

## The prevalence of apical periodontitis and endodontic treatment in two coagulation disorders

Prevalência de periodontite apical e tratamento endodôntico em dois distúrbios de coagulação

Prevalencia de periodontitis apical y tratamiento endodóntico en dos trastornos de la coagulación

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### **Abstract**

Coagulation disorders such as hemophilia and Von Willebrand's disease are characterized by changes in inflammatory responses and tissue repair. Inflammatory responses could be involved in the destruction of the periradicular bone and/or interfere with repair mechanisms following endodontic treatment. The aim of this study was to evaluate the prevalence of apical periodontitis (AP) and endodontic treatment in two coagulation disorders. Panoramic radiographs (106 from the study and 106 from the control groups) were examined for the presence of AP lesions in untreated and root canal-treated teeth. The number of teeth and the prevalence of root canal treatments were also recorded. Two endodontists evaluated all items separately. Statistical analyses were performed using the Statistical Package for Social Science (SPSS), version 21.0 (IBM, Armonk, NY, USA) and the level of statistical significance was established at 5% ( $p < 0.05$ ). The prevalence of AP was not significantly different between the study and control groups ( $p=0.574$ ). However, the comparative analyses between them revealed statistically significant differences in variables such as the presence of endodontic treatment ( $p=0.007$ ), adequate filling ( $p=0.014$ ),

endodontic treatment with AP ( $p < 0.0001$ ), and the presence of AP in well-filled and restored teeth ( $p = 0.003$ ). The coagulation disorders evaluated here did not influence the manifestation of AP, however, they affected the inflammatory responses and tissue repair mechanisms.

**Keywords:** Apical periodontitis; Hemophilia A; Hemophilia B; Inflammation; von Willebrand diseases.

### Resumo

Os distúrbios de coagulação, como hemofilia e doença de Von Willebrand, são caracterizados por mudanças nas respostas inflamatórias e na reparação de tecidos. As respostas inflamatórias podem estar envolvidas na destruição do osso perirradicular e / ou interferir nos mecanismos de reparo após tratamento endodôntico. O objetivo deste estudo foi avaliar a prevalência de periodontite apical (PA) e tratamento endodôntico em diferentes distúrbios da coagulação. Radiografias panorâmicas (106 do grupo de estudo e 106 do controle) foram examinadas para a presença de lesões perirradiculares em dentes não tratados e tratados endodônticamente. O número de dentes e a prevalência de tratamentos endodônticos também foram registrados. Dois endodontistas avaliaram todos os itens separadamente. As análises estatísticas foram realizadas por meio do programa Statistical Package for Social Science (SPSS), versão 21.0 (IBM, Armonk, NY, EUA) e o nível de significância estatística foi estabelecido em 5% ( $p < 0,05$ ). A prevalência de PA não foi significativamente diferente entre os grupos ( $p = 0,574$ ). No entanto, as análises comparativas revelaram diferenças estatisticamente significativas em variáveis como presença de tratamento endodôntico ( $p = 0,007$ ), preenchimento adequado ( $p = 0,014$ ), tratamento endodôntico com PA ( $p < 0,0001$ ) e presença de PA em dentes bem obturados e restaurados ( $p = 0,003$ ). Os distúrbios da coagulação não influenciaram na manifestação da PA, porém afetaram as respostas inflamatórias e os mecanismos de reparo tecidual.

**Palavras-chave:** Doenças de von Willebrand; Hemofilia A; Hemofilia B; Inflamação; Periodontite apical.

### Resumen

Los trastornos de la coagulación como la hemofilia y la enfermedad de Von Willebrand se caracterizan por cambios en las respuestas inflamatorias y la reparación de tejidos. Las respuestas inflamatorias podrían estar involucradas en la destrucción del hueso perirradicular y / o interferir con los mecanismos de reparación después del tratamiento endodóntico. Evaluar la prevalencia de periodontitis periapical (PA) y tratamiento endodóntico en dos trastornos de la coagulación. Se examinaron radiografías panorámicas (106 del estudio y 106 de los grupos de control) para detectar la presencia de lesiones AP en dientes no tratados y tratados con endodoncia. También se registró el número de dientes y la prevalencia de tratamientos de conducto. Dos endodoncistas evaluaron todos los elementos por separado. Los análisis estadísticos se realizaron utilizando el Paquete Estadístico para Ciencias Sociales (SPSS), versión 21.0 (IBM, Armonk, NY, EE. UU.) Y el nivel de significancia estadística se estableció en 5% ( $p < 0.05$ ). La prevalencia de PA no fue significativamente diferente entre los grupos de estudio y control ( $p = 0,574$ ). Sin embargo, los análisis comparativos entre ellos revelaron diferencias estadísticamente significativas en variables como la presencia de tratamiento endodóntico ( $p = 0,007$ ), relleno adecuado ( $p = 0,014$ ), tratamiento endodóntico con PA ( $p < 0,0001$ ), y la presencia de PA en Dientes bien obturados y restaurados ( $p = 0,003$ ). Los trastornos de la coagulación evaluados aquí no influyeron en la manifestación de la PA, sin embargo, sí afectaron las respuestas inflamatorias y los mecanismos de reparación tisular.

**Palabras clave:** Enfermedades de von Willebrand; Hemofilia A; Hemofilia B; Inflamación; Periodontitis periapical.

## 1. Introduction

Apical periodontitis (AP) is an inflammatory response caused by an infection of the root canal system of microbial etiology (Siqueira, 2011). Microbial invasion may be through a caries process, dental trauma or some iatrogenic procedure (Stashenko *et al.*, 1998; Figdor & Sundqvist, 2007).

Systemic conditions of the host may be associated with distinct responses to periradicular diseases as well as to endodontic treatment. Such responses may influence the hosts susceptibility to disease (Segura-Egea *et al.*, 2005; Rosania *et al.*, 2009) and they are referred to as disease modifiers. Although they are not the cause of the disease, they can influence the development, diagnosis, the severity of the disease and/or the response to treatment (Siqueira, 2011).

Coagulation disorders such as hemophilia and Von Willebrand's disease are characterized by changes in inflammatory response and tissue repair (Castellanos-Cosano *et al.*, 2013). Evidence points to an extensive relationship between inflammation, coagulation and fibrinolysis, where inflammation can activate coagulation, which can, in turn, affect the inflammation activity (Levi *et al.*, 2004; Danese *et al.*, 2007). Activation of coagulation and deposition of fibrin, due to

inflammation, can be seen as an essential part of the host defense system as it aims to contain the infection and the consequent inflammatory response to a limited area (Levi *et al.*, 2004).

The inflammatory response may also be involved in the destruction of the periradicular bone and/or interfere with the cure and repair mechanisms following endodontic treatment. Therefore, an increase in the number and/or size of APs might be expected in patients with coagulation disorders (Castellanos-Cosano *et al.*, 2013).

Coagulation disorders are potential disease modifiers, that is, even though they are not the main cause for the development of AP they can influence its evolution. However, studies on the prevalence of AP in patients with these disorders are still scarce.

Due to the lack of such studies, the objective of the present work was to evaluate the prevalence of AP and endodontic treatment in patients with two different coagulation disorders.

## 2. Methodology

A cross-sectional study was carried out to evaluate the relationship between coagulation disorders and AP. The research project was submitted and approved by the Research Ethics Committee of HEMORIO, State Institute of Hematology Arthur de Siqueira Cavalcanti, registered under No. 402/16. All procedures complied with the 1964 Helsinki declaration. Additionally, informed consent was obtained from all individuals participating in this study.

### Selection of cases

The study group was composed of 106 randomly selected patients with coagulation disorders, such as Hemophilia A, Hemophilia B or von Willebrand's disease, enrolled at the HEMORIO dental clinic and the control group was composed of 106 patients without coagulation disorders.

Patients under 18 years old; with less than 8 teeth; smokers; individuals with immunosuppressive (HIV positive and diabetics), osteoporosis or hypertensive diseases were excluded.

The patients were treated between 2009 and 2019 and their medical records included complete anamnesis and panoramic radiographs. The anamnesis information provided the demographic characteristics (age and gender) and the blood disorder (type, degree of severity according to the criteria of the world Federation of Hemophilia) (Srivastava *et al.*, 2020).

### Radiographic evaluation

Radiographs were examined for the number of teeth, the presence of AP, endodontic treatment, the quality of any canal fillings, and the quality of any coronary restorations.

The periapical index (PAI) for endodontic success was applied to assess the presence of AP lesions (Orstavik *et al.*, 1986). Following this criterion, AP was considered absent when the outline, the width and the structure of the periodontal ligament were radiographically normal, and the periodontal contour expanded only around the overfilling from the root canal due to fibrillary encapsulation.

Endodontic treatment was considered suitable when all canals of the same dental element were restored homogeneously, without spaces, and this filling was only from 0 to 2.0 mm below the radiographic apex. However, cases of over-filling of the canal were still considered appropriate, if they did not exceeded 2.0 mm in length. Coronary restorations were considered suitable when they were radiographically intact. In cases of multiradicular teeth, the root with the worst classification was considered in the study, that is, the worst pathological situation.

All items were evaluated by two endodontists separately. The Kappa coefficient was used at the end of the evaluation to analyze agreement between the 2 evaluators for the presence/absence of AP ( $k = 0.83$ ). Cases of disagreement were resolved by discussion.

### Statistical analysis

All analyzes were performed using the Statistical Package for Social Science (SPSS), Version 21.0 (IBM, Armonk, NY, USA). The normality of the quantitative variables was verified using the Kolmogorov-Smirnov and Shapira-Wilk tests, in addition to the graphic analyzes. The qualitative variables were expressed as absolute frequency and relative frequency [N (%)], while quantitative variables were expressed as mean (standard deviation), median (minimum - maximum). For the quantitative variables, the Mann-Whitney test was used in the comparison between the two groups (study and control groups), while the Kruskal-Wallis test was used to compare the four types of blood disorders (von Willebrand, Mild Hemophilia, Moderate Hemophilia and Severe Hemophilia). The qualitative variables were compared using the chi-square test or Fisher's exact test. The level of statistical significance established was 5% ( $p < 0.05$ ).

### 3. Results

The demographic data showed that the mean age of the patients in the study group was  $37.67 \pm 13.70$  years old (ranging from 18 to 69 years old) and in the control group  $45.58 \pm 9.89$  years old (ranging from 19 to 60 years old); thus showing a statistically significant difference ( $p < 0.0001$ ). In the study group 38 (36%) of the individuals were female and 68 (64%) were male while in the control group 72 (68%) of the patients were female and 34 (32%) were male ( $p < 0.05$ ).

In the study group 35% ( $n = 37$ ) had Mild Hemophilia, 5% ( $n = 5$ ) had Moderate Hemophilia, 17% ( $n = 18$ ) had Severe Hemophilia and 43% ( $n = 46$ ) had von Willebrand's disease. The averages of the AP frequencies according to the type of blood disorder showed no statistically significant difference ( $p = 0.402$ ) as can be seen in Table 1. The mean of AP in the study group was  $2.91 \pm 3.16$  and the mean in the control group was  $2.45 \pm 2.31$ ; thus there was no statistically significant difference ( $p = 0.574$ ).

**Table 1.** Average AP frequencies according to the type of blood disorder.

CONDITION	VALUE	P
Von Willebrand	$2.49 \pm 2.48$	0.402
Mild hemophilia	$2.97 \pm 2.26$	
Moderate hemophilia	$5.4 \pm 6.6$	
Serious hemophilia	$3.17 \pm 4.69$	

Data are reported as mean  $\pm$  standard deviation. Source: Authors.

The comparative analyzes between the study and control groups revealed statistically significant differences in variables such as: total number of teeth, endodontic treatment, endodontic treatment with AP, adequate fillings, and the presence of AP in well-filled and restored teeth. These data are shown in Table 2.

**Table 2.** Comparative analysis of the variables between the coagulation disorder and control groups.

	VALUE	P
<b>Total number of teeth</b>		
Coagulation disorders	26.40 ± 6.60	<0.0001*
Controls	23.17 ± 7.20	
<b>Number of lesions</b>		
Coagulation disorders	2.91 ± 3.16	0.574
Controls	2.45 ± 2.31	
<b>Endodontic treatment</b>		
Coagulation disorders	0.55 ± 1.09	0.007*
Controls	1.17 ± 1.80	
<b>Endodontic treatment with AP</b>		
Coagulation disorders	0.17 ± 0.48	<0.0001*
Controls	0.69 ± 1.08	
<b>Appropriate fillings</b>		
Coagulation disorders	0.28 ± 0.71	0.014*
Controls	0.64 ± 1.17	
<b>Suitable restorations</b>		
Coagulation disorders	3.70 ± 3.78	0.522
Controls	4.56 ± 4.74	
<b>Teeth with well-filled canals and adequate restoration with ap</b>		
Coagulation disorders	0.07 ± 0.25	0.003*
Controls	0.30 ± 0.69	

The parameters were evaluated with the Mann-Whitney test. Data are reported as mean ± standard deviation (\* p <0.05). Source: Authors.

#### 4. Discussion

This study was conducted in order to investigate the influence of coagulation disorders on the frequency of AP as there is a lack of data on this subject in the literature (Castellanos-Cosano *et al.*, 2013).

The parameters used in the radiographic analysis of this study have already been described in previous methodologies (Segura-Egea *et al.*, 2011; Lopéz-Lopéz *et al.*, 2012; Castellanos-Cosano *et al.*, 2013). The PAI scoring system was used to evaluate the periapical radiolucencies as in previous works (Orstavik *et al.*, 1986; Ridao-Sacie *et al.*, 2007; Ríos-Santos *et al.*, 2010; López-López *et al.*, 2011).

Panoramic radiographic images, which were used to diagnose periradicular radiolucencies, enabled all teeth to be seen in the same radiography with relatively low exposure to ionizing radiation. According to a previous study, panoramic radiographs are useful tools for this kind of diagnosis (Nardi *et al.*, 2018) and they can be obtained more quickly than a complete periapical radiographic exam (Gulsahi *et al.*, 2008). This type of radiography is a highly viable tool which has been used in several epidemiological studies (Ridao-Sacie *et al.*, 2007; Gutmann *et al.*, 2009; Lopéz-Lopéz *et al.*, 2012; Castellanos-Cosano *et al.*, 2013).

The hypothesis proposed by the present study was not proven because there was no statistically significant difference (p = 0.574) between groups in relation to the frequency of AP lesions. These findings differ from other authors (Castellanos-Cosano *et al.*, 2013) who found a higher prevalence of AP in patients with coagulation disorders (p = 0.038). Differences between countries and populations relating to socioeconomic status, level of schooling, cultural habits may have influenced the

results (Jiménez-Pinzón *et al.*, 2004). In this work, all participants belonged to the same socioeconomic status (relatively low income). The larger size of our sample may also have contributed to a closer representation of reality.

The strict exclusion criterion, which was followed here, excluded the participation of smokers, patients with immunosuppressive (HIV positive and diabetic), autoimmune or hypertensive diseases and patients with osteoporosis. In an earlier study (Castellanos-Cosano *et al.*, 2013), the inclusion of smokers in the study group influenced the prevalence of AP. There are several works in the literature that suggest that smoking is associated with an increase in the prevalence of AP and that it is a risk factor for the disease (Aleksejuniene *et al.*, 2000; Kirkevang & Wenzel, 2003; Kirkevang *et al.*, 2007; López-López *et al.*, 2011; Segura-Egea *et al.*, 2011; Segura-Egea *et al.*, 2015).

There was a statistically significant difference in relation to the total number of teeth, with a larger average in the study group. This difference can be explained by the dental follow-ups offered by HEMORIO to patients with coagulation disorders. Sonbol *et al.* (2001) verified a lower prevalence of dental caries in patients with blood disorders when compared to their control group. According to those authors the result is a consequence of the effectiveness of preventive dental treatments.

There was a statistically significant difference for endodontic treatment with AP between the two groups, with a higher frequency in the control patients. AP associated with root canal treatment may also represent a persistent chronic condition of a lesion or incomplete healing. Therefore, in this study some obturated teeth with periradicular radiolucency may still be in the process of healing, depending on the time since the treatment (Dugas *et al.*, 2003). This is a known limitation of transverse studies in which the confusion factors are difficult to control, particularly when other factors such as caries, quality of coronary restorations, trauma history can influence AP. Another limitation of transversal studies is the fact that the mean time since the endodontic treatment is unknown (Marques *et al.*, 1998).

Important parameters such as the quality of the root canal fillings and the quality of coronary restorations were evaluated in the present work. There was a significant difference in adequate fillings, with a greater frequency in the control group, as well as the frequency of well-filled teeth with adequate restoration and presence of AP. Tavares *et al.* (2009) reported that appropriate coronary restorations had equally high success rates for cases with adequate or inadequate obturation in their study with healthy patients. On the other hand, Kalender *et al.* (2013) suggested that the absence or presence of restorations was not associated with the outcome of endodontic treatment and the presence of AP. Corroborating with this idea some studies have reported that the quality of obturation plays a key role independently of the quality of coronal restorations (Kayahan *et al.*, 2008; Gündüz *et al.*, 2011).

## 5. Conclusion

Although coagulation disorders are characterized by changes in inflammatory response and tissue repair, they did not show any influence on the frequency of AP lesions in this study. Due to the inconsistencies between the findings in the literature and considering the limitations of cross-sectional studies, new studies with longitudinal designs and more controlled variables should be carried out to elucidate such issues.

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