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**MICROBIOLOGICAL PROFILE OF PURULENT-SEPTIC DISEASES
IN MAXILLOFACIAL SURGERY**

by
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The defense materials are available in the Library of Medical University "Prof. Dr. Paraskev Stoyanov" – Varna, Bulgaria, as well as on the official website of the university.

CONTENTS

1. ABBREVIATIONS USED	5
2. INTRODUCTION	6
3. PURPOSE	8
4. GOALS	9
5. MATERIALS	11
5.1. Study Object and Period	11
5.2. Studied Contingent	11
5.3. Inclusion Criteria for the Study	11
5.4. Exclusion Criteria from the Study	12
6. METHODS	13
6.1. Study Design and Data Collection	13
6.2. Microbiological Methods	14
6.3. Statistical Data Analysis	15
6.3.1. Approach to Polymicrobial Infections	15
6.3.2. Directions of Analysis	15
7. RESULTS	17
7.1. Demographic and Seasonal Characteristics of the Studied Contingent	17
7.2. General Characteristics and Structure of Microbiological Findings	21
7.3. Comparative Analysis of Findings in Odontogenic and Non-odontogenic Infections	24
7.3.1. Comparison of the General Microbiological Profile	24
7.3.2. Comparison of the Etiological Structure	26
7.4. Etiological Structure of Isolated Pathogens	28
7.5. Comparative Analysis of Etiology and Localization	33
7.5.1. Anatomical Distribution of Odontogenic Infections	33
7.5.2. Anatomical Distribution of Non-Odontogenic Infections	34
7.6. Distribution of Bacterial Pathogens According to Gram Staining	35
7.7. Species Composition of Leading Pathogen Groups	37
7.7.1. Species Distribution within the Enterobacteriaceae Family	37
7.7.2. Species Distribution Among Coagulase-Negative Staphylococci (CoNS)	39
7.7.3. Species Distribution within the Streptococcus viridans Group	41
7.7.4. Species Distribution within the Candida Genus	43
7.8. Discussion of Expected Antibiotic Susceptibility and Clinical Significance	45
7.8.1. Expected Antibiotic Susceptibility of Gram-Positive Cocci	45
7.8.2. Expected Antibiotic Susceptibility of Gram-Negative Bacteria	46
7.8.3. Expected Antibiotic Susceptibility of Anaerobic Bacteria	46
7.8.4. Concluding Clinical Implications from the Etiological Analysis	46
8. DISCUSSION	47
8.1. Diagnostic Challenge: Dominance of Resident Microflora and High Proportion of Samples Without Etiological Diagnosis	47

8.2. Etiological Landscape: Beyond Statistics – The Role of Key Pathogens	48
8.3. Localization of the Infectious Process: Anatomical and Clinical Correlations	49
8.3.1. Microbiological Profile of Odontogenic Infections	49
8.3.2. Microbiological Profile of Non-Odontogenic Infections	49
8.4. Dynamics Over Time. The <i>Staphylococcal Shift</i> and the Influence of the Pandemic	50
8.5. Specific Diagnostic Challenges	51
8.5.1. Isolation of Anaerobic Bacteria	51
8.5.2. The Role of Fungal Pathogens – From Commensals to Co-pathogens	52
8.6. Clinical Vigilance for Rare and "Exotic" Findings	53
8.7. Dominance of Gram-Positive Bacteria and Clinical Role of Gram-Negative Bacteria.....	54
8.8. Clinical Significance and Practical Recommendations	55
8.9. Limitations of the Study	58
9. CONCLUSIONS	60
10. CONTRIBUTIONS	62
11. SCIENTIFIC PUBLICATIONS RELATED TO THE DISSERTATION	64
12. ACKNOWLEDGEMENTS	65

1. ABBREVIATIONS USED

AB – Antibiotic

AGPC – Anaerobic Gram-Positive Cocci

AMR – Antimicrobial Resistance

ARICU – Anesthesiology, Resuscitation and Intensive Care Unit

CO₂ – Carbon Dioxide

CoNS – Coagulase-Negative Staphylococci

COPD – Chronic Obstructive Pulmonary Disease

COVID-19 – Coronavirus Disease 2019

CSRE – Commission on Scientific Research Ethics

CT – Computed Tomography

DKA – Diabetic Ketoacidosis

ESBL – Extended-spectrum beta-lactamase

GAS – Group A Streptococcus (*Streptococcus pyogenes*)

HIV – Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome

MDR – Multi-Drug Resistance

MFS – Maxillofacial Area / Region

MFSurg – Maxillofacial Surgery

MRI – Magnetic Resonance Imaging

MRSA – Methicillin-Resistant *Staphylococcus aureus*

MRSE – Methicillin-Resistant *Staphylococcus epidermidis*

n – number (absolute frequency)

OPG – Orthopantomography

PAMPs – Pathogen-Associated Molecular Patterns

PRRs – Pattern Recognition Receptors

SOPs – Standard Operating Procedures

spp. – species pluralis (multiple species)

UMHAT – University Multiprofile Hospital for Active Treatment

VGS – *Viridans* Group Streptococci

WHO – World Health Organization

2. INTRODUCTION

The human face is much more than an anatomical feature – it is the focal point of identity, communication, and a primary gateway for sensory perceptions. Due to its complex structure and constant contact with the external environment, it is highly susceptible to microbial invasion. In the clinical practice of the MFSurg (maxillofacial surgeon), acute purulent-inflammatory diseases of the head and neck are an everyday and urgent problem. These conditions transform this vital area from a center of communication into a source of severe pain, functional disorders, and a potential systemic threat. A patient presenting with an asymmetrical, swollen, and painful face often seeks emergency care, which is a clinical signal for the onset of a complex pathophysiological cascade requiring immediate and decisive intervention.

Anatomical and Pathophysiological Aspects

The clinical severity and dramatic course of these infections are rooted in the complex and often treacherous anatomy of the head and neck. Beneath the surface of the skin and mucous membranes lies an intricate network of connective tissue sheaths called fasciae. These structures enclose muscles, glands, and blood vessels, but simultaneously form interfascial spaces – virtual cavities with low resistance that serve as insidious pathways for the rapid spread of purulent exudate. For instance, an infection originating from the apex of a tooth root can spread within hours along these anatomical corridors, following the path of least resistance, and evolve into an extensive phlegmon.

The consequences of such rapid dissemination can be catastrophic. Edema and compression of the upper airway can lead to asphyxia. Penetration of the infection downwards along the retropharyngeal space can cause descending necrotizing mediastinitis – a condition with mortality rates reaching up to 40% even with aggressive treatment. Furthermore, venous spread can cause cavernous sinus thrombosis or the formation of a brain abscess. These severe complications transform purulent processes from a local into a systemic problem, requiring a multidisciplinary approach and intensive care.

Etiology of Infections

The primary source of this microbial aggression is, in most cases, odontogenic. The oral cavity is home to one of the most complex and densely populated microbial communities in the human body. In health, this oral microbiome exists in a delicate balance with the host. However, processes such as dental caries, pulpitis, and periodontitis disrupt the integrity of natural barriers, allowing oral bacteria to invade hitherto sterile tissues. The etiology of odontogenic infections is a classic example of polymicrobial synergy. The process typically begins with facultative anaerobic streptococci (primarily from the VGS), which create a hypoxic environment ideal for the subsequent growth of strict anaerobes. It is these anaerobic bacteria (*Prevotella*, *Porphyromonas*, *Fusobacterium*, *Peptostreptococcus* spp.) that are responsible for the most severe tissue destruction and necrosis.

Therapeutic Strategy and Challenges

The therapeutic strategy for managing this complex problem rests on two fundamental pillars: surgical treatment and AB therapy. Surgical incision and adequate drainage are absolutely mandatory and life-saving procedures. They remove the bulk of microorganisms and necrotic tissues and improve local blood supply. However, surgery alone is insufficient. Here, systemic AB therapy, which must be initiated immediately, plays a key role.

The choice of initial, empirical AB is one of the most critical decisions in the treatment process. It faces an enormous challenge – the global pandemic of AMR. The spread of MRSA, ESBL-producing strains, and multidrug-resistant Gram-negative bacteria has rendered many standard AB ineffective. The microbial landscape is a dynamic and geographically heterogeneous system, which is why the application of therapeutic protocols based on international guidelines, without considering local epidemiological data, can lead to treatment failure.

The microbial landscape is a dynamic and geographically heterogeneous system. The etiological profile and resistance levels in a given hospital or region can differ drastically from those in other parts of the world. For this reason, applying therapeutic protocols based on international guidelines without considering local epidemiological data can lead to therapeutic failure. This highlights the critical need for continuous monitoring of the local microbiological ecosystem. Conducting retrospective analyses of the etiology of purulent-septic diseases is of fundamental importance for developing an adequate, evidence-based strategy for empirical AB therapy. Such studies serve as a "microbiological map" of the region, guiding the clinician to the most likely causative agents and allowing for a more informed choice of treatment, which in turn improves patient clinical outcomes and contributes to limiting the further spread of resistance. The present work aims to contribute precisely in this direction, by providing an in-depth analysis of the microbiological profile of these severe infections in one of the leading clinical centers in Bulgaria over the last ten years.

3. PURPOSE

The aim of the present scientific study is to conduct an in-depth retrospective analysis of the microbiological profile in purulent-septic diseases in the maxillofacial area (MFS), treated in one of the leading clinical centers in Bulgaria – University Hospital "St. Marina" – Varna, Bulgaria, for a period of ten years (2015-2024). This aim is dictated by the growing challenge that antimicrobial resistance (AMR) poses to modern clinical practice. In conditions of a dynamically changing etiological landscape and the emergence of multidrug-resistant strains, the choice of adequate empirical antibiotic therapy becomes increasingly difficult and uncertain. International guidelines provide general directions, but their effectiveness is directly dependent on local epidemiological specificities. Therefore, the study aims not merely to describe the isolated pathogens, but to create an up-to-date "microbiological map" for the Varna region. This map will serve as a scientifically grounded database to assist clinicians in their daily work. Through the analysis of a large volume of data, the study aims to identify the leading causative agents, outline key trends in their distribution over time, and establish existing differences in etiology according to the origin of the infection.

The ultimate aspiration of this work is to provide valuable scientific information that will serve to optimize local therapeutic protocols, improve the effectiveness of empirical treatment, contribute to limiting the spread of antimicrobial resistance, and ultimately improve the prognosis and clinical outcome for patients with these severe and potentially life-threatening diseases.

4. GOALS

To fulfill these goals the following tasks were set:

1. **To determine the overall etiological structure of purulent-septic infections in the MFS, treated at the Clinic of Maxillofacial Surgery at University Hospital "St. Marina" - Varna, Bulgaria, over a 10-year period (2015-2024).**

The first and most fundamental task is to create a comprehensive and quantitative profile of all microorganisms isolated from purulent processes in the MFS. This includes identifying all bacterial and fungal pathogens down to species level, calculating their absolute and relative frequency (n), and establishing a hierarchy of the most significant causative agents. This task aims to answer fundamental questions such as: Which are the dominant pathogens in the overall sample? What is the proportion of Gram-positive versus Gram-negative bacteria? What is the place of anaerobes and fungi in the overall etiological landscape? The fulfillment of this task will provide the "big picture" of microbiological etiology, serving as a basis for all subsequent analyses.

2. **To perform a comparative analysis of the microbiological profile in infections of odontogenic and non-odontogenic origin.**

This task focuses on one of the key distinctions in clinical practice. It is essential to establish whether and what statistically significant differences exist in the causative agents of infections originating from dental structures compared to those of other origins (cutaneous, traumatic, sialogenic, etc.). The task involves dividing the entire sample of isolates into two groups according to clinical diagnosis and a detailed comparison of the etiological spectra. This analysis is expected to confirm or refute classic notions of streptococcal and anaerobic dominance in odontogenic infections and staphylococcal dominance in non-odontogenic ones. The results will have immense practical value, as they can guide a more precise choice of empirical therapy at the patient's initial examination.

3. **To track the dynamics of the main etiological agents over time, comparing two 5-year periods – before and after the COVID-19 pandemic.**

The third task introduces a temporal dimension to the analysis, aiming to ascertain whether the microbiological landscape is static or undergoing changes. For this purpose, the ten-year study period will be divided into two equal five-year intervals: 2015-2019 (pre-pandemic) and 2020-2024 (pandemic and post-pandemic). A comparative analysis of the frequency of key pathogenic groups (e.g., *Staphylococcus* spp., *Streptococcus* spp., *Enterobacteriaceae*) will be performed between the two periods. This task aims to test the hypothesis of the so-called "staphylococcal shift" and to evaluate the potential influence of the COVID-19 pandemic, associated with changes in AB consumption and hospital hygiene, on the etiological spectrum of infections.

4. **To analyze the frequency of polymicrobial infections and samples without a proven etiological agent and to discuss the possible reasons for this.**

The final task is directed towards two important aspects of routine microbiological diagnostics. Firstly, the exact proportion of polymicrobial infections (isolation of two or more pathogens from one sample) will be determined, as they are often associated with a more severe course and therapeutic difficulties. Secondly, the large proportion of samples without an etiological diagnosis (sterile cultures or only resident flora) will be analyzed. This task aims to quantitatively assess this diagnostic problem and discuss its most probable causes, such as previous AB therapy and methodological difficulties in isolating fastidious anaerobic microorganisms. The results will highlight the limitations of routine diagnostics and reinforce the importance of local epidemiological data for clinical practice.

5. MATERIALS

A retrospective, descriptive microbiological study was conducted. The present study has a retrospective, observational, and descriptive design, based on the analysis of existing data. This design choice was made to evaluate the etiological structure of purulent-septic diseases in the MFS and to track the dynamics of causative agents over time. By utilizing routinely collected laboratory data from clinical practice, the study provides a valuable epidemiological profile directly applicable to improving local clinical protocols.

5.1. Study Object and Period

The object of the study included all results from microbiological cultures of materials (pus, aspirates, wound secretions) taken from patients with a clinical diagnosis of purulent-septic disease. The patients were treated at the Clinic of Maxillofacial Surgery at **University Hospital "St. Marina" - Varna, Bulgaria**. Data for a full 10-year period, covering the time from January 1, 2015, to December 31, 2024, were analyzed, ensuring a sufficiently large sample for statistical reliability and trend tracking.

5.2. Studied Contingent

The study included data from all patients ($n=1735$) from whom material for microbiological examination was taken within the specified period.

The studied group was divided into two main subgroups based on clinical diagnosis and the probable primary source of infection:

- Patients with odontogenic infections ($n=1033$): This group included patients with infections originating from the teeth and their supporting structures, such as periapical abscesses, phlegmons with a dental periodontitis source, and pericoronitis.
- Patients with non-odontogenic infections ($n=702$): This group comprised patients with infections of other origins, such as traumatic, dermatogenic, sialogenic (from salivary glands), rhinogenic (from the nasal cavity), or tonsillogenic (from tonsils) origin.

5.3. Inclusion Criteria for the Study

Only patients who simultaneously met all of the following criteria were included in the present analysis:

- Hospitalization in the Clinic of Maxillofacial Surgery (**MFSurg**) within the ten-year period (2015-2024).
- Clinical diagnosis of "abscess" or "phlegmon" in the **MFS**, confirmed by examination by a maxillofacial or oral surgeon through palpatory detection of a purulent infiltrate.
- Undergone surgical intervention (incision, lavage, and drainage), during which a varying amount of pus was evacuated.

- Conducted microbiological examination of intraoperatively collected material.
- Availability of preserved medical documentation allowing for comprehensive data analysis.

5.4. Exclusion Criteria from the Study

All patients meeting at least one of the following criteria were excluded from the analysis:

- Patients treated as outpatients, without having been hospitalized.
- Patients treated outside the ten-year study period (before 2015 or after 2024).
- Patients with a clinical diagnosis other than "abscess" or "phlegmon."
- Cases where no purulent collection was found and evacuated intraoperatively.
- Patients for whom no microbiological examination was performed.
- Cases with incomplete or missing medical documentation that did not allow for the collection of necessary data.

The study was approved by the Commission on Scientific Research Ethics (CSRE) at "Prof. Dr. Paraskev Stoyanov" Medical University – Varna, Bulgaria (Protocol No 2/04.07.2024).

6. METHODS

6.1. Study Design and Data Collection

The study was planned and executed as a retrospective, observational study, based on the analysis of data from a single clinical center. This study design is suitable for investigating the etiological spectrum of diseases within a specific geographical and clinical environment. Data were collected from the archive of the Microbiological Laboratory of University Hospital "St. Marina" - Varna, Bulgaria, which serves a wide range of patients, including those with maxillofacial infections. The covered period of 10 years (from 2015 to 2024) ensures a sufficiently large sample for reliable statistical analysis.

In all patients, the diagnosis of "abscess" or "phlegmon" was confirmed both clinically and intraoperatively.

- In patients with odontogenic infections, the diagnosis was established after identification of the causative tooth. This was achieved through physical examination (detection of caries, radices, periodontal pockets) and imaging studies (most commonly OPG), which visualized granulomas, radices, jaw cysts, etc.
- In patients where the above data were not established, the infection was assumed to be of non-odontogenic origin.

For each patient, the following key indicators were extracted from the laboratory records, which served as the basis for our analysis:

- **Year of study:** This indicator allowed for tracking the dynamics of the etiological spectrum over time and identifying possible trends.
- **Type of infection:** Samples were classified based on the clinical diagnosis documented by clinicians as odontogenic (originating from teeth or periodontium) or non-odontogenic (of other origins, such as trauma, dermatogenic infections, sinusitis, etc.).
- **Result of microbiological examination:**
 - **No growth (sterile culture):** A result indicating the absence of microbial growth under the culture conditions used.
 - **Resident (normal) microflora:** Identification of microorganisms considered part of the normal microflora of the respective anatomical area.
 - **Isolated pathogenic microorganism:** Identification of one or more microorganisms considered causative agents of the infection.
- **Species of isolated pathogen(s):** This information included the full taxonomic identification of the microorganism down to species level (e.g., *Staphylococcus aureus*, *Streptococcus pyogenes*).

6.2. Microbiological Methods

All examined samples were processed according to the SOPs of the microbiological laboratory, ensuring a unified and reproducible approach.

- **Material Collection and Transport:** Materials (pus, aspirates, wound secretions) were collected by clinicians under aseptic conditions to minimize contamination. Samples were collected in sterile containers or, for fastidious microorganisms, with sterile swabs in a transport medium that ensured the viability of pathogens until their arrival at the laboratory. Rapid transport of samples is critical, especially for strict anaerobic bacteria, which are sensitive to oxygen.
- **Inoculation:** Materials were inoculated onto a wide range of culture media to provide optimal conditions for the growth of various types of microorganisms. The set of media typically includes:
 - **Blood Agar and Chocolate Agar:** Non-selective media suitable for the growth of most aerobic and facultatively anaerobic bacteria, including streptococci and staphylococci.
 - **MacConkey Agar:** A selective medium used for the isolation and differentiation of Gram-negative bacteria from the family *Enterobacteriaceae*.
 - **Sabouraud Agar:** A medium specifically designed for the isolation of fungi, such as *Candida spp.*, by inhibiting bacterial growth.
- **Incubation:** Inoculated cultures were incubated at physiological temperature (35-37°C) to simulate conditions in the human body. Various atmospheric conditions were used for culturing diverse microorganisms:
 - **Aerobic conditions:** For bacteria that require oxygen for growth (e.g., *Pseudomonas spp.*).
 - **Microaerophilic conditions:** An environment with reduced oxygen and increased CO₂ content, ideal for culturing streptococci.
 - **Anaerobic conditions:** An oxygen-free environment, critical for the isolation of strict anaerobes, which play an important role in purulent-septic infections.
- **Identification:** Identification of isolated microorganisms was performed through a sequence of methods, including:
 - **Macromorphological and cultural characteristics:** Observation of the size, shape, color, and consistency of colonies.
 - **Microscopic analysis:** Gram staining to determine morphology and cell wall reaction (Gram-positive or Gram-negative).
 - **Biochemical tests:** A series of tests (e.g., oxidase, catalase, coagulase) for species differentiation. In modern microbiology, these methods are supplemented or replaced by automated systems for rapid and accurate identification.

6.3. Statistical Data Analysis

The collected data were entered, systematized, and analyzed using spreadsheet software (Microsoft Excel). To address the study's objectives, descriptive statistical analysis was applied. The main statistical indicators calculated included absolute frequencies (**n**) and relative proportions (%) for each data category, allowing for a clear and quantitative presentation of the results.

6.3.1. Approach to Polymicrobial Infections

Special attention was paid to cases of polymicrobial infections, where more than one pathogen was isolated from the same sample. To accurately reflect the entire etiological spectrum and assess the contribution of each microorganism, a unique approach was applied: each isolated pathogenic microorganism was counted as a separate isolate. For example, if *Staphylococcus aureus* and *Klebsiella* spp. were isolated from one sample, they were counted as two separate isolates. This provides a more complete and precise picture of the microbial etiology than if only a single predominant pathogen were reported, or if mixed infections were counted as a single case. This method is crucial for understanding the complex synergy between different microorganisms in purulent-septic processes in the MFS.

6.3.2. Directions of Analysis

Data analysis was conducted in three main, interconnected directions:

1. **Calculation of the total proportion of samples with a proven causative agent:** This analysis aims to determine the overall effectiveness of routine microbiological diagnostics in clinical settings, differentiating between samples with sterile cultures, samples with resident microflora, and those with an isolated pathogen. Calculating this percentage is critical for assessing diagnostic challenges, such as the impact of prior AB therapy.
2. **Determination of the etiological structure of all isolates and comparative analysis:**
 - **General etiological profile:** A detailed analysis was performed on the frequency of all isolated microorganisms, grouped by genus and species, to establish the overall etiological landscape of infections in the MFS.
 - **Comparative analysis:** A comparison of the microbial profile in odontogenic and non-odontogenic infections was conducted. This analysis is key, as it provides specific information that can guide empirical AB therapy before microbiological results are available. It allows for the identification of typical pathogens for each group of infections (e.g., *Streptococcus* spp. in odontogenic and *Staphylococcus* spp. in non-odontogenic infections).
3. **Analysis of the dynamics of causative agents over time:**
 - **Two-period time analysis:** To track possible changes in the etiological landscape, data were divided into two equal 5-year intervals. This approach allows for a comparison of the frequency of individual pathogens before and after certain

events, such as the COVID-19 pandemic, which may have influenced AB use and the selection of AMR strains.

- **Detailed monitoring:** A detailed analysis of the trends of the most commonly encountered pathogen groups was performed to determine whether their proportion was increasing or decreasing. This included tracking the frequency of staphylococci, streptococci, and Gram-negative bacteria, which allows for the formulation of hypotheses about the causes of the observed changes. This analysis is particularly important from a public health perspective and in the fight against AMR.

7. RESULTS

7.1. Demographic and Seasonal Characteristics of the Studied Contingent

A total of 1735 samples from patients with purulent-septic diseases in the MFS were included in the present study, covering the period 2015-2024. Analysis of demographic data shows that the mean age of patients was 42.5 ± 17.2 years, ranging widely from 18 to 88 years. This distribution indicates that purulent-septic infections in the MFS affect all active age groups, highlighting their clinical significance.

The gender distribution demonstrates a significant predominance of males. Of the total number of patients, 1018 (58.7%) were men, and 717 (41.3%) were women, forming a male:female ratio of approximately 4:1. This difference is consistent with data from other studies and can be explained by the higher incidence of trauma and risk behaviors (e.g., lower oral hygiene) in the male population, as noted by (Brook, 2017).

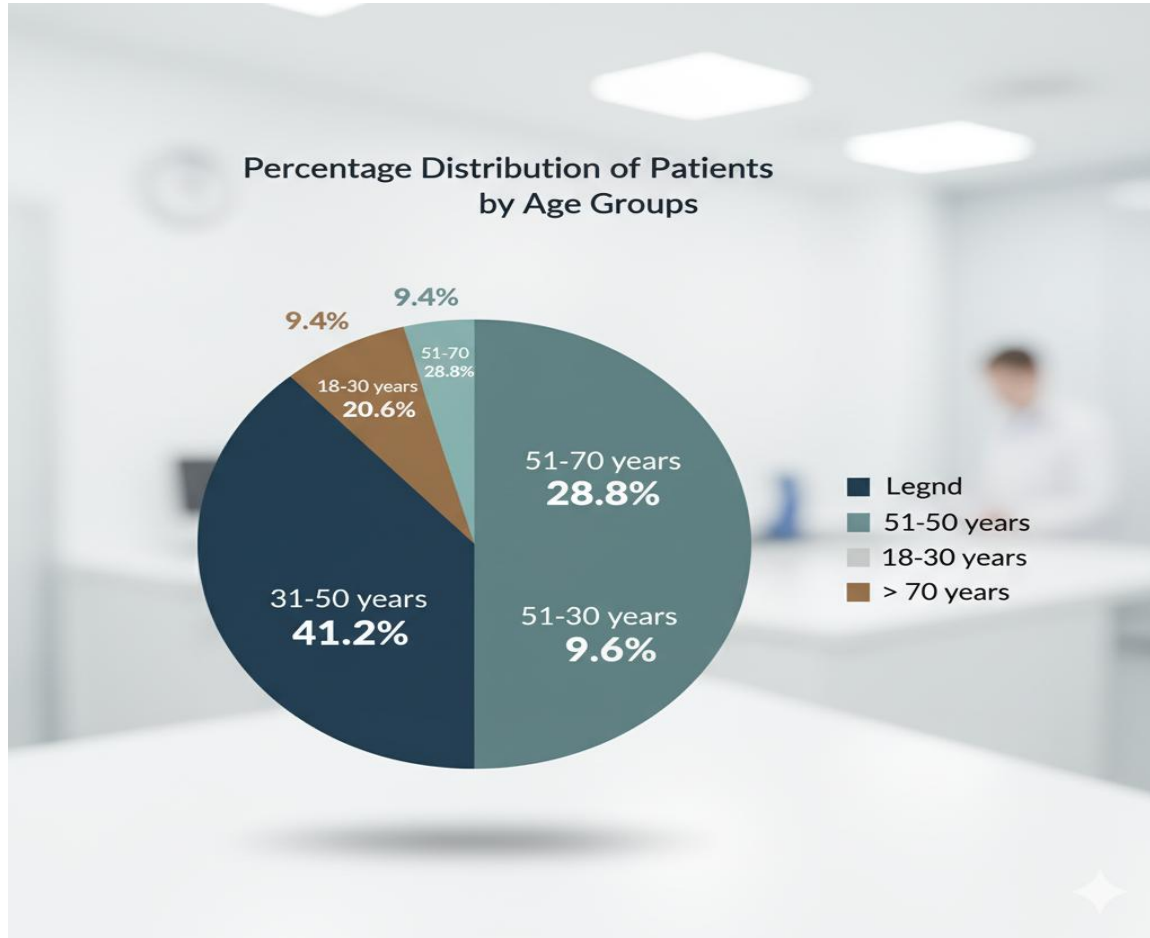
To provide a more detailed picture, an additional analysis of the age distribution of patients, broken down by age groups, was performed. The results are presented in Table 1.

Table 1. Age distribution of patients (n=1735).

Age Group	Number of Patients (n)	Share (%)
18-30 years	358	20.6%
31-50 years	715	41.2%
51-70 years	499	28.8%
> 70 years	163	9.4%
TOTAL	1735	100.0%

The data from Table 1 show that the most affected age group are patients aged between 31 and 50 years, who constitute over 40% of all cases. This group is the most active and often exposed to risk factors such as dental caries, periodontitis, and trauma, which explains the high number of infections. It is also noticeable that cases in the age group over 70 years are significantly fewer, which may be due to a smaller number of preserved teeth and associated odontogenic problems, as confirmed by studies by (Bahl et al., 2014).

Figure 1. Percentage distribution of patients by age groups



As Figure 1 clearly illustrates, the distribution of patients by age groups shows that purulent-septic infections in the maxillofacial area most strongly affect the group of patients between 31 and 50 years. This segment represents the largest sector of the pie chart with a share of 41.2%, which is almost double the next largest group.

This distribution is of significant clinical importance and is consistent with demographic and behavioral factors. The 31 to 50 age group is the most active part of the population, which is most exposed to risks associated with odontogenic infections (dental caries, periodontitis). These results emphasize that MFS infections are not solely a problem of the young or elderly but are significant for a large part of the active population.

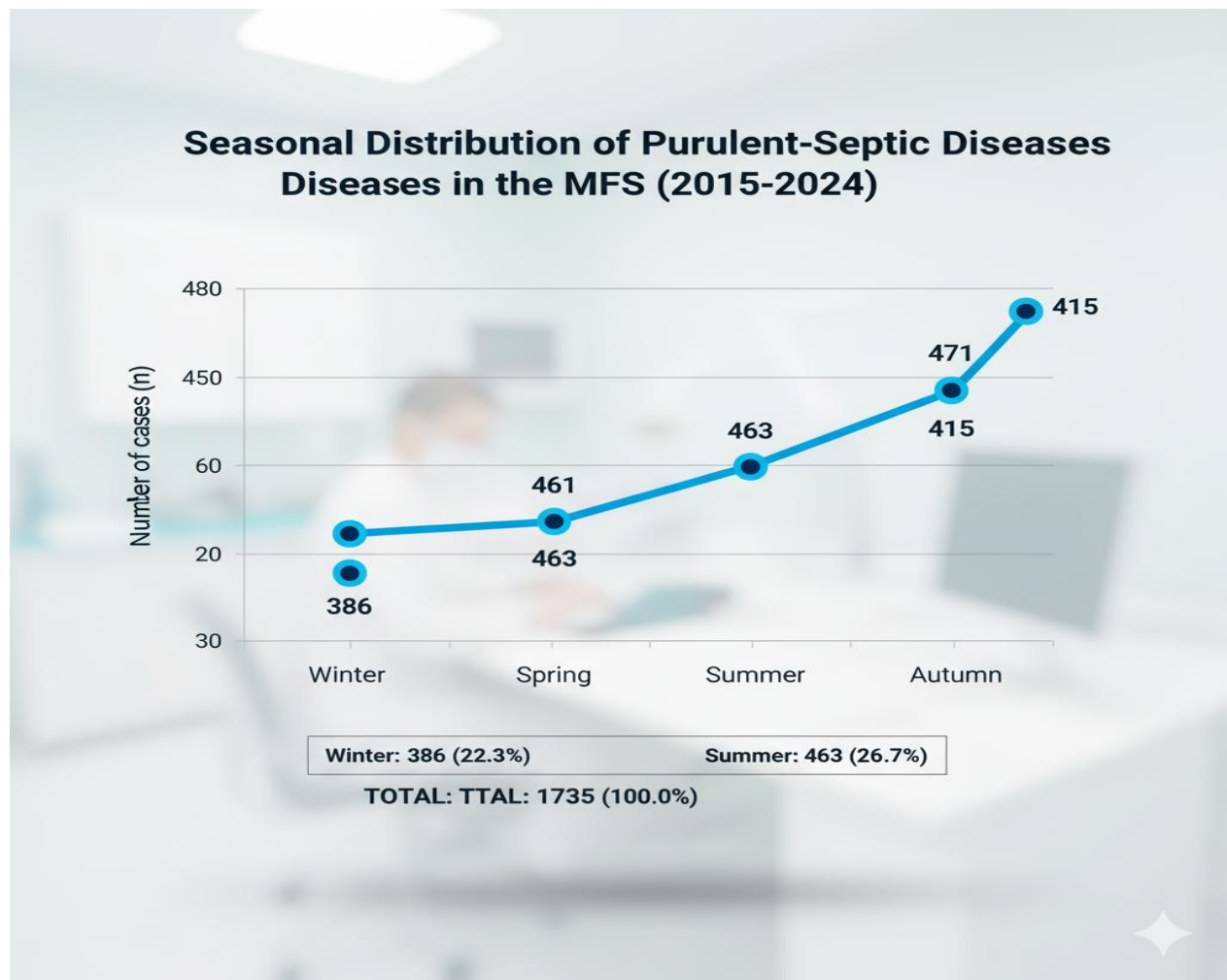
It is also noticeable that the number of cases decreases significantly in the age group over 70 years, which constitutes only 9.4% of all cases. This can be explained by a smaller number of preserved teeth in this age group, which consequently reduces the frequency of odontogenic problems leading to infections.

The analysis of cases by seasons shows a slight peak of purulent-septic diseases during the spring and summer months. The distribution is presented in Table 2.

Table 2. Distribution of patients by months and seasons (n=1735)

Month	Number of Cases (n)	Season	Number of Cases (n)	Share (%)
December	138	Winter	386	22.3%
January	128			
February	120			
March	153	Spring	471	27.1%
April	151			
May	167			
June	162	Summer	463	26.7%
July	147			
August	154			
September	148	Autumn	415	23.9%
October	125			
November	142			
TOTAL	1735		1735	100.0%

Figure 2. Seasonal distribution of purulent-septic diseases in the MFS for the period 2015-2024



The presented line chart illustrates the seasonal dynamics of purulent-septic diseases in the MFS for the ten-year study period. The data show that the incidence of infections tends to increase during the spring and summer months, reaching its peak in spring (471 cases) and summer (463 cases). In contrast, a slight decrease in the number of cases is observed during the winter and autumn months (386 and 415 respectively).

This seasonal variation can be explained by various factors, including changes in human behavior and external risk factors, which is consistent with other studies (Hupp et al., 2019). The higher incidence of trauma and sunburns during the summer, as well as the spread of viral infections that

can predispose to bacterial superinfections in the spring, are possible causes for the observed fluctuations. However, the difference is not drastic, indicating that purulent-septic diseases in the MFS are relevant throughout the year.

This analysis complements the presented demographic data and provides a more complete overview of the epidemiological profile of the studied infections.

7.2. General Characteristics and Structure of Microbiological Findings

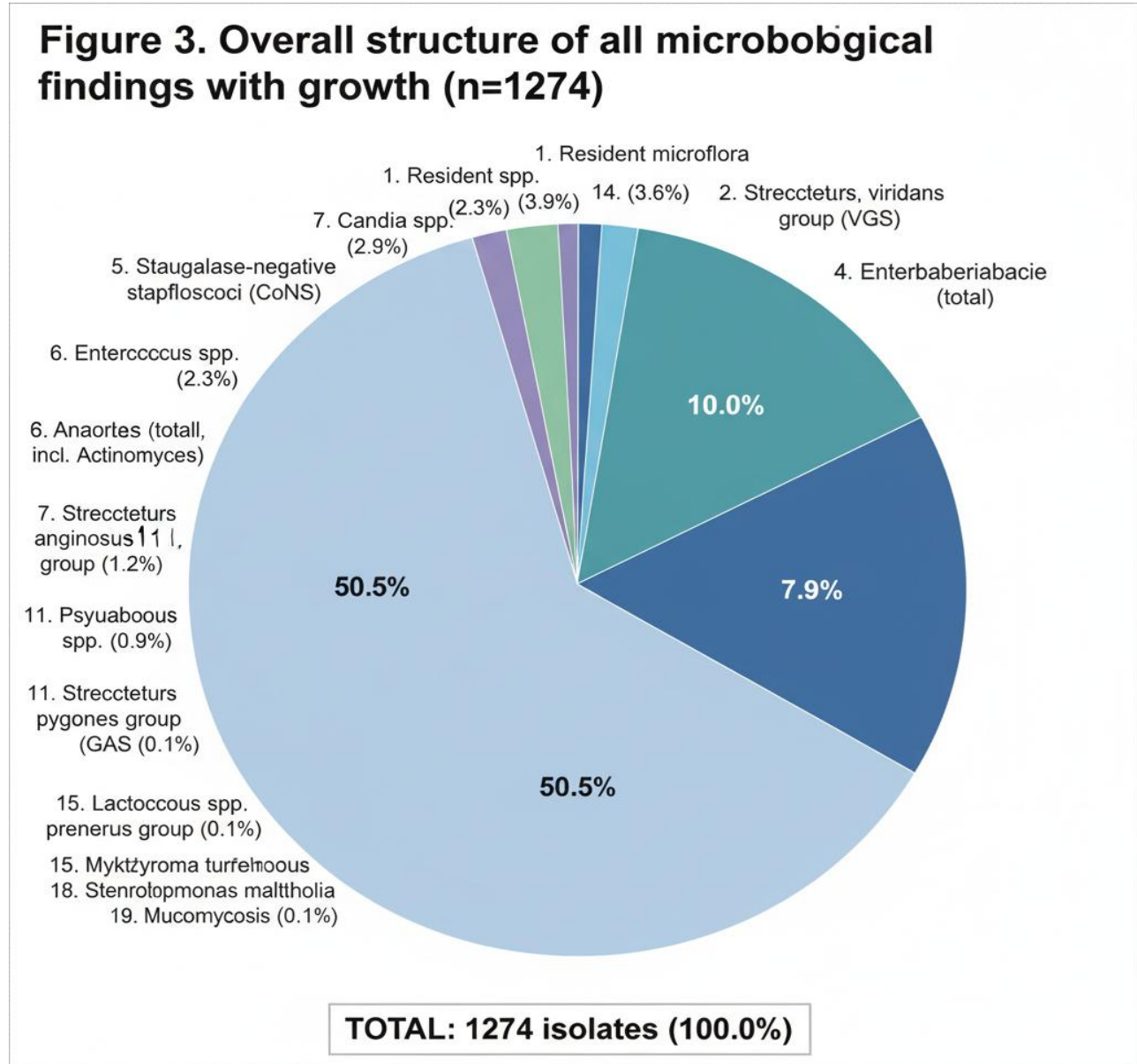
Of all 1735 clinical samples examined, microorganism growth was established in 1239 (71.4%) of them, while 496 (28.6%) remained sterile. This result is consistent with other studies in maxillofacial surgery and microbiology, which also report a significant proportion of samples without an isolated pathogen (Brook, 2017). The reasons for this high percentage can be multifactorial, including prior **AB** therapy which suppresses bacterial growth, as well as difficulties in isolating fastidious or anaerobic microorganisms under routine conditions.

The detailed distribution of samples shows that a confirmed pathogenic agent was isolated in 596 (34.4%) of all samples, and only resident microflora was found in 643 (37.1%). The percentage of samples with an isolated pathogen is higher in non-odontogenic infections (38.7%) compared to odontogenic ones (31.4%), which is explained by the higher degree of contamination with oral resident microflora in the latter (Table 3).

Table 3. Detailed structure of all microbiological findings with growth (n=1274).

Rank	Microbiological Finding	Number (n)	Share (%)
1.	Resident microflora	643	50.5%
2.	Coagulase-negative staphylococci (CoNS)	145	11.4%
3.	<i>Streptococcus</i> , viridans group (VGS)	127	10.0%
4.	<i>Enterobacteriaceae</i> (total)	101	7.9%
5.	<i>Staphylococcus aureus</i>	71	5.6%
6.	<i>Candida</i> spp.	50	3.9%
7.	<i>Enterococcus</i> spp.	29	2.3%
8.	<i>Acinetobacter</i> spp.	20	1.6%
9.	Anaerobes (total, incl. <i>Actinomyces</i>)	15	1.2%
10.	<i>Streptococcus anginosus</i> group	14	1.1%
11.	<i>Pseudomonas</i> spp.	12	0.9%
12.	<i>Streptococcus pyogenes</i> group (GAS)	9	0.7%
13.	<i>Corynebacterium</i> spp.	5	0.4%
14.	<i>Streptococcus pneumoniae</i>	3	0.2%
15.	<i>Mycobacterium tuberculosis</i>	2	0.2%
16.	<i>Lactococcus</i> spp.	1	0.1%
17.	<i>Burkholderia</i> spp.	1	0.1%
18.	<i>Stenotrophomonas maltophilia</i>	1	0.1%
19.	Mucormycosis	1	0.1%
	TOTAL	1274	100.0%

Figure 3. Overall structure of all microbiological findings with growth (n=1274)



The data from Table 3 and Figure 3 clearly show that the absolute most common microbiological finding in the examined samples is resident microflora, accounting for 50.5% of all cases with growth. This is consistent with the general conclusions of the study and highlights the diagnostic challenges in isolating specific pathogens, especially when the oral cavity is the source of the infection. This high proportion of resident microflora contributes to the significant number of samples without an isolated specific pathogen.

Among the isolated pathogenic microorganisms, CoNS play a leading role with 11.4%, followed by the *Streptococcus viridans* group (VGS) (10.0%) and *Enterobacteriaceae* (7.9%). This ranking is important as it indicates the increasing clinical significance of CoNS as opportunistic pathogens.

7.3. Comparative Analysis of Findings in Odontogenic and Non-odontogenic Infections

To understand the specifics of the two main types of infections, a comparative analysis was performed on both the general sample profile and the specific etiological structure.

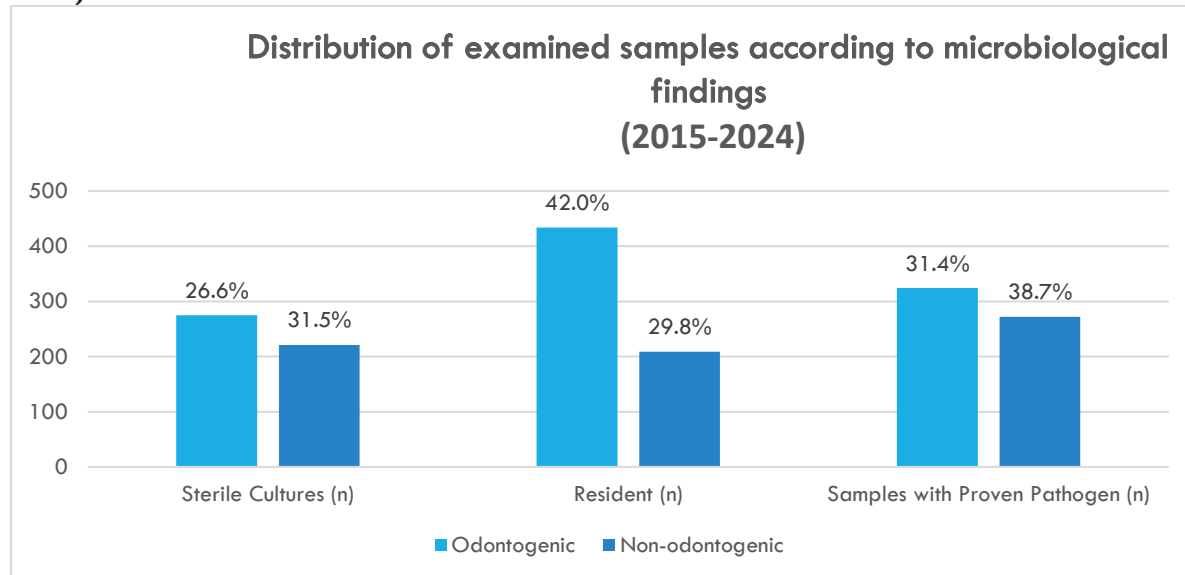
7.3.1. Comparison of the General Microbiological Profile

Analysis of the sample distribution shows significant differences in the microbiological picture between the two types of infections (Table 4).

Table 4. Distribution of examined samples according to microbiological findings (2015-2024).

Category	Total Samples (n)	Sterile Cultures (n)	Resident Microflora (n)	Samples with Proven Pathogen (n)	Share with Proven Pathogen (%)
Non-odontogenic	702	221	209	272	38.7%
Odontogenic	1033	275	434	324	31.4%
TOTAL	1735	496	643	596	34.4%

Figure 4. Distribution of examined samples according to microbiological findings (2015-2024).



The observed difference in the percentage of samples with a proven causative agent between the two main groups of infections is significant and poses important diagnostic challenges. As the data show, the percentage of samples with an isolated pathogen is higher in non-odontogenic infections (38.7%) compared to odontogenic ones (31.4%). This difference is not coincidental and can be explained by several key factors that are important for future clinical practice.

1. Influence of resident microflora

Firstly, samples from odontogenic sources are exposed to a much higher degree of contamination with oral resident microflora. As Table 4 shows, almost 42% of samples from odontogenic infections (434 out of 1033) yielded growth of only resident microflora, which significantly complicates the isolation of the true pathogen. This phenomenon, where resident microflora predominates, is one of the main reasons for the lower percentage of proven pathogens in odontogenic samples, as emphasized in the general conclusions. This finding highlights the need for strict sampling technique to minimize contamination with normal flora. In contrast, non-odontogenic infections, which are often associated with skin microflora or traumatic contamination, are easier to isolate under standard aerobic conditions.

2. Effect of prior antibiotic therapy

Secondly, the high proportion of samples without an isolated causative agent in odontogenic infections (275 sterile cultures) also supports the hypothesis of the influence of prior antibiotic therapy. Patients with odontogenic infections often receive antibiotics from general practitioners or dentists even before hospital admission. This treatment, although sometimes ineffective for complete cure, can suppress bacterial growth *in vitro*, making microbiological diagnosis impossible. The lack of accurate information about this anamnesis is a major limitation of our retrospective study.

3. Diagnostic challenge and the importance of empirical therapy

These results underscore the diagnostic challenge faced by clinicians and prove that empirical antibiotic therapy, based on local epidemiological data, is critically important. In the presence of an unfavorable microbiological finding (sterile sample or only resident flora), the clinician must rely on their knowledge of the most probable causative agents to choose appropriate treatment. Our study provides precisely this valuable information, outlining the profile of the most common pathogens in the region and their antibiotic susceptibility, which can serve as a basis for developing local therapeutic protocols.

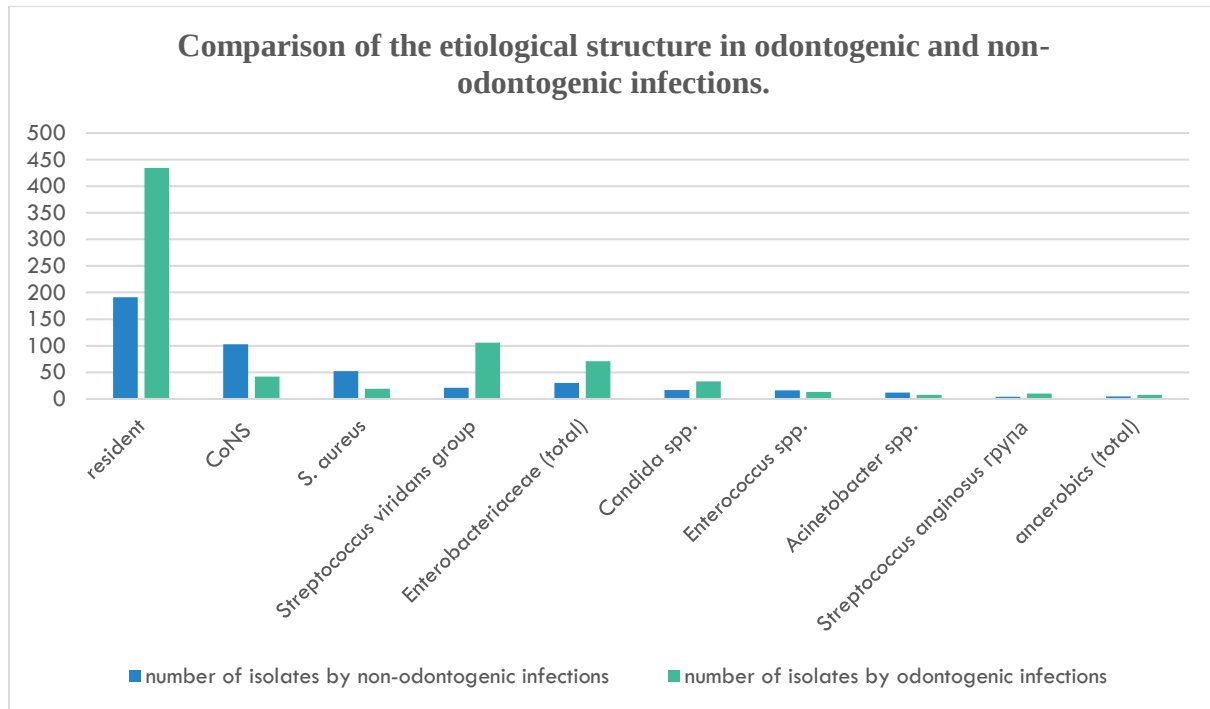
7.3.2. Comparison of the Etiological Structure

Detailed analysis of isolated pathogens and resident flora reveals a completely different etiological profile in the two groups of infections (Table 5).

Table 5. Leading findings in non-odontogenic and odontogenic infections

Microbiological Finding	Non-odontogenic (n)	Odontogenic (n)
Resident microflora	209	434
Coagulase-negative staphylococci (CoNS)	103	42
<i>Staphylococcus aureus</i>	52	19
<i>Streptococcus</i> , viridans group	21	106
Enterobacteriaceae (total)	30	71
<i>Candida</i> spp.	17	33
<i>Enterococcus</i> spp.	16	13

Figure 5. Comparison of the etiological structure in odontogenic and non-odontogenic infections.



Key findings from the comparative analysis:

A clear difference in etiology between the two types of infections is observed, as noted in the general conclusions of the study.

- **Dominance of staphylococci in non-odontogenic infections.**

As seen, CoNS (103) and *Staphylococcus aureus* (52) are significantly more common causative agents in non-odontogenic infections, with a total of 155 isolates, confirming their role as primary pathogens in skin, traumatic, and postoperative infections. The high frequency of *S. aureus* (52 isolates) in this group is indicative of its potential to cause severe purulent processes.

- **Dominance of oral flora in odontogenic infections.**

On the other hand, streptococci from the Viridans group are dominant in odontogenic infections, with 106 isolates, highlighting their key contribution as part of the normal oral microflora, which under certain conditions can become pathogenic.

7.4. Etiological Structure of Isolated Pathogens

From the 596 samples with proven infection, a total of 631 pathogenic microorganisms were isolated. This ratio of 1.05 isolates per sample unequivocally indicates that a large proportion of purulent-septic infections in the MFS are of polymicrobial etiology. This is consistent with the generally accepted understanding that infections in this area are rarely monomicrobial and are usually caused by the synergistic action of several types of bacteria (S. D. Hupp et al., 2019). This fact is extremely important for the choice of antibiotic therapy, as it is necessary to ensure coverage for both aerobic and anaerobic pathogens.

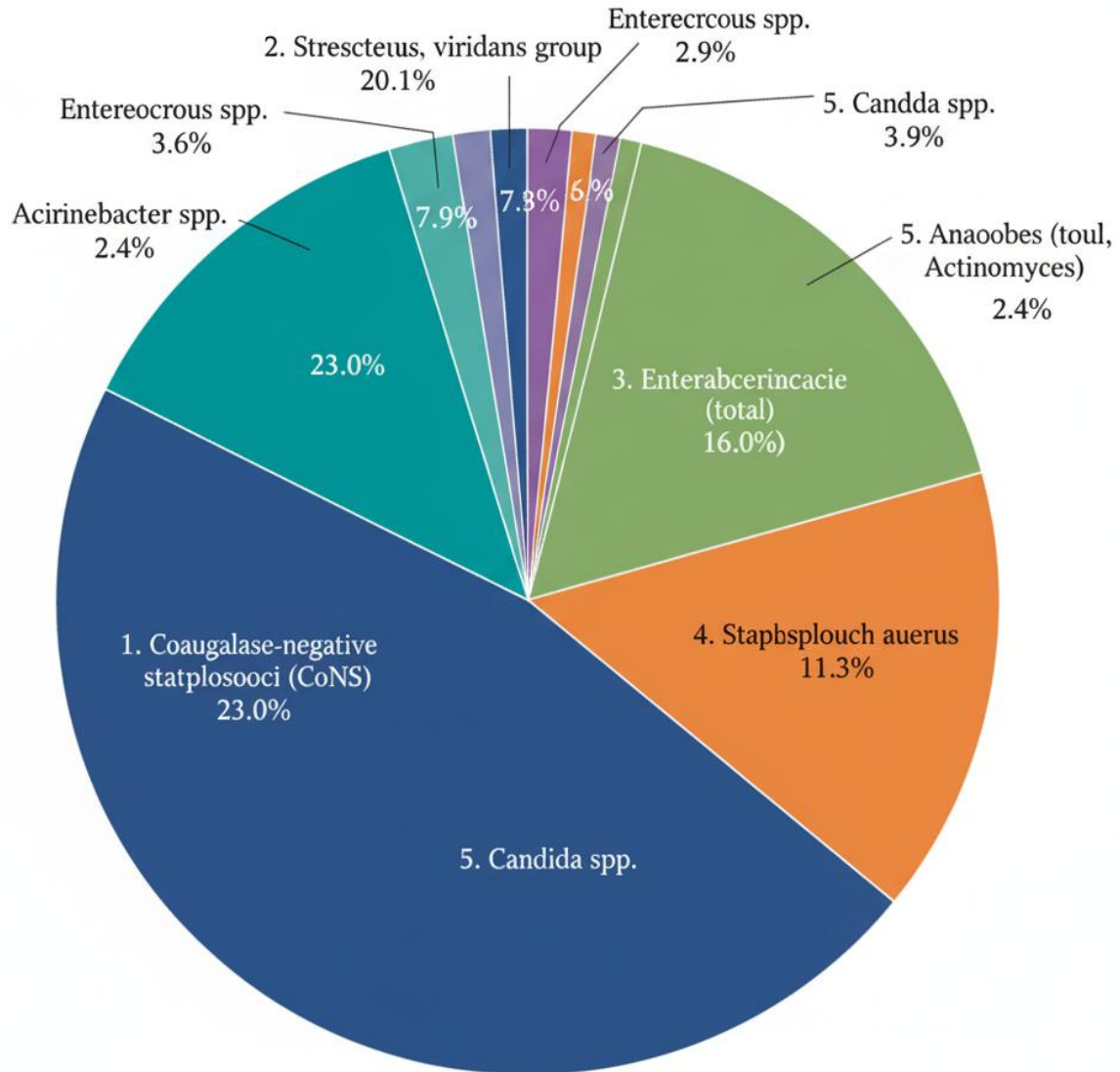
The detailed etiological structure of all 631 isolates, grouped by genus and species, is presented in Table 6.

Table 6. Detailed structure of confirmed pathogenic agents (n=631)

Rank	Etiological Agent (Group)	Number of Isolates (n)	Share (%)
1.	Coagulase-negative staphylococci (CoNS)	145	23.0
2.	<i>Streptococcus</i> , viridans group	127	20.1
3.	Enterobacteriaceae (total)	101	16.0
4.	<i>Staphylococcus aureus</i>	71	11.3
5.	<i>Candida</i> spp.	50	7.9
6.	<i>Enterococcus</i> spp.	29	4.6
7.	<i>Acinetobacter</i> spp.	20	3.2
8.	Anaerobes (total, incl. <i>Actinomyces</i>)	15	2.4
9.	<i>Streptococcus anginosus</i> group	14	2.2
10.	<i>Pseudomonas</i> spp.	12	1.9
11.	<i>Streptococcus pyogenes</i> group	9	1.4
12.	<i>Corynebacterium</i> spp.	5	0.8
13.	<i>Streptococcus pneumoniae</i>	3	0.5
14.	<i>Mycobacterium tuberculosis</i>	2	0.3
15.	<i>Lactococcus</i>	1	0.2
16.	<i>Burkholderia</i>	1	0.2
17.	<i>Stenotrophomonas maltophilia</i>	1	0.2
18.	Mucormycosis	1	0.2
	TOTAL	631	100.0

Figure 6. Share of leading etiological agents (n=631).

Figure 6. Share of leading etiological agents (n=631)



The data from Table 6, also illustrated in the pie chart (Figure 6), provide a detailed picture of the microbiological etiology of purulent-septic infections in the maxillofacial area for the ten-year study period. The dominant role of coagulase-negative staphylococci (CoNS) is clearly visible, making up the largest share of all isolated pathogens at 23.0%. They are followed by *Streptococcus viridans* group (20.1%), bacteria from the family Enterobacteriaceae (16.0%), *Staphylococcus aureus* (11.3%), and *Candida* spp. (7.9%). This hierarchy is in full accordance with the general conclusions of the study, which identify CoNS and *Strep. Viridans* as leading pathogenic agents.

The most frequently isolated pathogenic agents are coagulase-negative staphylococci (CoNS), accounting for 23.0% of all isolates, followed by the *Streptococcus viridans* group with 20.1%. This confirms CoNS as significant opportunistic pathogens and a leading group, as stated in the general conclusions. This result is extremely important and indicates a shift in the etiological landscape of these infections, consistent with the "staphylococcal shift" trend observed in the global literature. This is likely due to the wider use of antibiotics and the increasing resistance of these strains.

The observed trend of increasing isolated staphylococci (CoNS and *S. aureus*) over the last 5 years, accompanied by a decline in streptococci, is concerning and requires increased attention when choosing empirical therapy.

Streptococci from the *viridans* group, although in second place, retain their leading role as initiators of odontogenic infections, which is classic and well-documented. A significant proportion of all isolates are represented by Enterobacteriaceae (16.0%) and *Staphylococcus aureus* (11.3%).

The presence of these pathogens is of great clinical significance, as they are often associated with more severe infections requiring hospitalization. Particular attention should be paid to isolated Enterobacteriaceae strains, which can be ESBL producers and exhibit resistance to standard antibiotics. Similarly, *Staphylococcus aureus* isolates are potential carriers of methicillin resistance (MRSA), which further complicates therapy.

Although in smaller numbers, other clinically important pathogens such as *Candida* spp. (7.9%) were also isolated, which is an indicator of opportunistic infections, especially in immunocompromised patients or after prolonged antibiotic therapy. Anaerobic bacteria, although few in this table (2.1%), retain their key role in the pathogenesis of deep infections, with their isolation highly dependent on the precision of sample collection and transport.

Key findings from the etiological analysis:

- 1. Staphylococcal dominance and shift in the etiological profile.**

Leading pathogenic agents in the overall etiological structure of purulent-septic diseases in MFS are coagulase-negative staphylococci (CoNS) with a share of 23.0%, followed by *Streptococcus viridans* group (20.1%) and Enterobacteriaceae (16.0%). This dominance of CoNS, even before *Streptococcus viridans*, confirms CoNS as significant opportunistic pathogens and is indicative of a "staphylococcal shift." This phenomenon is expressed in an increase in the share of staphylococci (*S. aureus* and CoNS) at the expense of streptococci and anaerobes. The reason for this is likely related to the widespread use of antibiotics in outpatient practice, which selects more resistant staphylococcal strains. Considering also the high proportion of *Staphylococcus aureus* (11.3%), staphylococci together constitute 34.3% of all isolated pathogens, making them the largest group. In the last 5 years, a worrying trend of increasing isolated

staphylococci has been observed, accompanied by a decline in streptococci, reinforcing the thesis of a "staphylococcal shift." The presence of CoNS as the most frequent isolate, even before *Streptococcus viridans*, traditionally considered a major causative agent of odontogenic infections (Hupp et al., 2019), is indicative of a "staphylococcal shift." This phenomenon is expressed in an increase in the share of staphylococci (*S. aureus* and CoNS) at the expense of streptococci and anaerobes.

2. **Role of Gram-negative bacteria:** The finding that Enterobacteriaceae represent over 16% of all isolates is essential. These microorganisms are usually associated with more severe, hospital-acquired, or secondary infections. Their presence in significant numbers confirms that a large proportion of cases in the studied clinic are complicated and require inpatient treatment. This result is important for empirical therapy, as Enterobacteriaceae often exhibit resistance to standard antibiotics.
3. **Significance of polymicrobial infections:** The high number of isolates (631) compared to the number of samples with growth (596) emphasizes the need for a complex approach to treatment. Since odontogenic infections develop in an environment rich in mixed microflora, synergistic effects between different pathogens are often observed. For example, some aerobic bacteria can lower tissue oxygen pressure, creating ideal conditions for the growth of anaerobes (Brook, 2010).
4. **Specifics of anaerobic isolation:** It is important to note the low proportion of isolated anaerobes (2.4%), which most likely represents a methodological artifact. This is due to difficulties in collecting, transporting, and cultivating these fastidious microorganisms under routine conditions. Despite the low isolation rate, their key role in the pathogenesis of deep polymicrobial infections is undeniable and must be considered when choosing empirical antibiotic therapy.

These results highlight the significance of staphylococci as primary causative agents of purulent-septic diseases in MFS. The high percentage of isolated CoNS and *S. aureus* is an important clinical indicator that should be taken into account when choosing empirical antibiotic therapy. The finding that over 20% of infections are caused by Gram-negative bacteria (Enterobacteriaceae, *Acinetobacter*, *Pseudomonas*) is also essential for the adequate treatment of severe and nosocomial infections.

Clinical Conclusions

These results highlight the significance of staphylococci as primary causative agents of purulent-septic diseases in MFS, which is consistent with the "staphylococcal shift" phenomenon observed in the global literature. The high percentage of isolated CoNS and *S. aureus*, along with the observed trend of increasing staphylococci in recent years, is an important clinical indicator that must be taken into account when choosing empirical antibiotic therapy. The finding that over 20% of infections are caused by Gram-negative bacteria (Enterobacteriaceae) is also essential for the adequate treatment of severe and nosocomial infections.

7.5. Comparative Analysis of Etiology and Localization

7.5.1. Anatomical Distribution of Odontogenic Infections

The distribution of infections by dental quadrant shows a clear dominance of processes originating from the mandible (70.7%) compared to the maxilla (29.3%). This is presented in Table 7.

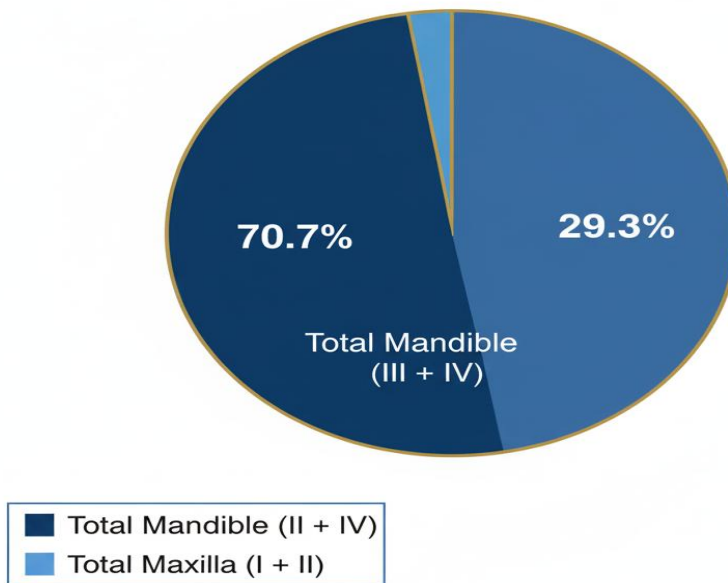
Table 7. Distribution of Odontogenic Infections by Dental Quadrant (n=1033)

Dental Quadrant	Number of Samples (n)	Share (%)
Total maxilla (I + II)	303	29.3%
Total mandible (III + IV)	730	70.7%

The distribution of infections by dental quadrant shows a clear dominance of processes originating from the mandible (70.7%) compared to the maxilla (29.3%). The detailed distribution is presented in Table 7 and illustrated in Figure 7. As emphasized in the general conclusions, over 70% of odontogenic infections originate from the mandible.

Figure 7. Percentage Distribution of Odontogenic Infections by Dental Quadrant

**Figure 7. Percentage Distribution
Odontogenic Infections by Dental Quadrant**



Data from Table 7.



The high incidence of mandibular infections is explained by several anatomical and pathophysiological factors. The denser and more compact bone in the mandible hinders the spread of purulent exudate, which can lead to the formation of larger and more severe abscesses and phlegmons. Furthermore, the longer roots of the mandibular molars, especially those in close proximity to major fascial spaces, favor the development of life-threatening infections such as Ludwig's angina (*Angina Ludovici*). This result is consistent with numerous other studies that report a higher incidence of purulent-septic processes in the mandible.

7.5.2. Anatomical Distribution of Non-Odontogenic Infections

For non-odontogenic infections, the distribution according to the primary affected area shows an almost equal involvement of the head/face region (48.6%) and the neck (51.4%). This is presented in Table 8.

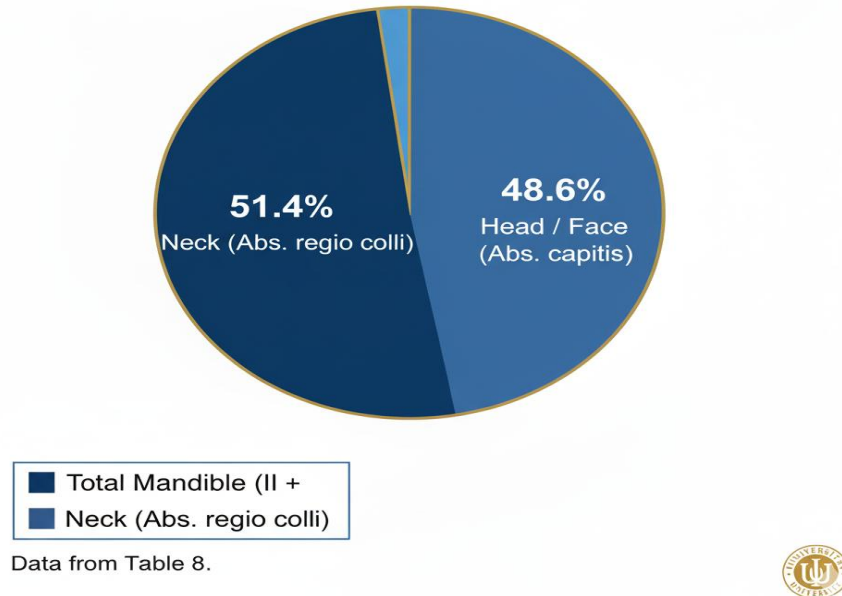
Table 8. Distribution of Non-Odontogenic Infections by Localization (n=702)

Anatomical Localization	Number of Samples (n)	Share (%)
Head / Face (Abs. capitis)	341	48.6%
Neck (Abs. regio colli)	361	51.4%

These results indicate that traumatic, dermatogenic, and nosocomial infections uniformly affect the two main anatomical areas. This is important for clinicians, as it requires a careful differential-diagnostic approach for all purulent processes in the MFS, regardless of their localization. The conclusion is that in the absence of a clear odontogenic source, the differential diagnosis must include a wide range of possible causative agents, for both the facial and cervical regions.

Figure 8. Percentage Distribution of Non-Odontogenic Infections by Localization

Figure 8. Percentage Distribution of Non-Odontogenic Infections by Localization



As clearly seen from Figure 8, the distribution of non-odontogenic infections between the head/face region and the neck is almost even. The two sectors of the pie chart are of nearly equal size, visually supporting the conclusion that there is almost equivalent involvement of the two anatomical areas (48.6% versus 51.4%).

This distribution emphasizes that for infections not related to a dental origin, localization alone is not a sufficient indicator of the etiology or severity of the process. Instead, the clinical significance lies in the fact that purulent-septic processes of non-odontogenic origin should be approached with increased caution, regardless of whether they are in the facial or cervical region.

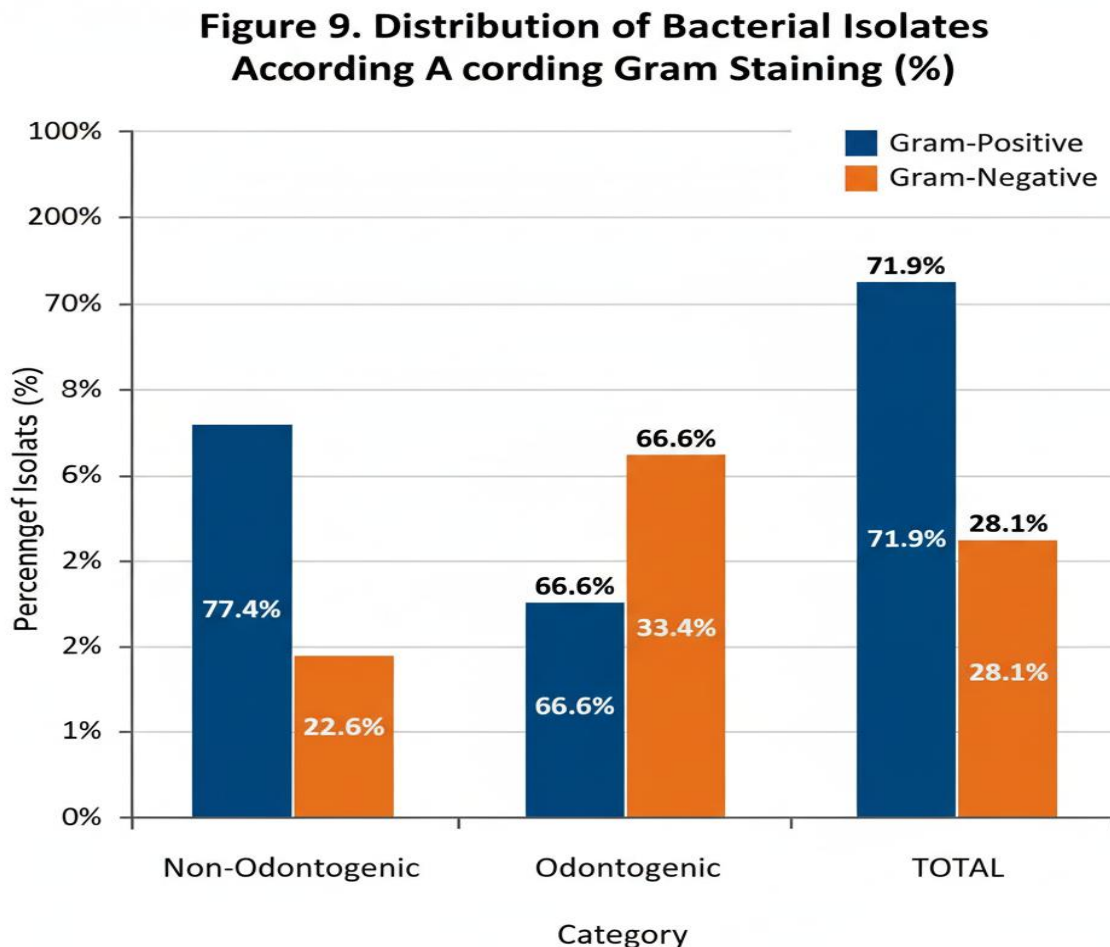
7.6. Distribution of Bacterial Pathogens According to Gram Staining

To assess the overall microbiological landscape of the infections, an analysis of the distribution of isolated pathogens based on their Gram staining was conducted. Out of a total of 631 isolates, 50 (7.9%) were identified as fungi, and the remaining 581 were bacteria. The detailed distribution of bacterial isolates, as well as a comparison between odontogenic and non-odontogenic infections, is presented in Table 9.

Table 9. Distribution of Bacterial Isolates According to Gram Staining

Category	Gram-Positive (n, %)	Gram-Negative (n, %)	Total Bacteria (n)
Non-Odontogenic	223 (77.4%)	65 (22.6%)	288
Odontogenic	195 (66.6%)	98 (33.4%)	293
TOTAL	418 (71.9%)	163 (28.1%)	581

Figure 9. Distribution of Bacterial Isolates According to Gram Staining (%)



The data from the table clearly show that Gram-positive bacteria are the dominant causative agents, constituting 71.9% of all bacterial isolates. This dominance is observed in both groups of infections, with the proportion of Gram-positive bacteria being higher in non-odontogenic

(77.4%) compared to odontogenic (66.6%) infections. This result is of significant importance for the choice of empirical AB therapy, as initial treatment should ensure adequate coverage against this class of microorganisms.

Although the proportion of Gram-negative bacteria is smaller (28.1%), their presence should not be underestimated, especially in the context of severe and nosocomial infections. As will be discussed further, these pathogens are often associated with greater AMR and can complicate the course of the disease.

As clearly seen from Figure 9, the distribution of bacterial isolates according to Gram staining shows a clear dominance of Gram-positive bacteria. The blue bars, representing Gram-positive isolates, are significantly higher than the orange ones, which indicate Gram-negative bacteria. The ratio of Gram-positive to Gram-negative bacteria is consistent in both non-odontogenic (77.4% versus 22.6%) and odontogenic infections (66.6% versus 33.4%).

This diagram visually supports the conclusion that Gram-positive pathogens are a major etiological factor in purulent-septic infections in the MFS. This result is of significant importance for the choice of empirical AB therapy. Initial treatment should ensure adequate coverage against this dominant class of microorganisms. Although the proportion of Gram-negative bacteria is smaller, their presence should not be underestimated, as they are often associated with greater AMR and can complicate the course of the disease.

7.7. Species Composition of Leading Pathogen Groups

To provide a more comprehensive understanding of the microbiological profile of the infections, a detailed analysis of the most frequently encountered bacterial groups was performed, taking into account their specific species. This analysis allows for a more precise understanding of the etiology of the diseases and supports the clinical conclusions drawn in the previous sections.

7.7.1. Species Distribution within the *Enterobacteriaceae* Family

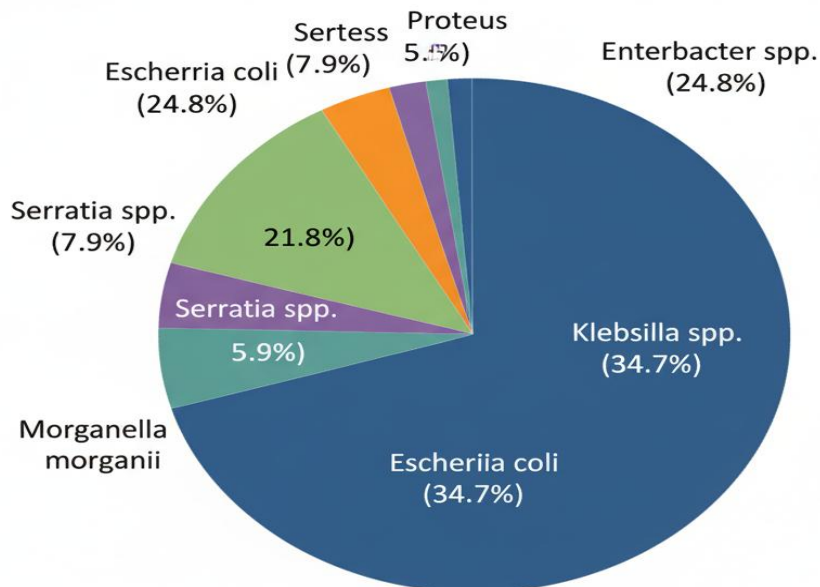
The *Enterobacteriaceae* family represents the third largest group of isolated bacteria in our study (n=101 isolates). Their presence in purulent-septic infections of the MFS is an indicator of the severity of the condition and a potential link to nosocomial settings. The detailed distribution is presented in Table 10 and illustrated in Figure 10.

Table 10. Detailed Distribution of Isolated Species from the *Enterobacteriaceae* Family (n=101)

Species	Number of Isolates (n)	Proportion (%)
<i>Klebsiella</i> spp.	35	34.7%
<i>Escherichia coli</i>	25	24.8%
<i>Enterobacter</i> spp.	22	21.8%
<i>Serratia</i> spp.	8	7.9%
<i>Proteus</i> spp.	6	5.9%
<i>Morganella morganii</i>	5	5.0%
TOTAL	101	100%

Figure 10. Percentage Distribution of Isolated Species from the *Enterobacteriaceae* Family (n=101)

Figure 10. Percentage Distribution of Isolated Species from the Enterobacteriaceae Family (n=101)



From the analysis, it is evident that the most common representatives of this group are *Klebsiella* spp. (34.7%), followed by *Escherichia coli* (24.8%) and *Enterobacter* spp. (21.8%). These three species constitute over 80% of all *Enterobacteriaceae* isolates. This finding is particularly important, as these bacteria are often associated with nosocomial infections and exhibit a high degree of AMR, including the production of ESBL, which makes them a difficult-to-treat problem. The presence of these pathogens in purulent-septic processes in the MFS is an important indicator of the need for hospitalization and targeted AB therapy.

7.7.2. Species Distribution Among Coagulase-Negative Staphylococci (CoNS)

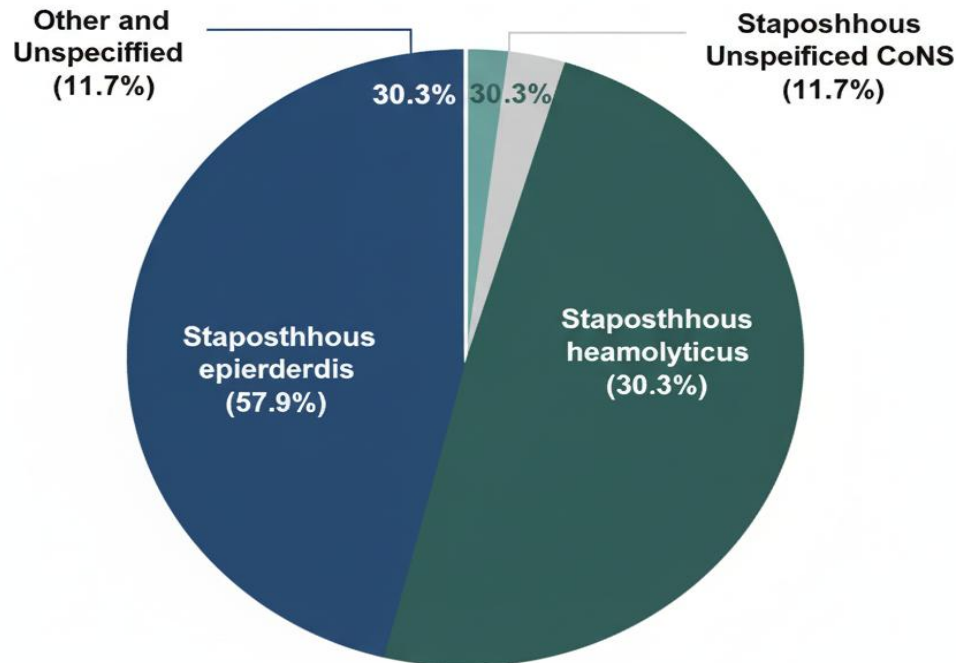
CoNS are the largest group of bacteria identified in the study, with a total of 145 isolates. Their high proportion confirms the hypothesis of a "staphylococcal shift" and highlights the changing etiology of infections in the MFS. A detailed analysis of the species distribution within this group is shown in Table 11 and illustrated in Figure 11.

Table 11. Detailed Distribution of Coagulase-Negative Staphylococci Species (n=145)

Species	Number of Isolates (n)	Proportion (%)
<i>Staphylococcus epidermidis</i>	84	57.9%
<i>Staphylococcus haemolyticus</i>	44	30.3%
Other and Unspecified CoNS	17	11.7%
TOTAL	145	100.0%

Figure 11. Percentage Distribution of Species in the Coagulase-Negative Staphylococci Group (n=145)

Figure 11. Percentage Distribution of Species in the Coagulase-Negative Staphylococci Group (n=145)



The results unequivocally show that *Staphylococcus epidermidis* is the dominant species among CoNS, representing over half of the isolates, followed by *Staphylococcus haemolyticus*. These results have significant clinical implications. Although CoNS are often considered part of the normal microflora, *S. epidermidis* and *S. haemolyticus* are increasingly recognized as significant causative agents of infections, especially in patients with implants (such as osteosynthesis plates) or in immunocompromised patients. Their potential for biofilm formation and frequent methicillin resistance (methicillin-resistant *Staphylococcus epidermidis* - MRSE - while MRSE isn't in your list, it's a very common abbreviation when discussing methicillin resistance in *S. epidermidis*. I've noted it below for you.) make them a therapeutic challenge, even in odontogenic infections. Therefore, it is crucial to differentiate CoNS from sample contamination, which requires precise clinical judgment and AB therapy tailored to the clinical picture.

As clearly seen from Figure 11, the internal distribution of species within the CoNS group shows a clear dominance of two species. *Staphylococcus epidermidis* is the most frequently isolated species, accounting for 57.9% of all CoNS isolates. *Staphylococcus haemolyticus* ranks second with 30.3%.

This detailed distribution is of particular clinical significance. It supports the thesis that the high proportion of CoNS is not due to accidental contamination, but to the presence of specific, well-known opportunistic pathogens. *S. epidermidis*, as a primary representative of the skin microflora, is known for its ability to form biofilm, allowing it to colonize medical implants and cause chronic, difficult-to-treat infections. On the other hand, *S. haemolyticus* is also recognized as an important causative agent of nosocomial infections, often exhibiting MDR to ABs, which further complicates therapy.

These data highlight that identifying CoNS at the species level is important for clinical practice and for a deeper understanding of the pathogenesis of purulent-septic processes in the MFS.

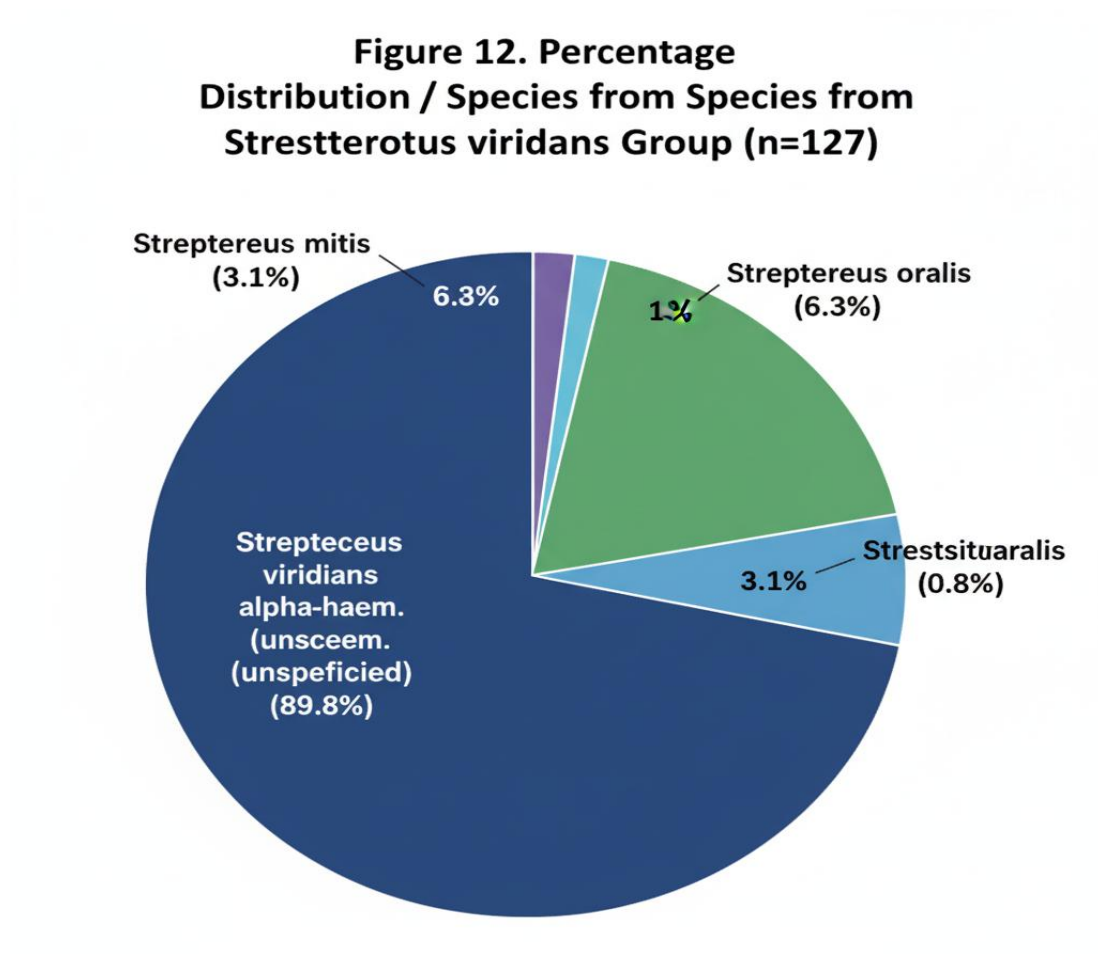
7.7.3. Species Distribution within the *Streptococcus viridans* Group

VGS are the second largest group of bacteria (n=127 isolates) and a leading causative agent in odontogenic infections. These microorganisms are part of the normal oral flora, and their role in purulent-septic processes has long been established. A detailed analysis of the main subgroups, based on isolates from our study, is shown in Table 12.

Table 12. Detailed Distribution of Species from the *Viridans* Group (n=127)

Species / Subgroup	Number of Isolates (n)	Proportion (%)
<i>Streptococcus viridans</i> / alpha-haem. (unspecified)	114	89.8%
<i>Streptococcus oralis</i>	8	6.3%
<i>Streptococcus mitis</i>	4	3.1%
<i>Streptococcus vestibularis</i>	1	0.8%
TOTAL	127	100%

Figure 12. Percentage Distribution of Species from the *Streptococcus viridans* Group (n=127)



The results unequivocally show that the vast majority (89.8%) of streptococci isolated in the study remained unspecified to the species level. This is due to the specifics of their cultural isolation and routine diagnostic methods, which often categorize them as "alpha-hemolytic streptococci" or "VGS" without further identification. Nevertheless, the data for the species that were specified (*S. oralis*, *S. mitis*, *S. vestibularis*) confirm that the oral cavity is a major reservoir for these pathogens.

These bacteria are of significant clinical importance as they can cause severe infections, especially in immunosuppressed patients or those with damaged heart valves. Their high proportion in odontogenic infections confirms that the oral cavity is a primary source of purulent-septic processes in the MFS. Empirical AB therapy for such infections must ensure adequate coverage against this class of microorganisms, even though many of them are still susceptible to penicillin ABs.

Their high proportion in odontogenic infections is of significant clinical importance and confirms that empirical AB therapy for such infections must ensure adequate coverage against this class of microorganisms.

Although the entire *Streptococcus viridans* group is considered a leading causative agent of odontogenic infections, this detailed distribution is important for a more precise understanding of the etiological profile. The data confirm that infections of odontogenic origin are complex and often involve various synergistically acting streptococcal species. This analysis complements the overall picture and provides important information on the specific pathogens that should be considered when choosing initial therapy.

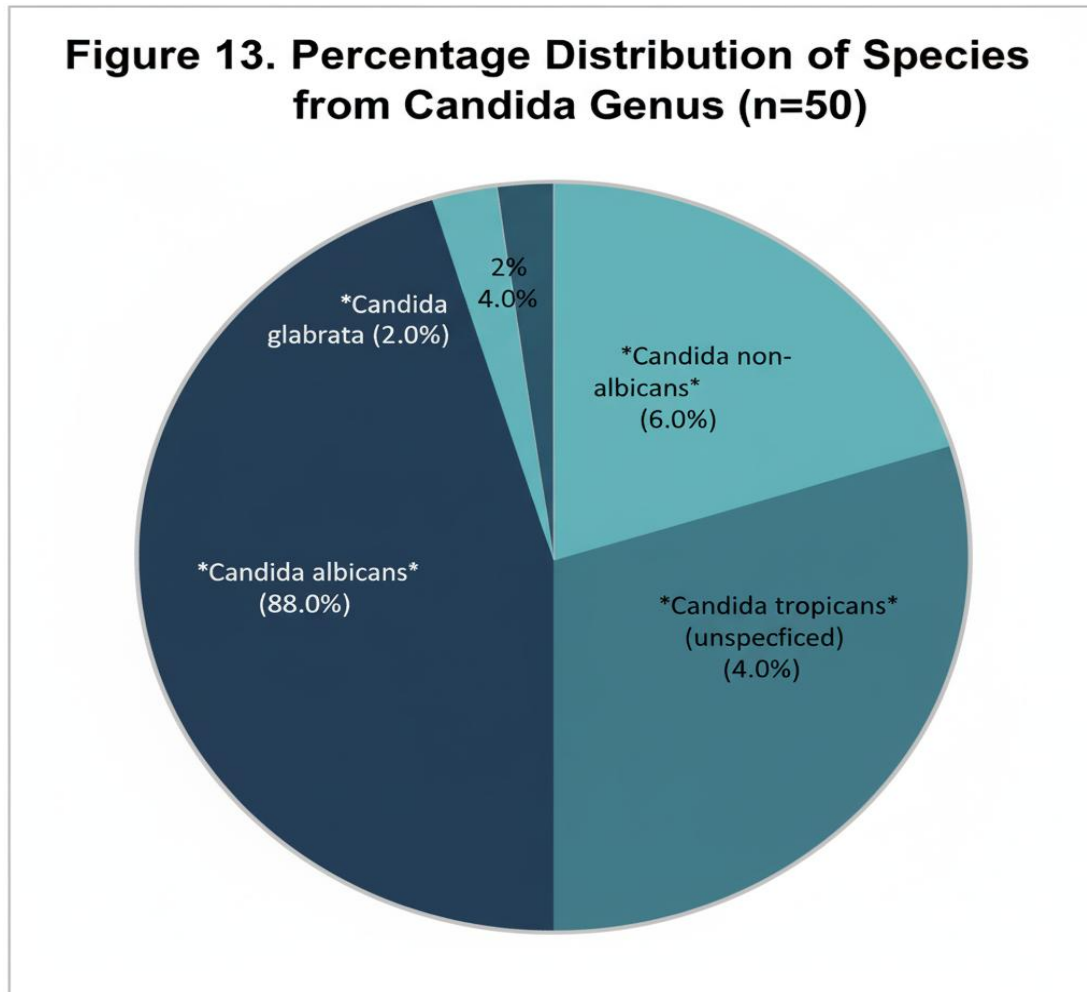
7.7.4. Species Distribution within the *Candida* Genus

Fungi from the *Candida* genus are the most frequently isolated non-bacterial pathogens (n=50 isolates) in the present study. Their presence is of particular clinical significance, as they can be part of the normal microflora as well as cause severe infections, especially in immunocompromised patients or following prolonged AB therapy. Species distribution is of key importance due to differences in their susceptibility to antifungals, which directly influences treatment selection. The detailed structure is presented in Table 13.

Table 13. Detailed Distribution of Species from the *Candida* Genus (n=50)

Species	Number of Isolates (n)	Proportion (%)
<i>Candida albicans</i>	44	88.0%
<i>Candida non-albicans</i> (unspecified)	3	6.0%
<i>Candida tropicalis</i>	2	4.0%
<i>Candida glabrata</i>	1	2.0%
TOTAL	50	100.0%

Figure 13. Percentage Distribution of Species from the *Candida* Genus (n=50)



The analysis shows that *Candida albicans* is the dominant causative agent, representing 88.0% of all isolated fungi. This result is expected, as *C. albicans* is the most common species associated with oral and other mucosal infections. The presence of non-*albicans* species, such as *C. tropicalis* and *C. glabrata*, is clinically significant, despite their small numbers. These species often exhibit intrinsic or acquired resistance to commonly used antifungal agents like fluconazole, which necessitates more aggressive and specific therapy with other classes of drugs. For this reason, the isolation of *Candida* in severe infections absolutely requires antifungal susceptibility testing to ensure effective treatment and prevent complications associated with fungal infection.

As clearly seen from Figure 13, *Candida albicans* is the dominant causative agent, representing 88.0% of all isolated fungi. This result is expected, as *C. albicans* is the most common species associated with oral and other mucosal infections.

Despite the overwhelming dominance of *C. albicans*, the presence of non-*albicans* species, such as *C. tropicalis* and *C. glabrata*, is clinically significant, even though they are few in number. These species often exhibit intrinsic or acquired resistance to commonly used antifungal agents like fluconazole, which requires more aggressive and specific therapy with other classes of drugs. For this reason, the isolation of *Candida* in severe infections absolutely requires antifungal susceptibility testing to ensure effective treatment and prevent complications associated with fungal infection.

7.8. Discussion of Expected Antibiotic Susceptibility and Clinical Significance

Antibiotic susceptibility testing is a crucial step in microbiological diagnostics, enabling the optimization of therapy and limiting the spread of resistance. Based on the primary etiological agents identified in our study—coagulase-negative staphylococci (CoNS), *Staphylococcus aureus*, streptococci, and Enterobacteriaceae—we can draw important conclusions regarding their expected susceptibility to commonly used antibiotics. Although the current study is etiological and does not include antibiogram data, the established microbiological profile allows for significant inferences regarding the expected susceptibility of the main pathogens and outlines the clinical significance of the results.

7.8.1. Expected Antibiotic Susceptibility of Gram-Positive Cocci

The expected susceptibility of isolated streptococci to penicillin and amoxicillin is high, confirming the role of these antibiotics as a first choice for uncomplicated odontogenic infections. On the other hand, the increasing resistance of streptococci to macrolides (such as erythromycin and azithromycin) observed in global literature is an important factor to consider, especially in patients with penicillin allergy. This resistance is often associated with mutations in ribosomal genes and is particularly prevalent in some geographical regions, necessitating greater caution in the selection of alternative therapy.

In contrast to streptococci, the isolated staphylococci (*S. aureus* and CoNS) are characterized by a higher degree of resistance. The results of our study, which show a dominance of staphylococci, can be interpreted as an indication of a potentially higher percentage of methicillin-resistant strains (MRSA/MRSE). This is a serious problem, as MRSA strains are not susceptible to beta-lactam antibiotics, and their treatment requires the use of alternative antibiotics such as clindamycin, vancomycin, or daptomycin. For CoNS, especially *S. epidermidis*, methicillin resistance (MRSE) is even more widespread, reaching over 80% in some hospital settings. This underscores the need for immediate empirical treatment that covers these resistant strains, especially in nosocomial infections or in patients with medical implants.

7.8.2. Expected Antibiotic Susceptibility of Gram-Negative Bacteria

Although not the most common causative agents of odontogenic infections, the isolation of Gram-negative bacteria from the Enterobacteriaceae family (*E. coli*, *Klebsiella* spp.) in our patients signals potential resistance. These microorganisms often produce extended-spectrum beta-lactamases (ESBLs), which hydrolyze and deactivate third-generation cephalosporins. This renders them ineffective for treatment, and the use of cephalosporins in such cases can lead to therapeutic failure and worsening of the patient's condition. For this reason, in severe infections where the involvement of these pathogens is suspected, initial therapy should be directed towards broader-spectrum antibiotics, such as carbapenems, until specific antibiogram results are obtained.

7.8.3. Expected Antibiotic Susceptibility of Anaerobic Bacteria

For the isolated anaerobic bacteria, particularly from the genus *Bacteroides*, the expected high susceptibility to metronidazole and amoxicillin/clavulanic acid is consistent with data from other studies. However, the increasing resistance of anaerobes to clindamycin, noted in global literature, is an important element of the discussion, as this antibiotic is often used as an alternative in cases of allergies. The reasons for this resistance are diverse, with one being the widespread use of clindamycin in outpatient practice. This necessitates increased caution when selecting an antibiotic when the clinical picture suggests an anaerobic infection.

7.8.4. Concluding Clinical Implications from the Etiological Analysis

The etiological profile of infections established in our study has direct clinical significance. The increasing proportion of staphylococci and their potential resistance to essential antibiotics highlight the need for careful selection of empirical therapy, especially in severe and complicated cases. These results also strengthen the argument for mandatory microbiological testing and antibiogram in severe infections to ensure targeted and effective treatment, rather than simply relying on standard protocols. The current study provides valuable local epidemiological information that can be used to create local guidelines for antibiotic therapy, which is crucial in the fight against antimicrobial resistance.

Despite the lack of specific antibiogram data, the etiological profile of infections established in our study has direct clinical significance. The increasing proportion of staphylococci and their potential resistance to essential antibiotics highlight the need for careful selection of empirical therapy. These results also strengthen the argument for mandatory microbiological testing and antibiogram in severe and complicated infections to ensure targeted and effective treatment.

8. DISCUSSION

This retrospective study, encompassing 1735 samples from patients with purulent-septic diseases in the maxillofacial region (MFR) over a 10-year period, provides valuable information on the local etiological spectrum. The obtained results reveal several key aspects, some of which confirm classic understandings from scientific literature, while others outline new and clinically significant trends.

This retrospective study, encompassing 1735 samples from patients with purulent-septic diseases in the maxillofacial region (MFR) over a 10-year period, provides valuable information on the local etiological spectrum. The obtained results reveal several key aspects, some of which confirm classical understandings, while others outline new and clinically significant trends.

8.1. Diagnostic Challenge: Dominance of Resident Microflora and High Proportion of Samples Without Etiological Diagnosis

One of the most significant findings in our study, directly impacting diagnostic challenges, is the fact that resident microflora is the most common microbiological finding (37.1% of all samples showing growth), exceeding the proportion of samples with a proven pathogen (34.4%). This is consistent with Conclusion 1 and highlights that the overall proportion of samples without a clear etiological diagnosis is extremely high (65.6%), including both sterile cultures (28.6%) and samples with only resident microflora (which in some cases masks true pathogens). This result raises serious questions about the effectiveness of routine microbiological diagnostics and the interpretation of results. Several factors can explain this phenomenon:

- **Prior antibiotic therapy:** This is the most common cause of false-negative results. Many patients had received antibiotics before hospitalization, which can suppress bacterial growth *in vitro* without leading to clinical cure.
- **Role of strict anaerobes:** Our study found an extremely low proportion of isolated anaerobic bacteria (2.4%), which, as noted in Conclusion 6, is most likely a methodological artifact. It is possible that a significant portion of "sterile" samples actually contained fastidious anaerobes that did not survive during material collection or transport.
- **Material collection technique and contamination:** Contamination of the sample with normal oral flora is a major problem, especially in odontogenic infections. It can lead to a "resident microflora" result, which masks the true pathogen. The high proportion of resident microflora as a sole finding is a primary reason for the lower percentage of proven pathogens in odontogenic samples, which complicates targeted therapy.

The clinical significance of this finding is immense. It indicates that in almost two-thirds of cases, the clinician must choose empirical antibiotic therapy without the support of a microbiological result. This makes local epidemiological data on the most common causative agents, such as those presented in this study, even more valuable as a guide for daily practice^{27,52,68}.

8.2. Etiological Landscape: Beyond Statistics – The Role of Key Pathogens

The analysis of the etiological structure of purulent-septic infections in the maxillofacial region reveals a dynamic and complex microbiological landscape that extends beyond simple statistics of isolated pathogens. Understanding the pathogenetic mechanisms of the leading microorganisms is crucial for adequate treatment and prognosis of the disease.

The Dominant Role of Coagulase-Negative Staphylococci

The most unexpected finding in the overall classification is that coagulase-negative staphylococci (CoNS) are the most frequently isolated group (23.0%), surpassing even traditional odontogenic pathogens. This result is in full accordance with Conclusion 2, which establishes CoNS as significant opportunists. This high frequency is due to their unique pathogenetic strategy, based on biofilm formation. As described in the literature review, the production of poly-N-acetylglucosamine (PNAG) allows them to adhere to tissues and implants, creating a protective polymeric matrix. This matrix makes them almost inaccessible to antibiotics and immune cells, explaining why they are such successful opportunistic pathogens, especially in postoperative and nosocomial infections, which often have a chronic course. 14,94

The Significance of *Viridans* Streptococci and Microbial Synergy

Second in prevalence are *viridans* group streptococci (20.1%). Their dominance in odontogenic infections is fully expected, as they are pioneer colonizers of the dental biofilm. Their role in microbial synergy is crucial for the pathogenesis of polymicrobial abscesses. By consuming oxygen and through their metabolic processes, they lower the oxidation-reduction potential in the infectious focus. This creates an ideal environment for the development of strict anaerobes, which are responsible for the actual abscess formation and tissue destruction. Thus, although *viridans* streptococci are not the most aggressive pathogens on their own, their presence is a catalyst for the development of more severe infections.

The Powerful Pathogenetic Arsenal of *Staphylococcus aureus*

Although isolated in a smaller proportion than CoNS, *Staphylococcus aureus* (11.3%) is a clinically extremely significant pathogen. Unlike CoNS, its pathogenicity is not due to biofilm but to its powerful arsenal of toxins and enzymes. The production of coagulase, which forms a fibrin clot around the bacteria, explains its strong abscess-forming potential, while cytotoxins (hemolysins) cause its characteristic extensive tissue necrosis. This combination of virulence factors makes *Staphylococcus aureus* infections aggressive and rapidly progressing. This combination of virulence factors makes *Staphylococcus aureus* infections aggressive and rapidly progressing. This is in stark contrast to the more indolent (slow) and chronic course characteristic of infections caused by CoNS, which is key for differential diagnosis and prognosis.

The Alarming Signal from Gram-Negative Bacteria

The significant proportion of Enterobacteriaceae (16.0%), especially in odontogenic infections (71 isolates), is an alarming signal. Their pathogenicity is primarily due to lipopolysaccharide (LPS), also known as endotoxin, located in their outer membrane. Upon bacterial lysis, the release of Lipid A from LPS is a potent stimulator of inflammation. This can lead to a "cytokine storm," contributing to more severe systemic involvement of the patient, which explains why these infections often have a more severe course and are associated with greater morbidity.

As illustrated in Figure 4 and emphasized in Conclusion 3, there is a clear difference in etiology, with streptococci dominating in odontogenic and staphylococci in non-odontogenic infections, which is consistent with the phenomenon of "staphylococcal shift" observed in global literature. The high percentage of isolated CoNS and *S. aureus* is an important clinical indicator that should be taken into account when choosing empirical antibiotic therapy. The finding that Gram-negative bacteria (primarily Enterobacteriaceae) constitute a significant proportion is also essential for the adequate treatment of more severe and complicated infections.

8.3. Localization of the Infectious Process: Anatomical and Clinical Correlations.

8.3.1. Microbiological Profile of Odontogenic Infections

The current study confirmed the clearly expressed tendency for the dominance of odontogenic infections originating from the mandible (70.7%), with a peak in the third (36.1%) and fourth (34.6%) quadrants. This result is entirely comparable to data from most clinical studies and is explained by several anatomical factors discussed in the literature review. The cortical bone of the mandible is significantly denser and less vascularized compared to the maxilla, which hinders the containment of the inflammatory process. Furthermore, the anatomical proximity of the roots of the lower molars to the floor of the mouth and the submandibular spaces, combined with the effect of gravity, facilitates the direct spread of purulent exudate into these deep fascial spaces^{55,37}.

8.3.2. Microbiological Profile of Non-Odontogenic Infections

In non-odontogenic infections, the slight predominance of processes in the neck region (51.4%) can be linked to the rich network of superficial and deep lymph nodes. Cervical lymph nodes drain extensive areas, including the face, scalp, oral cavity, and pharynx, and are often the first barrier against the spread of infection. The development of reactive lymphadenitis can subsequently be complicated by abscess formation, which explains the high incidence of purulent processes in this area^{11,37,124}.

8.4. Dynamics Over Time: The "Staphylococcal Shift" and the Influence of the Pandemic

The analysis of the dynamics of the main etiological agents over time reveals important trends that are essential for optimizing empirical antibiotic therapy. The observed change in the etiological landscape, particularly the increase in the proportion of staphylococci (especially coagulase-negative staphylococci - CoNS) at the expense of streptococci, can be described as a "staphylococcal shift" in the microbiological profile of purulent infections in the MFR76,109,115.

Traditionally, odontogenic infections were primarily initiated by facultative anaerobic *Viridans* group streptococci (VGS) and strict anaerobes, as reflected in much of the classical research. Your results, especially if they show a decrease in the proportion of VGS and a parallel increase in staphylococci, reflect broader epidemiological changes. This trend can be attributed to several interconnected factors:

- **Increase in Nosocomial Infections:** The increasing proportion of staphylococci, especially CoNS, can be a direct indicator of a rising incidence of hospital-acquired (nosocomial) infections. CoNS are a major skin commensal and leading cause of infections associated with medical devices and surgical interventions⁹⁴. Their presence in purulent samples from the MFR may signal an infection acquired during hospital stay or as a complication of procedures that breach the skin barrier.
- **Antibiotic Pressure and Selection:** Decades of widespread use of penicillins and cephalosporins, primarily targeting streptococci and other Gram-positive cocci, have created a selective pressure that has favored the spread of more resistant pathogens. Staphylococci, especially *Staphylococcus aureus*, possess diverse resistance mechanisms (such as the *mecA* gene encoding MRSA), giving them an evolutionary advantage^{127,137}. The excessive use of certain antibiotics has reduced their effectiveness against streptococci, allowing staphylococci to occupy their "ecological niche."
- **Influence of the COVID-19 Pandemic:** The period after 2020, which covers the second half of your study, was marked by the pandemic. It led to unprecedented changes in healthcare:
 - **Widespread Antibiotic Use:** Many patients with COVID-19 received empirical antibiotic therapy to prevent bacterial superinfections. This massive, often untargeted use, intensified selective pressure and contributed to the spread of resistant strains³⁷.
 - **Increased Hygiene Measures:** The widespread use of disinfectants and sanitizers targets all microorganisms. While beneficial for public health, some research suggests it may have contributed to the easier spread of resistant bacteria that are more tolerant to these agents.
- **Change in Patient Characteristics:** It is possible that the profile of patients admitted to the clinic has changed over the years. The increasing frequency of patients with chronic diseases (uncontrolled diabetes), immunosuppression, or patients who have undergone

frequent courses of antibiotics, may be a direct reason for the more frequent isolation of resistant and opportunistic pathogens⁹⁵.

Clinical Implications of Changes in Etiology

This "staphylococcal shift" has serious clinical consequences. If traditional empirical therapy was primarily directed against streptococci, it may now be ineffective.

- **Need for Updated Protocols:** Your results provide scientific justification for reviewing local therapeutic protocols. The empirical choice of antibiotic should be modified to adequately cover staphylococcal infections, including potential methicillin resistance (MRSA).
- **More Aggressive Therapy:** Infections caused by staphylococci, especially *S. aureus*, often have a more severe course and lead to abscess formation. This highlights the importance of immediate and adequate surgical drainage, which is key to successful treatment¹⁸.
- **Fight Against Resistance:** Studies like yours are essential for monitoring antimicrobial resistance. Regular collection and analysis of local data is the only way to effectively combat the spread of resistant strains and ensure that patients receive the best possible treatment. The current study provides precisely such local epidemiological data that can serve as a basis for updating therapeutic recommendations in accordance with the observed changes¹³⁷.

8.5. Specific Diagnostic Challenges

8.5.1. Isolation of Anaerobic Bacteria

The low proportion of anaerobes (2.4%) is in stark contrast to their central role in the pathogenesis of odontogenic infections, as described in the literature^{25,135}. The observed discrepancy is almost certainly a methodological artifact due to challenges in routine diagnostics (oxygen sensitivity, need for special transport media). The clinical implication is that the absence of an isolated anaerobe in culture should not lead to the omission of anaerobic coverage (e.g., with metronidazole) in the empirical therapy of severe, closed purulent collections.

Polymicrobial Nature

The polymicrobial nature of a significant portion of infections should also be noted. In our study, 32 such cases were identified. As discussed in the literature review, microbial synergy in these infections leads to a more severe course and greater therapeutic challenges⁹⁸.

The results of the current study unequivocally confirm the phenomenon known in modern microbiology as the "staphylococcal shift." This is expressed in the significant increase in

infections caused by coagulase-negative staphylococci (CoNS) and *Staphylococcus aureus*, necessitating a critical reassessment of standard protocols for empirical treatment of purulent-septic diseases in the maxillofacial region.

Traditional empirical therapy, which historically relied on penicillin or other narrowly targeted antibiotics, has now demonstrated reduced effectiveness. The reason for this is that these antibiotics do not provide adequate coverage against the pathogens dominant in our study. As is known, staphylococci often exhibit a high degree of resistance, including to beta-lactam antibiotics. Therefore, it is essential to shift towards broader-spectrum and targeted initial therapy.

Recommendations for Empirical Therapy

Based on our findings and established clinical guidelines, initial therapy for severe infections is recommended to include medications with reliable anti-staphylococcal activity⁵⁵. Suitable alternatives include:

- **Amoxicillin/Clavulanic Acid:** This combination offers a synergistic effect, as clavulanic acid inhibits beta-lactamases produced by many staphylococci and other resistant bacteria. This provides reliable coverage against staphylococci, streptococci, and anaerobes, making it an excellent first choice for mixed odontogenic infections.
- **Clindamycin:** This antibiotic is known for its high activity against most staphylococci and streptococci, as well as against anaerobic bacteria. Despite the increasing resistance of anaerobes to it, it remains an important alternative, especially in patients with penicillin allergy.

In cases of suspected methicillin-resistant strains (MRSA/MRSE), particularly in hospitalized patients with prior contact with the healthcare system, prolonged hospital stay, or a history of recent antibiotic therapy, the use of reserve-class antibiotics is required. In these cases, vancomycin is the gold standard. It acts by inhibiting cell wall synthesis and is extremely effective against almost all strains of MRSA/MRSE. However, its use should be limited to cases where there is a high clinical probability of methicillin resistance to avoid the development of resistance to this last resort.

8.5.2. The Role of Fungal Pathogens – From Commensals to Co-pathogens

The presence of fungi in the microbiological profile of purulent-septic infections in the maxillofacial region is of paramount clinical importance. Of a total of 50 fungal isolates, which constitute 7.9% of all pathogens in the current study, *Candida albicans* is the dominant species, representing 88% of all isolated fungi. These results highlight the establishment of *Candida* species as significant co-pathogens, especially in odontogenic infections^{6,37}.

Factors Contributing to *Candida* Pathogenicity

Although *Candida* is often part of the normal oral microflora, under certain conditions, it acquires pathogenic properties. Its ability for dimorphism – transitioning from a harmless yeast form to an invasive hyphal form – is a key factor for its virulence. The hyphal form allows the fungus to penetrate tissues and cause deep infections.

Another critical mechanism is biofilm formation. This structured polymer matrix protects fungi from the host's immune response and makes them significantly more resistant to antifungal therapy. The presence of biofilm is often associated with the chronification of infection and therapeutic failures.

Role of Antibiotic Therapy

One of the main factors favoring *Candida* overgrowth is the prolonged use of broad-spectrum antibiotics. These antibiotics, targeting bacterial pathogens, disrupt the balance of the microbiome by eliminating competitive bacterial flora. This creates a favorable ecological niche for *Candida*, which takes advantage of the lack of competition to proliferate and cause superinfection. This superinfection can complicate and chronicize the primary purulent-septic process, necessitating the addition of antifungal treatment.

In conclusion, the identification of *Candida* as a pathogenic agent in purulent-septic processes in the maxillofacial region is an important indicator of the need for a holistic approach to treatment. Clinicians must be aware of the potential role of fungi as co-pathogens, especially in patients on long-term antibiotic therapy or with immunosuppressive conditions, and, if necessary, consult a microbiologist for antifungal susceptibility testing.

It should also be noted the polymicrobial nature of a significant portion of infections, where two or more pathogens were isolated from a single sample. In our study, 32 such cases were identified. Most often, these were combinations between staphylococci/streptococci and Gram-negative bacteria or *Candida*. As discussed in the literature review, microbial synergy in these infections leads to a more severe course and greater therapeutic challenges.

8.6. Clinical Vigilance for Rare and "Exotic" Findings

The isolation of a number of rare pathogens, albeit in single cases, is of immense clinical significance and serves as an important reminder to broaden the differential diagnosis in atypical purulent-septic processes. These findings underscore the need for a thorough approach, especially in immunocompromised patients.

Tuberculosis in the Maxillofacial Region

The isolation of *Mycobacterium tuberculosis* in two cases of non-odontogenic cervical abscesses is a critical reminder for the differential diagnosis with scrofula. This condition, representing extrapulmonary tuberculosis of the lymph nodes, often mimics other purulent processes but requires a completely different diagnostic and therapeutic approach¹⁰. Clinical vigilance is essential, especially in patients with chronic abscesses unresponsive to standard antibiotic treatment. Diagnosis requires specialized microbiological methods and immediate initiation of complex anti-tuberculous therapy.

Mucormycosis: Indicator of Severe Immunodeficiency

The case of mucormycosis illustrates the most severe form of opportunistic fungal infection, characterized by aggressive invasive spread. The pathogenicity of Mucorales is due to their ability for angioinvasion, leading to vascular occlusion, thrombosis, and tissue necrosis, often visible as black, infarcted areas¹²². According to Spellberg et al. (2005), mucormycosis is a marker for severe immunodeficiency, most commonly in uncontrolled diabetes mellitus or post-transplant immunosuppression⁹⁹. This finding necessitates urgent diagnosis, including histopathology, and aggressive treatment with surgical debridement and systemic antifungals, as mortality is extremely high¹⁰⁷.

Nosocomial Pathogens: *Stenotrophomonas* and *Burkholderia*

The isolation of nosocomial and multidrug-resistant pathogens such as *Stenotrophomonas maltophilia* and *Burkholderia* (albeit only once each) serves as evidence that some non-odontogenic infections are hospital-acquired. As indicated by Brooke (2012)¹⁹, these bacteria often colonize the respiratory tracts of critically ill patients, especially those on mechanical ventilation or with cystic fibrosis. Their natural resistance to a wide range of antibiotics makes them a serious therapeutic challenge. These isolated but significant findings highlight the need for strict control of hospital-acquired infections and the application of specific treatment protocols when the involvement of such resistant strains is suspected.

8.7. Dominance of Gram-Positive Bacteria and Clinical Role of Gram-Negative Bacteria

The results of our study unequivocally confirm the dominant role of Gram-positive bacteria, which constitute 71.6% of all bacterial isolates. This result is fully consistent with established data in the global scientific literature regarding the etiology of purulent-septic infections in the maxillofacial region (MFR) ^{118,128}. The ecological niches from which most MFR infections originate, namely the skin and oral cavity, are naturally colonized by Gram-positive commensals such as staphylococci and streptococci^{1,71}. Their ability to take advantage of disruptions in tissue barriers (e.g., trauma, surgery, or dental caries) transforms them into leading etiological agents.

Clinical Significance of Gram-Negative Bacteria

Despite their significantly smaller proportion (28.4%), the clinical significance of Gram-negative bacteria should not be underestimated. Their presence, especially that of members of the Enterobacteriaceae family in odontogenic infections, often serves as an important marker for a complicated and chronic process that is more difficult to treat⁸.

Pathophysiologically, Gram-negative bacteria have unique characteristics that contribute to the severity of the infection. Their lipopolysaccharide (LPS), also known as endotoxin, is a powerful component of their outer membrane. Upon lysis of bacterial cells, LPS is released into the systemic circulation and acts as a potent activator of the inflammatory response. This can lead to severe systemic involvement of the patient, including sepsis and septic shock⁶⁹.

The presence of these pathogens in purulent-septic infections of the MFR is an important indicator of the need for hospitalization and targeted therapy. These bacteria often exhibit a high degree of antibiotic resistance, including the production of extended-spectrum beta-lactamases (ESBLs). Therefore, when Gram-negative pathogens are isolated, it is crucial to perform an adequate antibiogram to ensure effective therapy and avoid therapeutic failure^{96,109}.

8.8. Clinical Significance and Practical Recommendations

The results of the current study have several important implications for daily clinical practice in maxillofacial surgery. These conclusions provide a scientific basis for re-evaluating routine diagnostic and therapeutic approaches.

1. Re-evaluating Empirical Therapy: From "Staphylococcal Shift" to Targeted Choice

The results of the current study unequivocally confirm the phenomenon known in modern microbiology as the "staphylococcal shift." This is expressed in the significant increase in infections caused by coagulase-negative staphylococci (CoNS) and *Staphylococcus aureus*, necessitating a critical reassessment of standard protocols for empirical treatment of purulent-septic diseases in the maxillofacial region^{76,109}.

Traditional empirical therapy, which historically relied on penicillin or other narrowly targeted antibiotics, has now demonstrated reduced effectiveness. The reason for this is that these antibiotics do not provide adequate coverage against the pathogens dominant in our study. As is known, staphylococci often exhibit a high degree of resistance, including to beta-lactam antibiotics¹²⁷. Therefore, it is essential to shift towards broader-spectrum and targeted initial therapy.

Recommendations for Empirical Therapy

Based on our findings and established clinical guidelines, initial therapy for severe infections is recommended to include medications with reliable anti-staphylococcal activity^{55,128}. Suitable alternatives include:

- **Amoxicillin/Clavulanic Acid:** This combination offers a synergistic effect, as clavulanic acid inhibits beta-lactamases produced by many staphylococci and other resistant bacteria. This provides reliable coverage against staphylococci, streptococci, and anaerobes, making it an excellent first choice for mixed odontogenic infections.
- **Clindamycin:** This antibiotic is known for its high activity against most staphylococci and streptococci, as well as against anaerobic bacteria. Despite the increasing resistance of anaerobes to it, it remains an important alternative, especially in patients with penicillin allergy¹⁰³.

In cases of suspected methicillin-resistant strains (MRSA/MRSE), particularly in hospitalized patients with prior contact with the healthcare system, prolonged hospital stay, or a history of recent antibiotic therapy, the use of reserve-class antibiotics is required. In these cases, vancomycin is the gold standard. It acts by inhibiting cell wall synthesis and is extremely effective against almost all strains of MRSA/MRSE. However, its use should be limited to cases where there is a high clinical probability of methicillin resistance to avoid the development of resistance to this last resort¹²⁷.

2. Importance of Infection Origin for Antibiotic Selection

The results of the current study unequivocally prove that the origin of purulent-septic infection in the maxillofacial region is of fundamental importance for the selection of adequate empirical antibiotic therapy. The observed differences in the microbiological profile of odontogenic and non-odontogenic infections necessitate a different therapeutic approach.

Therapeutic Approach for Non-Odontogenic Infections

In non-odontogenic infections, which often originate from skin trauma, postoperative complications, or nosocomial conditions, the main focus of therapy should be directed towards Gram-positive cocci, and specifically towards staphylococci. Data from our study, which show the dominant role of *Staphylococcus aureus* and coagulase-negative staphylococci (CoNS), confirm this necessity²⁴.

These pathogens are primary causative agents of superficial and deep skin infections that can develop in the maxillofacial region. Of particular importance is considering potential methicillin resistance (MRSA) in at-risk patients – those with previous contact with a hospital environment, with more severe infections, or with a history of recent antibiotic use. In these cases, empirical therapy should include antibiotics with anti-MRSA activity, such as vancomycin or clindamycin.

Therapeutic Approach for Odontogenic Infections

In contrast to non-odontogenic infections, for odontogenic processes, the therapeutic focus should be on providing broad-spectrum coverage of the oral microflora. This environment is rich in various types of microorganisms that can act synergistically. Our results highlight the leading role of streptococci, but also the significant presence of Enterobacteriaceae²⁰.

A key element of empirical therapy that must be emphasized is the need for coverage of anaerobic bacteria, even if they are not isolated in laboratory settings. As already indicated, the low isolation rate of anaerobes is likely due to methodological limitations rather than their absence. Anaerobes play a critical role in the pathogenesis of deep odontogenic infections, creating an environment favorable for the growth and spread of aerobic bacteria. Therefore, a combination of antibiotics targeting both aerobic and anaerobic pathogens (e.g., amoxicillin/clavulanate or a combination of penicillin with metronidazole) is crucial for successful treatment and prevention of serious complications. This combined approach ensures that all probable causative agents are targeted, increasing treatment effectiveness.

3. Need for Improvement in Microbiological Diagnostics

The extremely low proportion of isolated strict anaerobic bacteria (2.4%) is a serious limitation of the current study and at the same time highlights a critical need to improve the pre-analytical stage in clinical practice. This result is in sharp contrast to established literature data, which indicate that anaerobic bacteria, particularly strains such as *Fusobacterium* spp. and *Bacteroides* spp., are primary etiological agents of deep and severe odontogenic infections (Hupp et al., 2019; Brook, 2017). The reason for their insufficient isolation is directly related to the method of sample collection and transport, which compromises the viability of these oxygen-sensitive microorganisms^{55,27}.

To overcome this challenge, systematic training of medical personnel is necessary. Clinicians should be encouraged to collect material by needle aspiration instead of a simple swab²⁰. Aspiration ensures that the sample is obtained from the central, purulent part of the infectious focus, minimizing contamination with superficial microflora and avoiding exposure to air.

Furthermore, the use of special anaerobic transport media¹³⁵ is critical. These media contain reducing agents and are hermetically sealed, maintaining an oxygen-free environment and preserving the viability of anaerobic bacteria until they reach the microbiological laboratory. This approach significantly increases the chance of isolating these key pathogens, which in turn provides the opportunity for adequate antibiogram testing and targeted therapy.

In conclusion, improving microbiological diagnostics, especially concerning anaerobic bacteria, is crucial for more accurate determination of the etiological profile of purulent-septic diseases in the maxillofacial region. This step will lead to more effective treatment, reduced therapeutic failures, and better clinical outcomes for patients.

4. Always Consider "Exotic" Pathogens.

Although extremely rare findings, the presence of *Mycobacterium tuberculosis* and mucormycosis in the studied contingent (0.3% and 0.2%, respectively) is of immense clinical significance. These cases serve as an important reminder that in atypical courses of purulent-septic diseases or in patients with known or undiagnosed immune deficiencies (e.g., uncontrolled diabetes, HIV, or after organ transplantation), the differential diagnosis should be significantly broader and include unconventional causative agents.

These "exotic" infections, though rare, are life-threatening and require rapid, specific diagnosis and aggressive treatment that differs radically from standard protocols for purulent processes. For example:

- **Mucormycosis**, caused by fungi of the order Mucorales, is an opportunistic infection that primarily develops in patients with uncontrolled diabetes or severe immunosuppressive conditions. It is characterized by rapid invasive spread, which can lead to the destruction of tissues and organs, involvement of the orbital cavity and brain, and has an extremely high mortality rate. Early diagnosis, based on histopathological examination, and immediate surgical debridement of affected tissues, combined with systemic antifungal treatment, are crucial for patient survival.
- **Tuberculosis in the maxillofacial region** is also rare but should be suspected in the presence of chronic lymphadenitis or abscesses unresponsive to standard antibiotic treatment. This infection can be primary or a result of dissemination of pulmonary tuberculosis. Diagnosis requires specialized microbiological methods (e.g., PCR) and specific anti-tuberculous treatment, which is prolonged and complex.

The presence of systemic symptoms, such as high fever, night sweats, and weight loss, which are not explained by a standard bacterial infection, as well as the lack of therapeutic response to standard antibiotic therapy, should direct the clinician towards searching for such "exotic" causative agents. Clinical vigilance and collaborative work with microbiologists and infectious disease specialists are key to the timely recognition of these rare but extremely dangerous conditions¹²².

8.9. Limitations of the Study

Every scientific study has its limitations, and these are particularly important for interpreting the results and planning future research. The current dissertation, as a retrospective study, is heavily dependent on the completeness and quality of available medical documentation. This is the primary limitation, which imposes certain constraints on the possibilities for analysis.

Key Drawbacks

1. **Lack of data on prior antibiotic therapy:** One of the most significant drawbacks is the lack of accurate data on prior antibiotic therapy. Many patients with odontogenic infections are admitted to the hospital after having already received antibiotics from general practitioners or dentists. This prior therapy, even if ineffective, may have influenced the ability to isolate pathogens, explaining the high percentage of "sterile" samples in our study. The absence of this information makes it impossible to analyze the effect of prior treatment on microbiological findings.
2. **Lack of antibiotic susceptibility data:** The second significant drawback is that the analysis does not include antibiotic susceptibility data. Although we rely on literature data for expected resistance, the lack of our own local antibiogram data is a serious omission. This data is critical for developing local therapeutic protocols, as the resistance profile can vary significantly depending on the geographical region and specific hospital center. The available study data provide only guidance on the most probable causative agents, but not on the most effective empirical treatment.
3. **Single-center study:** Although this is one of the largest centers in the country – **University Hospital "St. Marina" - Varna, Bulgaria**, the results reflect only the local epidemiological profile and should be extrapolated to other regions with increased caution.

Despite these limitations, the current study provides the most extensive and detailed picture of the microbiological profile of purulent-septic diseases in the maxillofacial region in one of the largest clinical centers in Bulgaria over the past 10 years. The analysis of over 1700 clinical samples yields statistically significant data that can be used as a basis for future studies and for improving clinical practice. The results, especially regarding the dominant role of staphylococci and Gram-negative bacteria, are of paramount importance for selecting adequate empirical therapy and for overcoming increasing antibiotic resistance.

9. CONCLUSIONS

Based on the retrospective analysis of 1735 samples from patients with purulent-septic diseases in the maxillofacial region, hospitalized and treated at the Clinic of Maxillofacial Surgery at **University Hospital "St. Marina" - Varna, Bulgaria**, for the period 2015-2024, the following conclusions can be drawn:

1. Diagnostic Challenge and the Role of Resident Microflora

The analysis of microbiological findings reveals a complex picture, with resident microflora consisting of more than one bacterial species being the most frequently observed (50.50% of all samples with growth). This highlights the challenges in etiological diagnostics, as it is difficult to determine a dominant pathogen in these cases. The next most frequent findings are monoinfections with specific pathogens, among which coagulase-negative staphylococci (CoNS - 11.40%), *Streptococcus viridans* group (10.00%), and Enterobacteriaceae (total - 7.90%) account for the highest proportion. These results necessitate the use of local epidemiological data for adequate empirical antibiotic therapy, especially in polymicrobial infections and in patients who have received antibiotics.

2. Leading Etiological Agents and the Significance of CoNS

Among the pathogenic agents, coagulase-negative staphylococci (CoNS - 23.0%) and *viridans* group streptococci (20.1%) are leading. The high proportion of CoNS establishes them as significant opportunistic pathogens, not merely contaminants.

3. Clear Etiological Differentiation Based on Infection Origin

There is a clear difference in the etiology of infections: streptococci (especially the *viridans* group) dominate in odontogenic infections, while staphylococci (*S. aureus* and CoNS) are leading in non-odontogenic infections. This conclusion is essential for the choice of initial antibiotic therapy.

4. Anatomical Correlations and Origin of Odontogenic Infections

Over 70% (70.7%) of odontogenic infections originate from the mandible. This correlation is consistent with the anatomical predispositions for infection spread in this area, related to greater bone density and the anatomical position of the teeth.

5. Trend of "Staphylococcal Shift"

Over the last 5 years, an alarming trend of increasing isolated staphylococci has been observed, accompanied by a decrease in streptococci. This phenomenon supports the "staphylococcal shift" observed in the global literature.

6. Methodological Limitations and the Role of Anaerobes

The low proportion of isolated strict anaerobic bacteria (2.4%) is most likely due to a methodological artifact related to sample collection and transport. This necessitates mandatory anaerobic coverage in the empirical therapy of abscesses and phlegmons, despite low isolation rates.

7. Significant Role of Fungi as Co-pathogens

Candida spp. represent a significant proportion of isolates (7.9%), establishing them as an important co-pathogen, especially in odontogenic infections. Their presence calls for increased attention to the risk of fungal superinfections, particularly in patients with compromised immune status or after prolonged antibiotic therapy.

10. CONTRIBUTIONS

The current study makes the following original and confirmatory contributions:

Original Contributions:

1. Large-scale Retrospective Analysis of Microbiological Profile

For the first time in Bulgaria, such a large-scale (10-year, covering over 1700 samples) retrospective analysis of the microbiological profile of purulent-septic diseases in the maxillofacial region (MFR) is presented. This study covers patients from one of the leading clinical centers in the country – University Hospital "St. Marina" - Varna, Bulgaria, providing exceptionally valuable local epidemiological data.

2. Detailed Demographic Analysis

For the first time, a detailed demographic analysis (age, gender, seasonality) and an analysis of the anatomical localization of purulent-septic processes in the maxillofacial region are performed on such a large sample of patients with this pathology in Bulgaria. This analysis allows for the identification of clear risk groups and specific areas of predisposition to infections, which is essential for prevention and guiding health policy.

3. Documentation of the "Staphylococcal Shift" and Dynamics of the Etiological Spectrum

For the first time, the dynamics of the etiological spectrum over time are analyzed and documented. The study identifies and describes the phenomenon of the "staphylococcal shift" over the last five years, which has a direct impact on the choice of empirical antibiotic therapy.

4. Updated "Microbiological Map"

The study provides an up-to-date "microbiological map" of purulent infections in the MFR for the region, which can be used to optimize local therapeutic protocols and improve clinical practice.

Confirmatory Contributions:

1. Confirmation of Etiological Differentiation

For the conditions in Bulgaria, the classical differentiation in the etiological profile between odontogenic infections (dominated by oral flora) and non-odontogenic infections (dominated by staphylococci) is confirmed, strengthening the understanding of the pathogenesis of these conditions in a local context.

2. Confirmation of Anatomical Correlations

The study data confirm the anatomical prerequisites for the more frequent involvement of the mandible in inflammatory purulent diseases of odontogenic origin. This result is consistent with international data and highlights the importance of understanding the anatomy of the MFR.

3. Confirmation of Diagnostic Challenges

The significant proportion of samples where resident microflora is the most common microbiological finding, instead of an isolated etiological agent, is confirmed. This finding highlights the diagnostic challenges and methodological limitations in routine clinical practice, as well as the need to improve the pre-analytical stage of microbiological diagnostics for more precise differentiation of true pathogens from commensals.

11. SCIENTIFIC PUBLICATIONS RELATED TO THE DISSERTATION

1. Yankov YG, Mechkarova ID. Etiological spectrum of odontogenic and non-odontogenic abscesses in oral and maxillofacial surgery. *Scr Sci Med Dent*. 2023, 9: 68-74.
10.14748/ssmd.v9i1.9130
2. Yankov YG, Mechkarova ID. Microbiological spectrum, clinic and treatment of patients with phlegmons of the mouth floor. *Int J Med Sci Clin Invent*. 2023, 10(5): 6704-10.
10.18535/ijmsci/v10i5.02

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