"OVIDIUS" UNIVERSITY FROM CONSTANTA
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ABSTRACT OF DOCTORAL THESIS

ENT MANIFESTATIONS IN IMMUNOSUPPRESSED PATIENTS

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Contents

Keywords: ENT, manifestations, SARS-CoV2, HIV, neoplastic disease

GENERAL PART

INTRODUCTION

The ENT manifestations of HIV-positive patients cause problems through the aggression of the pathogen that is difficult to respond to treatment, through the sometimes unfavorable evolution of the disease, through their difficult monitoring, through very aggressive drug treatment, or through surgical treatment difficult to approach. Oral manifestations are: oral candidiasis; hairy leukoplakia; recurrent aphthous stomatitis; neoplasms (Kaposi's sarcoma and lymphomas); conditions caused by herpes simplex, herpes zoster, and human papillomavirus (HPV); periodontal disease; and oral tuberculosis. Nasosinusal manifestations are: acute and chronic rhinosinusitis; allergic rhinitis; neoplasms (Kaposi's sarcoma and lymphomas). Manifestations in the neck are: enlarged lymph nodes; salivary gland involvement. Otological manifestations are: acute and chronic otitis media; secretory otitis media; otitis externa; polyps in the external auditory canal; neoplasm (Kaposi's sarcoma); sensorineural hearing loss; peripheral facial paralysis. The immune response is defined as a cascade of phenomena that occur as a result of the specific interaction of the immune system with the antigen, leading to the activation, proliferation, and differentiation of immune competent cells, resulting in the emergence of effector cells and memory cells, which structure individual immunity. Immunosuppression is defined as "a state of temporary or permanent dysfunction of the immune response resulting from insults to the immune system. This can be the consequence of medical causes (diseases or procedures) or induced by drugs that suppress the immune system. The number of patients with immunosuppression in a population is difficult to estimate. However, American specialists estimate that approximately 3% of the US population is in this situation, due to some identified causes. Little is known about ENT surgical outcomes in these patients. Based on these considerations, studies were conducted to identify common ENT surgical diagnoses and treatments for HIV/AIDS patients as a primary objective and to evaluate surgical outcomes in these patients as a secondary objective.

1. CURRENT STATE OF KNOWLEDGE

The body's defense mechanisms always respond when it is faced with the invasion of antigens that have a different structure to the body's normal cellular structures (self). The greater the difference, the more aggressive the reaction against it will be. Defense against

antigens, which are called non-self structures, is carried out by the immune system. The optimal functioning of the immune system is conditioned by the tolerance towards self structures. When autoantibodies are formed or autoreactive lymphocytes differentiate that no longer recognize the self, tolerance disappears and the immune response is directed against the normal own structures, which become autoantigens or self-antigens.

Infection with the SARS-CoV 2 virus was considered a possible triggering factor of some long-lasting manifestations, which were defined as the prolonged form of the "Long COVID" disease, based on autoimmune mechanisms. The research carried out during these 2 years of the pandemic allowed the identification of the production of autoantibodies as markers of the genesis of the acute evolution, towards this chronic form recognized today in the medical world, as Long COVID. Deep molecular research in patients with COVID-19 found the presence of autoantibodies in peripheral blood at initial diagnosis. This was the main risk factor of the 4 identified, which predicted whether a patient with acute disease could evolve to long-term COVID-19. The other significant early predictors of Long COVID symptoms which the researchers called “post-acute sequelae” were type 2 diabetes, SARS-CoV 2 viremia, and Epstein-Barr virus (EBV) viremia. EBV viremia suggested that latent EBV infection has been reactivated.

ENT manifestations in HIV infection

The ENT manifestations of HIV-positive patients cause problems for people infected with the human immunodeficiency virus (HIV) through the aggression of the pathogen that is difficult to respond to treatment, through the sometimes unfavorable evolution of the disease, through their difficult monitoring, through very aggressive drug treatment, or through surgical treatment difficult to approach. Antiretroviral treatment combined with aggressive ENT drug treatment poses major difficulties for HIV-infected patients due to high toxicity.

ENT manifestations in SARS-CoV 2 virus infection

The literature on ENT manifestations of COVID-19 is still poor. Therefore, it is worthwhile to study the ENT manifestations of this new virus and there is a demand to accurately identify the defining epidemiological and clinical features of COVID-19.

Remarkably, a percentage of patients with COVID-19 had OSA; although the direct association between OSA and COVID-19 has not yet been reported, untreated OSA patients suffer from chronic intermittent hypoxia leading to hypertension, heart failure,

cerebrovascular disease, and obesity; these are risk factors for greater severity of COVID-19 . Angiotensin-converting enzyme 2 (ACE2) is the entry receptor of COVID-19 in patients with OSAS, dysregulation of the renin-angiotensin system occurs. Therefore, the effect of disturbed sleep on the immune system and the protection of OSA patients from COVID-19 should be considered. In addition, it should be taken into account that patients who have recovered from severe cases of COVID-19 may be at risk of OSA due to pulmonary fibrosis. Otorhinolaryngological manifestations in COVID-19 are not rare but prominent in COVID-19, especially in mild or moderate disease, and should be considered as potential clinical features. Timely identification of otorhinolaryngological symptoms can lead to early detection of otherwise asymptomatic carriers.

ENT manifestations in the radio-treated neoplastic patient

Chemotherapy in such cases is often considered an organ-preserving treatment; however, such treatment may be difficult to tolerate in HIV-positive patients. Chemotherapy can increase the risk of infection, especially in patients whose immune systems are compromised. Patients with CD4 counts less than 200 cells/mm^3 experience increased toxicity from therapy.

Radiotherapy in HIV-positive patients can cause severe mucositis. Adequate radiation treatments require good compliance and strong physical condition during treatment.

THE PERSONAL PART

2. General methodology

2.1 OBJECTIVES AND PURPOSE OF THE WORK

Immunosuppression is defined as “a state of temporary or permanent dysfunction of the immune response resulting from insults to the immune system. Immunosuppression can be the consequence of medical causes (diseases or procedures) or induced by drugs that suppress the immune system. The number of patients with immunosuppression in a population is difficult to estimate. However, American specialists estimate that approximately 3% of the US population is in this situation, due to some identified causes.

The current thesis aims to evaluate the influence of different types of immunosuppression on the incidence of ENT pathology, the clinical aspects, their evolution,

and treatment. The option for a surgical cure requires a complex, complete clinical-biological approach as well as a special preparation for these patients.

We designed the research in three studies: - ENT diseases in patients: with major acquired immunodeficiency (HIV/AIDS); with neoplasms subjected to radio/chemotherapy treatment and in patients with possible autoimmunity induced after infection with SARS-CoV 2 and post-vaccine. The main objectives of my research consisted in the evaluation of various ENT manifestations in immunosuppressed patients, such as in people infected with the human immunodeficiency virus (HIV), in radio and chemotherapy-treated neoplastic people, but also people infected with the SARS-CoV 2 virus. A second objective is to establish some variables whose influence had an impact and led to the improvement of their quality of life.

The purpose of the study consisted of the division and classification by site of ENT manifestations in the immunosuppressed patient and how the therapeutic behavior responded according to the particular complexity of the immunosuppressive pathology for each patient. If the relationship between the studied variables and the ENT manifestation itself is conclusive, then the final goal of the paper is to develop an ENT guide for the immunosuppressed patient, which requires a much more specific, careful, and meticulous approach to the therapeutic conduct, the local ENT exam, of paraclinical examinations, additional investigations and follow-up of favorable or unfavorable evolution.

2.2 Material and method

The study was carried out in the HIV/AIDS Day Clinic of the Constanța Infectious Diseases Clinical Hospital, in the psycho-social care department for HIV/AIDS patients of the Baylor Marea Neagra Foundation, in the Constanța County Emergency Clinical Hospital, in the Clinical Hospital Colțea Bucharest, and in CF Cluj-Napoca Clinical Hospital during 2018-2022.

The research included 3 studies that included patients infected with the Human Immunodeficiency Virus, patients with radio and chemotherapy-treated neoplasms, patients infected with the SARS-CoV 2 virus, who manifested ENT diseases during the immunosuppression period, as follows: Study 1: a group of 223 patients immunosuppressed by the Human Immunodeficiency Virus with ENT complications admitted to the departments of Infectious Diseases Constanța, Constanța County Emergency Clinical Hospital, Alexandru Gafencu Constanța Military Emergency Hospital, Colțea Clinical Hospital Bucharest and CF Cluj-Napoca Clinical Hospital, in the period 2018-2022 with ENT diagnosis depending on

the location of the manifestations, with drug treatment and/or surgical treatment. The patients were selected from a group of 600 people infected with HIV.

Study 2: a group of 75 immunosuppressed patients due to radiotherapy and chemotherapy treatment who showed ENT complications at the oncology visit and required an ENT consultation in Constanța County Emergency Clinical Hospital, Alexandru Gafencu Constanța Military Emergency Hospital, Colțea Clinical Hospital Bucharest, CF Cluj-Napoca Clinical Hospital, during 2018-2022. The patients were selected from a group of 400 people with neoplasms located in different regions.

Study 3: a group of 73 patients infected with the SARS-CoV 2 pandemic virus who presented ENT complications at the consultation, both during the acute period of COVID-19 infection and in the post-Covid period. The patients presented themselves at the ENT consultation at Constanța County Emergency Clinical Hospital, Alexandru Gafencu Constanța Military Emergency Hospital, Colțea Clinical Hospital Bucharest, Cluj-Napoca Clinical Hospital during 2020-2022. From the study group, there was a small number of patients who were admitted to the ENT department and presented a positive Covid RT-PCR test.

From the 3 study groups, we analyzed each group of immunosuppressed patients separately, having a significant number of common variables such as age, sex, background, educational level of the patient, associated conditions, exposure to risk factors, the number of CD4 lymphocytes, site of ENT manifestations, ENT evolution, surgical interventions, quality of life after ENT treatment, mortality, DASS-21 scale, VAS scale. During the pandemic period, the status of the patient with ENT manifestations was established (Covid vaccinated/not vaccinated and if he had a history of infection with the SARS-CoV 2 virus).

2.3 Statistical data analysis

The experimental data were processed using the statistical processing program IBM SPSS Statistics 25. The data are presented as mean ± standard deviation (SD) for continuous variables in the case of symmetric distributions, as median and IQR (Interquartile range) for continuous variables in the case of asymmetric distributions, or as frequencies and percentages in the case of categorical variables. The condition of normality was determined with the Kolmogorov-Smirnov and Shapiro-Wilk tests. The procedures used were: Descriptive statistics (for the characterization of categorical and continuous variables defined at the database level), Graphs, Parametric statistical tests: the OneWay ANOVA test (for

comparing the mean values of three or more independent groups), Non-parametric statistical tests: the $\chi 2$ of the association (of the link) between two categorical variables, z Test for comparing two proportions, Kruskal-Wallis H Test (used to test the difference between three or more independent groups), Median Test, Wilcoxon T Test (used to test the difference between two dependent groups) In all situations the significance level chosen was $\alpha = 0.05$.

The immunosuppressed patient presenting with ENT clinical manifestations was studied and analyzed in the working cohorts as follows: in study I, immunosuppressed patients with HIV infection were evaluated, in study II, immunosuppressed patients with radio-treated or radio- and chemo-treated neoplasms were evaluated, and in study III immunocompromised patients with covid-19 infection were evaluated, representing the most current and representative research study for the support and publication of this doctoral thesis.

3. Study I

Objectives

- Clinical evaluation of ENT manifestations in HIV positive patients
- Establishing the opportunity and results of ENT surgical treatment
- Analysis of the patient's evolution after ENT treatment by means of the VAS, DASS-21 evaluation scales

3.1 Material and method

The study included 223 patients infected with Human Immunodeficiency Virus who presented with clinical ENT complications and who were treated concurrently for both infectious disease and remission of ENT manifestations. The people included in the study were clinically and biologically evaluated both at the time of being recorded as HIV-positive patients and at the time of presenting to ENT clinics for complications in this sphere. Patients during hospitalization completed questionnaires to obtain quality of life data after concurrent ENT treatment with that of the infectious disease, but also before ENT treatment to determine whether there was an improvement in health status. Depending on the site of ENT manifestations, patients infected with the Human Immunodeficiency Virus were included in the study as follows: 85 patients with pathologies of the oral cavity, 41 patients

with pathologies of the throat, 51 patients with pathologies of the ear, and 46 patients present pathologies at the rhinosinus level.

Inclusion criteria

+ Patients infected with human immunodeficiency virus from 2018-2022

+ ENT manifestations in HIV positive patients

Exclusion criteria

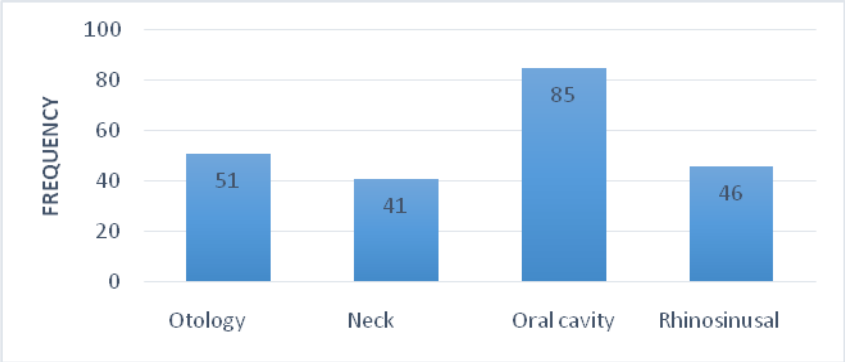
- Patients with other pathologies from the ENT and Infectious Diseases departments

- Patients infected with human immunodeficiency virus without ENT manifestations

- HIV positive patients without complete clinical data in FOCG

3.2 Results for Study I

ENT events headquarters



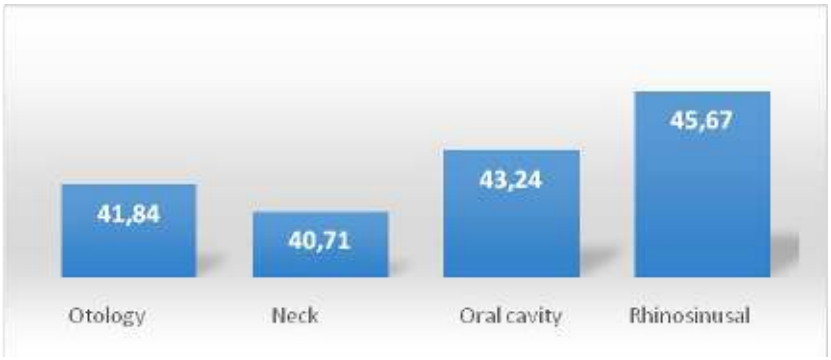
ENT manifestations headquarters

Figure 1 Graphical representation Column for the variable Center of ENT manifestations in patients from the study group.

Most patients had persistent oropharyngeal candidiasis. Correlating with the retrospective studies that showed that the most frequent site is the oral cavity, we can say that we have an equal result compared to these researches. The second site of ENT manifestations in the immunosuppressed patient is the ear (otological site), represented by 51 patients who presented to the ENT clinic for acute suppurative otitis media, otitis externa, chronic suppurative otitis media or otomycosis, while serous otitis they had a lower share. Compared to seronegative patients, these otitis or otomycosis had a more severe evolution and required aggressive and long-term local treatment. The third site of ENT manifestations in the immunosuppressed patient is the nose (the rhinosinusal site) represented by 46 patients who presented themselves in the ENT clinic. The fourth site of ENT manifestations in immunocompromised patients is the throat, represented by 41 patients who presented to the

ENT clinic for later cervical adenopathies, toxoplasmosis, mononucleosis, adenitis, acute laryngitis, reflux laryngitis, paralysis of the vocal cords, polyps on the vocal cords, laryngeal neoplasms and Non-Hodgkin's lymphomas.

Distribution of HIV-positive patients with ENT manifestations by age group

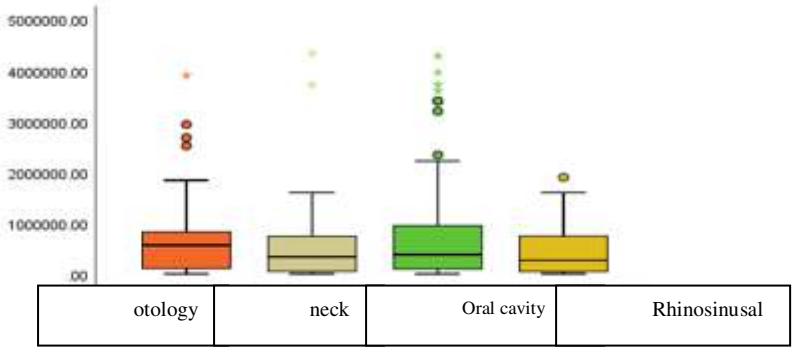


ENT manifestations headquarters

Figure 3 Bar-Error Graphic Representation for the variable Age (years) according to the categories of the variable Location of ENT manifestations in patients from the study group.

The study notes that the average age of HIV-infected patients is 40 years, representing a young and active population. Although these patients are very young, severe chronic complications were observed in the study. Advanced antiretroviral treatment represents a positive dynamic. Because of this, ENT treatment responds favorably if the HIV-positive patient is stable from the point of view of antiretroviral treatment.

Distribution of HIV-positive patients with ENT manifestations according to HIV RNA viremia value at the time of enrollment



ENT manifestations headquarters

Figure 4 Box-Plot graphic representation for the HIV RNA Viremia variable at the time of recording according to the categories of the variable Location of ENT manifestations in the patients in the study group.

A high value of viremia at the time of taking HIV into account indicates that the patients accessed the medical services late, they are in an advanced stage of immunodepression, and it is necessary to urgently institute treatment against HIV infection. This determination of viremia is mandatory from the first stage of infection, in case of detection of seroconversion, as close as possible to the moment of infection.

Distribution of HIV-positive patients with ENT manifestations according to the value of HIV RNA viremia at the time of detection of ENT manifestations

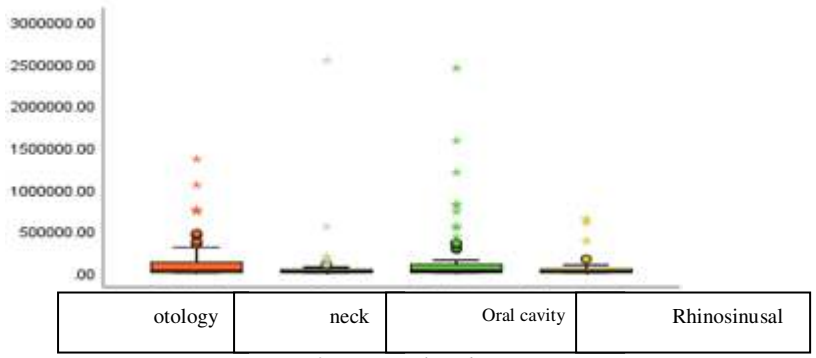
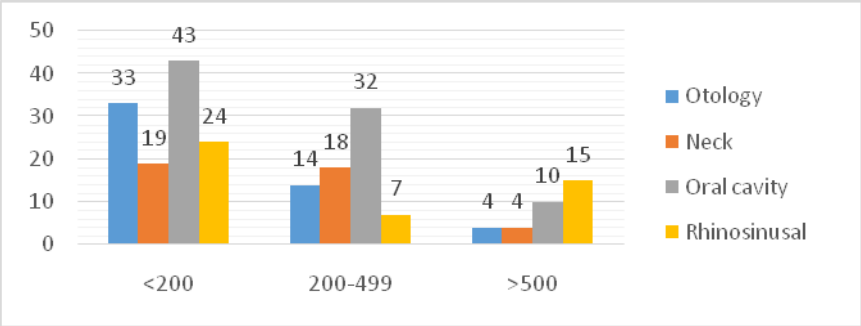


Figure 5 Box-Plot graphic representation for the variable HIV RNA viremia at the time of detection of ENT manifestations according to the categories of the variable Location of ENT manifestations in patients from the study group.

The average value of HIV RNA viremia at the time of detection of ENT manifestations is 153,062, being much lower than the average of HIV RNA viremia at the time of detection of HIV infection (581,000). Appropriate antiretroviral treatment stabilized the condition of the infected patient. If the viremia at the time of detection of ENT manifestations had been much higher, then the response of the pathogens to the treatment would have been much more aggressive. 44.39% of the total of 223 patients infected with the Human Immunodeficiency Virus had a favorable evolution of the disease. In conclusion, increased HIV RNA viremia at the time of detection of ENT manifestations can influence the evolution of ENT conditions. When the viremia would have been much lower, probably from the total of 223 HIV-positive patients, the percentage of patients with a favorable evolution would have increased above 50-60%.

Distribution of HIV patients by CD4 count at the time of HIV diagnosis

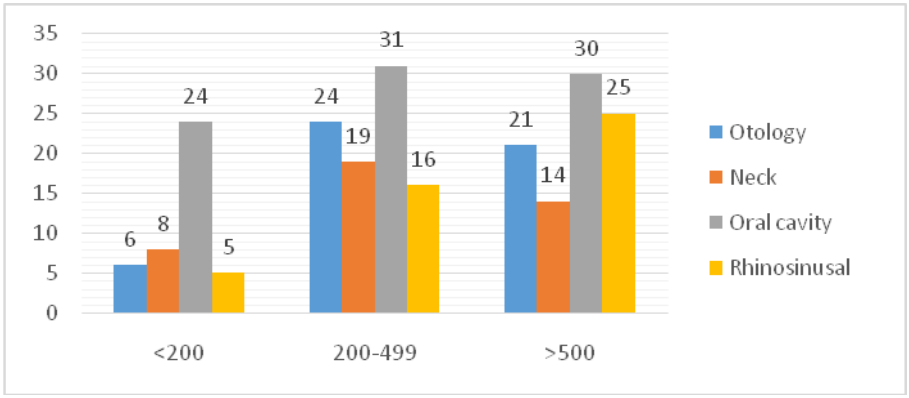


CD4 at the time of HIV detection

Distribution of HIV patients by CD4 count at the time of HIV diagnosis

It is shown that most patients have a CD4 lymphocyte count < 200 at the time of detection of human immunodeficiency virus infection (119 patients out of a total of 223), due to late presentation to the infectious disease doctor. Retrospective studies indicate that patients have a very low CD4 count when they are diagnosed with HIV. The lowest values in this study can be found in otological diseases (64.71%), followed by rhinosinusal diseases (52.17%). There is a dependency relationship (an association, a link) between the CD4 variables at the time of HIV detection and the Center of ENT manifestations: $\chi 2calc = 21.578$, $df = 6$, $p = 0.001 < \alpha = 0.05$ ($\chi 2$ test of the association between two categorical variables).

Distribution by CD4 value at the onset of ENT manifestations



CD4 at the time of HIV detection

Figure 13 Graphical representation Column for the variable CD4 at the occurrence of ENT manifestations according to the categories of the variable Location of ENT manifestations in patients from the study group

In this study, it is demonstrated that the value of CD4 lymphocytes at the time of onset of ENT disease is higher compared to the time of detection of HIV infection. To proceed with a surgical intervention, the CD4 value in HIV-positive patients must be >200. The value of

CD4 lymphocytes limits the therapeutic approach because to benefit from surgical intervention, the patient must have a value of CD4 lymphocytes >200. In this paper, an increased share of CD4 > 200 lymphocytes is observed for the rhinosinusal site. Patients presenting pathologies in the oral cavity have low values of CD4 lymphocytes (CD4<200, in the percentage of 28.24%), and this suggests that they are severely immunosuppressed and are in a critical condition.

Distribution of HIV-positive patients with ENT manifestations by HIV disease stage

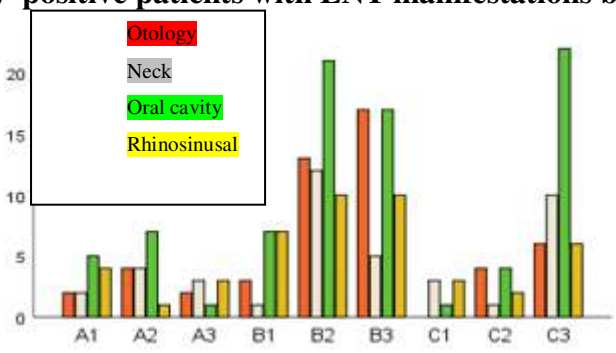
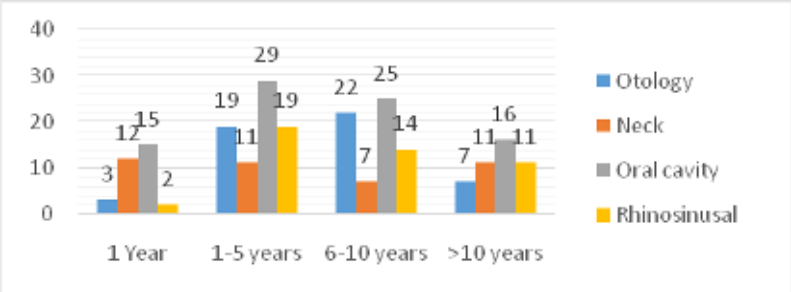


Figure 15 Graphical representation Column for the HIV Disease Stage variable according to the categories of the variable Location of ENT manifestations in patients from the study group

It is noteworthy how the stage of HIV disease B2 (values of CD4 lymphocytes between 200-499) is most frequently identified in all ENT pathologies at the level of the ear, throat, oral cavity, or rhinosinusal level. In stage B3, the infected patient presents specific symptoms, and the most common ENT pathologies are at the level of the ear. During the ENT clinical examination, otoscopic, muco-purulent otorrhea that is difficult to treat, or fungal secretions are observed. The most affected sites for stage C3 HIV disease were the throat and oral cavity. Persistent oral candidiasis, later cervical lymphadenopathy, angular cheilitis, leukoplakia, Kaposi's sarcoma, laryngeal neoplasms, mononucleosis, or toxoplasmosis have been seen in HIV-positive patients at stage C3.

Distribution of HIV-positive patients with ENT manifestations by time of onset of ENT manifestations

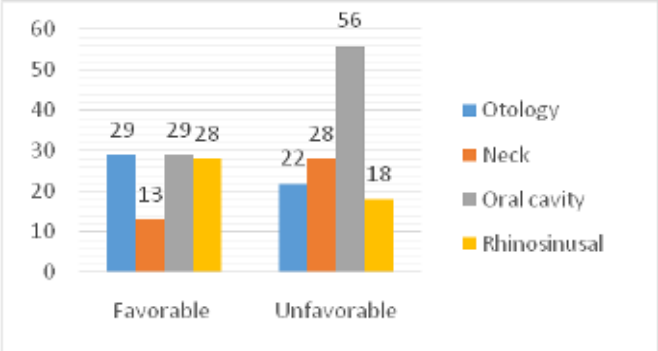


The moment of the appearance of ENT manifestations

Figure 17 Graphical representation Column for the variable Time of onset of ENT manifestations according to the categories of the variable Location of ENT manifestations in patients from the study group

In our group, it can be observed that in the first 5 years, the infected people presented ENT complications in an approximately equal percentage in all anatomical locations in the ENT sphere: 37.25% at the level of the ear, 26.83% at the level of the throat, 34.12% at the level of the oral cavity, 41.30% at rhinosinusal level. Between 6-10 years after the detection of HIV infection, the patients in the study presented complications of an otological nature, such as middle and outer ear infections or severe sensorineural hearing loss.

Distribution of HIV-positive patients with ENT manifestations according to the evolution of ENT complications.

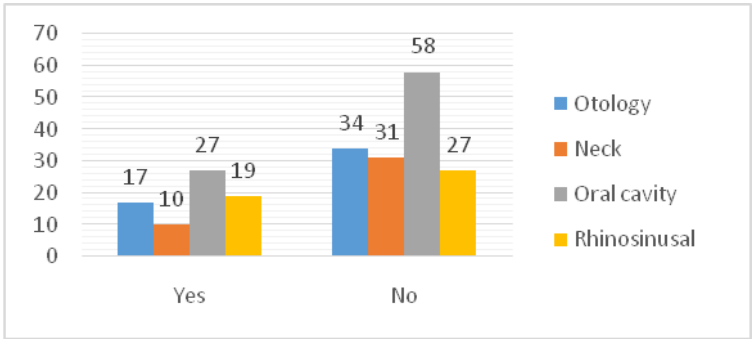


The evolution of ENT

Figure 18 Graphical representation Column for the variable ENT Evolution according to the categories of the variable Location of ENT manifestations in patients from the study group

In this study, there is an association between the evolution of ENT and the location of ENT complications stating that patients with otological conditions such as otitis, otomycosis, otomastoiditis, hearing loss and had a cure rate of 56%. Patients who experienced rhinosinusal complications showed a favorable evolution in 60%. People with diseases in the oral cavity and in the throat (examples: persistent oral candidiasis, stomatitis, herpes, acute tonsillitis, later cervical adenopathies, Kaposi's sarcoma, lymphomas, laryngitis, laryngeal neoplasms) presented unfavorable developments in a proportion of 65%.

Distribution of HIV-positive patients with ENT manifestations according to the percentage of vaccination for 2020 SARS-CoV 2 pandemic virus

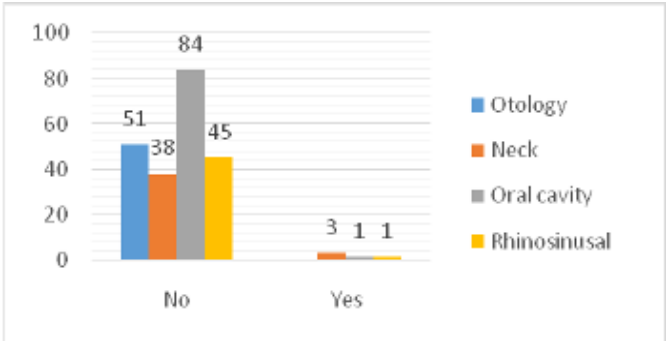


Vaccinated COVID

Figure 16 Graphical representation Column for the variable COVID vaccinated according to the categories of the variable Center of ENT manifestations in patients from the study group

This study demonstrates that the majority of HIV-infected patients, although immunosuppressed and in need of special health care, are not vaccinated against SARS-CoV 2 (only 32% of them were vaccinated). In this study, it is demonstrated that the excess of ENT diseases is due to non-vaccination for the SARS-CoV 2 virus. The majority of patients who were not vaccinated presented complications in the oral cavity and in the ear (58 patients for oral cavity manifestations and 34 patients for otological).

Distribution of HIV-positive patients with ENT manifestations by mortality



Mortality rate

Figure 21 Graphical representation Column for the variable Mortality according to the categories of the variable Location of ENT manifestations in patients from the study group

In our study, it is observed that the life span of HIV-infected patients has increased due to effective antiretroviral treatment, and ENT complications with a risk of death are represented by neoplasms. 2.24% of monitored patients died due to ENT complications. The most common post-radiotherapy complications were oral mucositis, but the advanced stage of HIV disease together with severe ENT manifestations led to the death of the immunocompromised patient.

Distribution of HIV-positive patients with ENT manifestations according to the DASS-21 (Depression, Anxiety, and Stress Scales) score.

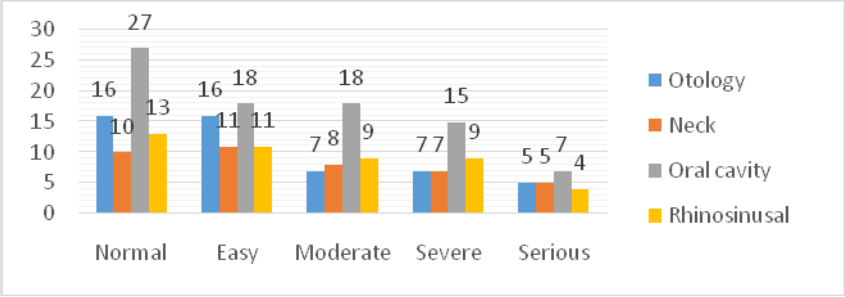


Figure 22 Graphical representation Column for the variable DASS-21 according to the categories of the variable Location of ENT manifestations in patients from the study group

The DASS-21 score takes into account the patient's emotional state at discharge. Most of the patients have a normal or slightly influenced score due to the stress caused by the disease, and between 13-20% of the patients have a severe score because they patients are depressed, anxious, and fearful, without being able to understand the purpose of medical or surgical treatment and without could understand the reason for an ENT check. Patients with neck pathologies have a severe DASS-21 score (12.20%). Such patients need understanding and periodic monitoring so that the trauma suffered has a course with a good outcome.

3.3 Discussion and Conclusions for Study I

- ENT manifestations in the immunosuppressed patient predominate in people with an average age of 40 years, most of them having a favorable evolution due to their relatively young age.
- The most common ENT complications in patients infected with the Human Immunodeficiency Virus are persistent oral candidiasis, laterocervical adenopathies, acute tonsillitis, acute and chronic rhinosinusitis, ear otomycosis and acute suppurative otitis media.
- The value of CD4 lymphocytes at the time of the onset of ENT manifestations is between 200-499 in 40% percent and greater than 500 in approximately 40% percent. Patients with CD4 lymphocyte counts greater than 200 have a better prognosis and better response to treatment.
- The patients in the study presented associated comorbidities such as neoplasm, cirrhosis, tuberculosis, diabetes, and hepatitis, complicating the evolution and therapeutic conduct. ENT treatment concurrently with the management of these associated conditions

generated difficulties in the management of patients, requiring the adoption of an appropriate strategy within a multidisciplinary team.

- The most frequent cases were detected between 1 and 10 years after HIV positive patients were recorded. The patient with ENT manifestations who presented approximately 1 year after HIV was detected has a more precarious status due to the increased viremia, the number of CD4 lymphocytes in low limits. Patients with ENT manifestations who presented to the ENT clinic 10 years after HIV detection have a better status, due to low viremia and the effectiveness of combined antiretroviral therapy.
- Analysis of the DASS-21 score for calculating the stage of depression, anxiety, and stress in patients immunosuppressed by infection with the Human Immunodeficiency Virus who had ENT diseases was dominated by a mild form of the depression scale.
- 32.74% of the HIV-positive patients in the study were vaccinated against the Covid-19 disease. The rest of the unvaccinated people were reluctant to this preventive measure.

4. Study II

Objectives

- Evaluation of various ENT manifestations in neoplastic patients treated with radiochemotherapy
- Establishment of ENT surgical treatment for neoplastic patients treated with radiochemotherapy
- Analysis of the patient's evolution after ENT treatment by means of the VAS, DASS-21 evaluation scales

4.1 Material and Method

Study II includes 75 patients with different neoplasms treated with radiochemotherapy or treated with surgical cure, in all clinical-anatomical centers who presented ENT clinical complications and who were treated for the remission of ENT manifestations. The techniques used to develop the cohort were observation sheets, medical letters, analyses, complete ENT clinical examination, endoscopic examination, fiberscopic examination, micro-otoscopic examination, CT/MRI imaging examinations, histopathological examination, and surgical interventions.

Inclusion criteria

+ Neoplastic patients treated with radiation and/or chemotherapy

+ Neoplastic patients with ENT manifestations

Exclusion criteria

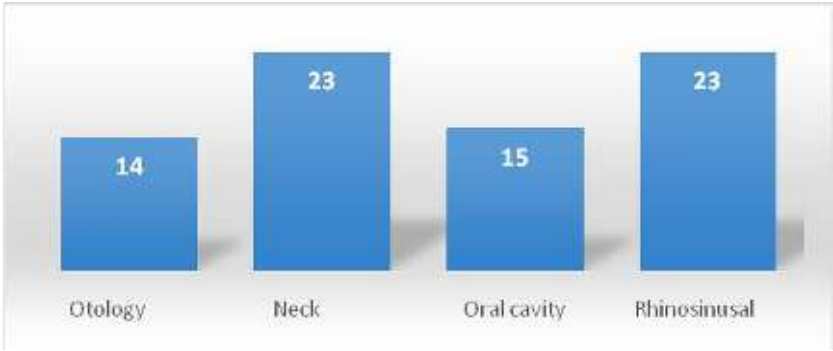
- Neoplastic patients without monitored treatment

- Neoplastic patients without ENT manifestations

- Neoplastic patients without complete clinical and paraclinical data

4.2 Results for Study II

ENT events headquarters

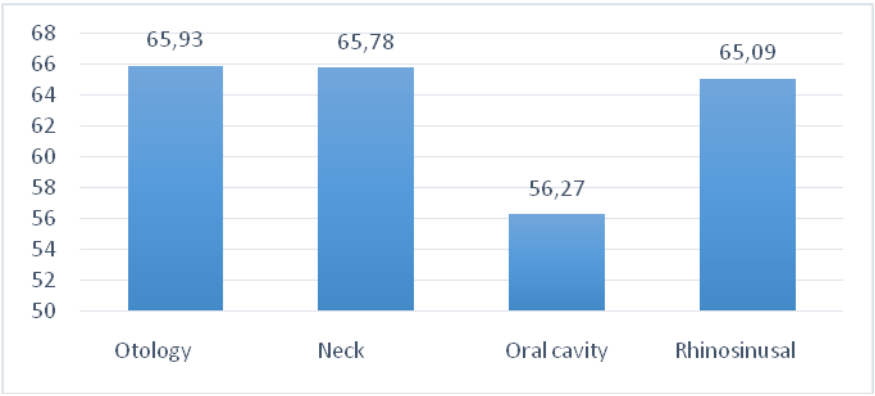


ENT manifestations events headquarters

Figure 24 Graphical representation Column for the variable Location of ENT manifestations in patients from the study group.

In this study, the most common anatomical locations of ENT manifestations are at the neck and the rhinosinusal level. The next site of ENT manifestations in the neoplastic patient is the oral cavity with a percentage of 20%. The ear is the least affected office with a percentage of 18.67%. In our study, neoplastic patients were found who presented ENT complications such as cerumen plug, otitis externa, acute purulent otitis media, otomycosis, sudden deafness, tinnitus, transmission hyperacusis, and serous otitis.

Distribution of neoplastic patients with ENT manifestations according to age



ENT manifestations events headquarters

Figure 26 Bar-Error Bar graphic representation for the variable Age (years) according to the categories of the variable Location of ENT manifestations in patients from the study group

The age of neoplastic patients with ENT manifestations included in the study was between 42-87 years, with an average value of 63.69 years and a standard deviation of 9.17 years.

Distribution of neoplastic patients with ENT manifestations according to sex

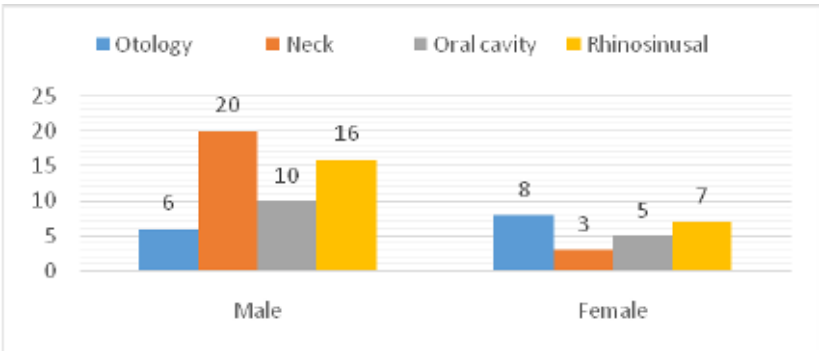
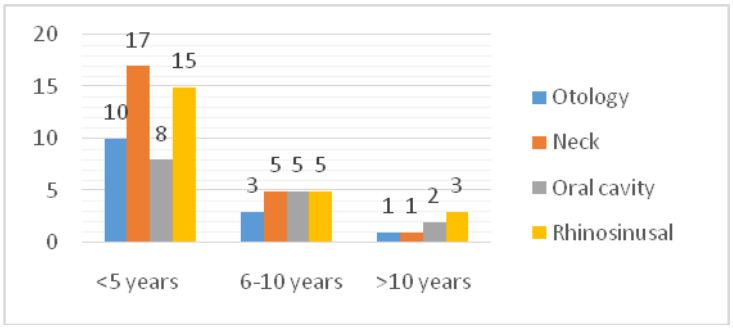


Figure 30 Graphical representation Column for the variable Sex according to the categories of the variable Location of ENT manifestations in patients from the study group

Our study found that women are more prone to ENT complications of an otological nature. Laryngeal tumor formation is much more common in men (86.96%) who presented with inoperable tracheostomy, bleeding from the stoma, fistulas, granulation tissue, bleeding adenopathy blocks, tracheal necrosis, severe dysphagia, recurrences or neoplasms secondary.

Distribution of neoplastic patients with ENT manifestations according to the age of the neoplasm.

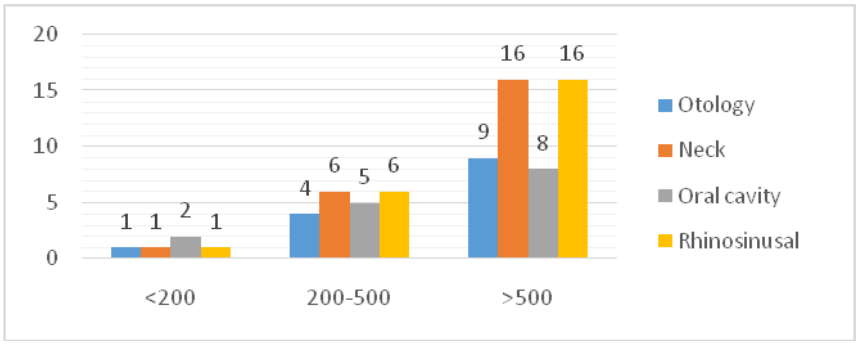


The age of the neoplasm

Figure 32 Graphical representation Column for the variable Age of the neoplasm according to the categories of the variable Location of ENT manifestations in patients from the study group

Most of the patients in study II have neoplasms less than 5 years old. Oral mucositis, oropharyngeal candidiasis, chronic tonsillitis, and oropharyngeal tumor formations continued to appear 5 years after the neoplasm diagnosis.

Distribution of neoplastic patients with ENT manifestations according to the number of CD4 lymphocytes at the time of ENT manifestations



CD4 at the time of ENT manifestations

Figure 35 Graphical representation Column for the variable CD4 at the time of ENT manifestations according to the categories of the variable Location of ENT manifestations in patients from the study group

In the study cohort, the value of CD4 lymphocytes with the location of ENT manifestations remains constant, with an approximately equal weight compared to the postradiotherapy moment in all locations, except for CD4 lymphocytes with a value greater than 500. The highest frequency of smaller CD4 lymphocytes of 200 at the time of ENT manifestations is still found in the oral cavity but with a much lower percentage value compared to the post-radiotherapeutic moment. The most frequent pathologies with values between 200 and 500 CD4 lymphocytes are at the level of the oral cavity. Furthermore, dental foci, tonsillitis, hypertrophy of the palatine tonsils, and persistent oral candidiasis are more likely to occur in radio-treated neoplastic patients who have a value of less than 200

CD4 lymphocytes. It is noted that the number of patients with CD4 values greater than 500 is more at the time of ENT manifestations than at the time of radiotherapy. It is worrying when the patient remains with a CD4 lymphocyte count below 200.

Distribution of radiotherapy-treated neoplastic patients with ENT manifestations according to the percentage of vaccination for the 2020 SARS-CoV 2 pandemic virus

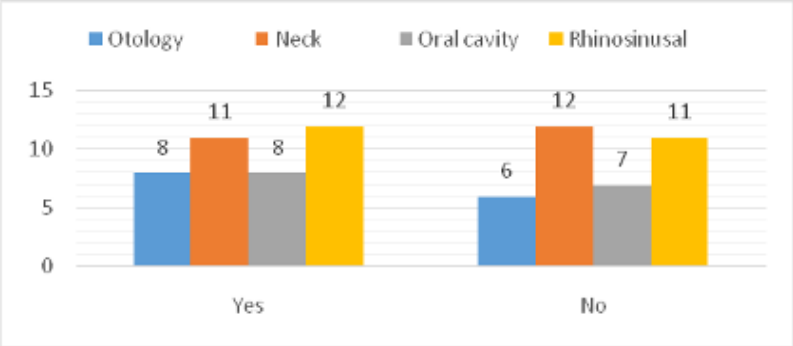


Figure 38 Graphical representation Column for the variable Vaccinated according to the categories of the variable Location of ENT manifestations in patients from the study group

In terms of the percentage of vaccination against the SARS-CoV 2 pandemic virus, 52% of neoplastic patients treated with radiation were vaccinated. The rest of the patients did not agree to the vaccination due to the fear of adverse reactions.

Distribution of radiotherapy-treated neoplastic patients with ENT manifestations by time of onset of ENT manifestations

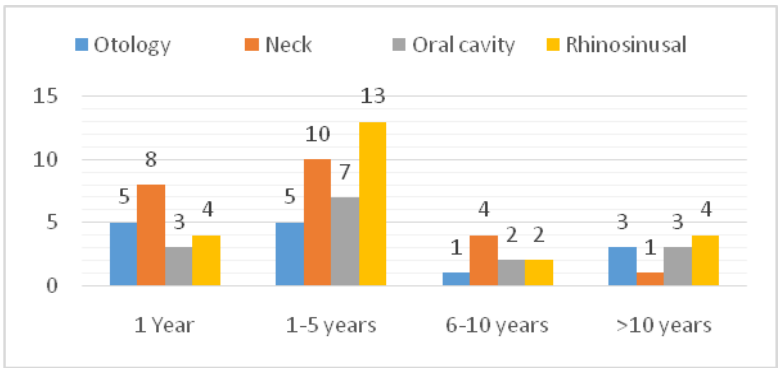


Figure 39 Graphical representation Column for the variable Time of onset of ENT manifestations according to the categories of the variable Location of ENT manifestations in patients from the study group

In this study, it is observed that ENT manifestations occur most frequently between 1 and 5 years after the diagnosis of cancer. It is found that immunosuppression by radiotherapy

predisposes to the appearance of oral manifestations. Most complications occurring between 1-5 years are epistaxis, non-functional tracheostomes, relapses, mucositis, chronic sinusitis, and otomycosis. Between 5 and 10 years, ENT complications are rare, and after 10 years after cancer detection, complications of an otological nature and from the oral cavity occur most frequently.

Distribution of radio-treated neoplastic patients with ENT manifestations according to the percentage of neoplastic mortality

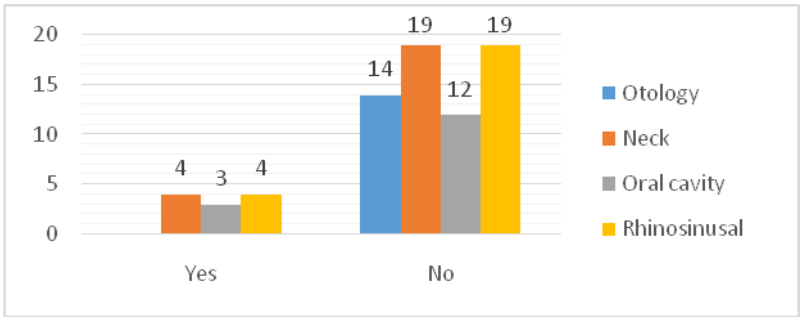


Figure 41 Graphical representation Column for the variable Mortality according to the categories of the variable Location of ENT manifestations in patients from the study group.

The mortality rate for radiotherapy-treated neoplastic patients with ENT comorbidities is 14.67%. Most of them died due to the unfavorable evolution of the tumor formations and due to the advanced stage of the neoplastic disease. Part of the patients presented with relapses, secondary tumor formations, metastases, and palliative oncological treatment.

Distribution of radiotherapy-treated neoplastic patients with ENT manifestations consulted during the covalescence period of SARS-CoV 2 virus infections

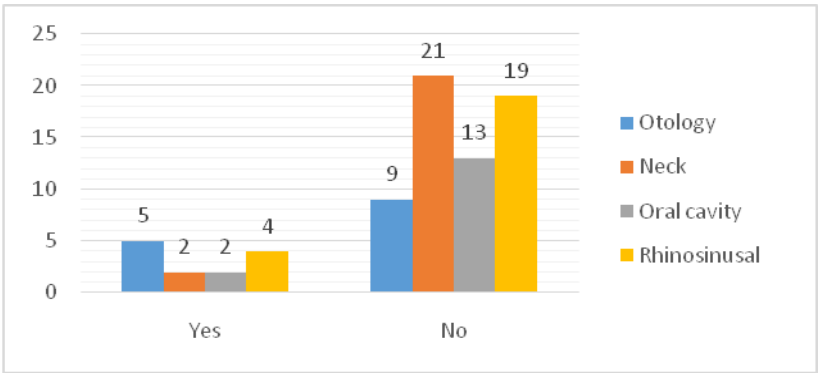
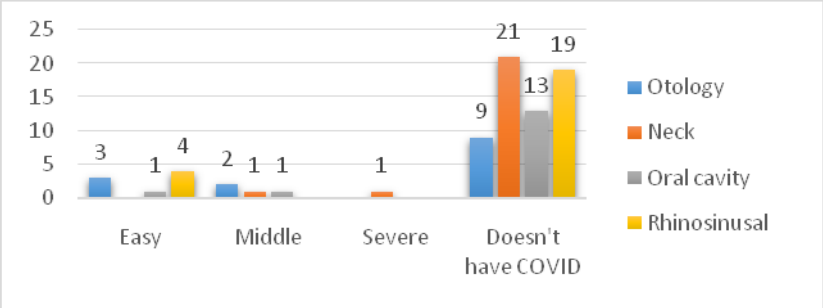


Figure 42 Graphical representation Column for the positive COVID variable according to the categories of the variable Location of ENT manifestations in patients from the study group

Of the total number of radiotreated neoplastic patients in the study cohort, 13 were positive for SARS-CoV 2 virus infection. They presented ENT manifestations during the

convalescence period. The immunosuppression acquired by radiotherapy was accentuated by SARS-CoV 2 virus infection.

Distribution of radiotherapy-treated neoplastic patients with ENT manifestations according to the severity of anamnestic SARS-CoV 2 infection.

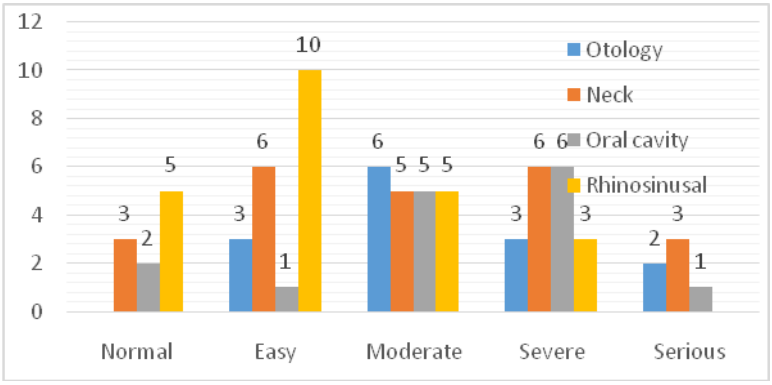


Severity of the COVID disease

Figure 43 Graphical representation Column for the variable Severity of the COVID disease according to the categories of the variable Location of ENT manifestations in patients from the study group

Most of the radiotherapy-treated neoplastic patients with ENT manifestations were not infected with the SARS-CoV 2 pandemic virus (82.67%). What is surprising in the study, the radiation-treated neoplastic patients who went through the COVID-19 disease had mild form or they were asymptomatic . In a proportion of 10.67%, patients infected with the SARS-CoV 2 virus (with mild form or asymptomatic) presented to the otorhinolaryngologist for tinnitus, sensorineural hearing loss, benign paroxysmal positional vertigo, acute otitis media, epistaxis, hyposmia, hypertrophic rhinitis, angina acute pultacea, acute nasopharyngitis. It was found that most neoplastic patients who went through the COVID-19 disease presented themselves at the ENT clinic for ear conditions (21.43%) and nose conditions (17.39%).

Distribution of radio-treated neoplastic patients with ENT manifestations according to the DASS 21 score (Depression, Anxiety, and Stress Scales)



DASS-21

Figure 45 Graphical representation Column for the variable DASS-21 according to the categories of the variable Location of ENT manifestations in patients from the study group

Chronic otitis media, severe treatment-resistant otomycosis, sensorineural hearing loss, benign paroxysmal positional vertigo, repeated epistaxis, lateral-cervical adenopathy, severe dysphagia, swallowing problems, laryngitis, and oral candidiasis have a low-level of tolerability, and because of this, patients with these conditions have a moderate DASS-21 Score.

4.3 Discussions and Conclusions for Study II

This study notes that the incidence of common malignancies is increasing in the elderly population, and radiation therapy remains the mainstay of treatment for some patients. These patients are considered immunosuppressed due to the existence of high radiotoxicity after treatment.

- The most frequently affected otorhinolaryngological sites in radio-treated neoplastic patients are the neck and the rhinosinusal level. In this study, pathologies such as deviated nasal septum, anterior epistaxis, acute and chronic rhinitis, and chronic rhinosinusitis were encountered at the rhinosinus level. In the neck, conditions such as laterocervical adenopathies, bleeding adenopathy blocks, inoperable tracheostomy, fistulas, peristomal granulation tissue, vocal cord paresis, oropharyngeal and laryngeal tumor formations predominated.
- The visual analog scale for the pain felt by the radio-treated neoplastic patient (VAS) when detecting ENT manifestations was approximately 5 points. After discharge from the ENT clinic, a score reduction of approximately 2-3 points was observed. The dominant symptom in the otorhinolaryngological sphere is pain, felt by the patient in a certain location, and for the ENT doctor, pain relief is very important in the therapeutic approach.
- There is a contextual correlation between the age of the neoplasm of the patient who underwent radiotherapy and other oncological therapeutics and the time of occurrence of otorhinolaryngological complications. Most of the patients had an age of the neoplasm less than 5 years, and the ENT manifestations in most of them appeared less than 1 year after radiotherapy in percentage 26.67% and between 1 and 5 years in 56.67 % of them.
- The analysis of the DASS-21 score for calculating the stage of depression, anxiety, and stress in radiation-treated neoplastic patients who had ENT diseases showed that most of

them go through mild depression in a percentage of 26.67%, moderate depression at 28% and depression at 24%.

5. Study III

Objectives

- Evaluation of various ENT manifestations of patients infected with the SARS-CoV 2 virus
- Establishment of ENT surgical treatment for post-Covid patients
- Analysis of the patient's evolution after ENT treatment by means of the VAS, DASS-21, FAS evaluation scales

5.1 Material and Method

Study III includes 73 immunosuppressed patients infected with SARS-CoV 2 virus who were cured and who presented ENT clinical complications and were treated for remission of ENT manifestations. Patients infected with COVID-19 were evaluated after ENT manifestations that were divided according to the site anatomically as follows: ear (otological headquarters), throat, oral cavity, and nose (rhinosinusal headquarters). All patients who presented to the ENT doctor during an acute bout of SARS-CoV 2 virus infection, or with a post-Covid condition who presented ENT manifestations associated with SARS-CoV 2 virus infection during June 2020, were included in the study - June 2022 in the ENT clinics of the Constanța Emergency Hospital, the Constanța County Emergency Clinical Hospital, the Colțea Clinic Hospital Bucharest and the CF Cluj-Napoca Clinical Hospital. The data were processed from the anamnesis, from the local ENT clinical examination, from the discharge letters and tickets, and the patient's clinical and therapeutic monitoring.

Inclusion criteria

+ Covid-19 positive patients with ENT manifestations

+ Patients with a positive Real Time PCR test

+ Covid-19 positive patients with clinical, paraclinical data that required additional ENT investigations

Exclusion criteria

- Patients with ENT manifestations without a positive Real Time PCR test

- Positive Covid-19 patients without complete clinical and paraclinical data

5.2 Results for Study III

ENT events headquarters

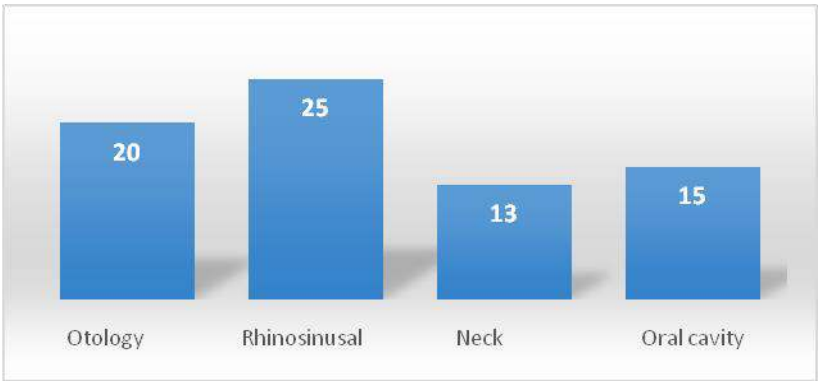


Figure 47 Graphical representation Column for the variable Location of ENT manifestations in patients from the study group

In my study, 73 patients infected with the SARS-CoV 2 virus who presented to the otorhinolaryngologist for complications were analyzed. It is observed that most of the patients had complications at the rhinosinusal level (34%). The second site of ENT manifestations in patients infected with the SARS-CoV 2 virus is the ear. The third site of ENT manifestations in patients infected with the SARS-CoV 2 virus is the oral cavity. At the level of the oral cavity, we have identified conditions such as acute tonsillitis, nasopharyngitis, peritonsillar phlegmons, oral candidiasis, oral thrush, xerostomia, etc. The fourth site of ENT manifestations of patients infected with the SARS-CoV 2 virus is the neck, in a smaller percentage (17.81%).

Distribution of post-Covid patients with ENT manifestations according to the value of the Visual Analog Scale for Fatigue.

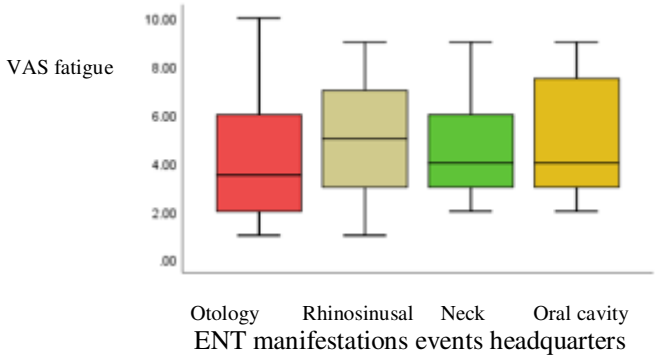


Figure 50 Box-plot graphic representation for the VAS fatigue score variable according to the categories of the variable Location of ENT manifestations in patients from the study group

It is noted that fatigue does not go away after the SARS-CoV 2 virus infection is cured. In our study, patients with post-Covid ENT manifestations completed a questionnaire that calculates the VAS score for fatigue. All patients who presented themselves in the ENT clinic stated that the fatigue persists even after being cured of COVID-19. Fatigue was classified as mild fatigue, moderate fatigue, and persistent severe fatigue. The highest degree of fatigue (score 10) was present in ENT pathologies of a rhinosinus nature such as acute and chronic sinusitis, nasal septum deviations, viral and hypertrophic rhinitis, and nasal polyps.

The location of ENT manifestations according to the associated conditions

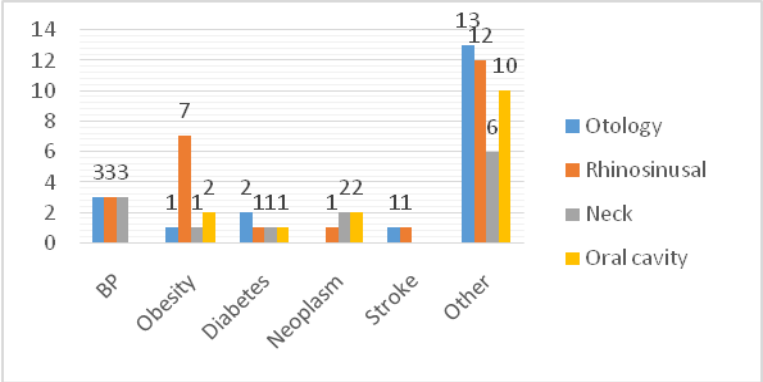


Figure 52 Graphical representation Column for the variable Associated diseases according to the categories of the variable Location of ENT manifestations in patients from the study group

We took into account the most important risk factors for death in confirmed cases of COVID-19 infection, namely cardiovascular diseases, chronic kidney diseases, cancers, diabetes, chronic lung diseases, chronic liver diseases, and severe neurological diseases. The study cohort included patients with otorhinolaryngological manifestations after recovery from the Covid-19 disease.

Distribution of post-Covid patients with ENT manifestations according to the percentage of vaccination for the 2020 SARS-CoV 2 pandemic virus

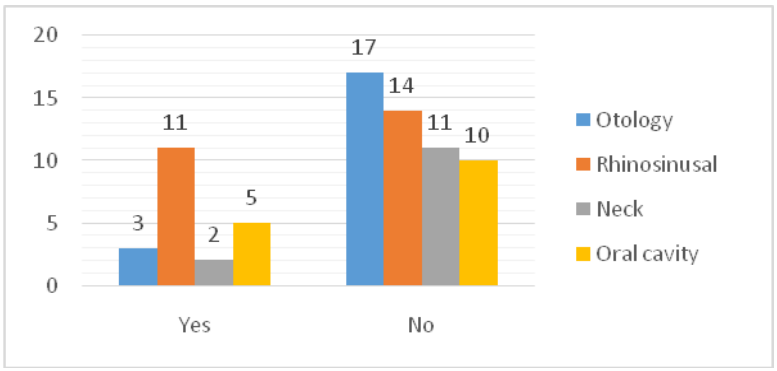


Figure 53 Graphical representation Column for the variable COVID vaccinated according to the categories of the variable Location of ENT manifestations in patients from the study group

In this study most patients were not vaccinated (71%). In the period after the imposed restrictions, ENT pathology was the usual one for patients who had access to consulting rooms. When presenting to the ENT clinic, the vaccinated patients had mild forms or were asymptomatic. Some of the vaccinated patients with a history of Covid-19 infection had otorhinolaryngological manifestations after the covalescence period. Strengthening immunity is essential for the prevention of otorhinolaryngological diseases.

Distribution of post-Covid patients with ENT manifestations according to acute disease severity

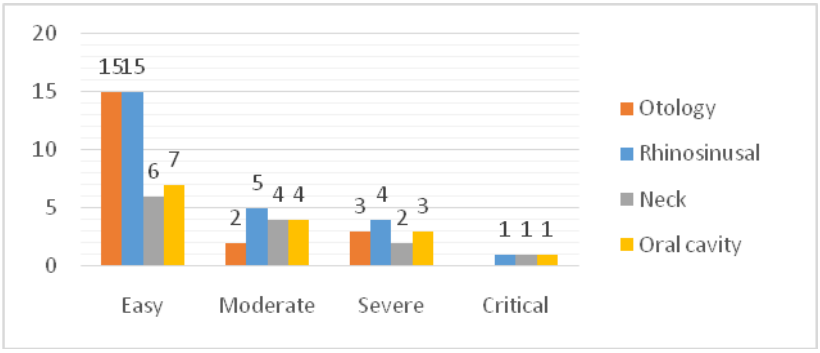
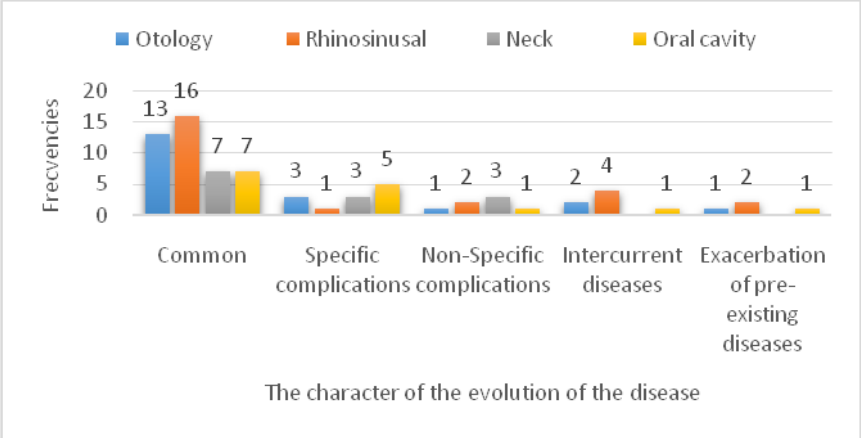


Figure 54 Graphical representation Column for the variable Severity of the disease according to the categories of the variable Location of ENT manifestations in patients from the study group

In this study, epidemiological investigations were analyzed and it was found from the anamnesis and ENT clinical examination that patients infected with the SARS-CoV 2 virus had mild, moderate, severe, and critical forms. From the point of view of the severity of the COVID-19 disease, most patients had a mild form, and compared to the anatomical headquarters in the ENT sphere, a large part of them presented for otological conditions (75%), followed by patients suffering from rhinosinusal nature (60%).

The distribution of post-Covid patients with ENT manifestations according to the nature of the evolution of the Covid-19 disease



The character of the evolution of the disease

Figure 56 Graphical representation Column for the variable Character of the evolution of the disease according to the categories of the variable Location of ENT manifestations in the patients of the study group

The patients were divided according to the otorhinolaryngological center according to the following evolutionary characteristics of SARS-CoV 2 virus infection: common infection, infection with specific complications, infection with non-specific complications, infection with intercurrent diseases, and infection with exacerbation of pre-existing diseases. Most of the patients in the study cohort were with common infections (58.9%). Exacerbation of pre-existing diseases such as high blood pressure, chronic heart failure, and cardiac arrhythmias were present in 5.5% of the patients in the study.

The distribution of post-Covid patients with ENT manifestations according to the time of onset of the conditions

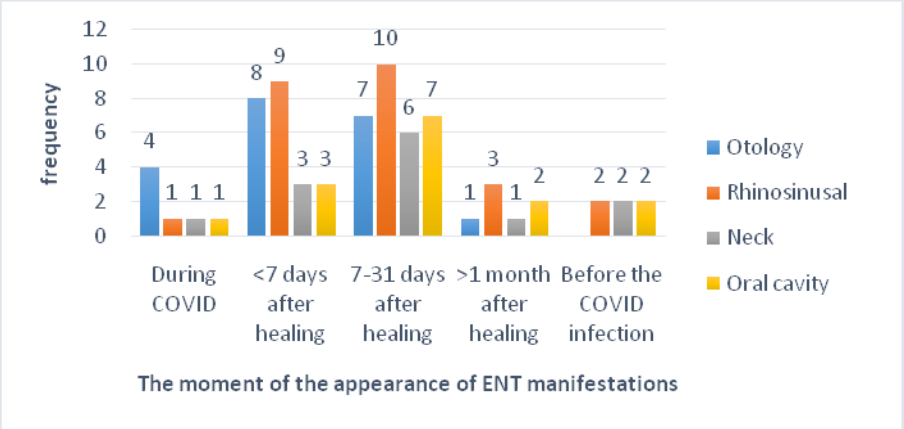


Figure 59 Graphical representation Column for the variable Time of onset of ENT manifestations according to the categories of the variable Location of ENT manifestations in patients from the study group

It was found that during SARS-CoV 2 virus infection, 9.6% of patients presented ENT complications. Previous epistaxis, suppurative acute otitis media, acute laryngitis, and peritonsillar phlegmon were observed at the ENT consultation. Most patients presented for ENT complications within the first 31 days after healing. Benign paroxysmal positional vertigo, acute sinusitis, etc. have been observed in these people.

Distribution of post-Covid patients with ENT manifestations according to the percentage of mortality

The mortality rate for patients with ENT manifestations infected with the SARS-CoV 2 virus is 1.4%. The patient died due to the unfavorable evolution of the neoplasm (stage IV B). SARS-CoV 2 infection did not complicate the evolution of the neoplastic patient's health.

The distribution of post-Covid patients with ENT manifestations according to the degrees of smell

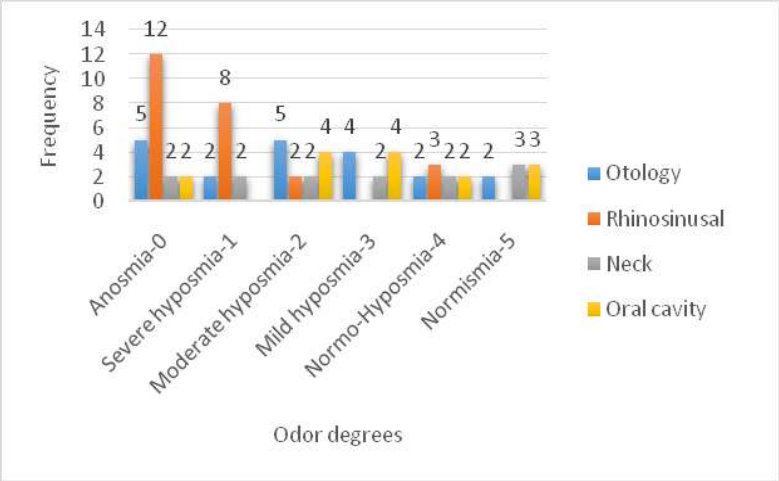


Figure 61 Graphical representation Column for the variable Degree of smell according to the categories of the variable Location of ENT manifestations in patients from the study group

In the study, it was observed that most patients with ear conditions had moderate anosmia and hyposmia. People with rhinosinusal disorders showed severe hyposmia and anosmia (32.48%). It was found that most patients who presented with neck complications had normal hyposmia or did not mention smell disturbances. It is also noted that patients with acute tonsillitis, peritonsillar phlegmons, canker sores, post-Covid glossitis, and pharyngitis reported mild and moderate hyposmia.

Distribution of post-Covid patients with ENT manifestations after surgical interventions

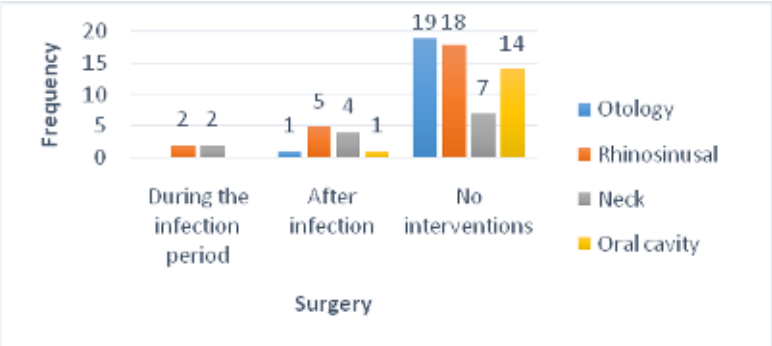


Figure 62 Graphic representation Column for the variable Surgical interventions according to the categories of the variable Location of ENT manifestations in the patients of the study group.

The surgical interventions that occurred after the cure of the COVID-19 disease are in the percentage of 20% for the rhinosinusal headquarters and 30% for patients with neck pathologies. It is observed that in 79.5% of patients no surgical treatment was instituted and long and well-targeted drug treatment was successful.

Distribution of post-Covid patients with ENT manifestations according to the Depression, Anxiety, and Stress Scale

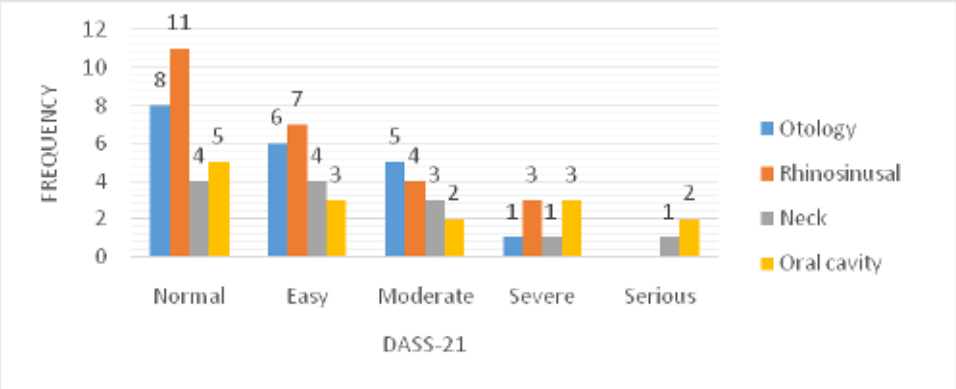


Figure 63 Graphical representation Column for the variable DASS-21 according to the categories of the variable Location of ENT manifestations in patients from the study group

In our study, 38.4% of patients cured of Covid-19 have a normal DASS-21 score. In this research, it is observed that patients with rhinosinusitis, although they have disturbances of smell and taste, are in a positive emotional state without developing depression. This study demonstrates that patients with a history of COVID-19 infection who presented with ear conditions have mild and moderate depression, anxiety, and stress. Most people with neck disorders have a mild to moderate DASS-21 score. Patients with ENT manifestations in the oral cavity who have a history of COVID-19 infection have mild, moderate, and severe depression in a percentage of 13-20%. The study identified some cases of patients with severe DASS-21 scores, having pathologies such as osteomyelitis, tonsillar cancer, severe dysphagia with xerostomia, and laryngeal squamous carcinoma.

Distribution of post-Covid patients with ENT manifestations after post-Covid lifestyle changes

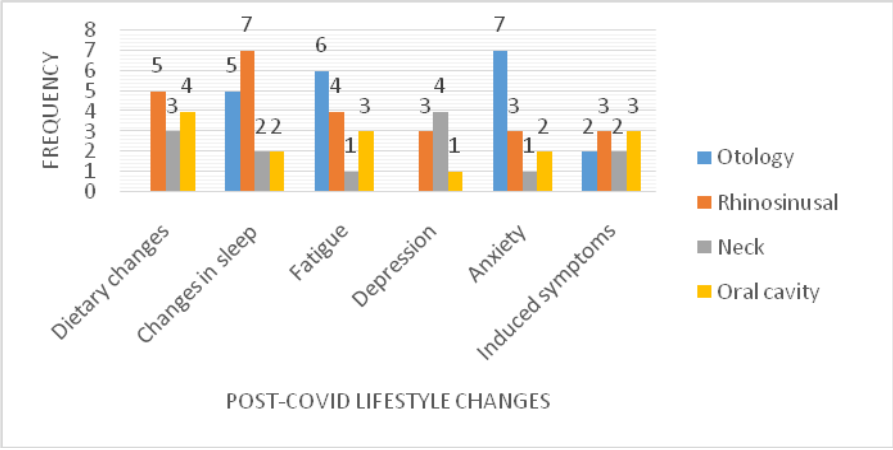


Figure 65 Graphical representation Column for the variable Changes in the post-COVID lifestyle according to the categories of the variable Location of ENT manifestations in patients from the study group

In this study, we grouped lifestyle changes into 6 categories: dietary changes, sleep changes, fatigue, depression, anxiety, and induced symptoms. Empirically, it was found that the patients who presented themselves in the ENT clinic had dietary changes in a percentage of 16.4%. Most of them presented complications at the level of the oral cavity (26.7%), at the level of the throat (23.1%), and at the level of the rhinosinus (20%). The ENT pathologies encountered had no connection with this lifestyle change. 21.9% of patients cured of the infection Covid-19 who presented to the ENT clinic presented with changes in sleep. Fatigue is felt in 19.2% of patients who had post-Covid ENT manifestations. Anxiety and depression were present in patients with ear and throat manifestations in 35% and 30.8%, respectively. In this study, it was observed that some of the patients (13.7%) generated induced symptoms such as cough, nausea, vomiting, dyspnoea, panic attacks, dysphagia and odynophagia, nasal obstruction, rhinosinusal, pharyngeal or esophageal foreign body sensation, without could make a concrete, local clinical, fibroscopic, endoscopic, paraclinical and imaging diagnosis.

5.3 Discussions and Conclusions for Study III

With the appearance of this virus, more and more patients with a history of infection with the SARS-CoV 2 virus presented themselves to the otorhinolaryngologist for the appearance of symptoms in this area.

The most common pathologies encountered in patients cured of Covid-19 were benign paroxysmal positional vertigo, acute purulent otitis media, otomycosis, acute otomastoiditis, oral thrush, tonsillitis, peritonsillar phlegmons, severe dysphagia, acute laryngitis, acute nasopharyngitis, sensorineural hearing loss, neuronitis, tinnitus, anterior epistaxis, chronic hypertrophic rhinitis, viral rhinitis, acute and chronic sinusitis, anosmia and hyposmia, xerostomia, dysgeusia and ageusia, glossitis, vocal cord paralysis.

The average age of patients with a history of COVID-19 infection with ENT manifestations is 48 years, 79.5% of them are from the urban environment, with a greater predominance for the female sex.

In this study, it was found that during infection with the SARS-CoV 2 virus, 20% of patients presented with ear conditions. Most patients presented for ENT complications in the first 31 days after healing. These patients presented benign paroxysmal positional vertigo,

acute sinusitis, viral rhinitis, anosmia, hyposmia, severe dysphagia, ageusia, xerostomia, oral thrush, and acute laryngitis. After one month of recovery from COVID-19 infection, 12% of patients presented rhinosinusal manifestations such as acute and chronic re-acute sinusitis, anosmia, hyposmia and 13% of the patients presented oral cavity conditions such as peritonsillar phlegmons, acute tonsillitis, xerostomia, ageusia, glossitis, severe dysphagia, vocal cord paralysis.

Patients with a history of SARS-CoV 2 virus infection diagnosed with ENT disorders such as benign paroxysmal positional vertigo, anosmia, hyposmia, xerostomia, ageusia, dysgeusia, severe dysphagia, sensorineural hearing loss, angina pectoris have an unfavorable evolution. The most frequent cases (64%) with unfavorable evolution are found in patients with rhinosinusal diseases due to periods of re-acuteness or persistent symptoms. Most of the time, 83.6% of patients developed acute forms.

Surgical interventions during the pandemic occurred in 5.5% of the patients in the study. The most common operations were laterocervical node biopsies and emergency tracheotomies. After the recovery of patients from COVID-19, surgical interventions occurred in 15.1% of patients presented with otorhinolaryngological complications.

In this study, the fatigue rating scale was carried out, which demonstrated that 37% of patients felt minimal fatigue after recovery from COVID-19 with a higher proportion of patients with ENT manifestations at the level of the throat, ear, and oral cavity. The average fatigue occurs in patients with rhinosinusal and ear manifestations, and severe fatigue is felt in 20.5% of patients with a history of COVID-19 who presented ENT complications. Fatigue is a trigger for changing the patient's lifestyle and emotional state.

In this study, it was observed that patients cured of the SARS-CoV 2 virus show significant lifestyle changes: diet, sleep, physical and mental state, emotional state, and cognitive disturbances. Dietary changes are presented in 16.4% of the patients in the study with a higher proportion in those with manifestations in the nose, throat, and oral cavity.

6. GENERAL CONCLUSIONS

1. The study of the particularities of the development of ENT diseases with the state of the immune system represents a challenge that generated this research.
2. The state of the immune system, in patients with acquired immunodepression (HIV), or therapeutically induced (radio/chemotherapy), can cause specific conditions in the ENT

sphere, such as oropharyngeal candidiasis, hairy leukoplasia of the tongue, regional adenopathies.

3. In the absence of a known immunological diagnosis, they can represent the moment of detection and diagnosis of a state of immunodepression, including the ENT specialist in the multidisciplinary assistance team of these patients.
4. Studies show that the severity of ENT conditions is not influenced in cases of therapeutically controlled immunosuppression, instead, the duration of convalescence and healing increases.
5. The therapeutic approach of the ENT patient known to be immunosuppressed must optimize the interference between the therapy specific to the organ condition (invasive or non-invasive) and the concomitant therapies (antiretroviral therapy, respectively oncological therapy).
6. The most common ENT complications in patients infected with HIV are persistent oral candidiasis, laterocervical adenopathies, acute tonsillitis, acute and chronic rhinosinusitis, ear otomycosis, acute suppurative otitis media, hairy leukoplakia of the tongue.
7. The most common surgical interventions for HIV-positive patients in this study were biopsies of cervical adenopathy, endoscopic maxillary antrostomies for chronic sinusitis, and tonsillectomy for recurrent purulent angina.
8. Post-radiotherapy mucositis in patients with head and neck neoplasms must be treated with special attention and permanent monitoring of patients, as they represent a possible severe complication.
9. Conditions such as laterocervical adenopathies, bleeding adenopathy blocks, inoperable tracheostomy, fistulas, peristomal granulation tissue, vocal cord paresis, oropharyngeal and laryngeal tumor formations predominated in the neck.
10. The diseases in the otorhinolaryngological sphere had as a cardinal symptom the pain, felt by the patient in a certain location, the evaluation of its intensity and its improvement being important in the therapeutic conduct.
11. The visual analog scale for the pain felt by the radio-treated neoplastic patient (VAS) when detecting ENT manifestations was approximately 5 points. The specialized therapeutic cure determined the relief of pain and implicitly, the improvement of the quality of life, the score being approximately 2-3 points.
12. The most frequent neoplasms that also developed ENT manifestations were those located proximally: laryngeal, oropharyngeal, and oral floor neoplasms. I have recorded it. also, ENT manifestations associated with bronchopulmonary, breast, cervical, and colon neoplasms

13. The emergence of the SARS-CoV 2 virus, which triggered the COVID 19 pandemic, has increased the addressability of patients who have passed the disease to the otorhinolaryngologist for the development of symptoms in this sphere since the onset of the disease.
14. Due to the effects on immunity determined by the SARS-CoV 2 virus (autoimmunity phenomena), patients diagnosed with ENT complications such as benign paroxysmal positional vertigo, anosmia, hyposmia, xerostomia, ageusia, dysgeusia, severe dysphagia, sensorineural hearing loss, angina a dragging evolution, difficult to control therapeutically.
15. Of the total ENT clinic presentations, pandemic surgery was 5.5% for patients in the study group. The most common operations were biopsy of the lateralocervical ganglia and emergency tracheotomies. After curing patients of Covid-19, surgery occurred in 15.1% of patients with otolaryngological complications.
16. In patients cured by COVID 19, significant lifestyle changes occurred: nutrition, sleep, physical and mental state, emotional state, cognitive disturbances, due to conditions with an impact on their quality of life such as neurosensory hypoacusis, tinnitus, otomycosis, severe dysphagia, aggressive angina and phlegmons, chronic respiratory failure.
17. Cough, dysphagia, dizziness, headache, nausea and vomiting, nasal obstruction, dysgeusia, tinnitus, hypoacusis, are some signs and symptoms that can induce variable degrees of depression, for which the patient presents to the otolaryngologist during the convalescence period.
18. The studies carried out reveal the new position of the ENT doctor in current medicine, more involved in deeper knowledge of the patient, in the initially complex assessment, especially of the immune status, this is a decisive fact of an optimized conduct with maximizing the therapeutic efficiency.
19. Developing the Guide for specialists in the field is an important step in the multidisciplinary approach of ENT pathology, by facilitating an early diagnosis and a prompt attitude.

Considering all these aspects discussed in the doctoral thesis, taking into account the complexity of the immunosuppressive disease, the data that are necessary to be able to treat such a patient medically or surgically, the multidisciplinary team that is needed (the otolaryngologist, the infectious disease doctor, the anesthetist, the oncologist, the radiotherapist, the radiologist, the laboratory doctor and the psychotherapist), we considered it necessary to design an ENT guide for the immunosuppressed patient.

7. Elements of originality of the thesis

1. The work represents the first research dedicated to the analysis of ENT pathology aspects in patients with immune system impairment (immunodepression, immunotolerance, etc.);

2.The pandemic context favored the assessment of the impact of SARS-CoV 2 infection and specific vaccination in ENT pathology.

3. It is the first approach to the impact of ENT pathology on patients' quality of life;

4. The thesis materialized in the development of the first Illustrated Guide to ENT conditions in patients with immunodepression, dedicated to fellow Otorhinolaryngologists, but equally to other specialists.

8. LIST OF PUBLICATIONS

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