



Epidemiology of Chronic Pulpitis, Dental Caries, and Periapical Disease and Their Possible Risk Factors in an Adult Chinese Population in the Northern Regions of China

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Abstract

Background: Dental diseases and disorders are reported to affect specific ages, genders, and races of patients. Therefore, epidemiological investigations are necessary for understanding dental diseases and disorders.

Objectives: This cross-sectional study aims to determine the prevalence and potential risk factors of chronic pulpitis, dental caries, and periapical disease in adults seeking treatment at the Tianjin Stomatological Hospital, Tianjin, a major referral center in the Northern region of China.

Methods: A total of 3,245 males and females visited the Department of Adult Dentistry and the Department of Endodontics of the Tianjin Stomatological Hospital, Tianjin, China, for oral health concerns from January 17, 2020, to November 18, 2023. Among these patients, 615 (19%) were receiving treatment for chronic pulpitis, dental caries, and/or periapical diseases at the institute. Demographic parameters and clinical examination results of 496 patients (119 patients were excluded due to missing information) who were being treated for chronic pulpitis (long-term inflammation of the dental pulp), dental caries (a biofilm-mediated, sugar-driven, multifactorial, dynamic disease), and/or periapical disease (inflammation around the tooth root) with varying severity (moderate or severe) were included in the study.

Results: Of the 496 patients, 300 (60%) were females, 328 (66%) were aged 60 years or older, and 295 (59%) had issues with mandibular teeth. Among the patients, 250 (50%), 301 (61%), and 151 (30%) were diagnosed with dental caries, chronic pulpitis, and periapical disease(s), respectively. Female gender ($P = 0.041$), age ≥ 60 years ($P = 0.045$), and issues with mandibular teeth ($P = 0.046$) were found to be associated with chronic pulpitis, dental caries, and periapical diseases in the patients.

Conclusions: The prevalence of dental diseases and disorders in Han Chinese adults is 19% in the Northern regions of China. Chronic pulpitis and dental caries are the most prevalent dental diseases, while periapical diseases occur less frequently among Han Chinese adults in the Northern regions of China. Females, individuals aged ≥ 60 years, and issues with mandibular teeth are independent risk factors for the development of chronic pulpitis, dental caries, and periapical disease in adult patients in Northern regions of China. Policymakers in China should consider the findings of this study to reduce dental diseases and disorders in Chinese adults, especially in the Northern regions of China.

Keywords: Chronic Pulpitis, Dental Caries, Dental Diseases, Dentistry, Mandibular Teeth, Periapical Disease, Oral Health, Tooth

1. Background

Dental pulps react with carriers and are responsible for periapical disease in adult patients (1). The pulp and resistance responses of patients lead to the development of reversible or irreversible inflammation, which can cause necrosis (2). These issues may extend to

other areas of the periodontium due to periodontal tissues and bacterial infections (1). The prevalence of chronic pulpitis, dental caries, and periapical disease in adult patients varies across different racial populations (3-5). The dental pulp is susceptible to ischemic conditions, as it is affected by trauma, chronic dental caries injuries, inflammation, and pulpitis (6). Generally,

root canals are preferred to prevent infections in the periapical tissues (7). Dental diseases and disorders are reported to be more prevalent in specific ages, genders, and races of patients (8). Dental diseases and disorders among the Chinese population have evolved over time (9). Oral diseases continue to be highly prevalent in China, impacting the health of the population (10). However, specialized dental care is generally not accessible and is often unaffordable due to limited insurance coverage, posing a significant public health challenge for policymakers (11). According to Chinese national oral health epidemiological investigations conducted in 1983, 1995, 2005, and 2015, there is an imbalance in oral health knowledge, and the incidence of dental caries and periapical disease remains relatively high (12). The pooled prevalence of caries in the Tianjin Northern regions of China from 1980 to 2018 is 58.4% (13). However, data for other dental diseases and disorders (those included in this manuscript) for the Tianjin Northern regions of China are not available. As a result, these data are not reported in the manuscript, and the current study was performed to fill this gap. Several national epidemiological investigations have been carried out on this topic, and different policies for the care of dental diseases and disorders have been recommended by various groups in China (11), but no specific policies have been developed for the care of dental diseases and disorders in the Northern regions of China. Therefore, an epidemiological investigation is necessary to assess the prevalence of dental diseases and disorders in this region. We are part of the Endodontics Department at the institute, where we treat adult patients with complaints of chronic pulpitis, dental caries, and periapical disease. Thus, we have focused this study solely on chronic pulpitis, dental caries, and periapical disease to evaluate their prevalence and relationships, excluding other diseases or conditions.

2. Objectives

This cross-sectional study aims to determine the prevalence and potential risk factors of chronic pulpitis, dental caries, and periapical disease in adults seeking treatment at the Tianjin Stomatological Hospital, a major referral center for the Northern region of China.

3. Methods

3.1. Study Design, Period, and Setting

In this cross-sectional study, data from January 17, 2020, to November 18, 2023, at the Tianjin Stomatological Hospital, School of Medicine, Nankai

University, Tianjin, China, were extracted from the electronic medical records.

3.2. Inclusion Criteria

Patients receiving treatment for chronic pulpitis, dental caries, and/or periapical disease were included in the study.

3.3. Exclusion Criteria

Patients with incomplete data due to the absence of any required parameters were excluded from the study.

3.4. Sample Size Calculation

Sample size calculation was based on the assumption that a minimum of 15% of males and females have dental diseases and disorders requiring treatment among individuals visiting the department of adult dentistry and the department of endodontics for oral-related issues (the 15% prevalence rate was selected from prior studies). Additionally, with a 5% type I error, 10% type II error, and a 95% confidence interval (CI), using XLSTAT Statistical Software for Excel, it was determined that 3,200 individuals (males and females) would need to visit the endodontics department of the hospitals for oral-related reasons (2). This hypothesis assumes that 15% of those visiting the endodontics department for various oral conditions have chronic pulpitis, dental caries, and/or periapical disease requiring treatment.

3.5. Outcome Measures

3.5.1. Demographical and Clinical Parameters

Demographic and clinical parameters were extracted from the electronic medical records of patients in the department of endodontics at the hospitals.

3.5.2. Clinical Examinations

Extra and intraoral examinations of all patients were performed by clinicians from adult dentistry and the department of endodontics. Pulp sensitivity tests for hot and cold, electrical tests, palpation, horizontal and vertical percussion, periodontal probing, and mobility were conducted. Additionally, a dentoalveolar radiograph was taken for the affected tooth. One tooth, one surface was examined for dental caries during the clinical examination, with radiographic findings used to assess chronic pulpitis and periapical disease, following institutional protocol.

3.5.3. Chronic Pulpitis

Long-term inflammation of the dental pulp (14).

3.5.4. Dental Caries

Dental caries is a biofilm-mediated, sugar-driven, multifactorial, dynamic disease that may lead to phasic demineralization and recrystallization of dental hard tissues (15). Superficial caries are classified as moderate caries, while deep caries are considered severe caries (16).

3.5.5. Periapical Disease

Inflammation around the tooth root (17).

3.5.6. Severity of Dental Diseases and Disorders

The severity of dental diseases and disorders was classified into two categories: Moderate (primitive, mild, or moderate) and severe (more than moderate or severe). These classifications were determined by clinicians from the department of adult dentistry and the department of endodontics (8). The assessment of severity was based on international guidelines.

3.6. Statistical Analyses

GraphPad 3.01 Software, San Diego, CA, USA, was used for statistical analysis. Categorical, non-normal continuous, and normal continuous variables are presented as frequencies with percentages in parentheses, median values with Q3 - Q1 in parentheses, and mean \pm standard deviation (SD), respectively. The Soup Calculator[®] was used to calculate quartile values. The Kolmogorov-Smirnov test was used to evaluate the linearity of continuous variables. Parametric analyses were performed for normal continuous variables, non-parametric analyses for non-normal continuous variables, and chi-square (χ^2) or Fisher's exact test was performed for categorical variables. A univariate *t*-test or χ^2 -test was performed, followed by logistic regression analysis for significant parameters in univariate analyses to develop a relationship between demographic parameters and clinical examination results (any type of dental disease or disorder) (9). All results were considered significant at a 95% CI and a *P*-value less than 0.05.

3.7. Ethics Approval and Consent to Participate

The protocol for the established study was designed by the authors and approved by the Human Ethics Committee of Nankai University (project number TJYXZDXK-078D, dated January 15, 2020). The study adheres to the laws of China and the 2008 Declaration

of Helsinki. All enrolled patients signed an informed consent form for participation and for the publication of one or more articles from the study before the study commenced. The study followed both national and international ethics guidelines for human research, including obtaining informed consent from participants and approval from an ethics committee.

4. Results

4.1. Study Population

During the study period, 3,245 males and females visited the Department of Endodontics and the Department of Adult Dentistry at the Tianjin Stomatological Hospital, School of Medicine, Nankai University, Tianjin, China, for various oral health-related reasons and objectives. Among these 3245 individuals, a total of 615 (19%) were receiving treatment for chronic pulpitis, dental caries, and/or periapical disease at the Department of Endodontics of the Tianjin Stomatological Hospital, School of Medicine, Nankai University, Tianjin, China. However, the complete data for 119 patients were unavailable in the hospital records, and therefore, data from these 119 patients were excluded from the study. The demographic, clinical, and radiographic parameters of the remaining 496 patients receiving treatment for chronic pulpitis, dental caries, and/or periapical disease were included in the study. The flow diagram of the cross-sectional study is presented in Figure 1.

4.2. Demographical and Clinical Parameters

Among the 496 patients, a total of 300 (60%) were female and 196 (40%) were male. A total of 328 (66%) patients were aged 60 years or more at the time of diagnosis, while 168 (34%) patients were under 60 years old at the time of diagnosis. The majority of the patients were Han Chinese. Additionally, 295 (59%) patients had issues with the mandibular teeth, while 201 (41%) patients had issues with the upper teeth. Among the patients, 250 (50%) were reported to have dental caries, 301 (61%) were reported to have chronic pulpitis, and 151 (30%) had periapical disease(s). The details of the demographic and clinical parameters of the enrolled patients are provided in Table 1.

Moderate conditions of dental diseases and disorders were more prevalent in male patients, patients under 60 years of age, and those with dental issues in the upper teeth. Severe conditions of dental diseases and disorders were more common in female patients, patients aged 60 years or older, and those with dental issues in the

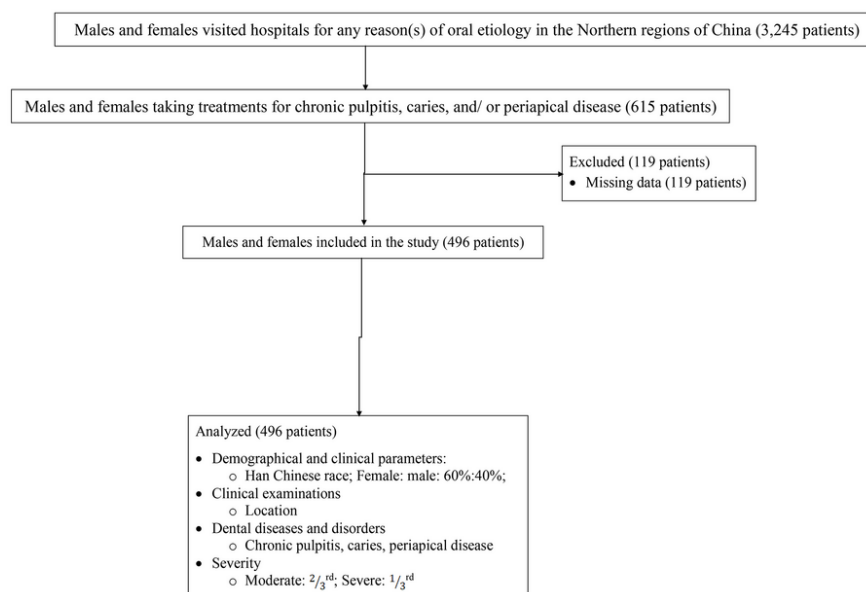


Figure 1. The flow diagram of the cross-sectional study

mandibular teeth. The details of the severity of dental diseases and disorders according to demographic and clinical parameters are presented in [Table 2](#).

Two-thirds of the patients had moderate dental diseases and disorders, while the remaining one-third had severe dental diseases and disorders. The details of the severity of different dental diseases and disorders are presented in [Table 3](#). The study chart, categorized by dental diseases and disorders, is presented in [Figure 2](#).

4.3. Relationship Between Demographical Parameters and Clinical Examination Results

An unpaired *t*-test was performed and showed that female gender, age over 60 years, mandibular teeth involvement, Han Chinese ethnicity, and urban or suburban residential area in the Northern regions of China had significant differences in patients with moderate or severe dental diseases and/or disorders (chronic pulpitis, dental caries, and periapical disease) compared to those without reported diseases or disorders among Chinese adult individuals. (Details of univariate analyses, including P-values and other statistical measures, are not reported here; parametric analyses for normal continuous variables, non-parametric analyses for non-normal continuous

variables, and the χ^2 -test or Fisher's exact test for categorical variables were used.)

Further logistic regression analysis revealed that female gender ($P = 0.041$), age over 60 years ($P = 0.045$), and mandibular teeth involvement ($P = 0.046$) are associated with chronic pulpitis, dental caries, and periapical diseases (any type of dental disease or disorder) in Chinese adult patients. Additionally, female gender ($P = 0.043$), age over 60 years ($P = 0.046$), and mandibular teeth involvement ($P = 0.047$) were found to be associated with moderate dental diseases and disorders (chronic pulpitis, dental caries, and periapical disease) in Chinese adult patients. Furthermore, female gender ($P = 0.045$), age over 60 years ($P = 0.048$), and mandibular teeth involvement ($P = 0.048$) are associated with severe dental diseases and disorders (chronic pulpitis, dental caries, and periapical disease) in Chinese adult patients. The details of the relationship among demographic parameters and clinical examination results are presented in [Table 4](#).

5. Discussion

The current study reported that chronic pulpitis was the most prevalent dental disease, while periapical disease(s) were less common among the study population during the study period. The results of the

Table 1. Demographical and Clinical Parameters of Patients Enrolled in the Cross-Sectional Study from the Northern Regions of China ^{a, b}

| Parameters | Study Population |
|--|------------------|
| Numbers of patients | 496 |
| Gender | |
| Male | 196 (40) |
| Female | 300 (60) |
| Age (y) | |
| Median (Q3 - Q1) | 61 (62 - 55) |
| ≥ 60 | 328 (66) |
| < 60 | 168 (34) |
| Ethnicity | |
| Han Chinese | 457 (92) |
| Mongolian | 34 (7) |
| Tibetan | 5 (1) |
| Dental issue (location) | |
| The mandibular teeth of dentistry | 295 (59) |
| The upper side of dentistry | 201 (41) |
| Dental diseases and disorders | |
| Chronic pulpitis | 301 (61) |
| Dental caries | 250 (50) |
| Periapical disease | 151 (30) |
| Subjects/diseases | |
| Chronic pulpitis | 100 |
| Dental caries | 83 |
| Periapical disease | 50 |
| Residential area of the Northern regions of China | |
| Rural | 275 (55) |
| Urban or suburban | 221 (45) |

Abbreviations: Q3, third quartile; Q1, first quartile.

^a Values are expressed as No. (%) unless otherwise indicated.

^b Patients may have one or more dental diseases and/or disorders.

prevalence of dental diseases in the current study are consistent with those of retrospective studies (1, 12) and case series (4, 18). Chronic pulpitis was the most prevalent dental disease, and periapical disease(s) were less frequently occurring dental diseases among adult individuals in the Northern Chinese population during the study period.

Female gender was associated with dental diseases and disorders (both moderate and severe). The results of the association between gender and dental diseases in the current study are consistent with those of retrospective studies (1, 12), a meta-analysis (8), a cross-sectional study (2), and a case series (4). Women tend to be more concerned about their oral diseases and disorders (1). Chinese women are more concerned about their oral health, as evidenced by their higher healthcare utilization and more frequent visits to the dentist, which explains the observation of more severe disease statistics among women (19). Female gender is

an independent parameter for dental diseases and disorders in adults in the Northern regions of the Chinese population.

Age 60 years or older was associated with dental diseases and disorders (moderate and severe). The results of the association between age and dental diseases in the current study are consistent with those of retrospective studies (1, 12), a meta-analysis (8), a cross-sectional study (2), and case series (18), but are not consistent with the findings of other cross-sectional studies (20, 21). The large sample size in the cross-sectional study (20) may account for these contradictory results. Oral health tends to deteriorate with age (1), and older individuals generally have more time for the care of oral health (1). Age 60 years or older is an independent parameter for dental diseases and disorders in adults in the Northern regions of the Chinese population.

Table 2. Severity of Dental Diseases and Disorders According to Demographical and Clinical Parameters of Patients Enrolled in the Cross-Sectional Study from the Northern Regions of China ^{a, b, c}

| Parameters and Severity of Dental Diseases and Disorders | Study Population (N= 496) |
|--|---------------------------|
| Male | |
| Moderate | 118 (24) |
| Severe | 78 (16) |
| Female | |
| Moderate | 139 (28) |
| Severe | 161 (32) |
| Age (≥ 60 y) | |
| Moderate | 143 (29) |
| Severe | 185 (37) |
| Age (< 60 y) | |
| Moderate | 100 (20) |
| Severe | 68 (14) |
| The mandibular teeth of dentistry | |
| Moderate | 179 (36) |
| Severe | 116 (23) |
| The upper side of dentistry | |
| Moderate | 150 (30) |
| Severe | 51 (11) |

^a Values are expressed as No. (%).

^b The severity of dental diseases and disorders is classified by clinicians from adult dentistry and the department of endodontics.

^c The international guidelines were used for the assessment of severity.

Table 3. Severity for Different Dental Diseases and Disorders of Patients Enrolled in the Cross-Sectional Study from the Northern Regions of China ^{a, b, c, d}

| Dental Diseases and Disorders and Severity | Study Population (N = 496) |
|--|----------------------------|
| Chronic pulpitis | |
| Moderate | 182 (37) |
| Severe | 119 (24) |
| Dental caries | |
| Moderate | 148 (30) |
| Severe | 102 (20) |
| Periapical disease | |
| Moderate | 101 (20) |
| Severe | 49 (10) |

^a Values are expressed as No. (%).

^b The severity of dental diseases and disorders is classified by clinicians from adult dentistry and the department of endodontics.

^c Moderate caries: Superficial caries, severe caries: Deep caries.

^d The international guidelines were used for the assessment of severity.

The mandibular teeth were associated with dental diseases and disorders (moderate and severe). The results of the association between the location of dental diseases and disorders in the current study are not consistent with those of a retrospective study (1). Due to the complex etiology and food habits of the Chinese population, mandibular teeth are more prone to dental

diseases and disorders (22). The mandibular teeth are an independent parameter for dental diseases and disorders in the Northern regions of the Chinese population. The greater involvement of the mandibular teeth in dentistry is primarily attributed to food habits, though other factors such as hygiene maintenance may also play a role and should be considered.

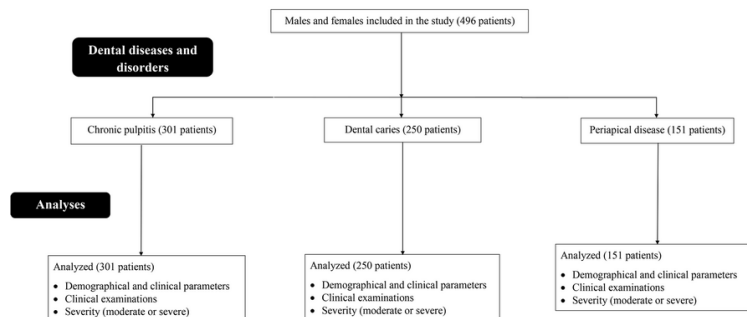


Figure 2. The study chart according to dental diseases and disorders. The international guidelines were used for the assessment of severity.

Table 4. Relationship Between Demographical Parameters and Clinical Examination Results (Any Type of Dental Disease or Disorder; Moderate or Severe)^{a, b}

| Parameters | OR | 95% CI | P-Value |
|--|--------|-----------------|---------|
| Gender (female vs. male) | 1.4561 | 1.1124 - 1.6411 | 0.041 |
| Age ($\geq 60, y$ vs. $< 60, y$) | 1.6452 | 1.2241 - 1.8521 | 0.045 |
| Ethnicity (Han Chinese vs. others) | 0.5412 | 0.4123 - 0.6123 | 0.6123 |
| Dental issue (mandibular teeth of dentistry vs. upper side of dentistry) | 1.8952 | 1.4581 - 2.0211 | 0.046 |
| Residential area (rural vs. urban or suburban) | 0.6145 | 0.5142 - 0.7123 | 0.9854 |

Abbreviations: OR, odd ratio; CI, confidence interval.

^a Multivariate analysis (logistic regression analysis).

^b An odd ratio of more than 1 and a P-value less than 0.05 were considered significant.

Table 5. Percentage Population of Dental Caries for Different Studies in Different Settings

| Studies | Population of Dental Caries in the Study Population (%) |
|---|---|
| Current study | 50 |
| Retrospective study on the Mexican population | 84.07 |
| CNOHEV 1983 | 56 |
| CNOHEV 1995 | 60.53 |
| CNOHEV 2005 | 50.34 |
| CNOHEV 2015 | 62.13 |
| Survey on oral health status of Chinese residents | 68.98 |
| Case series on North American population | 59.18 |
| Cross-sectional study on the Indian population | 26 |
| Meta-analyses on mainland China: Evidence from 1980 to 2018 | 52 |

Abbreviation: CNOHEV, Chinese National Oral Health Epidemiological Investigations.

A total of 50% of the study population reported dental caries. The results of the prevalence of dental caries in the current study are consistent with those of retrospective studies (1, 12), case series (4, 18), and a cross-sectional study (23) (Table 5 and Figure 3). Dental caries is the most common oral disease among the

Chinese population (11), and the population in the Northern regions of China faces serious dental caries issues.

The details of comparative studies on dental diseases and disorders included in the current study for comparison are presented in Table 6.

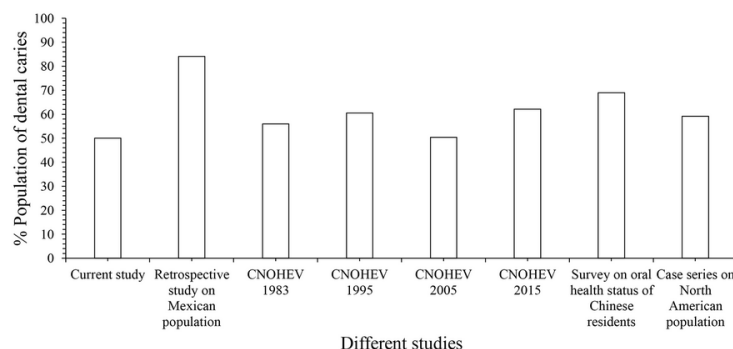


Figure 3. Graphical presentation of % population of dental caries for different studies. CNOHEV, Chinese National Oral Health Epidemiological Investigations.

Table 6. Comparative Studies on Dental Diseases and Disorders in Different Regions and Different Settings

| Study | Published Year | Study Population | Sample Size (N, Teeth) | Age Range (y) |
|---|----------------|---|------------------------|---------------|
| Retrospective study Perez et al. (1) | 2023 | Mexican | 683 | (0 to > 60) |
| Cross-sectional study Almeida et al. (2) | 2021 | Brazilian | 2,500 | 10 > to > 80 |
| Case series Scavo et al. (4) | 2011 | North America | 975 | 7 - 86 |
| Meta-analysis Janakiram et al. (8) | 2020 | Indian | 92,219 | Adults |
| Retrospective study Zhang et al. (12) | 2022 | Sichuan, Nanchong region of China | 537,878 | 3 - 74 |
| Case series Survey Si et al. (18) | 2019 | 31 provinces, cities, and autonomous regions of China except Hong Kong, Macao, and Taiwan | 172,425 | 3 - 75 |
| Cross-sectional study Liu et al. (20) | 2015 | Northeast China | 1,188 | 35 - 74 |
| Cross-sectional study Sadeghivand et al. (21) | 2023 | Tabriz, East Azerbaijan province, Iran | 300 | 37 ± 8.89 |
| Cross-sectional study Rambabu and Koneru (23) | 2018 | Indian | 1,800 | 2 |
| Survey Abrahamian et al. (24) | 2022 | Spanish | 174 | All age |

Despite different kinds of policies for dental diseases and disorders suggested by policymakers in China, the current study was performed to address the lack of specific policies for the care of dental diseases and disorders in the Northern regions of China. Although various groups have recommended different approaches for the care of dental diseases and disorders in China (12), no specific policies exist for the Northern regions. Therefore, epidemiological investigation is necessary to assess the prevalence of dental diseases and disorders in this area. Our study focuses specifically on the Northern regions of China, rather than the entire Chinese population.

In the limitations of the study, it is noted that chronic pulpitis was not further subdivided into reversible and irreversible forms. The moderate and severe categories of dental diseases are based on clinicians' opinions, and

there are possibilities of intra- and inter-variability (24). Another limitation is that definitions for the severity of diseases can vary from study to study, which may affect the results of the study. In the current study, we reported the severity for all subjects/diseases, without dividing by the specific dental diseases investigated, as is typically done in other studies. This approach follows our institutional instructions.

Further data regarding socio-economic status, dental care habits (e.g., tooth brushing methods, frequency, and toothpaste used), and other factors that could provide more insights, particularly for the elderly population and patients with co-morbidities (25), were missing from the electronic records of the patients. While these data could be collected through a survey, our institution does not currently gather them, which limits our ability to perform such analyses. Additionally,

the study did not consider the association between caries and diet.

Furthermore, only one study was conducted at a single center, which limits the ability to generalize the findings to the entire population of the Northern regions of China. We did not evaluate demographic risk or protective factors to prevent the occurrence of dental diseases and disorders, as such data were not available in the institutional records. The study population consisted of patients seeking treatments at one hospital, which introduces significant selection bias, as individuals with more severe disease are more likely to seek care, thus skewing the results. To mitigate this bias in future research, we suggest enrolling all patients with dental diseases and disorders, whether or not they are receiving treatment.

Finally, the study did not account for other confounding variables that could influence the findings. For example, the association between mandibular teeth and disease prevalence may be related to factors such as higher occlusal stress or accessibility for oral hygiene. Future studies should consider these potential confounding factors and explore methods to control for their influence.

5.1. Conclusions

A total of 19% prevalence of dental diseases and disorders was observed in Han Chinese adult males and females who visited the Tianjin Stomatological Hospital, School of Medicine, Nankai University, Tianjin, China, from January 17, 2020, to November 18, 2023. Chronic pulpitis and dental caries were the most prevalent diseases among Han Chinese adult patients in the Northern regions of China. Periapical disease(s) were less commonly reported dental diseases in adult patients in the Northern regions of China. Females, individuals aged 60 years or more, and those with mandibular dental issues were identified as independent parameters for the development of chronic pulpitis, dental caries, and periapical disease in the population of Northern China. The population in the Northern regions of China faces significant dental caries issues. Chinese women in these regions are more concerned about their oral health. Policymakers in China should consider the current study to address the issue of dental diseases and disorders in Chinese adults and improve oral health, especially in Northern China.

This study provides valuable insights into the prevalence of chronic pulpitis, dental caries, and periapical disease in an adult Chinese population. However, the study's methodological limitations prevent definitive conclusions about the relationship

between the identified risk factors and these conditions. Future research is needed to provide more robust evidence to address these limitations and contribute to a better understanding of the epidemiology of dental diseases.

Footnotes

Authors' Contribution: All the authors have read and approved the manuscript for publication. D. W. was the project administrator and contributed to the conceptualization, formal analysis, supervision, resources, methodology, validation, funding acquisition, and literature review of the study. M. L. contributed to the investigation, resources, conceptualization, visualization, formal analysis, methodology, funding acquisition, and literature review. Z. W. contributed to resources, data curation, formal analysis, methodology, funding acquisition, and literature review of the study and drafted and edited the manuscript for intellectual content. All authors agree to be accountable for all aspects of the work, ensuring its integrity and accuracy. D. W., M. L., and Z. W. confirmed the authenticity of the raw data.

Conflict of Interests Statement: All authors declared that they have no conflict of interest.

Data Availability: The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Ethical Approval: The designed protocol of the established study was prepared by the authors themselves and approved by the human ethics committee of Nankai University (project number TJYXZDXK-078D, dated 15 January 2020). The study follows the law of China and the v2008 declarations of Helinski.

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Informed Consent: All enrolled patients have signed an informed consent form for participation and publication of one or more articles from the study before commencing the study.

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