RESEARCH
www.commprac.com
ISSN 1462 2815

MICROBIOLOGICAL CHARACTERISTICS OF THE DISEASE IN PATIENTS WITH CHRONIC PURULENT OTITIS MEDIA - URGENCH BRANCH OF TASHKENT MEDICAL ACADEMY

Esamuratov Aybek Ibragimovich[1], Karimova Maksuda Ahmedjanovna[2]*, Sultanov Bekhzod Olimoyich[3], Olimova Madinabonu Maxmudovna[4] and Ortiqov Bobomurod Baymamatovich[5]

[1] Head of Department Otorphinolaryngology and Ophthalmology, Al-Khorazmiy St 28, Urgench City, Uzbekistan.
[2] PhD, Assistant, Department of Microbiology, Al-Khorazmiy St 28, Urgench City, Uzbekistan. *Corresponding Author E-Mail: ms.karimova86@mail.ru
[3] Assistant, Department of Otorphinolaryngology and Ophthalmology, Al-Khorazmiy St 28, Urgench City, Uzbekistan.
[4] Student, Urgench Branch of the Tashkent Medical Academy, Al-Khorazmiy St 28, Urgench City, Uzbekistan.
[5] PhD, Assistant, Tashkent Medical Academy, Farobiy st 2, Tashkent city, Uzbekistan.

DOI: 10.5281/zenodo.8365647

Abstract

The main goal of the research was to analyze the etiological and pathogenetic characteristics of the disease and to evaluate and scientifically substantiate the main factors of the type of microbe, growth pattern, environmental resistance in the development of the disease. According to our data, polyresistant strains of *S.aureus* and *Ps.aeruginosa* are the main cause of inflammation in the middle ear cavities. The microorganisms that grew at the highest level were *S. aureus* 59.3%, 45.1% and 49.7% in all three groups, *S. epidermidis* 16.3%, 38.2% and 32.1% respectively, and *Ps.aeruginosa* was observed in 24.1%, 16.7% and 18.2% of strains. In the obtained results, it was clearly determined that the incidence of *Pseudomonas aeruginosa* was 46.6% in mesotympanitis and 79.7% in epitympanitis. The same situation was observed in *Staphylococcus aureus* , in which it was 43.9% in mesotympanitis and 55.3% in epitympanitis. According to the results of determining the sensitivity of microbes to antibiotics, the change of *P.aeruginosa* strain isolation (IPM_10IU) 59.0%, to meropenem (MEM_10 IU) 71.0%, to ceftazidime (CAZ_10 IU) 69.0%, to amikacin (AMK-30 IU) 46.0%, to ciprofloxacin. (CIP-5 IU) was 78.0% and levofloxacin (LVX-5 IU) - 77.0%.

Keywords: Chronic Purulent Otitis Media, Microflora in the Middle Ear Cavity, Pseudomonas Aeruginosa, Staphylococcus Aureus, Sensitivity to Antibiotics.

INTRODUCTION

Chronic inflammation of the middle ear threatens intracerebral complications, mainly develops around chronic suppurative otitis media (CSO), requires in-depth study and urgent assistance, first of all, to adopt and develop effective measures for the prevention and treatment of the disease. In chronic purulent otitis media, microbiological diagnosis is appropriate for prevention of disease risk factors, early diagnosis, and improvement of the effectiveness of therapeutic and surgical treatment.

Chronic inflammation of the middle ear threatens intracerebral complications, mainly develops around chronic suppurative otitis media (CSO), requires in-depth study and urgent assistance, first of all, to adopt and develop effective measures for the prevention and treatment of the disease. In chronic purulent otitis media, microbiological diagnosis is appropriate for prevention of disease risk factors, early diagnosis, and improvement of the effectiveness of therapeutic and surgical treatment.

Factors that directly affect the course of acute purulent processes in the middle ear and cause the continuation of purulent inflammation in the whole body are important in the pathogenesis of chronic purulent otitis media (CPOM) [5, 11, 15, 20]. The upper respiratory tract, for example, adenoids, nasal septum curvature, chronic sinusitis, and hypertrophic rhinitis play an important role in the development of CPOM. The observed violation of the drainage and ventilation function of the auditory tube leads to the difficulty of evacuation of the existing tympanic cavity and the violation of aerosion of the middle ear cavity. This, in turn, prevents normal healing of the eardrum perforation after acute purulent otitis media, which leads to the formation of persistent perforation [12].

CPOM is an infectious condition, and is formed more often in childhood after measles, scarlet fever, and influenza [14, 17, 16, 18, 21]. These causes of the disease are observed in almost 75-80% of patients. For a long time, the main mechanism of the development of CPOM and the reason for its sudden transition have been recognized as foci of purulent infection, which formed distant parts of the middle ear and were not directly treated due to their topographical-anatomical absence [1, 2, 3, 6, 7].

Many microbes detected in the middle ear cavity are pathogenic. According to most authors, the main etiological factors in the development of purulent otitis media are bacterial and fungal proliferation of the middle ear cavity [4, 8, 9, 10, 13, 14, 19].

MATERIALS AND METHODS

After the diagnosis of CPOM, microbiological examination of the pus from the middle ear was taken from all patients admitted to the hospital, and samples from the tympanic cavity and antrum were also taken for examination during the sanitizing surgery of the ear.

Microbiological methods included the study of the species composition of the microflora taken from the ears in solid nutrient media, and after the identification of the isolated microflora by species, the sensitivity of different groups to antibiotics was checked by the method of diffusion on agar with standard indicator discs.

Microaerophilic conditions were created using 100% CO_2 for the preparation of streptococci and hemophilic bacillus cultures.

Also, smears were taken from the causative agent on the mucous membrane of the nasopharynx and nasal cavity to determine how its characteristics changed after treatment.

Treatment procedures were carried out in accordance with the standard of specialized medical care: antibiotic treatment, catheterization of the auditory tube (before ear drum perforation in cases of otitis media), transtympanic driving of drugs aimed at bacterial treatment (after ear drum perforation or paracentesis), vascular therapy (accompanying neurosensory deafness cases), in 20% of cases unilateral or bilateral tympanic cavity shunting was performed.

Microflora in the middle ear cavity was examined and its resistance to antibiotics was evaluated in order to evaluate the etiological significance of the microbial infection in all patients and obtain scientific results.

RESULTS AND THEIR DISCUSSION

The qualitative and quantitative composition of the microbial landscape and the degree of colony growth are presented in Table 1.

Table 1: Features of the microbial landscape depending on the degree of the inflammatory process in the middle ear

T/ r	From the middle ear separate received microbes	Group I (n=97)	Group II (n=79)	Group III (n=41)
1	*S. aureus*	59.3%	45.1%	49.7%
2	*S. epidermidis*	16.3 %	38.2%	32.1%
3	*Str. haemolyticus*	8.1%	16.4%	2.7%
4	*Str. pyogenes*	2.3%	2.7%	5.26%
5	*H. influenzae*	6.2%	5.8%	14.5%
6	*S. pneumonia*	2.6%	1.3%	1.96%
7	*Ps. aeruginosa*	24.1%	16.7%	18.2%
8	*E.coli*	10.3%	8.1%	10.7%
9	*Str. mitis*	3.1%	0.8%	2.7%
10	*Aspergillus* fungi	4.2%	5.8%	12.3%

Note: Statistically significant values, $p<0.05$

As can be seen from Table 1, patients diagnosed with chronic purulent otitis are divided into three groups depending on their clinical form. Patients diagnosed with mesotympanitis were included in group I (97 patients), and patients diagnosed with mesoepitympanitis and epitympanitis were included in group II (79 patients).

In the samples cultured in the established clinical groups, the growth rate of bacteria in *Str.pyogenes, Str.pneumonia* and *Str.mitis* was very low compared to other pathogens in all three groups (2.3% - 2.7% - 5, in groups I, II and III). 2%; 2.6% - 1.3% - 1.9%; 2.6% - 1.3% -1.9% and 3.1% - 0.8% - 2.7% suitable without). For this reason, they are of great importance to patients.

As it can be seen from the obtained analysis, the cultures of all strains were not the same, including the highest growth microorganisms *S. aureus* (59.3%, 45.1%, 49.7% in all three groups), *S. epidermidis* (16.3 %, 38.2 %, 32.1 %) and *Ps.aeruginosa* (24.1 %, 16.7 % and 18.2 %) strains were observed. Other different types of microorganisms were grown at different levels, namely, *Str.haemoliticus, E.coli, H.influenzae* (8.1% - 16.4% - 2.7%); H. influenzae (6.2% - 5.8% - 14.5% in appropriate cases).

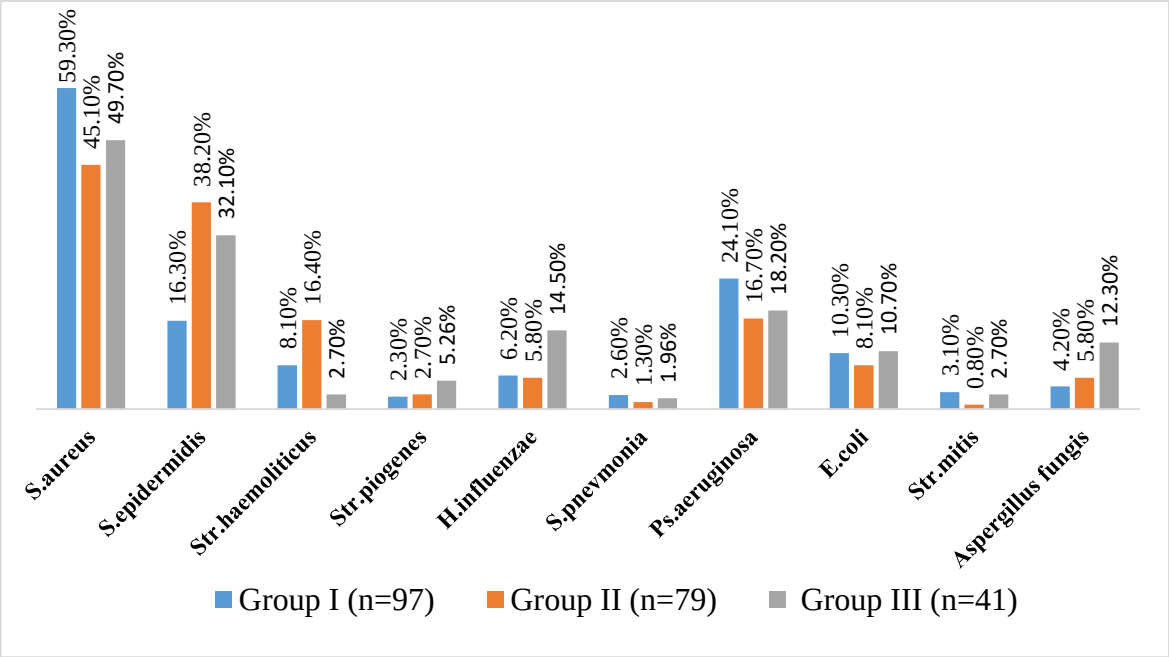

Fig 1: The results of the reproduction of microorganisms depending on the different clinical forms of chronic purulent otitis media

As can be seen from Figure 1, among the microorganisms of clinical importance, *S. aureus* was cultivated (59.3%, 45.1%, 49.7% in all three groups), the real causative agent of otitis media in its purulent forms, and *Ps.aeruginosa* (24.1%, 16.7% and 18.2%) and *E.coli* (10.3%, 8.1% and 10.7%) are seen and are the main causative agents.

Among the three clinical forms of purulent otitis media, in the results of the analysis for the comparative analysis of microorganisms, *S. aureus* (see Figure 2) was found in 59.3% of patients diagnosed with mesotymponitis in the first group, 49.7% in the group with epitympanitis (group III), and mesoepitympanitis in the second group stood out in 45.1%.

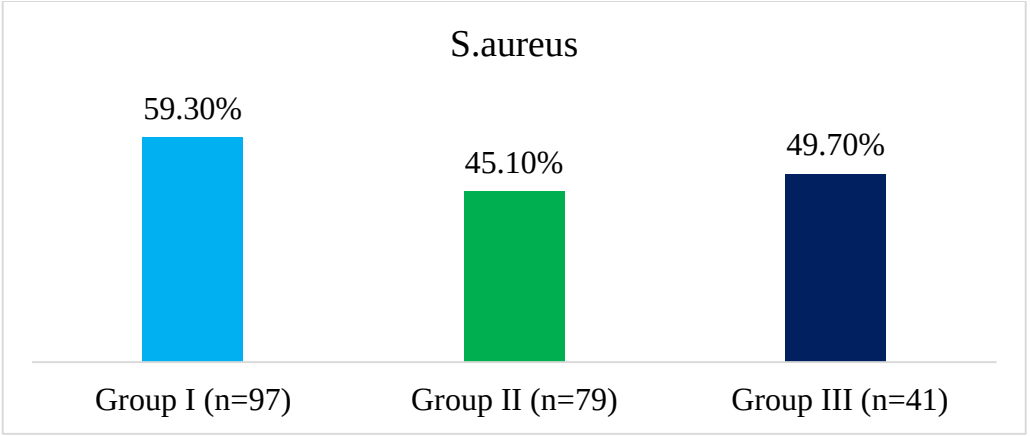

Fig 2: The results of the growth of seedlings depending on the clinical forms of *S.aureus* purulent otitis media

The middle ear of the three different clinical forms, the next most common clinically important pathogen cultured from purulent contents is *Ps.aeruginosa* (Fig. 3).

Thus, among the three clinical forms of purulent otitis, *Ps.aeruginosa* was the most common in the mesotymponitis form - 27.1%, and in the epitympanic form - 18.2% and in the mesotymponitis form - 16.7%.

In the analysis of secretions, it can be seen from the results of the analysis of *E.coli secretion among the three clinical forms that E.coli* was in the same proportion, in the mesotymponitis form - 10.3% and in the epitympanitis form - 10.7% (Fig. 4).

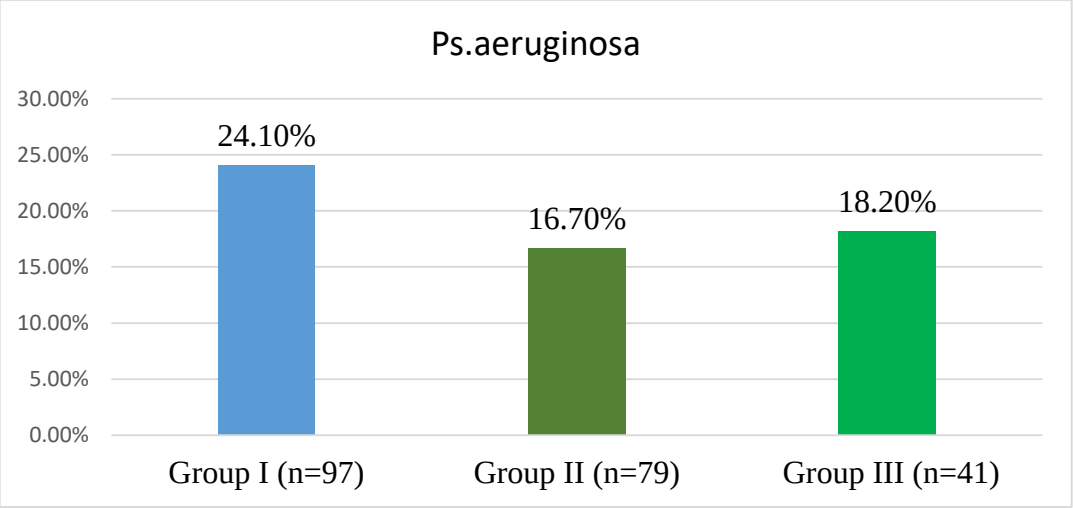

Fig 3: Growth rate of *Ps.aeruginosa* depending on the clinical forms of purulent otitis media

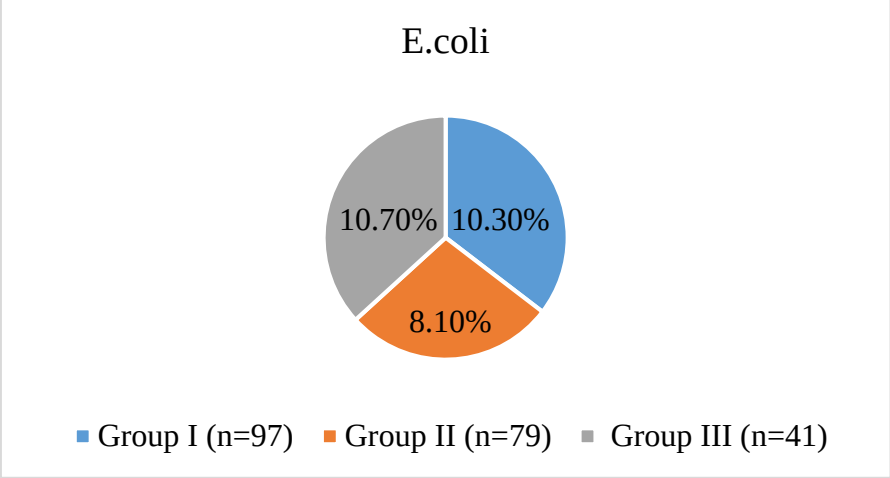

Fig 4: Growth rate of *E.coli microbe* , taking into account the clinical forms of purulent otitis media

Next, we aimed to study the growth of the groups of microorganisms in the above returned nasal cavity, and the following results were obtained from us, and these results are presented in Table 2.

Table 2: The growth rate of microorganisms taken from the nose by groups

T/ r	Microorganisms	Group I (n=97)	Group II (n=79)	Group III (n=41)
1	*S. aureus*	27 , 6%	18.0%	43.0%
2	*Ps. aeruginosa*	10.5%	22.0%	37.0%
3	*S. epidermidis*	12.5 %	11.6%	13.5%
4	*E.coli*	9.2%	8.1%	10.7%
5	*Str. pneumonia*	7.8%	6.0%	9.3%
6	*Str. haemolyticus*	7.7%	6.1%	9.2%
7	*Str. viridans*	6.5%	4.3%	8.5%
8	*Str. sangius*	5.2%	7.0%	10.2%
9	*S. saprophyticus*	2.9%	4.1%	5.0%
10	*Candida*	3.9%	2.3%	4.5%
11	*Str. mitis*	3.2%	3.4%	4.9%
12	*Str. salivarius*	1.9%	2.0%	4.1%

As can be seen from Table 2, the most common microorganisms in nasal swabs are *S. aureus* (in all three groups 27.6%, 18.0%, 43.0%), *Ps.aeruginosa* (10.5%, 22.0% and 37.0%) and *E.coli* (9.2%, 8 .1% and 10.7%).

Thus, the isolated *S.aureus* was 59.3% of the purulent contents of the middle ear isolated from the patients with mesotympanitis, and it was half less and 27.6% of the contents of the nose.

S. aureus was isolated from purulent contents of the middle ear (45.1%) and nasal contents (18.0%) in the mesoepitympanic form of the disease, it was also isolated from the nose twice as often.

At the same time, the detection of *S. aureus* in secretions from purulent contents of the middle ear (49.7%) and from the contents of the nose (43.0%) in patients with epitymponitis of the middle ear disease showed that this type of pathogen was released in the same amount (Fig. 5)

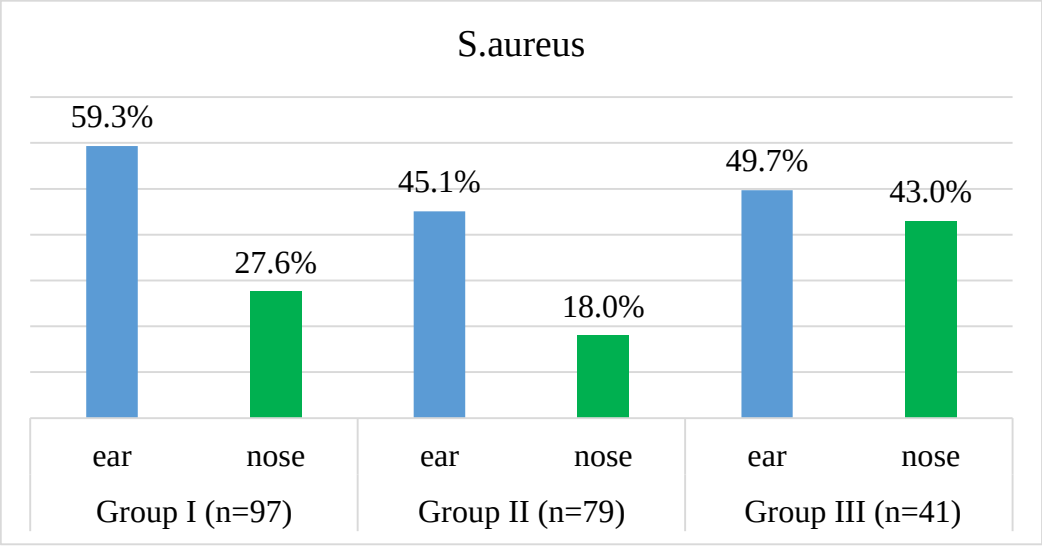

Fig 5: Comparative analytical results of *S.aureus* isolates from various clinical forms of chronic purulent otitis media depending on the type of biological material

Ps.aeruginosa isolation in biological material obtained from different clinical forms of purulent otitis media are presented in Figure 6.

According to the results of the comparative analysis of *Ps.aeruginosa secretions, depending on the pus composition in patients with different clinical forms of chronic purulent otitis media, the increase in Ps.aeruginosa pus secretions of the ear and nose in patients with various clinical* forms of chronic purulent otitis media shows that the increase in Ps.aeruginosa led to the worsening of the clinical signs and course of chronic purulent otitis media (Figure 6).

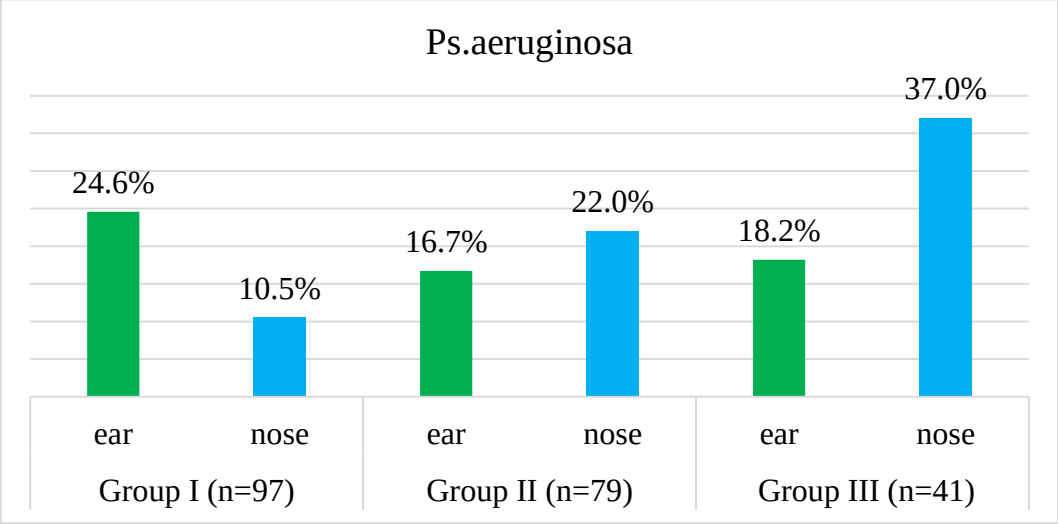

Fig 6: Comparative analysis of *Ps.aeruginosa isolation* in biological material obtained from different clinical forms of purulent otitis media

Thus, in patients with mesotympanitis, 24.1% and 10.5% of the purulent contents of the ear and nose, respectively, in the discharge of purulent discharge from the ear of a patient with mesoepitympanitis, Ps.aeruginosa was 18.0%, and Ps.aeruginosa was 22% in the discharge *from* the *nose*,0%, and in epitympanitis *Ps.aeruginosa* purulent secretions in the ear accounted for 49.7%, nasal secretions for 37.0%. This type of microorganism can be considered as the causative agent of the screening and, as a result of the separation of purulent content from the nose and ears, the disease can intensify the process by transitioning from mesotympanitis to epitympanitis.

A comparative analysis of *E.coli secretion* in patients with various clinical forms of chronic purulent otitis media depending on the purulent content of the ear and nose revealed the following (Figure 7), the release of this type of microorganism from the ear or nose created conditions for aggravating the clinical presentation of the disease.

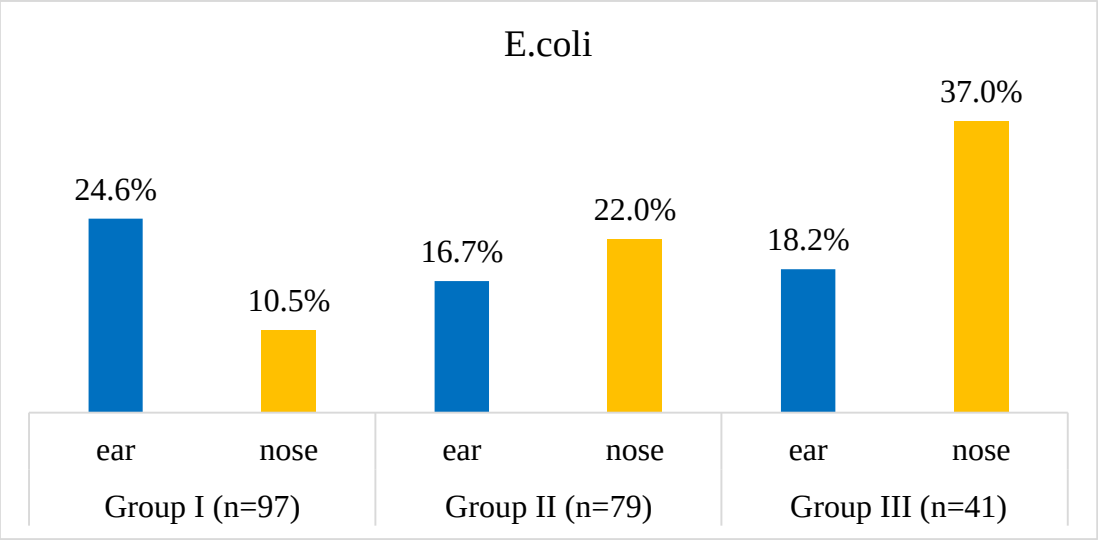

Fig 7: Comparative analysis of the isolation of *E.coli* depending on the type of biological material in different clinical forms of chronic purulent otitis media

In addition, in the isolated microorganisms, we studied the sensitivity to antimicrobial drugs by the disco-diffusion method. We evaluated the results based on the international EUCAST method for assessing the sensitivity of microorganisms to antimicrobial drugs.

Analysis of the sensitivity of microorganisms to antimicrobial drugs is clinically important *S.aureus, Ps.aeruginosa* and *E.coli.* carried out by microorganisms.

In the examination of microorganisms isolated to antibiotics, we separately investigated types of mesotympanitis and epitympanitis, which are clinically more difficult, of chronic purulent otitis media.

Table 3 shows the sensitivity results of *S. aureus isolated from patients diagnosed with mesotympanitis.*

In the EUCAST guideline dated 01-01-2020, version 10, in the evaluation of the susceptibility of staphylococci to cephalosporins, cefoxitin (FOX), cefixime, ceftazidime, ceftazidime-avibactam, ceftibuten and ceftolozane-tazobactam are prohibited in the treatment of staphylococci.

Table 3: Susceptibility of *S.aureus strains* isolated from patients diagnosed with mesotympanitis

Antimicrobial drugs	No	*S. aureus*		
		R %	I %	S %
FOX	57	20.0	0.0	80.0
CIP	57	7.0	0.0	93.0
LVX	57	4.0	0.0	96.0
LIGHT	57	12, 0	0.0	88.0
MOX	57	6.0	0.0	94.0
ERY	57	22.0	0.0	78.0
CLI	57	16.0	2.0	82.0
LNZ	57	1.0	0.0	99.0
RIF	57	1.0	0.0	99.0

S. aureus to antibiotics belonging to the fluoroquinolone class, ciprofloxacin, levofloxacin, norfloxacin and moxifloxacin were used in discs, and the antimicrobial resistance of *S. aureus* strains between them ranged from 4.0% to 12.0%.

To determine the sensitivity of *S.aureus* strains to antibiotics of the class of macrolides, a screening test such as erythromycin was used to evaluate the sensitivity to azithromycin, clarithromycin, roxithromycin.

Also, in the assessment of inducible resistance to clindamycin, antagonism between clindamycin macrolides and erythromycin can be determined. If antagonism is not detected, the isolate is evaluated according to the clinical cutoff values. In this regard, *S.aureus* strains were 22% resistant to macrolides, 99% sensitive to linezolid and rifampicin.

At the next stage, we analyzed the susceptibility of *S.aureus* strains isolated from patients with epitympanitis *(Table 4).*

Table 4: Susceptibility results of *S.aureus* strains isolated from patients diagnosed with epitympanitis

Antimicrobial drugs	No	*S. aureus*		
		R %	I %	S %
FOX	20	33.0	0.0	67.0
CIP	20	16.0	0.0	84.0
LVX	20	19.0	0.0	81.0
LIGHT	20	17.0	0.0	83.0
MOX	20	14.2	0.0	85.8
ERY	20	18.0	0.0	82.0
CLI	20	11.0	4.0	85.0
LNZ	20	0.0	0.0	100.0
RIF	20	1.0	0.0	99.0

In the chronic purulent form of epitympanitis, the proportion of *S. aureus* MRSA strains increased to 33.0%. We also found *that S. aureus* increased sensitivity to fluoroquinolone antibiotics in 14.2% to 19.0% of cases, respectively.

S.aureus strains are 100.0% and 99.0% sensitive to linezolid and rifampicin, respectively, is microbiologically evaluated, which is the basis for organizing the treatment in an efficient manner.

Thus, it appears that *S. aureus* strains isolated from patients diagnosed with epitympanitis have a more widespread susceptibility (Figure 7) than *S. aureus* strains isolated from patients diagnosed with mesotympanitis.

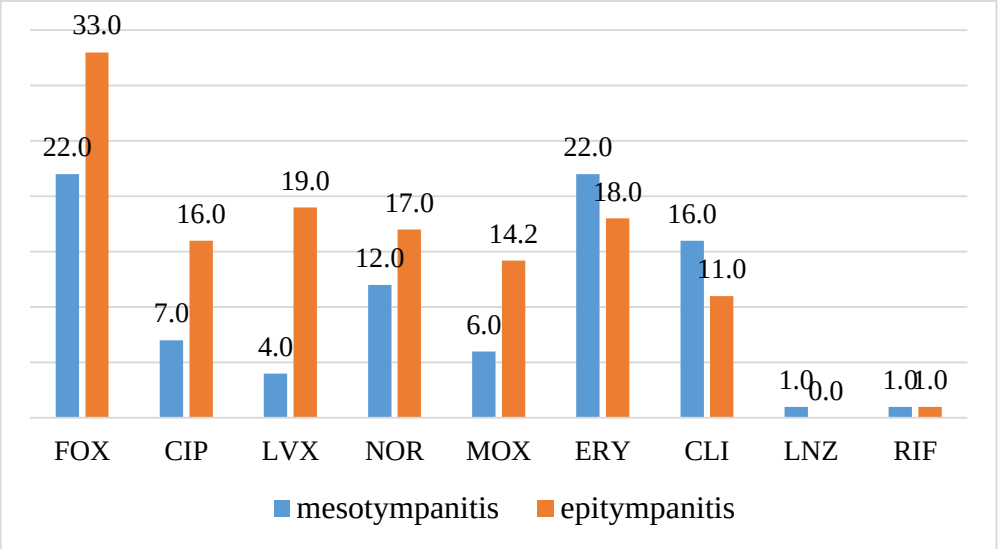

Fig 8: Comparative analysis of susceptibility of *S. aureus* from ear swabs of patients with chronic suppurative otitis media to antimicrobial drugs

Later, we analyzed the strains of *P.aeruginosa* in the secretions of patients diagnosed with mesotympanitis and epitympanitis, and the results are presented in Table 5.

As can be seen from the data presented in Table 5, the information on the sensitivity of *Ps.aeruginosa* to antibiotics is presented, and the table shows the characteristics of sensitivity to four antimicrobial drugs tested (amikacin (AMK -30IU) - 25, taking into account the high sensitivity of *Ps.aeruginosa* strains*)* 0%, imapenem (IPM -10 IU) – 48.0%, meropenem (MEM -1 IU) –50.0%, ceftazidime (CAZ -1 IU) – 64.0%, piperacillin-tazobactam (TZP -36 IU) – 65.0%, piperacillin (PIP -30 IU) - fluoroquinolones 62.5%, in particular ciprofloxacin (CIP -5 IU) – 69.0% and levofloxacin (LVX -5 IU) – 75.0%.

Table 5: Susceptibility of *P.aeruginosa strains* from ear swabs of patients diagnosed with mesotympanitis

Antimicrobial drugs	No	S%	I %	R %
PIP	23	37.5	0.0	62.5
TZP	23	35.0	0.0	65.0
CAZ	23	36.0	0.0	64.0
IPM	23	52.0	0.0	48.0
MEM	23	50.0	0.0	50.0
AMK	23	75.0	0.0	25.0
CIP	23	31.0	0.0	69.0
LVX	23	25.0	0.0	75.0

It can be seen that ciprofloxacin and levofloxacin have high sensitivity to fluoroquinolone-containing antibiotics.

Table 6 *P.aeruginosa* isolated from patients diagnosed with epitymponitis data on the sensitivity of strains, as well as *P.aeruginosa* isolated from patients diagnosed with mesotympanitis strains and *P.aeruginosa* strains isolated from patients diagnosed with epitympanitis had semi-permanent sensitivity.

Table 6: Susceptibility results of *P.aeruginosa* strains isolated from patients diagnosed with epitympanitis

Antimicrobial drugs	No	S%	I %	R %
PIP	8	50.0	0.0	50.0
TZP	8	33.0	0.0	67.0
CAZ	8	31.0	0.0	69.0
IPM	8	41.0	0.0	59.0
MEM	8	27.0	2.0	71.0
AMK	8	54.0	0.0	46.0
CIP	8	22.0	0.0	78.0
LVX	8	23.0	0.0	77.0

At the same time, patients diagnosed with epitympanitis and change in *P.aeruginosa* strain isolation (IPM_10IU) 59.0%, meropenem (MEM_10 IU) 71.0%, ceftazidime (CAZ_10 IU) 69.0%, amikacin (AMK-30 IU) 46.0% , ciprofloxacin (CIP-5 IU) was 78.0% and levofloxacin (LVX-5 IU) - 77.0%.

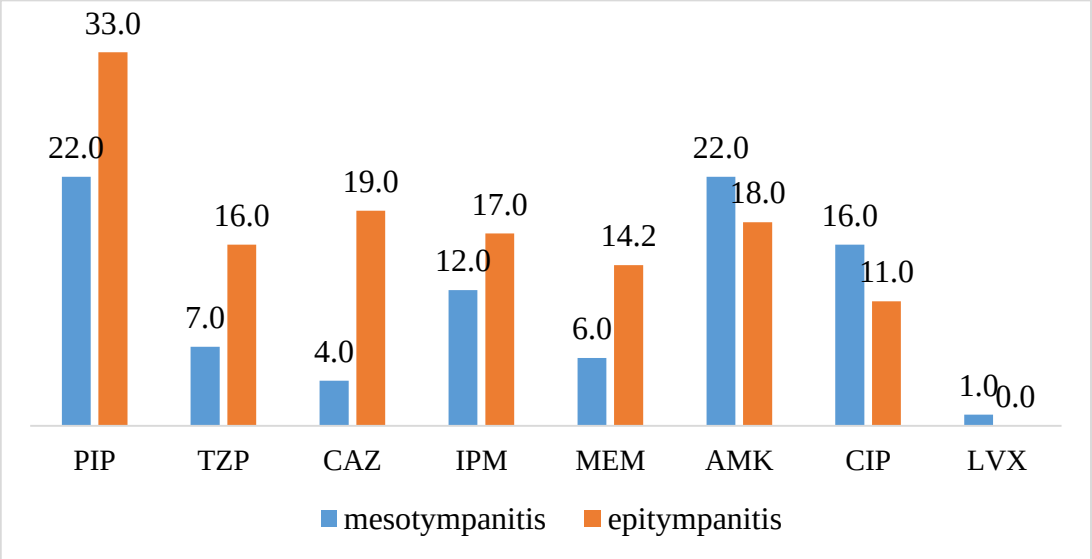

Fig 9: Comparative analysis of antimicrobial susceptibility of P.aeruginosa isolated from patients with chronic suppurative otitis media.

Thus, depending on the severity of the clinical form of CPOM, the cultivation rate of resistant *P.aeruginosa* strains increases.

CONCLUSIONS

1. In the control groups, the growth rate of bacteria in *Str.pyogenes, Str.pneumonia* and *Str.mitis* is very low in all three groups compared to other pathogens in groups I, II and III 2.3% - 2.7% - 5.2 %; 2.6% - 1.3% - 1.9%; 2.6% - 1.3% - 1.9% and 3.1% - 0.8% - 2.7%, respectively, were of great importance to patients.
2. Plantings were not the same in all the researched strains, including the highest growing microorganisms *S.aureus* in all three groups 59.3%, 45.1% and 49.7%, *S.epidermidis* respectively 16 , 3%, 38.2% and 32.1% and *Ps.aeruginosa* 24.1%, 16.7% and 18.2% were observed. Along with the growth of other types of microorganisms at different levels, *Str.haemoliticus, E.coli, H.influenzae* (8.1% -

16.4% - 2.7%); H. influenzae (6.2% - 5.8% - 14.5% in appropriate cases) was returned.

3. *In patients with isolated S.aureus,* there is twice as little discharge from the nose after the diagnosis of mesoepitympanitis from purulent contents of the middle ear (45.1%) and nasal contents (18.0%), as well as in patients with epitymponitis of the middle ear. The detection *of S.aureus in secretions* from purulent contents (49.7%) and nasal contents (43.0%) showed the same amount of this type of pathogen.
4. Patients diagnosed with epitympanitis and changes in *P.aeruginosa* strain isolation (IPM_10 IU) 59.0%, meropenem (MEM_10IU) 71.0%, ceftazidime (CAZ_10 IU) 69.0%, amikacin (AMK-30 IU) 46.0%, to ciprofloxacin (CIP-5 IU) was 78.0% and levofloxacin (LVX-5 IU) - 77.0%.

References

1) Agaronova Z.B., Akhmedov Sh.M., Mukhamedov I.T., Lekishvili M.V., Zhidkov I.L., Zelyanin A.S., Kocharyan E.Z. Surgical rehabilitation of patients with the disease of the operated ear // Russian otorhinolaryngology, 5, 2012, pp. 10-14.

2) Aleshkin A.V. Experience in the use of therapeutic bacteriophages in purulent-inflammatory diseases of the upper respiratory tract // Medical Council, 16, 2015, -pp. 96-101.

3) Volkov A.G., Kovalev A.A. Features of the course of chronic suppurative otitis media in patients with impaired carbohydrate metabolism // Medical Bulletin of the South of Russia, 2, 2012, pp. 46-48.

4) Gurov A.V. Features of antibacterial therapy of acute purulent sinusitis and acute purulent otitis media // Medical Council, 6, 2018, pp. 78-82.

5) Zargaryan B.M., Litvinov S.D. Simultaneous septo-turbino- and myringoplasty for chronic purulent otitis media // Bulletin of the Medical Institute Reaviz Rehabilitation, Doctor and Health, 6 (42), 2019, pp. 132-157.

6) Karneeva O.V., Polyakov D.P. A modern approach to the treatment of diseases of the upper respiratory tract and middle ear as a measure for the prevention of hearing loss // Pediatric Pharmacology, vol. 9, -No. 1, 2012, pp. 30-34.

7) Krivopalov A.A., Fanta I.V. Acute otitis media: epidemiology, classification, etiology and treatment //Medical Council, 4, 2016, pp. 53-55.

8) Kryukov A.I., Gurov A.V., Yushkina M.A., Izotova G.N., Sokolov S.S. Peculiarities of antibacterial therapy of purulent-inflammatory pathology of ENT organs //Medical Council, 18, 2016, pp. 18-22.

9) Kryukov A.I., Kunelskaya N.L., Gurov A.V., Izotova G.N., Elchueva Z.G. Evaluation of the effectiveness of the drug Ampisid in the treatment of external bacterial (non-pyocyanic) and acute otitis media Medical Council, 15, 2014, pp. 55-59.

10) Kustov M. O., Artyushkin S. A., Nacharov P. V., Verzhbitsky G. V., Artyushkina V. K. Microflora of the external auditory canal in patients with bacterial external diffuse otitis // Russian otorhinolaryngology. – 2012. 3. pp. 66-70.

11) Nurmukhamedova F. B., Amonov Sh. E. Assessment of the quality of life of patients with chronic suppurative otitis media before surgery // Journal of Theoretical and Clinical Medicine. – 2021. – 1.pp. 96-99.

12) Portenko G. M., Portenko E. G., Lokteva A. A. Latent aperforative otitis media - the current course of acute otitis media // Russian otorhinolaryngology, 2, 2009, pp. 139-143.

13) Ryazantsev S.V., Dyakov I.M., Konoplyov O.I. Antibacterial therapy for the disease of the operated ear //Medical Council, 8, 2018,pp. 34-35.

14) Semak L.I. Factors determining the outcome of purulent-septic complications of acute purulent inflammation of the middle ear //Medical news, 8 (251), 2015, pp. 77-82.

15) Hon E. M., Dzhenzhera G. E., Ovchinnikov A. Yu. Local antibacterial therapy for inflammatory diseases of the external and middle ear // Bulletin of Otorhinolaryngology. – 2012. – 3. pp. 92-94.

16) Kholmatov Jamol Isroilovich, and Makhamadiev A.A. Etiopathogenesis and treatment of chronic suppurative otitis media and sensorineural hearing loss // Bulletin of Avicenna, no. 4(57), 2013, pp. 104-110.

17) Kalinogorskaya O. S. et al. Antibiotic resistance and serotype composition of Streptococcus pneumoniae isolated from children in St. Petersburg in 2010-2013 // Antibiotics and Chemotherapy. - 2015. - T. 60. - No. 1-2. pp. 10-18.

18) Kurbanova N.N. and ot. The effect of new plant hepatoprotectors on the level of proinflammatory cytokines in acute toxic liver damage. //International Journal of Psychosocial Rehabilitation. – Vol. 24, Issue 08, 2020. pp. 8910-8920.

19) Karimova M. A., Nuralieva X. O. Description of the level of the effect of gene-modified soy on normal microflora in the experience. // International Journal of Health Sciences. – Vol. 6 no. 1 (2022) pp. 693-702.

20) Karimova M.A., Kurbanova N.N. Violation of the normal microflora of the large intestine of the influence of genetically modified soybeans in the experiment. //Medicine and innovations. – 2022. 3(7). pp. 162-166.

21) Karimova M.A, Esamuratov A.I, Olimova M.M. Experience in studying the effect of a geneticaly modified produkts on the colon microflora laboratory animals. Volume -12, issue-8 (2023).