MEDICAL UNIVERSITY

"PROF. DR. PARASKEV STOYANOV" - VARNA

Department of Infectious Diseases, Parasitology and Dermatovenerology

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CLINICAL, DIAGNOSTIC AND THERAPEUTIC STUDIES ON COMMON BACTERIAL SKIN INFECTIONS IN CHILDHOOD

ABSTRACT

On a dissertation for award
of an educational and scientific degree
"Doctor"

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Field of higher education: 7. "Health and sports"
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Scientific supervisor: Prof. Dr. Ilko Bakardjiev, MD.
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Prof. Dr. Snezhina Vasileva, MD.

Varna,2023

The dissertation work was discussed at a meeting of the extended departmental council of the Department of Infectious Diseases, Parasitology and Dermatovenerology at the Medical University of Varna and is directed for defense before a scientific jury

The dissertation contains 141 printed pages, of which 32 pages - literature review, aim and tasks of the study - 1 page, material and methods - 11 pages, results of own research - 41 pages, discussion of the results - 12 pages, conclusion - 3 pages, conclusions and contributions - 2 pages. Illustrated with 35 tables and 39 figures. It contains 26 pages - a bibliography with 339 titles - 12 in Cyrillic and 327 in Latin, reference to publications and participation in scientific forums related to the dissertation work - 1 page.

The public defense of the dissertation work will be held on 15.06.2023 at 12:30 p.m. at the MU - Varna.

The materials for the dissertation work will be available to those interested in the library of the MU - Varna, Marin Drinov St. N55

CONTENTS:

ABBREVIATIONS USED

AD	atopic dermatitis
AKA	amoxicillin/clavulanic acid
CBC	complete blood count
DBC	differential blood count
NF	normal flora
MIC	minimum inhibitory concentration
RLV	regional lymph nodes
CA-MRSA	Community-associated methicillin-resistant *Staphylococcus aureus*
FDA	U.S. Food and Drug Administration
GAS	Group A Streptococcal infection
GABHS	Group A β – hemolytic Streptococcus
MRSA	Methicillin resistant *Staphylococcus aureus*
MSSA	Methicillin sensitive *Staphylococcus aureus*
p.o.	per os
Sp, ssp	subspecies
TMP-SMX	Trimetoprim Sulfamethoxazole

1. Introduction

Under bacterial diseases of the skin - pyodermas, we mean all purulent-inflammatory processes of the skin caused by bacteria. In a narrow sense, this refers to diseases caused by pyogenic bacteria - pyococci - mainly staphylococci and streptococci. This subdivision is not always possible because many of the skin and mucosal infections can be caused by two microorganisms at the same time. Bacterial infections of skin and skin structures commonly seen in children include impetigo, ecthyma, folliculitis, furunculosis, carbuncles, infections of skin appendages - glands and nails, streptococcal intertrigo, erysipelas, cellulitis, streptococcal perianal dermatitis, toxic shock syndrome , necrotizing fasciitis, staphylococcal scalded skin syndrome, etc. (Hedrick, 2003). Skin infections can be acute, others subacute, recurrent, with clear clinical signs of inflammation: redness, swelling, increase in local temperature, pain, impaired functions. Environmental conditions also play a role in the development of purulent dermatitis. A hot climate, especially if it is humid, is a predisposing factor for the development of purulent dermatitis. Insects can be an additional reason for the development of purulent dermatitis. A risk factor is also the presence of another dermatological disease such as atopic dermatitis, scabies, lice (WHO, 2005).

Diagnosed early and treated correctly, skin infections are almost always curable. With delay in diagnosis, incorrect and/or insufficient treatment, some of the bacterial dermatoses have the potential to cause septicemia, nephritis, carditis, arthritis, even death. An important step is to determine the depth of the process and the intensity of the spread.

After making a correct diagnosis, the choice of the most appropriate therapy is of utmost importance. In children with mild or moderately severe bacterial infections of the skin and skin structure that do not require hospitalization or emergency surgery, prompt provision of oral antimicrobial therapy avoids the risk of worsening the inflammatory process. Empiric antimicrobial therapy should be directed at the most likely pathogens (Staphylococcus aureus or Streptococcus pyogenes), although some infections may be polymicrobial in origin. The resistance profile of the target pathogen, the therapeutic spectrum of the drug, and its pharmacokinetic properties must be considered when choosing an appropriate antimicrobial therapy. Other factors to be considered include the convenience of the dosage regimen, the acceptability and palatability of the administered oral formulation, and allergy data. Any treatment plan for bacterial infection of the skin and skin structures should aim to minimize the emergence of resistant organisms so that the risk of their spread to others in the community is reduced.

The lack of data on the characteristics of the demographic, social and risk factors in the Varna region, mode of infection, etiological dominance, peculiarities in their course and comorbidity, unclearly defined differential-diagnostic criteria and effective therapeutic agents, lack of mandatory registration and prevention of these social significant diseases, motivated us to conduct the present studies and answer some essential questions that would be useful for clinical practice in our country.

2. Purpose and tasks:

The **aim** of the dissertation is to study and analyze the dynamics, demographic and risk factors, clinical, diagnostic and therapeutic aspects of common bacterial skin infections in childhood.

To achieve this goal, we have set ourselves the following tasks:

1. To determine the frequency of bacterial skin infections in childhood among general pediatric pathology in Northeastern Bulgaria for the period 2012-2018;

2. To analyze the demographic and social structure of children with established common bacterial infections;

3. To investigate seasonality and risk factors for bacterial skin infections in childhood in the representative sample;

4. To study the peculiarities of the clinical course of different types of pyoderma;

5. To track the results of the applied clinical-laboratory and microbiological diagnostic methods;

6. To study, analyze and compare the therapeutic effectiveness of topical and systemic medications in the treatment of common bacterial skin infections in childhood.

3. Material and methods

Bases for the realization of the dissertation work are:

- Department of Infectious Diseases, Parasitology and Dermatovenerology, Department of Dermatovenerology, Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov", city of Varna;
- Department of skin and venereal diseases at UMBAL "St. Marina" EAD, Varna;
- Department of Social Medicine and Health Care, Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov", city of Varna;
- The clinical-laboratory, microbiological studies were carried out in the relevant laboratories of UMBAL "St. Marina" EAD, Varna.

3.1. Material

- The present study was conducted in the period 2012 - 2018 on outpatients, those referred for dermatological consultation from the I and II Children's Clinics, Clinic for Pediatric Oncohematology, Clinic for Orthopedics and Traumatology of UMBAL "St. Marina" EAD, Varna and patients hospitalized in the Department of Skin and Venereal Diseases at the same hospital;

- To fulfill the set tasks, the medical documentation (epicrisis, outpatient lists, laboratory tests) of 303 patients, divided into two groups - 154 patients with bacterial skin infection and those with other skin diseases - control group - 149, was studied;

- Determination of the age group of the patients examined by us is according to the distribution of the studied diseases: 0-28 days, 1-12 months, 13 months-4 years, 5-10 years, children over 11 years of age;

- The paraclinical laboratory tests were performed as follows: CBC - 146 patients, DBC -154 patients, S-RP - 143 patients, ESR in 37 patients, glucose - 126 patients.;

- Microscopic studies for morphological identification of bacteria and fungi:

o native preparation in 152 patients;

o Gram staining – 154 patients;

Microbiological studies – 154 patients;

Antibiogram by disc-diffusion method – 154 patients;

- Treatment with a local antibiotic (mupirocin, fusidic acid) and other local agents was carried out in 111 patients, with systemic therapy – in 151 patients; 111 patients were treated with combined therapy - local and systemic;

Systemic treatment of purulent dermatitis was performed with azithromycin in 40 patients, AKA - 19 patients, gentamicin - 56 patients, cefazolin - 11 patients, ceftriaxone - 25 patients.

Patient selection criteria:

Inclusion criteria – patients with bacterial skin infection:

1. Persons under 18 years of age.

2. Change on the skin, accompanied by objective local and systemic manifestations of bacterial inflammation, not due to other nosological entities.

3. Secondary bacterial skin infection in children with atopic dermatitis, insect dermatitis, scabies, etc.

4. Patients with a complicated skin bacterial infection that progressed to another disease (respiratory, renal, orthopedic, death).

5. Absence of another infectious disease during the examination or hospitalization (viruses, mycoses).

Exclusion criteria – patients with bacterial skin infections:

1. Patients over 18 years of age.

2. Skin disease with inconclusive clinical findings - lack of objective and subjective clinical data on skin infection.

3. Presence of other active infections during hospitalization – with viral or mycotic etiology.

Inclusion criteria – controls:

1. Persons under 18 years of age.

2. Patients with other non-bacterial skin diseases - alopecia, vitiligo, psoriasis, mild forms of AD, contact dermatitis, urticaria, seborrheic dermatitis, pityriasis rosea, pityriasis versicolor, formations, etc.

3. Absence of other active systemic infection, accompanied or not by a skin finding.

Exclusion criteria - controls:

1. Persons over 18 years of age.

2. Presence of other local and systemic active infections during hospitalization - with viral or mycotic etiology.

3.2. Methods

1. Documentary research methods:

A detailed analysis was carried out on the medical documentation for hospitalized, consulted and outpatient patients who passed through the reception-consultation office for skin and venereal diseases at UMBAL "St. Marina" EAD, Varna. Medical journals, epicrisis, outpatient lists, laboratory records of the pediatric patients who passed in the period 2012-2018 were thoroughly studied.

2. Clinical observation:

History: information was collected regarding the demographics and social structure of the patients - place of residence, gender, age; comorbid background, presence of sick brother/sister.

When determining somatic status, we focused on obesity, malnutrition, deformities;

For the dermatological status, data on the type, number, localization of rash units, involvement of regional lymph nodes and skin appendages were reported.

3. Laboratory research methods:

A) Clinical and laboratory tests of blood - CBC, DBC, ESR, C-RP, glucose.

- 3 hematological 5 Diff counters were used for the examination of CBC and DBC:
- Sysmex 1000XN and Siemens ADVIA 2120i apparatus work by fluorescence flow cytometry.

To determine the ESR, the following were used:

- Roller 20PN (Alifax S.p.A., Polverara, Italy) for examination of venous blood. The apparatus carries out photometric reading of the kinetics of erythrocyte aggregation;
- Manual Panchenko method with disposable kits in which 150 μl of capillary blood is mixed with sodium citrate in a ratio of 4:1.

The following devices were used to determine C-RP:

• Cobas 6000 and Advia Chemistry 1800, which work by immunoturbidimetry.

To determine the blood sugar level, the following are used:

• Cobas 6000 and Advia Chemistry 1800, which implement a two-step hexokinase enzymatic method.

Significant for the diagnostic process and determining the severity of bacterial skin infections in childhood are the increased values of white blood cells above 11.84 x 109, ESR - Panchenko: children 2 to 18 years - > 8 mm/h, newborns > 2 mm/ h, C-reactive protein - >5; blood sugar level – over 5.9 mmol/l.

B) Bacteriological studies:

To prove the disease-causing agents, microscopic and cultural studies were carried out, as well as a disk-diffusion method for determining antibiotic sensitivity.

Study progress:

1. Microscopic examination.

2. Preparation according to Gram

3. Cultural studies: the evaluation of the developed colonies was based on their surface and color, the presence of hemolysis, their ability to degrade various sugars, etc.

Staphylococci (*S. aureus*) were cultured on blood agar. These media are rich in nutrients and provide stable growth of *S. aureus* allowing additional observation of hemolysis.

S. aureus resistance to methicillin:

The main methods for demonstrating methicillin resistance against *S. aureus* are the Cefoxitin disk screening test, the latex agglutination test for PBP2a (penicillin binding protein 2a) (an enzyme encoded by mecA), and the oxacillin salt agar screening test (Sakoulas *et al.*, 2001).

Cultures of streptococci (*S. pyogenes* – GAS, GABHS) were performed on a complex "rich" medium, such as tryptone soy agar supplemented with 5% sheep blood, where large areas of β-hemolysis were visualized.

5. Disk-diffusion method for determining antibiotic sensitivity:

For Gram-positive microorganisms, Petri dishes with a diameter of 9-10 cm were used - and disks with benzylpenicillin, methicillin or oxacillin, erythromycin, tetracycline, gentamicin,

cephalothin, and when determining with 10 disks (15 cm Petri dishes) - additionally with ampicillin, chloramphenicol, kanamycin, amikacin.

To determine the sensitivity of Gram-negative microbes, petri dishes with 6 discs with ampicillin, gentamicin, cephalothin, tetracycline, chloramphenicol, nalidixic acid were used, and with 10 discs - additionally amikacin, azlocillin, cefotaxime, cefotiam, cefsulodin, cefoperazole, moxalatam, etc.

Interpretation of suppression zones:

The measured suppression zones were interpreted according to the three-level Bauer-Kirby categorization system, according to standardized tables. Strains can be:

- sensitive denoted by the symbol “S”;
- with intermediate sensitivity - symbol “I”;
- resistant - symbol "R".

4. Statistical methods:

The necessary information was collected in Excel-tables, in which all the necessary indicators were set to shape the demographic and social structure, the risk factors, the clinical picture, the diagnosis and the treatment of the patients in the group of cases with bacterial skin infections and the control group.

Descriptive analysis was used to describe the main characteristics of the sample and indicators included in the study. Central tendency measures such as the arithmetic mean, minimum and maximum values, and standard deviation were used as the basis of the analysis.

Independent T-test was used to compare the mean age at diagnosis between the two groups of patient-controls and cases. Differences between groups were statistically significant at $p \leq 0.05$.

Comparative analysis of the two studied groups was performed with a non-parametric **chi-square (x2) test** and **cross-tabulation**. It was used to search for significant differences in frequency representation across categorical values. Statistical significance was accepted for non-parametric tests at $p \leq 0.05$.

Spearman's correlation analysis (rho) was used to examine the relationships between different indicators to establish the strength of their mutual impact. The degree of association between variables was defined as significant at $r > 0.5 < r = 0.7$; large at $0.7 < r = 0.9$ and extremely large at $r > 0.9$ at $p \leq 0.05$.

Statistical processing of the data was performed using the statistical package IBM SPSS for Windows, version 25.0. Data were graphically presented using Microsoft Excel 2007, Windows 10.

4. Results and Discussion

4. 1. Analyzes on the morbidity of the studied population

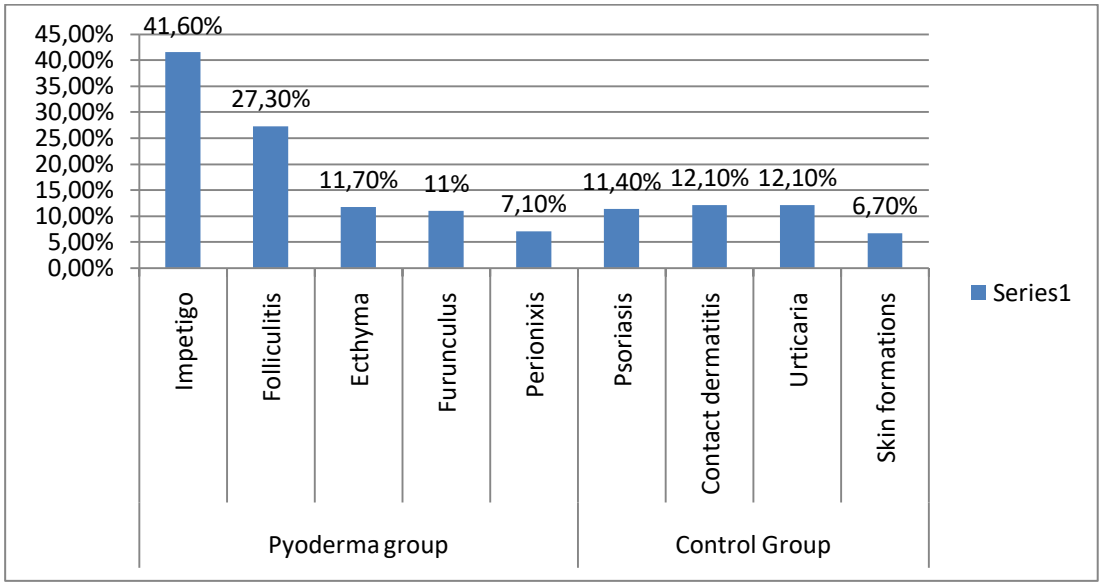

Fig. 1. *Morbidity in the studied groups of patients*

The data obtained from a comparative analysis regarding the frequency of diseases in the studied population found that the most common skin disease among children for the period 2012-2018 was impetigo (41.6%), followed by various forms of folliculitis (27.3%), ecthyma (11.7%), contact dermatitis (11.7%) and urticaria (11.7%), furunculus (11%) and psoriasis (11%), perionyxis (7.1%) and finally are the patients with skin formations – 6.7%. The reported data are similar to those presented by Gupta (2021). He classified childhood pyodermas as the most common dermatoses in children.

4. 1. 1. Study of the incidence of bacterial infections in childhood in the period 2012-2018.

The overall incidence of purulent dermatitis during the studied 6-year period varied between 13.98% (2012) and 10.49% (2018). The reason for the peaks observed in the period 2013 - 2015 are the established cases of nosocomial infections in the Department of Neonatology at SBAGAL - Varna. The gradual decrease in the frequency of children's bacterial infections after 2015 speaks of the unit's successful handling of this serious problem for medical facilities.

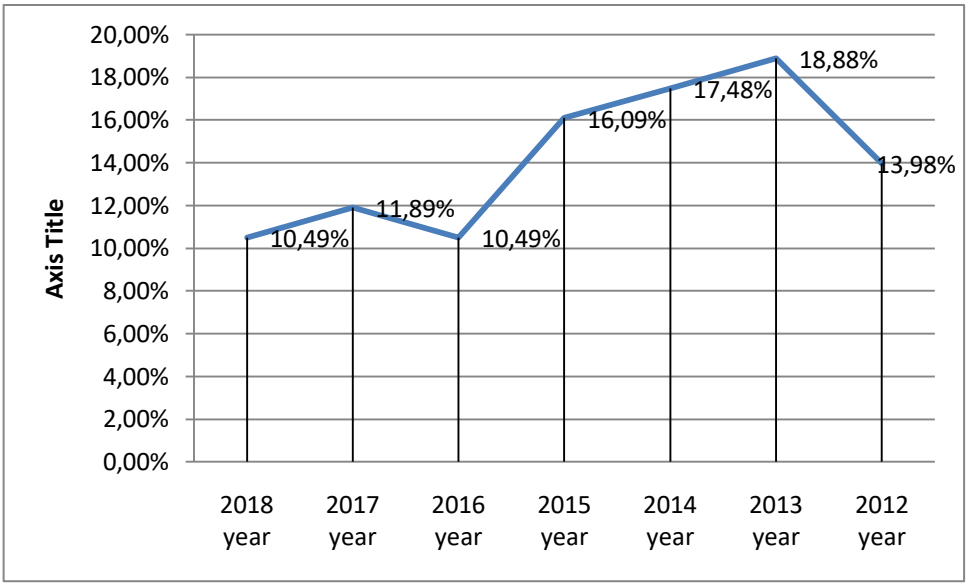

Fig. 2. *Incidence of common bacterial skin infections in childhood in the period 2012-2018.*

4. 2. Analysis of demographic and social structure in some common bacterial infections in children

4. 2. 1. Comparative analyzes to determine the average age of the patients in the studied groups

A t-test was used to compare the mean age at diagnosis between the two study groups, which found a mean value of 10,01 years for the patients with bacterial skin infections and 7,63 years for the control group.

Table 1. *Average age of patients in the studied groups*							
	Group	N	Arithmetic mean age	Standard deviation.	Standard error	T-test	95% CI
Age of diagnosis	Cases	154	**10,0145**	**6,71126**	.54081	**t=3,366, p=0,001**	[0,99-3,78]
	Controls	149	**7,6284**	**5,55323**	.45494		

4. 2. 2. Comparative study on morbidity in the studied groups, according to age and sex:

The study also found that the average age of boys with pyoderma was 9,3 years and that of girls was 10,72 years. The results regarding the average age of affected children in the study by Özçelik *et al*. (2018) are similar. He described that the mean age of onset of bacterial skin infection in girls was 10,52 years and 9,89 years in boys. The presented data show that the average age of the children is almost the same, even with the significant difference in the number of the studied population – 10 115 children in total, 2 491 of which have pyoderma.

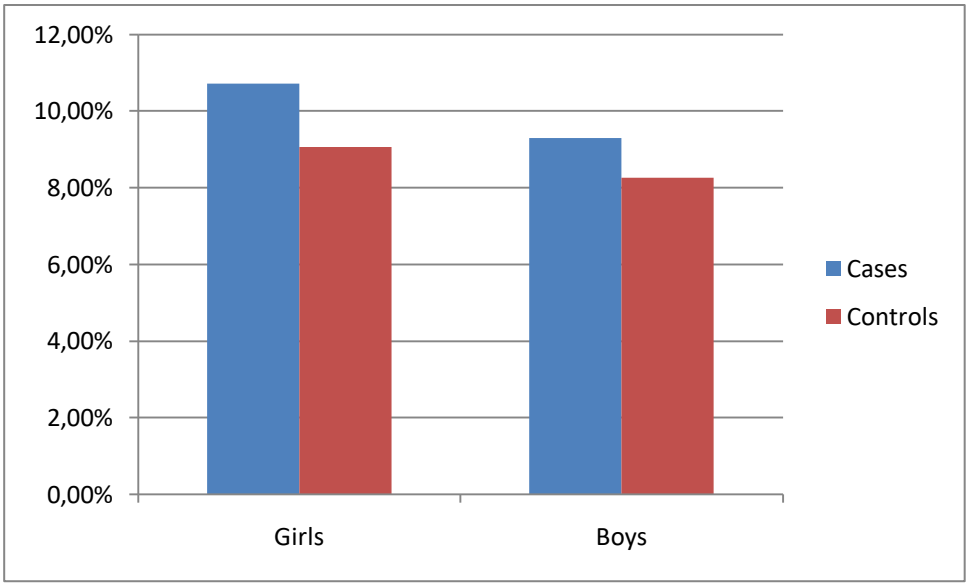

***Fig. 3**. Average age of the studied groups in relation to gender.*

4. 2. 3. Comparative analysis of patients with common childhood bacterial infections by gender

The statistical processing of the results of the study demonstrated that regarding the distribution by gender, the latter does not have a particular impact on morbidity - X2 =0.167, p=0.683. The data for the studied group show a ratio of boys/girls 1:1 (77 boys : 77 girls). Similar results were found by Jankovic *et al*. (2019). His team studied skin diseases in over 200 children between the ages of 5 and 16 and found no influence of gender on morbidity.

***Table 2.** Distribution of morbidity by gender*

X^2 =0,167, p=0,683			Gender		Total
			Girls	Boys	
Group	Cases	Number	77	77	154
		% in the studied group	**50,0%**	**50,0%**	100,0%
		% of total group	25,4%	25,4%	50,8%
	Controls	Number	71	78	149
		% in the studied group	**47,7%**	**52,3%**	100,0%
		% of total group	23,4%	25,7%	49,2%

4. 2. 4. Comparative analysis of patients in the studied groups according to their place of residence:

In January 2023, Ricciardo described a significantly higher incidence of purulent dermatitis in urban-dwelling children in countries with a high social standard compared to children and adults from

smaller settlements. The results found in the present study regarding the higher incidence of bacterial skin infections in urban areas (79,20%; n=122) directly correlate with the reported data. The regularity in the distribution of morbidity in the control group is similar. The described results show that there is a weak statistically significant difference in the morbidity of children from cities and villages (X2 =3,086, p=0,054).

Table 3. *Distribution of morbidity by residence*					
X^2 =3,086; p=0,054			Residence		Total
			Province	City	
Group	Cases	Number	32	122	154
		% in the studied group	20,8%	**79,2%**	100,0%
		% of total group	10,6%	40,3%	50,8%
	Controls	Number	44	105	149
		% in the studied group	29,5%	**70,5%**	100,0%
		% of total group	14,5%	34,7%	49,2%

4. 3. Study of seasonality and risk factors of common bacterial skin infections in childhood:

4. 3. 1. Comparative analysis of the distribution of patients with common bacterial infections in childhood, according to the season:

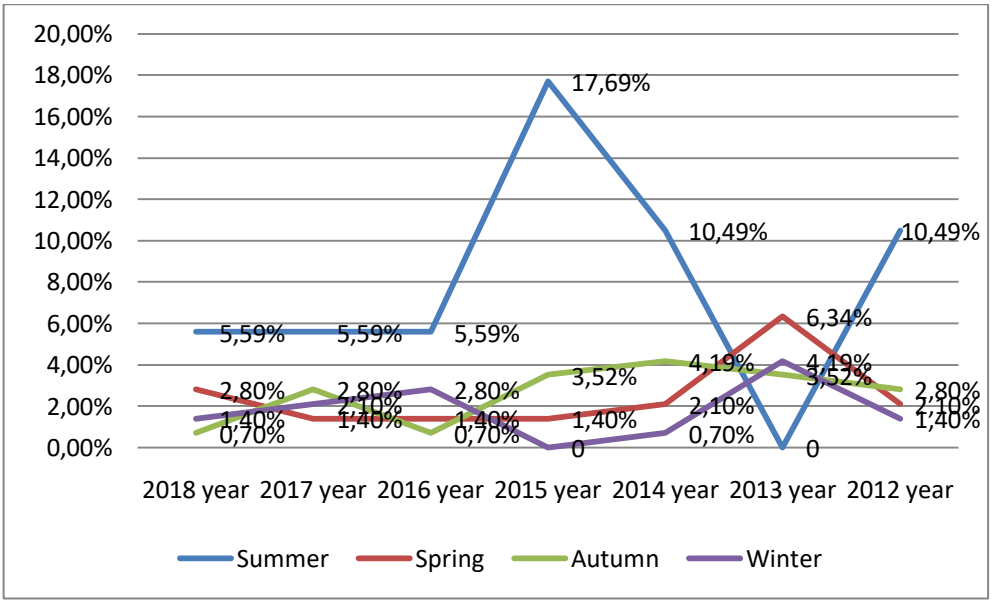

Fig. 4. *Distribution of the incidence of purulent dermatitis in children according to the seasons in the period 2012-2018.*

Our analyzes regarding the influence of a warm and humid climate and the associated increased skin surface exposed to direct contact with contaminated surfaces and closer contact between children show that purulent dermatitis occurs year-round, with a peak in the summer months – 48,10% , followed by spring (20,8%), autumn (16,2%) and winter – 14,9%. The data described show a weak but statistically significant difference in terms of seasonality of diseases between the two groups: X2 = 9,760; p = 0,021. In their analyses, Armitage *et al*. (2019) and Emodi *et al*.(2010) also found increased incidence during the warm and humid period from April to September in Nigeria. These data are also confirmed by published results from WHO (2005) and Banerjee *et al*., (2010).

4. 3. 2. Comparative analysis of the distribution of patients with common pyodermas in childhood, in relation to nasopharyngeal carriage, sick sibling, obesity and malnutrition for the development of pyodermas

Table 4. *Risk factors for bacterial skin diseases in childhood*

Factors	Nasopharyngeal carriage	Sick brother/sister	Obesity	Malnutrition
Cases	27,90%	18,20%	20,80%	13%
Controls	0%	0%	11,40%	6,70%
Total %	14,20%	9,20%	16,20%	9,9%
X^2	**48,485**	**29,85**	**4,904**	3,43
p	**0,001**	**0,001**	**0,027**	0,067

A risk factor for the development of a bacterial skin infection in childhood was registered in combination with carrying a pathogen in the nasopharyngeal area in 27,90% of pediatric patients in the studied Group, obesity – 20,80%, the presence of another child in the family with a skin infection – 18,20%, malnourished children – 13%. The presented data converge with the published results of Durupt (2007), who found a higher frequency of nasopharyngeal carriage of *S. aureus* in children with pyoderma. Falagas *et al*. (2009) reported an increased likelihood of skin infections in obese individuals and attributed this to the development of a pro-inflammatory state and reduced cell-mediated immune response, and Isaack H *et al*. (1992) reported a high risk of developing bacterial skin infections in children with marasmus and kwashiorkor.

Fig. 5. *Nasal carriage of S. pyogenes in a 9-year-old patient with impetigo. Erythema is visualized at the base of the left nostril, with a U-shaped erosion cutting through the philtrum, covered with yellowish-hemorrhagic crusts and fine scales.*

Fig. 6. *Nasal carriage of S. aureus in a 5-year-old patient with impetigo and angulus infectiosus oris. Numerous yellowish crusts and secretions are found in the area of the nostrils. Similar waste elements are observed in the corners of the mouth, accompanied by weak maceration.*

4. 3. 2. 1. Correlation analysis between nasopharyngeal carriage, infected sibling and pyodermas in childhood

Table 5. *Correlation analysis between some risk factors and pyodermas*

			Nasopharyngeal carriage	Sick brother/ sister	Impetigo	Ecthyma	Folliculitis
Spearman's rho	Nasopharyngeal carriage	rho	1.000	**.457****	**.591****	-.136	-.284**
		p	.	**.000**	**.000**	.092	.000
		N	154	154	154	154	154
	Sick brother/sister	rho	.457**	1.000	**.491****	-.067	**-.289****
		p	.000	.	**.000**	.411	**.000**
		N	154	154	154	154	154
	Impetigo	rho	.591**	.491**	1.000	-.266**	-.516**
		p	.000	.000	.	.001	.000
		N	154	154	154	154	154

	Ecthyma	rho	-.136	-.067	-.266**	1.000	-.041
		p	.092	.411	.001	.	.611
		N	154	154	154	154	154
	Folliculitis	rho	-.284**	-.289**	-.516**	-.041	1.000
		p	.000	.000	.000	.611	.
		N	154	154	154	154	154

The tests revealed a positive weak and moderate statistically significant correlation indicating that there is an association between a pediatric patient with nasopharyngeal carriage infecting another child in the family (rho = 0,457, p<0,05) and developing impetigo (rho = 0,591, p<0,05). Spearman analysis also found a moderate correlation for this child with impetigo to infect their sibling (rho=0,491; p<0,05). A negative, weak but statistically significant correlation was also found between an infected brother/sister and folliculitis (rho = -0,289; p<0,05), which indicates that in families where there is one person with a clinical manifestation of purulent dermatitis, it is likely if there is another child, they also have symptoms of a skin infection or disease. The data thus presented show us that it is advisable that the treatment/prevention be aimed at the whole family as a unit and not only at the patient as a case.

Fig. 7. *Impetigo in a 9-year-old child whose younger sister had S. aureus isolated from the nasopharyngeal region. Extensive golden-greenish dense crusts are visualized on the right buccal skin surface, as well as numerous similar lentiginous changes on the nose and chin.*

Fig. 8. *Two weeks after treatment with mupirocin twice a day. Discarded changes are missing. Residual erythema is established, due to the epithelialization that has occurred in the area.*

4. 3. 2. 2. Correlation analysis between obesity and pyodermas in childhood:

In their retrospective study of 248 775 patients, Mirmirani and Carpenter (2014) described a direct relationship between childhood obesity and diseases such as bacterial and fungal infections. In the present study, a low positive, statistically significant correlation was found in obesity and folliculitis - rho=0,189; p=0,019, indicating that inflammation of hair-sebaceous follicles may be associated with overweight in children.

Table 6. *Correlation analysis between obesity and some pyodermas*

			Obesity	Impetigo	Ecthyma	Folliculitis
Spearman's rho	Obesity	Correlation Coefficient	1.000	-.432**	-.037	**.189***
		p	.	.000	.650	**.019**
		N	154	154	154	154
	Impetigo	Correlation Coefficient	-.432**	1.000	-.266**	-.516**
		p	.000	.	.001	.000
		N	154	154	154	154
	Ecthyma	Correlation Coefficient	-.037	-.266**	1.000	-.041
		p	.650	.001	.	.611
		N	154	154	154	154
	Folliculitis	Correlation Coefficient	.189*	-.516**	-.041	1.000
		p	.019	.000	.611	.
		N	154	154	154	154

4. 3. 2. 3. Statistical analysis regarding the development of bacterial infections in children with atopic dermatitis

During the studies, 29 (18,8%) children with severe, impetiginized AD were registered in the group of cases with pyodermas (X2=4,686; p=0,03), and in the control group - 15 (10,1%) pediatric

patients with a mild form. The data presented correlate with those described by Alexander *et al*. (2020) recurrent and severe bacterial skin infections caused by *S. aureus* and S. pyogenes in children with AD. Another study placed AD impetigo as the second most common complication after molluscum contagiosum infection (Han, Yoon, Yook *et al*., 2022). Correlation analysis to look for dependencies between atopic dermatitis and impetigo registered a positive and statistically significant interdependence for a child with atopic dermatitis to develop impetigo, rho=0,268, p=0,001.

Table 7. *Correlation analysis between impetigo and AD.*

			Impetigo	AD
Spearman's rho	Impetigo	Correlation Coefficient	1.000	**.268****
		p	.	**.001**
		N	154	154
	AD	Correlation Coefficient	.268**	1.000
		p	.001	.
		N	154	154

Fig. 9. A 7-month-old child with impetiginized atopic dermatitis. In the mental and buccal areas, a diffuse erythema is visualized, more pronounced in the chin area, against the background of which numerous grouped pustules, scales and single crusts. Treatment with fusidic acid was carried out for 10 days.

Fig. 10. *A 7-month-old child with imetiginized atopic dermatitis - 3 weeks after treatment with fusidic acid and emollients. Weak, diffuse erythema with scant desquamation is observed.*

4. 4. Clinical observations on the features of different types of bacterial infections

4. 4. 1. Distribution of patients according to the localization of local manifestations

Table 8. *Localization of skin rashes.*			
Localisation	**Body**	**Face**	**Extremities**
Cases	46,10% n=71	**48,70%** **n=75**	**63%** **n=97**
Controls	43,30% n=66	56,40% n=84	51% n=76
Total	45,20% n=137	52,50% n=159	57,10% n=173
X^2	100	1,789	4,437
p	0, 752	0,181	0, 035

In the scientific literature, the limbs and face are indicated as the most common localization of pyoderma (Craft N *et al*., 2008; Bowen *et al*., 2015; Lim, 2018). Our observations on the topography of pyococcal infections are similar and have the following distribution of lesions on limbs - 63% and face - 48,7%. Craft N (2008) explained the increased frequency of lesions on the limbs with more frequent trauma, and the changes on the face with the dissemination of *S. aureus* from the nose to the facial skin surfaces. Another aspect of the study was to look for interdependence between season and location of rashes. Sprearman analysis showed a weak but significant negative correlation predicting more likely facial localization in spring and summer (rho=-0,182, p=0,02).

Fig. 11. *Impetigo in a 4-year-old child with involvement of the skin surface of the right upper limb. Extensive erosion with a dry surface, centrally located squamo-crusts and eriferous lamellar desquamation is found. Conducted fusidic acid treatment for 10 days.*

Fig. 12. *Five weeks after fusidic acid treatment of impetigo in a 4-year-old child.*

4. 4. 2. Comparative analysis in patients with some common bacterial skin infections in childhood according to the number of lesions

The comparative analysis of the examined groups revealed that in children with pyoderma, multiple rashes predominated - more than 4 lesions - 68,80%, and in Controls, the changes were more severe - with 3 or less rash units - 43%. The statistical difference is defined as weak but significant.

Table 9. *Number of lesions in the studied groups of patients*

Number	**n≤3**	**n≥4**
Cases	29,90% n=46	**68,80%** **n=106**
Controls	**43%** **n=64**	52,30% n=78
X^2	5,605	8,626
P	0,018	0,003

4. 4. 3. Comparative analysis of the types of rash units in the studied groups:

The results in the present study follow the evolutionary polymorphism observed in changes in bacterial skin infections. The predominant frequency is exudative elements (86,4%), followed by erythema (65,6%), erosions (64,3%) and crusts (60,4%). The difference in the frequency of different rash units is explained by the stage of the disease in which the patient sought medical help. The results thus obtained approximate those of Connor (1972) and Craft N *et al*. (2008).

Table 10. *Types of lesions – controls and cases*								
Criterion	Macules	Erythema	Edema	Papular rashes	Exudative rashes	Erosions	Flakes	Crusts
Cases	55,80%; n=86	**65,60%; n=101**	50,60%; n=78	44,20%; n=68	**86,40%; n=133**	**64,30%; n=99**	51,60% n=79	**60,40%; n=93**
Controls	**79,90%; n=119**	63,80%; n=95	37,60%; n=56	15,40%; n=23	1,30%; n=2	2%; n= 3	**50,80%; n=78**	4%; n=6
X^2	19,97	0,111	5,241	29,726	**221,596**	**131,505**	0,0809	**109,363**
p	0,001	0,74	0,022	0,001	0,001	0,001	0,776	0,001

4. 4. 4. Comparative analysis of mucosal changes in the studied groups of patients

Table 11. *Statistical significance regarding mucosal involvement.*					
X^2 = 31.101, p= 0, 001			Mocous membranes		Total
			No	Yes	
Group	Cases	Number	120	**34**	154
		% in the studied group	77,9%	**22,1%**	100,0%
		% of total group	39,6%	11,2%	50,8%
	Controls	Number	147	**2**	149
		% in the studied group	98,7%	**1,3%**	100,0%
		% of total group	48,5%	0,7%	49,2%

Regarding mucosal involvement, the comparative analysis showed a statistically significant difference between the two groups (X2=31,101; p=0,001) with priority involvement in children with pyoderma (22,1%) compared to patients in the control group – 1,3% . The prevalence of mucosal involvement in children with bacterial skin infections, Craft N (2008) explains the nasal carriage of pathogenic microorganisms.

4. 4. 5. Comparative analysis of the changes in the skin appendages in the studied groups of patients

Table 12. Statistical significance - involvement of skin appendages.					
X^2 = 9,502, p= 0, 002			Appendages		Total
			No	Yes	
Group	Cases	Number	96	**58**	154
		% in the studied group	62,3%	**37,7%**	100,0%

		% of total group	31,7%	19,1%	50,8%
	Controls	Number	117	32	149
		% in the studied group	78,5%	21,5%	100,0%
		% of total group	38,6%	10,6%	49,2%

Processing of the data from the objective assessment of changes in the skin appendages showed a dependence similar to that of mucosal involvement. In the Case Group, an almost 2-fold increased frequency (37.7%) of changes in the adnexa was found and a statistically significant difference according to this criterion between the two groups (X2=9.502; p=0.002). These data correlate with the scientific facts presented by Edlich (2005).

4. 4. 6. Comparative analysis regarding the increased RLN in the studied patient groups

Lymphadenopathy was found in respondents with bacterial skin infections in 27,3% of cases. The statistical difference between the two groups regarding the increase in RLN is strong and significant - X2 = 47,176; p = 0,001. Nardi, Schaefer (2022) considered a moderate increase in RLN to be a common symptom. Craft N (2008) assumes that lymphadenopathy is found in 90% of cases in children with prolonged purulent dermatitis.

Table 13. *Regional lymphadenopathy in children in the studied groups*

X^2 = 47.176 , p = 0, 001			Lymphadenopathy		Total
			No	Yes	
Group	Cases	Number	112	42	154
		% in the studied group	72,7%	**27,3%**	100,0%
		% of total group	37,0%	13,9%	50,8%
	Controls	Number	149	**0**	149
		% in the studied group	100,0%	**0,0%**	100,0%
		% of total group	49,2%	0,0%	49,2%

4. 4. 7. Comparative analysis of complications in the studied groups of patients:

The present study registered a statistically significant difference between the studied groups of children - X2 =21,831, p=0,001 and showed that 13,60% of pediatric patients with pyoderma developed complications - cellulitis (2,60%), pneumonia (4,54%), poststreptococcal glomerulonephritis (3,25%), sepsis (2,60%). Death occurred in one child (0,7%) from a second abnormal pregnancy at 1 month of age, male with congenital brain cysts, congenital herpes infection, suspected Calderon-Gonzalez-Cantu syndrome, who developed staphylococcal sepsis and subsequent exitus. Maculo-papules with a pale center and an erythematous shaft were visualized all over the body

and limbs. Subsequently, pustules appeared from which *P. mirabilis* and *S. aureus* were cultured. Blood culture also showed the presence of *S. aureus*. Our observations confirm the data from the literature sources regarding the higher risk of developing complications in patients with pyoderma. In the study by Abrha *et al*. (2020) 86% of children developed poststreptococcal glomerulonephritis, and 16.80% died.

Table 14. *Statistical significance in the development of complications*					
X^2 =21,831, p= 0,001			Complications		Total
			No	Yes	
Group	Cases	Number	133	**21**	154
		% in the studied group	86,4%	**13,6%**	100,0%
		% of total group	43,9%	6,9%	50,8%
	Controls	Number	149	0	149
		% in the studied group	100,0%	0,0%	100,0%
		% of total group	49,2%	0,0%	49,2%

4. 5. Statistical analyzes of the results obtained with the applied diagnostic methods - laboratory studies: paraclinical, microscopic, cultural

4. 5. 1. Comparative analyzes on some clinical laboratory indicators

According to Craft (2008), routine paraclinical examinations are not necessary for the diagnosis of superficial and uncomplicated purulent dermatitis. They are an important diagnostic and prognostic factor in complicated cases of pyoderma. The results of the paraclinical examinations carried out in the present study are significant for an inflammatory process. A statistically significant difference was found between the indicators of the patients in the studied groups. According to the various hematological and biochemical indicators, leukocytosis was found in 26% of children with pyoderma (X2= 34,645, p=0,001), increased ESR - in 9.7%; (X2=8,48; p=0,002) and elevated blood sugar levels in 13,6% (X2= 45,514; p=0,001) compared to the same parameters in patients in the control group.

Table 15. Paraclinical studies.					
Indicator	↑ Leuc	↑ Ly	↑C-RP	↑ ESR	↑Glucose
Cases	**n = 40; 26%**	n=1; 0,1%	n=31; 20,1%	**n=15; 9,7%**	**n=21;13,6%**
Controls	n=14; 9,5%	**n=21; 14,2%**	n=26; 17,6%	n=2; 1,4%	n=13; 8,8%
X^2	34,645	5,116	12,265	8,48	45,514
p	0,001	0,077	0,002	0,037	0,001

4. 5. 2. Comparative analyzes of microbiological results obtained by Gram stain, culture methods and disc diffusion tests

Data from microbiological tests demonstrated that in 83,3% of patients with purulent dermatitis, Gram-positive bacteria were found, of which - *S. aureus* (41,6%), MRSA (5,2%), *S. pyogenes* (3 ,9%), *S. epidermidis* (2,6%), *E. faecalis* (2,6%), *MRS epidermidis* (1,3%), and in 27,8% – Gram-negative microorganisms represented by *K. pneumoniae* (4,5%), *K. oxytoca* (1,9%) and *Acinetobacter spp.* (1,3%). Mixed infections were found in 2,1% of patients with purulent dermatitis. Similar results were presented by Ray *et al.*, who reported as early as 2013 that Gram-positive pathogens were identified in more than 80% of culture-positive skin infections, and *S. aureus* was the most common cause of culture-confirmed skin and soft tissue infections. infections in the United States.

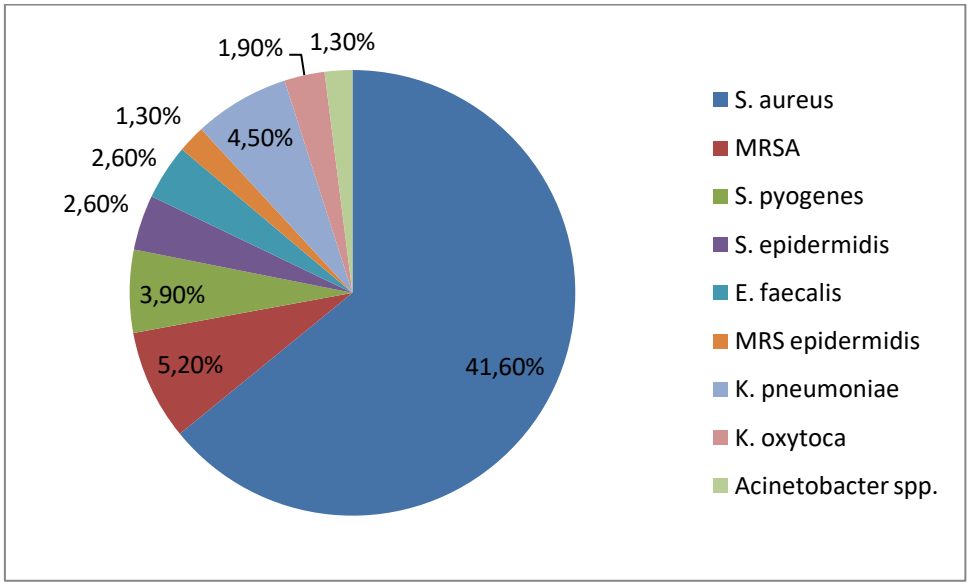

Fig. 20. *Isolates - percentage distribution.*

The establishment of the etiological bacterial agents is carried out on blood agar, which allows to recognize the macroscopic cultures of the causative agents, as well as to examine the presence of hemolysis.

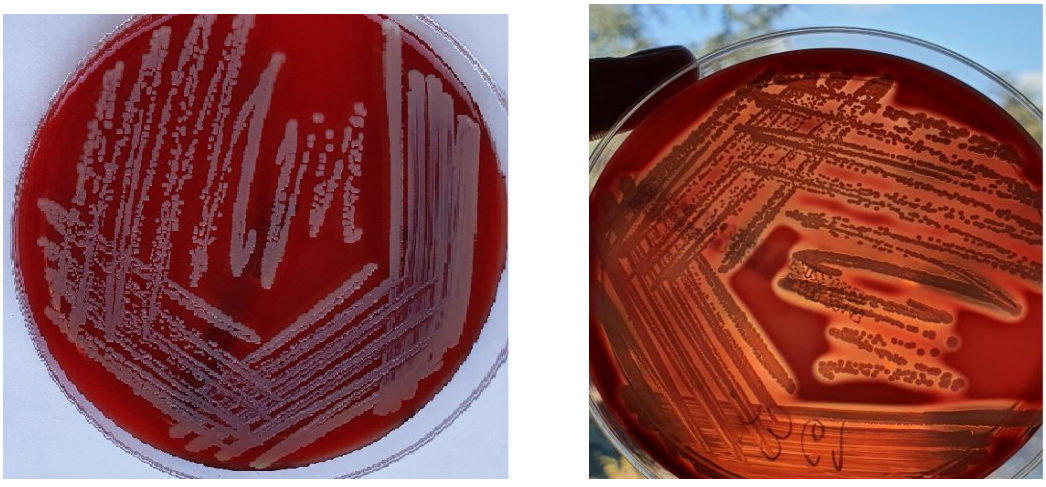

Fig. 21. *S. aureus colonies on blood agar.*

Fig. 22. Blood agar hemolysis caused by S. aureus, which visualized under illumination of the petri dish.

Fig. 23. *Complete hemolysis on blood agar caused by β-hemolytic S. pyogenes. Visualize small point-like colonies (1-2 mm) with a flat periphery, non-pigmented, almost transparent.*

4. 5. 2. 1. Studies on the antibiotic sensitivity of the isolated pathogens

The antibiotic sensitivity of the isolated pathogens was studied using the disc diffusion method:

Fig. 24. *Determination of antibiotic sensitivity by disc-diffusion method*

In our study, it was found that the isolates demonstrated the highest resistance to cefazolin - 14,3% ($p<0,05$), and the lowest - to ceftriaxone - 1,90%. In the local forms, the resistance of the isolates was registered with 1.30% ($p<0,05$) resistance to mupirocin and 2,60% ($p<0.05$) - to fusidic

acid. Our reported data are similar to the results presented by Fridkin *et al*., (2005) regarding the increasing multidrug resistance of pyococci in hospitalized and ambulatory patients.

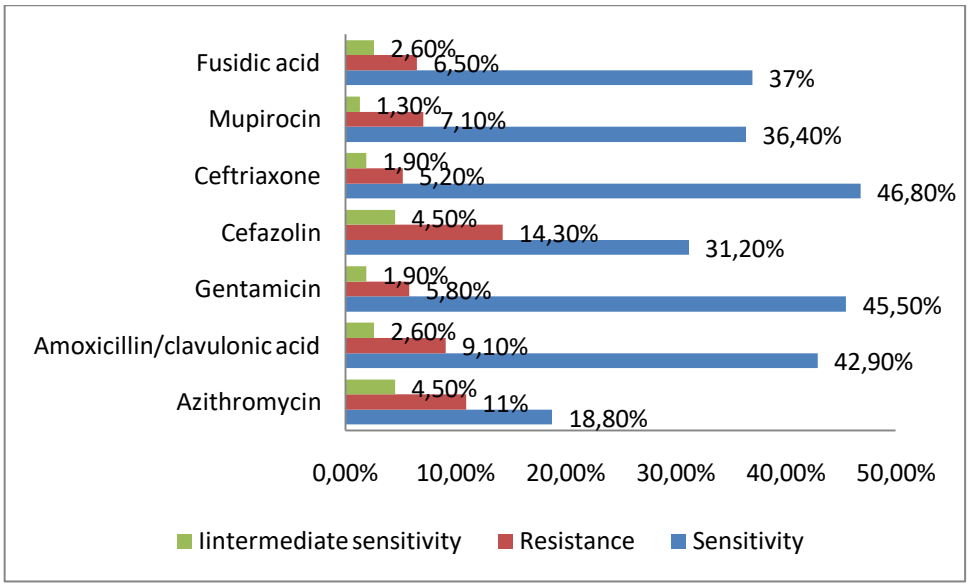

Fig. 25. *Antibiotic sensitivity of the isolated pathogens.*

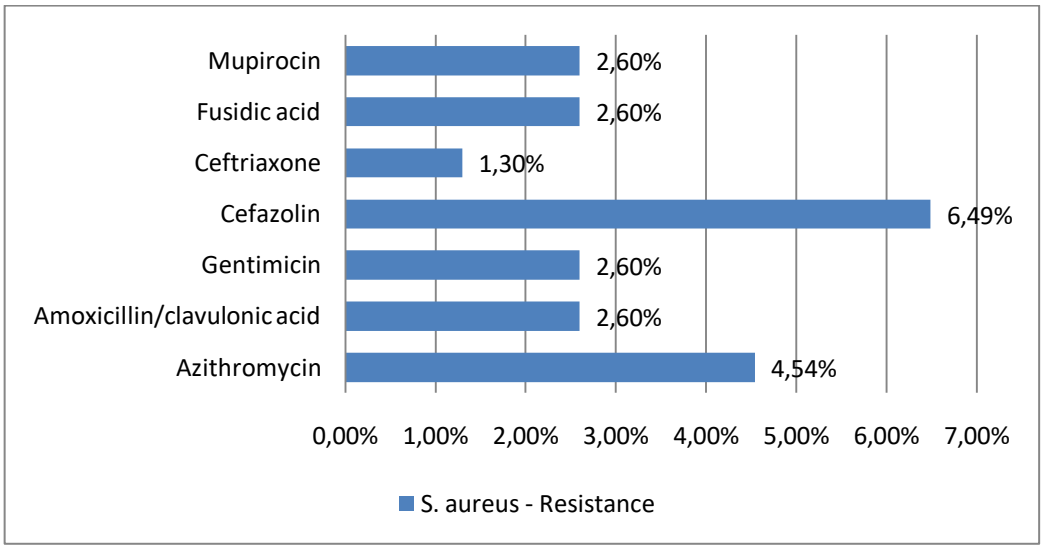

Fig. 26. *Antibiotic resistance of S. aureus to antibiotics for local and systemic use.*

Studies on the resistance of the more common pathogens responsible for purulent dermatitis in childhood demonstrated that *S. aureus* exhibited equal resistance to topical forms of mupirocin and fusidic acid at 2,60% each. Regarding systemic antimicrobials, the lowest resistance was registered to ceftriaxone – 1,30%, and the highest to cefazolin – 6,49%.

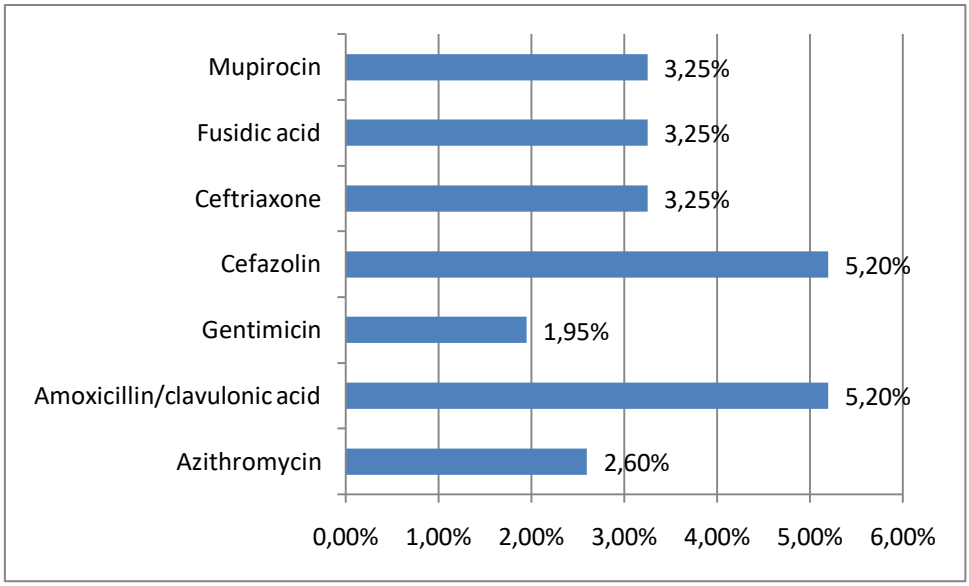

Fig. 27. *Antibiotic resistance of MRSA to antibiotics for local and systemic use.*

Analyzes of the resistance of MRSA to the antimicrobial agents, the subject of the current study, found the lowest resistance to gentamicin – 1,95%, to azithromycin – 2,60%, ceftriaxone – 3,25% and the highest to cefazolin and amoxicillin/ clavulonic acid – 5,20% each. The values regarding the local forms are equal again – 3,25% each.

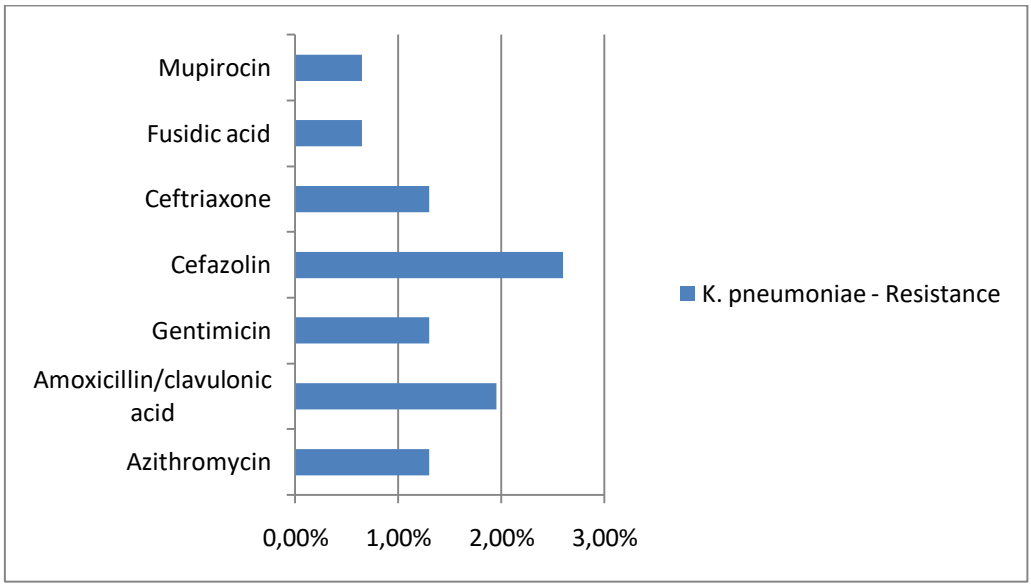

Fig. 28. *Antibiotic resistance of K.pneumoniae to antibiotics for local and systemic administration.*

Studies on *K. pneumonia* isolates demonstrated a tendency for the highest resistance to cefazolin at 2,60% and AKA – 1,95% of cases, azithromycin, gentamicin and ceftriaxone – 1,30% each, in local forms - 0, 65%.

4. 6. Study the therapeutic application and effectiveness of local and systemic medications in the treatment of common bacterial skin infections in childhood

4. 6. 1. Studies on the application of systemic antibiotics

As the most prescribed systemic antibiotics, Barbieri *et al*., (2022) highlight the combination of penicillin with beta-lactam inhibitors and macrolides. In the present study, systemic treatment was applied with preparations from the mentioned groups, respectively amoxicillin/clavulonic acid and azithromycin, as well as preparations from the group of aminoglycosides and cephalosporins, respectively with gentamicin, ceftriaxone and cefazolin. In 29,9% of the children, therapy was carried out with an antibiotic other than the investigated medication.

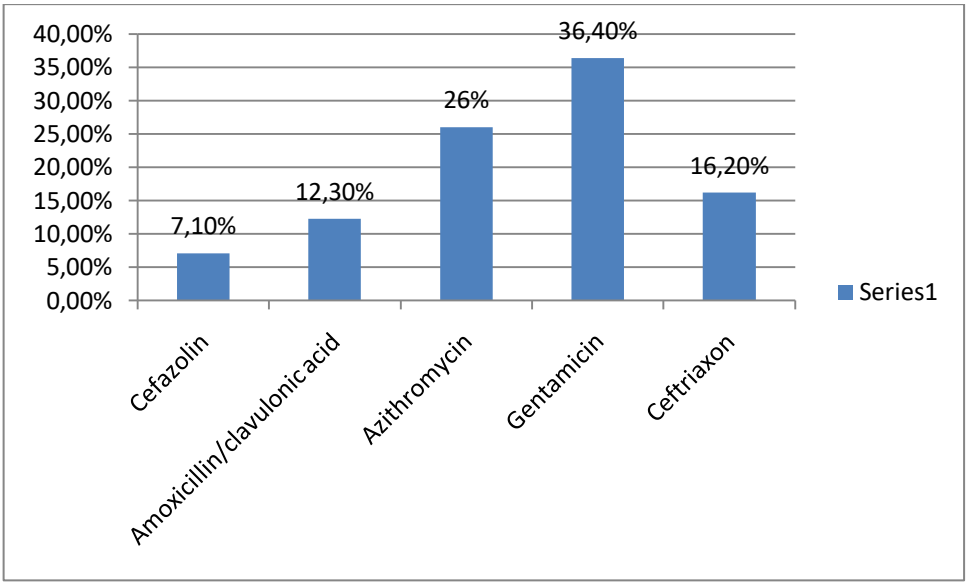

Fig. 29. *Systemic antibiotic therapy.*

Azithromycin - the present study found use in 40 patients (26%), in a daily dose for children - 10 mg/kg/24 h in a single dose for 3 to 5 days. The sensitivity of microorganisms to the macrolide was 18.80% of the examined individuals, resistance – 11% and intermittent sensitivity – 4.50% of the samples. According to Poiată A *et al*. (2006) and Hema-Ouangraoua *et al*. (2021) the resistance level of pathogens to azithromycin varied between 22% and 26,42%.

Amoxicillin/clavulanic acid was used for treatment in 19 (12,30%) children in a daily dose for mild cases of 20/5 to 40/10 mg/kg/24 h and 40/10 to 60/15 mg/kg/ 24 hours for severe skin infections, distributed in two/three doses. 42,90% of the microorganisms of the examined patients were sensitive to amoxicillin/clavulanic acid; 9,10% showed resistance and 2,60% - intermittent sensitivity. Thus, the results obtained regarding bacterial resistance to AKA reach those of Groppo FC *et al*., 2005.

Gentamicin was administered in a daily dose of 2,5 mg/kg every 8 hours. With the disc-diffusion method, sensitivity was found in 45.50% of the cases, resistance – 5,80%, intermediate sensitivity –

1,90%. Due to numerous scientific reports of frequent adverse reactions of gentamicin, it is absent from current recommendations for the treatment of skin and soft tissue infections in children (Stevens *et al*., 2014). However, due to its low cost, in the present study, aminoglycoside was the most widely administered antimicrobial (36,40%), which demonstrated a good safety profile and low pathogen resistance to it.

Cefazolin is administered in daily doses of 25 – 50 mg/kg/24 hours, 3-4 doses in mild to moderately severe infections; in severe cases - up to 100 mg/kg/24 hours, 3-4 applications. In the present study, a therapeutic effect with cefazolin was sought in 11 (7.10%) children. Microbiological tests demonstrated that despite its limited use, 14.30% of isolates showed microbial resistance to it and 4.50% showed intermediate sensitivity. According to Hepburn *et al*. (2004) in purulent dermatitis, a 5-day course of treatment was as effective as a ten-day course, provided clinical improvement was noted on day 5. The data presented support the thesis that in the treatment of bacterial skin infections in childhood, despite its good safety profile, cefazolin is not an appropriate therapeutic agent of first choice (Stevens *et al*., 2014).

Ceftriaxone crosses the blood-brain barrier and is used to treat severe skin infections at a daily dose of 20-80 mg/kg/24 hours. An advantage of ceftriaxone over other third-generation cephalosporins is its long serum half-life, which allows it to be administered to any 12 hours in children (Gainer, 1991). The object of our study were 25 (16.20%) patients treated with ceftriaxone, in which isolates were found to be sensitive to the preparation in 46.80% (n=72) of those treated, intermittent sensitivity – 1.90% (n= 3), resistance – 5.20% (n=8). From the obtained results, we can conclude that ceftriaxone is an antibacterial product with a convenient dosage regimen and a good safety profile.

4. 6. 2. Studies on the application of selected local antibiotic agents

In milder and superficial bacterial skin infections or in a combined approach of therapy with topical and systemic agents, Barbieri *et al*. (2022) suggest the use of at least one topical antibiotic. According to the authors, the most commonly prescribed agents were mupirocin (16%) and fusidic acid (9.6%). In the present study, fusidic acid was used in 59,10% of cases and mupirocin in 26% of patients. A reason for the difference in the use of these topical agents is that some patients (9,15%) reported subjective complaints such as burning and stinging when treated with mupirocin.

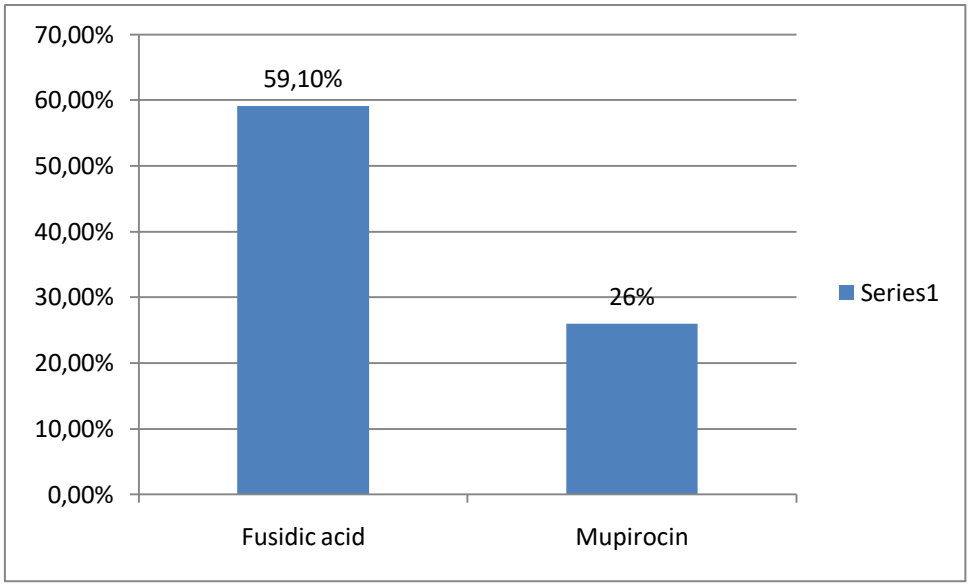

Fig. 30. *Local therapy.*

4. 6. 3. Comparative studies on the application of combined antibiotic therapy in bacterial infections in childhood

In children with multiple and extensive rash units, fever and complications, combined therapy of systemic and local agents was started. The comparative analysis of therapeutic behavior in the two groups showed a greater need for combined therapy in children with bacterial dermatoses (72,1%) compared to children in the control group (28,2%) (X2 =58,358; p= 0,001).

4. 6. 4. Comparative studies on the duration and effectiveness of treatment for bacterial infections in childhood

The effectiveness of the conducted therapy was reported up to and after the 7th day from its initiation. The involution of the signs of inflammation, absorption and drying of the exudative rash elements, the appearance of crusts, initial epithelization were registered. In patients with primary and superficial changes (17,5%), healing effect and completion of therapy was marked even before the 7th day. Longer treatment (over 7 days) was found in children with multiple rash units, impetiginized skin conditions, cellulitis and lower respiratory tract complications, renal involvement, sepsis, death (81,2%). There are no exact criteria to determine the duration of therapy. In MSSA infections, Stevens *et al*. (2014) recommended a five-day, twice-daily topical course of mupirocin or retapamulin for impetigo bullous and contagiosum, or a 7-day oral course of a penicillin antibiotic or cephalexin. For skin infections with MRSA - the authors' recommendations are for treatment with doxycycline, clindamycin, sulfamethoxazole-trimethoprim. In purulent skin infections, in addition to antimicrobial therapy of a duration tailored to the patient's condition, Stevens *et al*. (2014) recommend incision or drainage of the inflammatory lesion. For skin and soft tissue infections of the skin, the guidelines are

for systemic antimicrobial therapy lasting a minimum of 5 days, but this period should be increased if no progress in the healing process is observed.

Table 16. *Duration of treatment*		
Duration of treatment	<7 days	>7 days
Cases	17,5%; n=27	**81,2%; n=125**
Controls	24,8%; n=37	61,1%; n=91
X^2	2,422	14,94
p	0,12	0,001

4. 6. 5. Comparative studies on cases with an allergic drug reaction, as a result of the applied drug therapy for bacterial infections in childhood:

Table 17. *Allergic drug reactions*					
X^2=6,256, p=0, 012			Allergic reactions		Total
			No	Yes	
Therapy	Cases	Number	141	**13**	154
		% in the studied group	91,6%	**8,4%**	100,0%
		% of total group	46,5%	4,3%	50,8%
	Controls	Number	146	**3**	149
		% in the studied group	98,0%	**2,0%**	100,0%
		% of total group	48,2%	1,0%	49,2%
Total		Number	287	16	303
		% in the studied group	94,7%	5,3%	100,0%
		% of total group	94,7%	5,3%	100,0%

As a result of the antibiotic therapy, information was sought regarding the development of adverse drug reactions. A statistically significant difference was found between post-therapeutic events in children with pyoderma and the control group (X2=6,256, p=0,012). Erythemo-macular changes with centrifugal dissemination were found in 8,4% of patients with bacterial skin infection and in 2% of patients in the control group. In the group of pyodermas, in 1,3% of children a reaction was registered after therapy with azithromycin, in 3,9% - after treatment with amoxicillin/clavulanic acid, in 0,7% - with gentamicin, in 1,95% after treatment with another antibiotic that is not the subject of the study. Studies on local therapy demonstrated local intolerance, presented as subjective sensations of burning and stinging in 9,15% of children with purulent dermatitis.

5. Conclusions:

1. The frequency of bacterial skin infections in childhood on the territory of North-Eastern Bulgaria is 17,48% of the total pediatric pathology.

2. Analysis of the demographic and social structure of some common bacterial infections in children showed that:

2. 1. Gender does not influence morbidity ($p>0,05$);

2. 2. The average age of the patients was 10,1 years ($p<0,05$);

2. 3. The frequency of pyodermas is highest in patients between 11 and 18 years old, living mainly in urban conditions (79,2%, $p=0,054$).

3. The seasonality and risk factors study for bacterial skin infections in children shows:

3. 1. Bacterial skin infections occur year-round, with a peak in the summer season (48,19%, $p=0,21$).

3. 2. Risk factors for their development are the carrier of a pathogen in the nasopharyngeal region in 27,90%, obesity – 20,80% and atopic dermatitis – 18,80%.

4. The most common bacterial skin infections in the studied patients are:

4. 1. by diagnoses - impetigo - 41,60%, folliculitis - 27,30%, ecthyma - 11,70%, furunculus - 11% and perionyxis - 7,10%.

4. 2. by localization - in 63% of patients they are localized mainly on the limbs.

4. 3. The rash units are multiple - 68,80%, with a predominance of exudative lesions - 86,40%, followed by erosions - 64,30% and crusts - 60,40%.

5. Gram-positive bacteria predominate in the etiology of bacterial infections in childhood: *S. aureus* - 41,60%, MRSA - 5,20%. The highest resistance of pathogens to antibiotics was recorded for cefazolin - 14,30% ($p<0,05$), and the lowest for ceftriaxone - 5,20% ($p<0,05$).

6. Systemic antibiotic therapy of children with bacterial skin infections:

6. 1. Conducted parenterally in combination with the local forms of fusidic acid and mupirocin showed a statistically significant healing result ($p<0,05$).

6. 2. Is a predisposing factor for the development of allergic reactions in 8,40% of those treated compared to children from the control group, who received other systemic treatment 2% ($p= 0,012$).

6. Contributions:

6.1. Original

1. For the first time in the country, a comparative analysis was made of the frequency, demographic and social structure of common bacterial skin infections in childhood with general pediatric pathology.

6.2. Scientific and theoretical contributions:

1. For the first time in the country, data from an analysis of the clinical picture of pyodermas in childhood are presented, showing a high frequency of limb involvement;

2. For the first time in Bulgaria, the therapeutic application, effectiveness and safety of modern local and systemic medications in the treatment of common bacterial skin infections in childhood are analysed;

3. Significant antibiotic resistance was found in S. aureus, MRSA and K. pneumoniae, as the causative agents of pyodermas in childhood.

6.3. Scientific-practical and confirmatory contributions:

1. The study confirmed the established seasonality in bacterial dermatoses during the warm months of the year;

2. The study proves the role of atopic dermatitis, nasopharyngeal carriage of pathogens and obesity as risk factors for the development of pyodermas in childhood;

3. The analysis of the conducted microbiological studies confirms the main role of *S. aureus* in the etiology of pyodermas and establishes the frequency of MRSA as an etiological factor for the development of bacterial skin infections in childhood.

7. Publications related to the topic:

1. Stoyanova Zh., Bakardzhiev I., Bacterial skin infections in childhood, Varna medical forum, 2019, item 8, appendix 3;

2. Stoyanova Zh., Bakardzhiev I., Local therapy with fusidic acid in the treatment of bacterial skin infections in childhood, GP News, 11/2020;

Contributions related to the topic:

1. Stoyanova Zh., Bakardzhiev I., Microbiome, immunity and children's skin - Varna Spring Dermatology Days, Sunny Day, April 18-21, 2019.

2. Stoyanova Zh., Bakardzhiev I., Microbiome and skin, IX scientific session of the Medical College, Varna, March 23, 2021.

3. Stoyanova Zh, Bakardzhiev I, Epidemiology of bacterial skin infections in children in Varna Region, Varna Dermatology Days, Sunny Day, April 21-22, 2023.

8. Conclusion

Bacterial skin infections in childhood are among the most common diseases in developing countries. Their significance is related not only to quality of life impairment, morbidity and mortality, but also to a large economic impact. Precisely because of their high frequency and the trivial nature of the lesions, parents and medical professionals often neglect the conditions of skin diseases and thus significantly increase the risk of unwanted subsequent complications. These facts explain the need to raise the general medical culture of the population and focus the attention of doctors on outpatient care. Awareness and education about risk factors and ways to prevent these diseases should be part of the strategy of any health program (Gupta, 2021).

Dermatoses account for 8.4% of outpatient visits to primary care offices (Hancox *et al*., 2004). Bacterial skin infections are among the most common diseases of childhood, with the global pediatric population suffering from impetigo estimated at > 162 million. Between 2000 and 2015, the average childhood prevalence was estimated at 12.3% (Bowen *et al*., 2005).

Bacterial infections of the skin and skin structures that are common in children include impetigo, ecthyma, folliculitis, furunculosis, infections of skin appendages - glands and nails.

The incidence of bacterial skin diseases may be affected by climate change (Maraki and Tselentis, 2000). However, due to large environmental and climatic differences around the world, seasonality patterns vary from region to region. The combination of hot and humid climate, increased insect population in these areas, close body contact are predisposing factors for the development of pyodermas. A risk factor is also the presence of other dermatosis such as atopic dermatitis, scabies, lice (WHO, 2005).

A current problem with these infections is that they are contagious and, left untreated, can lead to serious and sometimes fatal outcomes, including invasive infection (eg, sepsis, osteomyelitis) and postinfectious complications (eg, acute rheumatic fever, acute poststreptococcal glomerulonephritis). (Hoy *et al*., 2012; Munro *et al*., 2018; Baker et.al, 2019; Campbell et.al, 2022).

The presented data and facts motivated us in the present dissertation to study and analyze the dynamics, demographic and risk factors, clinical, diagnostic and therapeutic aspects of some common bacterial skin infections in childhood.

In the present study, 303 patients were included - 154 of them with bacterial skin infections and 148 with other non-infectious skin diseases (control group).

The average annual incidence of bacterial skin infections in the Varna region is 14,20%. The comparative analysis of the age of the patients shows insignificant differences between the two sexes - 10,72 years - girls and 9,3 years - boys; Mean age of presentation of bacterial infections was 10,1 years. An increased incidence was found in children from 0 to 4 years of age and over 11 years of age. There is no gender bias. The influence of external environmental factors on the incidence of pyoderma

in childhood is year-round, with a peak in the summer months – 48,10% ($p<0,05$). There is an increased frequency of morbidity in children living in urban conditions (79,20%; n=122, $p<0,05$).

An essential factor for the development of bacterial skin infection in DV is the presence of accompanying diseases. Among them, children with AD - 18,80% ($p<0,05$), obesity - 20,80% ($p<0,05$) and carrying a pathogen in the nasopharyngeal area at 27,90% ($p<0,05$). A correlation was found between obesity and the development of bacterial skin infections in children, as well as between AD and impetigo.

Skin changes in pyodermas are mainly localized on the extremities in 63% ($p<0,05$), they are multiple - 68,80% ($p<0,05$), with a predominance of exudative rash lesions - 86,40% ($p<0,05$), followed by erosions - 64,30% ($p<0,05$) and crusts - 60,40% ($p<0,05$). Involvement of the mucous membranes, skin appendages and RLV in the pathological process is characteristic of pyodermas. There is a correlation between warm seasons and the localization of lesions on the face.

The three most common bacterial skin infections in childhood were impetigo 41,60% ($p<0,05$), followed by superficial folliculitis – 27,30% ($p<0,05$) and ecthyma 11.70% ($p <0,05$). Impetigo is a disease of younger children - mostly in the group between 0 and 4 years, while folliculitis is more common in adolescents over 11 years of age. In case of impetigo, accompanying diseases such as AD, insect dermatitis are a more likely predisposing factor, while in case of folliculitis - external factors, among which are mainly trauma, obesity. Both diseases peak in the warm months. Boys are more likely to develop impetigo, while girls are more likely to develop folliculitis or ecthyma.

Making a diagnosis of "pyoderma" is empirical, but establishing the etiological factor, as well as its antibiotic sensitivity, would refine the therapeutic behavior of the doctor and minimize the risk of developing microbial resistance. In the present study, the main etiological factor for the development of pyoderma is *S. aureus* – 41,60% ($p<0,05$). MRSA was responsible for 5,20% ($p<0,05$) of skin infections in children. Although in our study cefazolin has the most limited application, it also has the highest established resistance to it – 14,30% ($p<0,05$), and ceftriaxone - with the smallest – 5,20% ($p<0,05$).

Systemic antibiotic therapy carried out with amoxicillin/clavulanic acid, azithromycin, gentamicin, ceftriaxone and cefazolin, in combination or alone with the topical forms of fusidic acid and mupirocin, in an individually tailored dosage regimen, form and duration, have shown a good healing result with a relatively low rate of subsequent drug allergic reaction.

The above results allow us to conclude that, diagnosed in time and treated correctly, skin infections are almost always curable. With a delay in diagnosis or incorrect and/or insufficient treatment, some purulent dermatitis have the potential to cause severe complications. Good personal hygiene is key to the prevention of pyoderma in childhood. Cultural methods, as well as determination of antibiotic sensitivity of the isolates, would refine the treatment process and reduce the appearance of resistant microorganisms, and hence hospitalization, complications and lowering the quality of life

of pediatric patients and their parents. Despite the high prevalence and burden of skin diseases, they have been neglected as a priority in the development of health policies and an effective strategy to reduce the cost of hospital visits and improve the quality of life of patients.