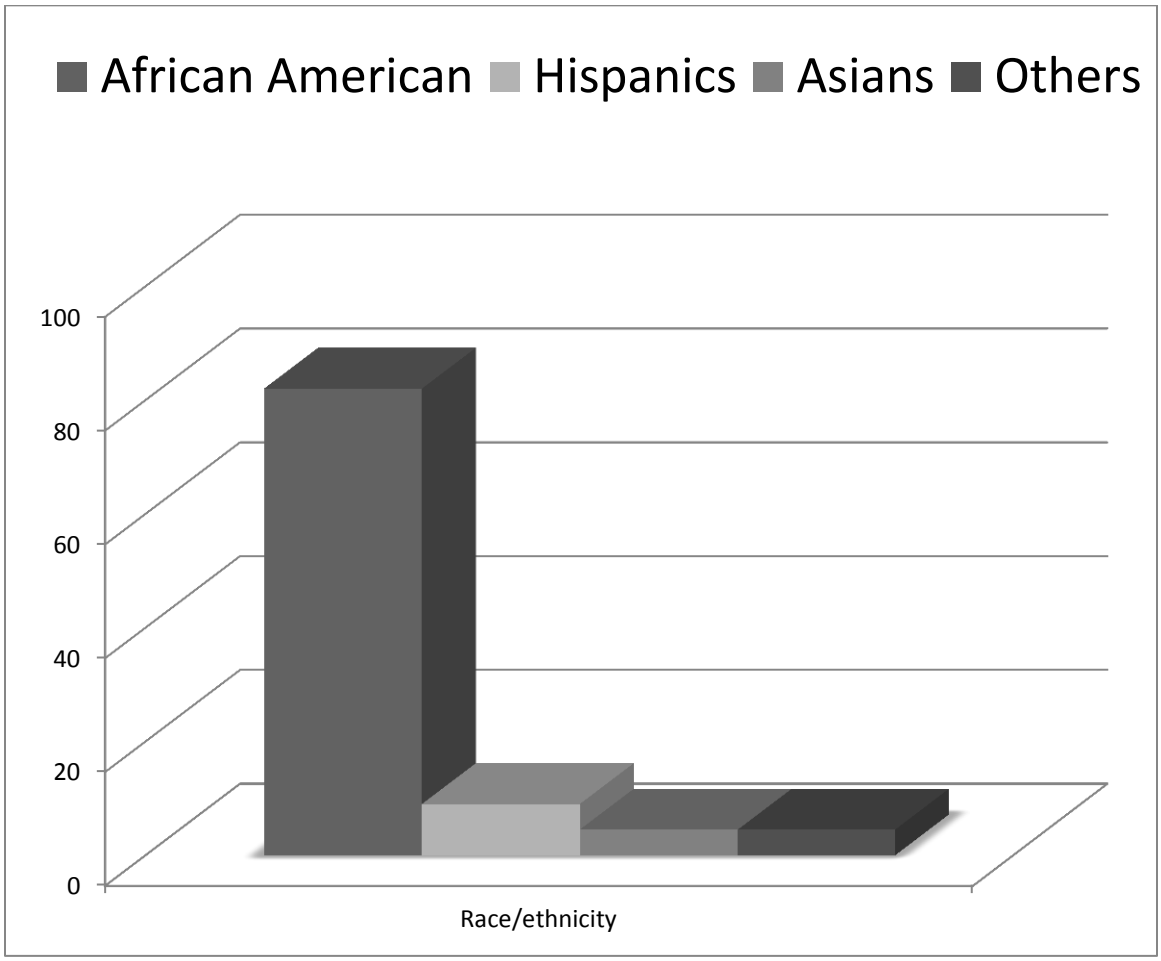

Figure 4. Percentage of cases by race

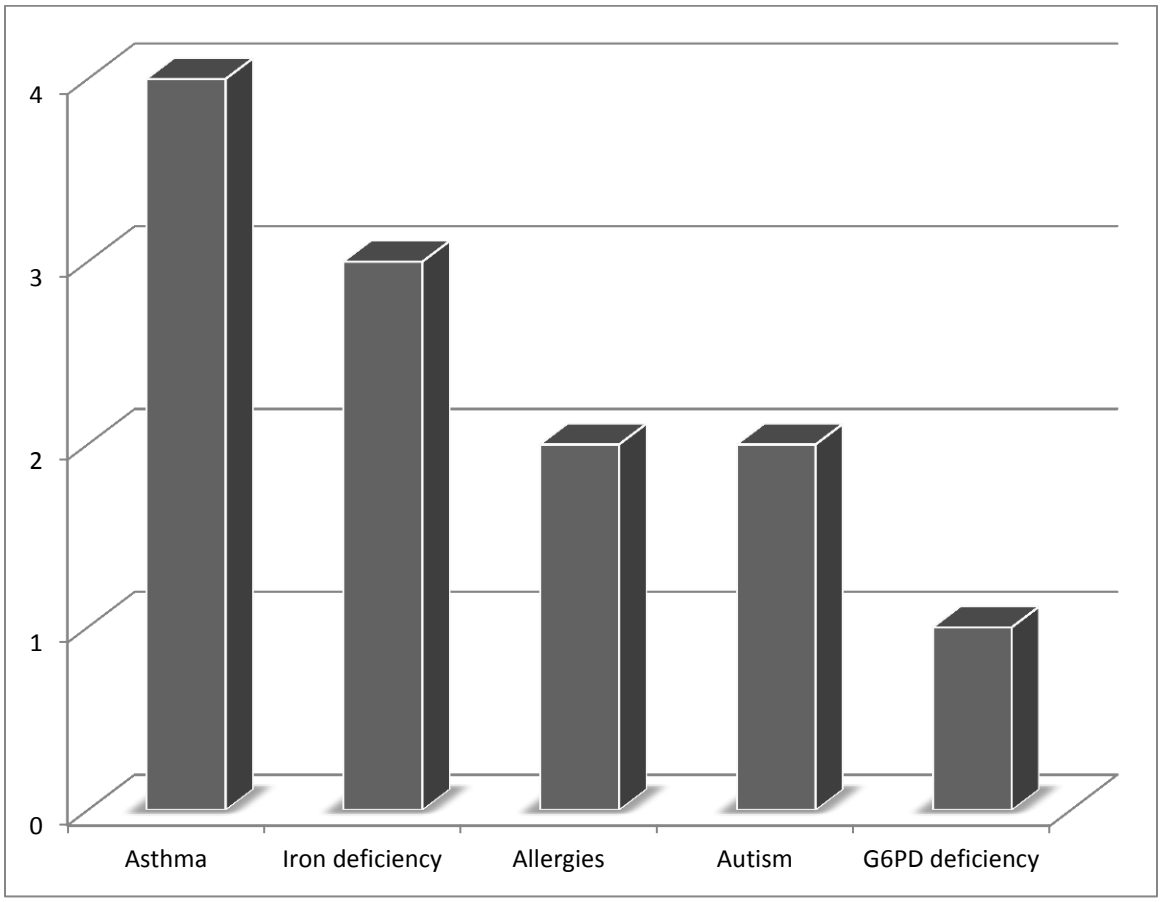

Figure 5. Number of cases with a medical diagnosis.

The diagnosis and non-surgical treatment required multiple visits.

Patients were treated with scaling and root planing, single and combination antimicrobials, some received open flap debridement and had other procedures such as guided tissue regeneration. Initial treatment with scaling and root planing was performed in 64% of cases, however, there was a 36% dropout before any treatment was initiated.

In 46% of cases microbial plaque testing was performed. Not all of the patients who were prescribed antibiotics had subgingival plaque samples taken for microbial analyses and antibiotic resistance testing. 59% of all patients received systemic antibiotics. Figure 6 shows how the method used to collect microbial samples using paper points.

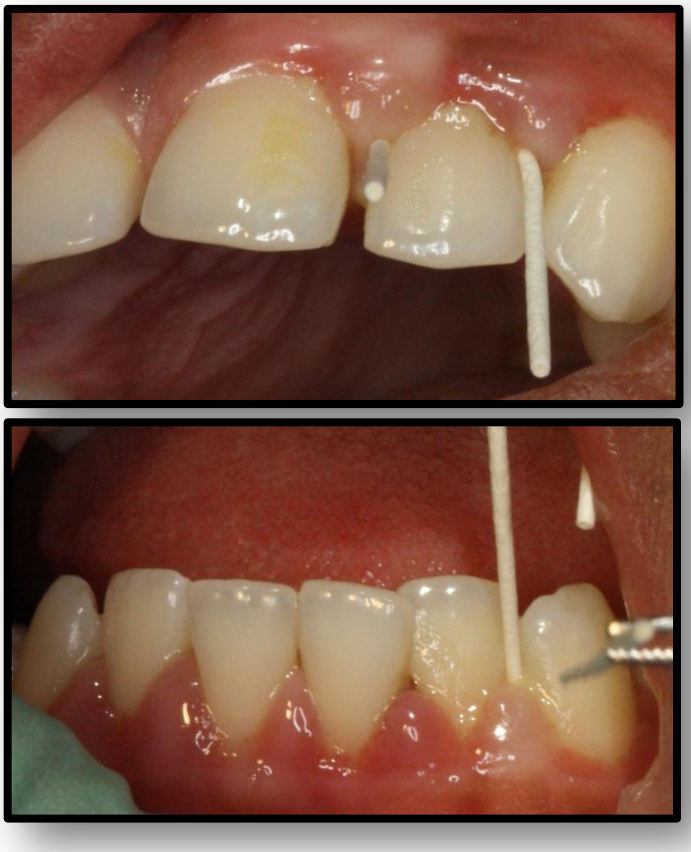

Figure 6. Subgingival plaque sample collection.

Figure 7 shows the percentage of cases distributed by the various antimicrobial regimens used. Some patients were prescribed a single antibiotic medication such as metronidazole, azithromycin and doxycycline. Combination therapy of amoxicillin and metronidazole was administered to 70% of patients for durations of 7-10 days.

Most of the patients were treated non-surgically with scaling and root planing and a combination-regimen antimicrobial therapy. Photographs of 1 patient (Figure 8) show retention of hopeless teeth 2 years post-operatively. The patient had initial phase therapy consisting of scaling and root planing, a course of antibiotics, and a 6 month maintenance recall. In only 5 patients (or 36%) the treatment had progressed beyond initial phase therapy to the surgical phase of treatment, such as open flap debridement, extractions, and guided tissue regeneration.

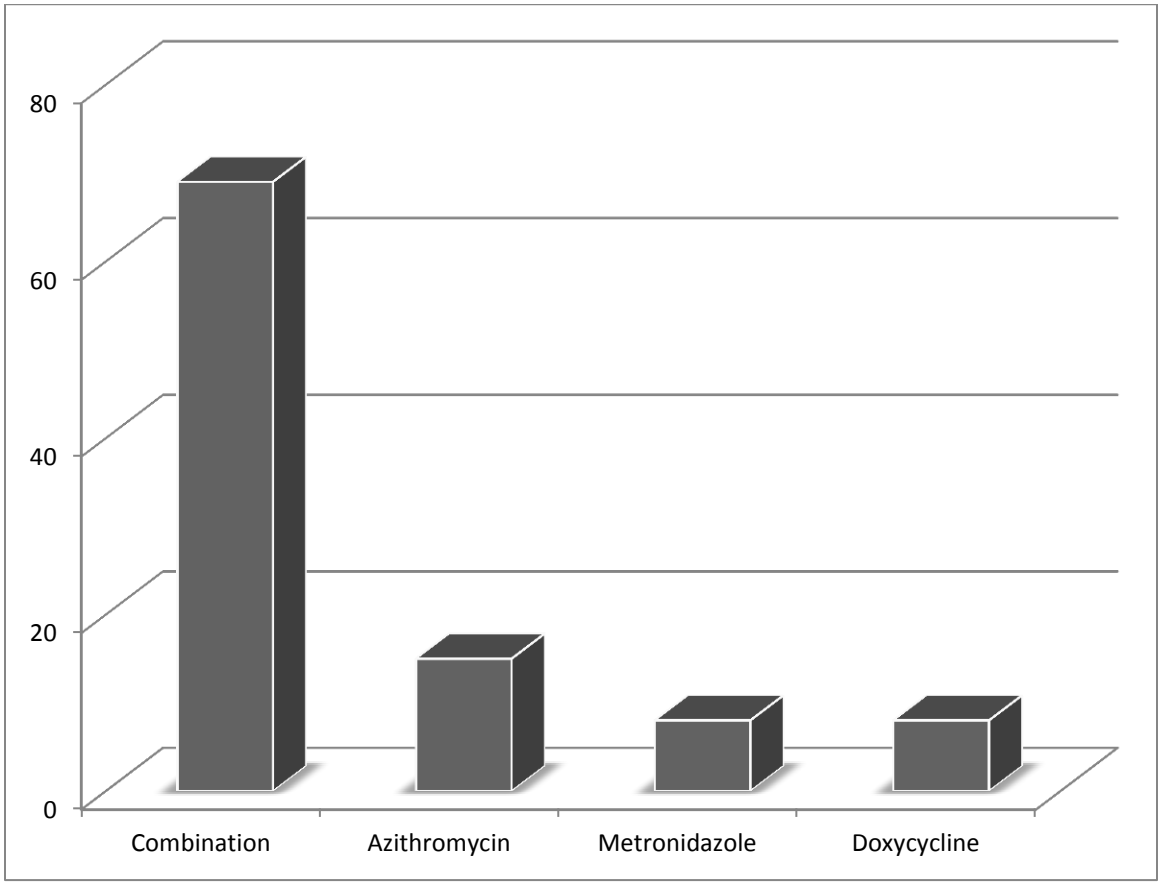

Figure 7. Percentage of cases by type of antibiotics.

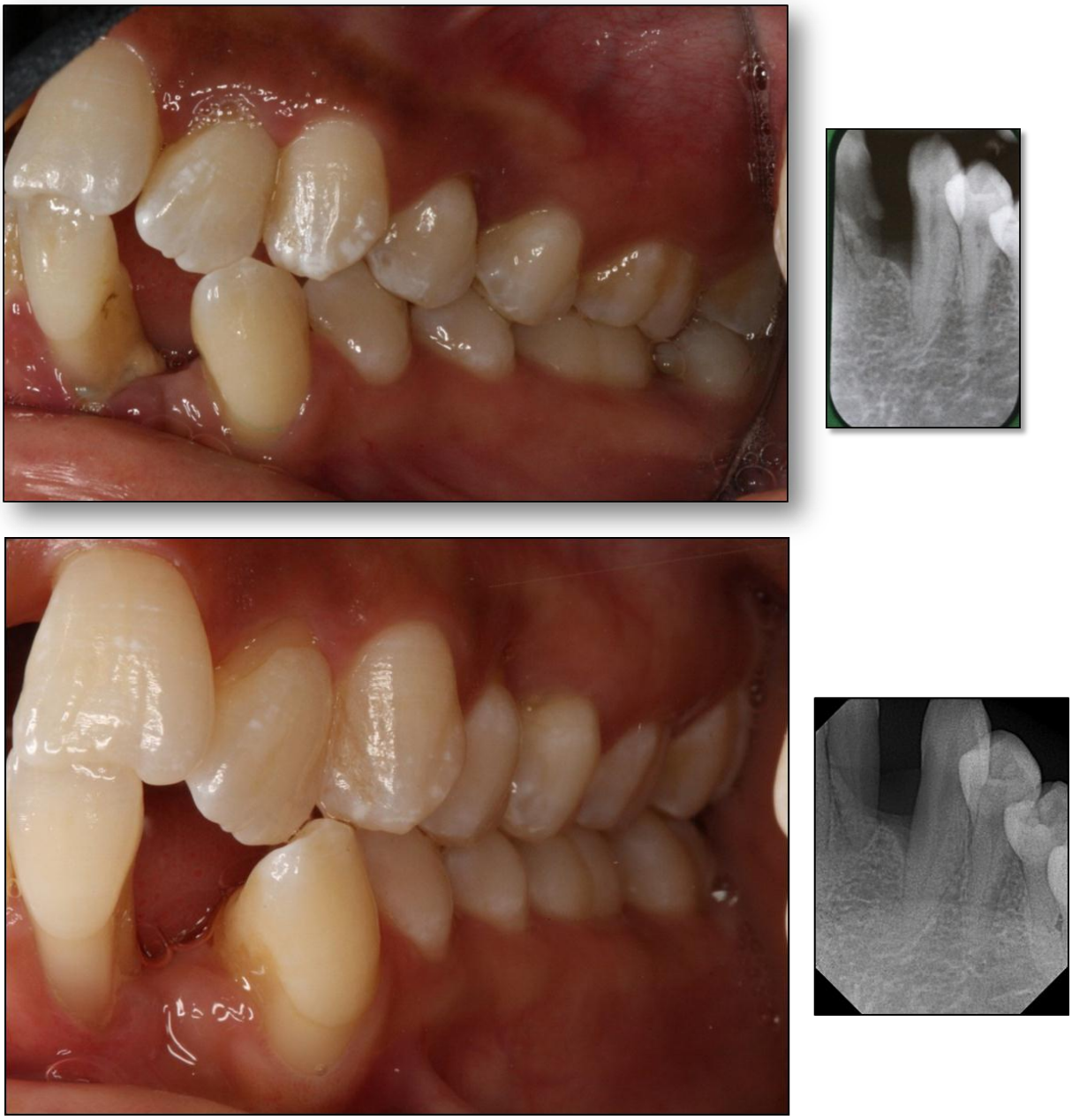

Figure 8. Typical patient at initial exam and 2 years after non-surgical treatment.

Initial clinical and radiographic patient presentation (above) and 1 year after scaling, root planig and combination antimicrobial therapy (below)

CHAPTER 4.

DISCUSSION

Temple University Kornberg School of Dentistry is located in an indigent area of Philadelphia. Many patients who seek care in this setting do not have the means to afford, what is determined by third-party payers, as specialty or elective treatment. Many are lacking basic dental care and are not compliant with set-forth treatment plans.

The majority of aggressive periodontitis cases, as evidenced by the sample of patient population in this report, are those of African-American race-ethnicity. This finding is consistent with previously published research showing a higher prevalence of early onset and aggressive periodontitis in those of African-American and Hispanic background. A survey of over 14,000 United States school children ages 13-17, showed the prevalence of localized, generalized and early onset forms periodontitis to be the lowest in whites and highest in African-American and Hispanic adolescents. This disease "affects about 10 percent of African-American, 5 percent of Hispanic and 1.3 percent of white U.S. adolescents."[16] Therefore, our findings cannot be simply attributed to the local demographics of the patient population.

When a patient presents with severe bone loss and symptoms leading to a diagnosis of aggressive periodontitis, initial, phase 1 treatment should be administered immediately and comprehensively. If left untreated, aggressive periodontitis results in marked tooth loss.[17]

Aggressive periodontitis has shown a familial predilection. Minnesota twin studies suggested a genetic influence in this disease.[18] Much debate still exists regarding the role of Mendelian genetics, patterns of inheritance, and specific genes involved in the

pathogenesis of aggressive periodontitis.[19,20] More recently, genetic polymorphisms of Il-1, Il-4, Fc-receptor, vitamin D receptor and other genes have been implicated in the aggressive periodontal disease process. If such a genetic pattern is suspected, a closer maintenance recall may be beneficial to reduce the excessive inflammation by arresting the aggregation of periodontal biofilm. Thorough evaluation of the patient's medical, social and family histories may provide additional information regarding a possible role of genetic predisposition in the etiology of this disease.[21]

The treatment protocol for aggressive periodontitis should include systemic antimicrobials as an adjunct to mechanical debridement. Approximately 59% of the cases in our patient sample were treated with systemic antimicrobials. The combination-regimen of amoxicillin and metronidazole was used in >60% of these patients for durations of 7-10 days. The combination-regimen of amoxicillin and metronidazole has shown to improve clinical attachment level gain in deeper pockets of periodontitis patients.[22] In a recent study, this combination regimen with scaling and root planing was compared to the control group of mechanical treatment alone. Subgingival plaque samples were analyzed for the presence of microbial species prior to treatment and at 3 and 6 months post-operatively. In the test group, *P. gingivalis* decreased significantly at 3 months and *T. forsythia* decreased significantly, below detection limits in comparison to the control group at 6 months ($P < 0.05$).[23] This, and other studies support using the polypharmaceutical approach of amoxicillin and metronidazole combination antimicrobial regimen together, with scaling and root planing in treatment of aggressive periodontitis.

Patient motivation and compliance is an important factor in successful treatment of aggressive periodontitis. Most of the subjects in this patient sample did not follow through with the proposed treatment or returned for maintenance. Since 72% (16/22) of the patients were minors, under 18 years old, the presence of a parent or guardian at all dental appointments would be required by law.[24] Multiple appointments in pre-doctoral clinic with subsequent referral to the graduate clinic for a comprehensive evaluation, microbial plaque sampling, individual quadrants of scaling and root planing, re-evaluation and maintenance may deter patients and their guardians from following through with treatment due to scheduling difficulties. It is recommended that the treatment of aggressive periodontitis be expedited by reducing the number of appointments of phase 1 treatment. This can be accomplished in an academic setting with referring these patients to the graduate clinic for all periodontal therapy including initial phase 1 treatment.

CHAPTER 5.

CONCLUSION

Aggressive periodontitis patients treated at the TUKSD are comprised mainly of African American race-ethnicity, with no predominance of a sex group. A combination regimen antibiotic therapy was often used together with nonsurgical periodontal therapy. Most patients did not present for treatment beyond the non-surgical phase, and some even before the treatment started. It is recommended that the treatment of aggressive periodontitis be expedited by referring the patients to the graduate clinic for all periodontal treatment including initial phase 1 treatment.

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