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Gender Features of Skin Microbiome and Antibiotic Resistance

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ABSTRACT

Sex, as a biological variable, determines immune responses to both self and foreign antigens. Human gender contributes to physiological and anatomical differences that influence the formation of the microbiome. In this regard, this article is aimed at identifying the features of microbial contamination of the skin in students (guys and girls) of the Institute of Natural Science and Medical Institute of Kaluga State University named after K. E. Tsiolkovsky. It was found that the number of microorganisms on the palms and the palmar part of the forearm in girls was 51.2% more than in guys. Most often, actinobacteria, staphylococci, streptococci, and corynebacteria were present. Moreover, the number of corynebacteria on the skin of young men was 1.6 times higher. It was noted that guys were sick more often than girls (except for cystitis), but less often they consulted a doctor for a prescription for antibiotics or used them on their own. Most of the students followed the standard course of antibiotic use or until symptoms disappeared. The most frequently used antibiotics were girls (63%), while guys used antibiotics 1.6 times less often. Only 2% of students never used antibiotics. Most often, students used tetracycline (31.8%), furazolidone (26%), ampicillin (27.8%), lincomycin (16.7%) and clarithromycin (11.1%), azithromycin (12.5%). A diffuse method was used to assess the resistance of microorganisms to antibiotics. The article presents the results of diffuse tests, which showed multi-resistance and gender differences in the resistance of skin microorganisms to antibiotics. The skin microflora of girls is more sensitive to the tested antibiotics than that of guys. Antibiotics to which microorganisms showed resistance were lincomycin (71.4% in guys and 45.3% in girls), fosfomycin (68.57% in guys and 53.85% in girls), benzylpenicillin (51.41% in for boys and 42.2% for girls), oleandomycin (51.43% for guys and 16.2% for girls), doxycillin (40% for guys and 29.1% for girls). The materials of the article are of practical value for understanding the gender characteristics of the skin microbiome and the resistance of microorganisms to antibiotics.

1. INTRODUCTION

Practical medicine has traditionally paid little attention to gender differences in the pathogenesis of many diseases, both infectious and somatic, and to the microbiome features of men and women. But in recent years,

academic and clinical medicine have begun to seriously study gender differences along with such factors as ethnicity and socioeconomic status. This has contributed to the development of a new field - gender medicine [1], [2].

Men and women are biologically and physiologically different, which is why they have different ways of carrying diseases, including infectious diseases. Sex, as a biological variable, determines immune responses to both their own and foreign antigens [3]. Human sex contributes to physiological and anatomical differences that affect microbiome formation [4], [5].

Recent advances have expanded our understanding of the human microbiome, including the skin microbiome. The skin is one of the largest habitats for microorganisms. There are 205 species of microorganisms representing 19 genera present on the human skin. Staphylococci, streptococci, micrococci, sarcinae, yeasts, corynebacteria, and opportunistic bacteria predominate on the surface of healthy human skin. Representatives of the genus Corynebacterium sometimes account for up to 70% of all cutaneous microflora [6], [7].

Although bacteria are distributed throughout the skin surface, microorganisms inhabiting the palms of the hands are of particular interest because it is one of the most dynamic habitats of skin microbes [8], [9]. Hands are the most important vector of microbial transmission between people, pets, various objects, and the environment [10].

Studies by various authors have noted gender peculiarities in the composition of the human skin microbiome [11- 13]. Men and women have different bacterial communities on the surface of their hands. Moreover, women's palms have more bacterial diversity than men's palms. This diversity may depend on the pH of the skin, the production of sweat or sebum, the frequency of moisturizers or cosmetics, and the thickness of the skin [14]. It may also be related to the interaction between the microbiome, hormonal balance, and the body's immune mechanisms [15].

The different biological status of men and women determines different reactions to prescribed medications, including antibiotics. Antimicrobial therapy played a crucial role in the treatment of human infectious diseases in the twentieth century, as the use of antibiotics significantly reduced human mortality from infections, shortened the clinical manifestations of diseases, and the number of postinfectious complications. Since the discovery of penicillin hundreds of antimicrobials have been developed and synthesized, dozens of which are now available for clinical use. Millions of people now survive infections that used to be life-threatening. But for several decades now, there have been increasing reports of antibiotic resistance of microorganisms [16-18].

Uncontrolled and unjustified use of antibiotics not only in clinical practice but also in animal husbandry and poultry production, has led to an avalanche-like increase in the number of bacterial strains resistant to various drugs. Bacteria have an effective genetic mechanism of resistance to antibacterial drugs. Therefore, there is a significant pool of antibiotic resistance genes in nature [19], [20]. Over the past few decades, a large number of cases of resistance acquisition in previously susceptible bacterial strains have been described [21], [22]. Antibiotic resistance leads to higher medical costs, longer hospital stays, and increased mortality. According to the World Health Organization, bacterial resistance to antibiotic drugs currently poses one of the greatest threats to humanity. Every day 1 out of 3 patients receives at least one antimicrobial. One in 15 patients in European hospitals has at least one of the hospital-acquired infections caused by multidrug-resistant bacteria [23], [24].

Currently, about 700,000 people die each year because of drug-resistant diseases, and it is predicted that there will be 10 million deaths per year in 2050, more than the 8.2 million cancer deaths today [25], [26].

Antimicrobial resistance also puts a strain on health care systems, which incur extremely high financial costs due to increased hospitalizations, longer hospital stays, and costly intensive care. Healthcare providers are forced to use a combination of more expensive antibiotics to treat various infections [26].

Thus, antibiotic resistance has become one of the leading problems of modern medicine. Antibiotic resistance can occur in anyone at any age and in any country. However, there are very few detailed studies nowadays examining the gender resistance of the human microbiome to antibiotics.

2. METHODS AND OBJECTS OF RESEARCH

The objects of the study were students of K. E. Tsiolkovsky Kaluga State University (n = 275). Students were interviewed about their morbidity and use of antibiotics. At the same time, we took flushes with sterile tampon probes from the skin of the palms and the palmar part of the forearm. Quantification of microorganisms (colony forming units - CFU) was performed using standard microbiological methods. Microorganisms were identified taking into account their morphological and biochemical characteristics. The species composition of isolated microorganisms was studied by mass spectrometry on a MALDI-TOF MS autoflex speed analyzer (Bruker company).

The sensitivity of bacteria to antibiotics was determined by the diffusion method using antibiotic-soaked disks (Table 1).

Table 1 List of antibiotics used

No.	Name	Concentration	No.	Name	Concentration
1	Azithromycin (ARN)	15 mcg	13	Oleandomycin (OLE)	15 mcg
2	Ampicillin (AMP)	10 mcg	14	Optokhin (OP)	6 mcg
3	Benzylpenicillin (PEN)	10 units	15	Ofloxacin (OF)	5 mcg
4	Doxycycline (DOC)	30 mcg	16	Tetracycline (TET)	30 mcg
5	Clarithromycin (KTM)	15 mcg	17	Tylosin (TLZ)	15 mcg
6	Levomycetin (LEV)	3.0 mcg	18	Tobramycin (TOB)	10 mcg
7	Levofloxacin (LFC)	5 mcg	19	Cefoperazone (CPR)	75 mcg
8	Lincomycin (LIN)	15 mcg	20	Cefoxitin (CEF)	3 mcg
9	Lomefloxacin (LOM)	10 mcg	21	Ciprofloxacin (CIP)	5 mcg
10	Neomycin (NEO)	30 mcg	22	Fosfomycin (FOS)	200 mcg
11	Novobiocin (NB)	5 mcg	23	Furadonin (FD)	300 mcg
12	Oxacillin (OCS)	10 mcg	24	Furazolidone (FRN)	300 mcg

The principle of the disc-diffusion method is based on the phenomenon of inhibition of surface, visible growth of microorganisms on the agar nutrient medium by the antibiotic. The concentration gradient of the antibiotic in the nutrient medium is created by its diffusion from the cardboard disc. The disc with the antibiotic is placed on the surface of the nutrient medium immediately after sowing (inoculating) the culture of the microorganism under study. Two processes begin almost simultaneously: diffusion of antibiotics from the disc and growth of microorganisms on the surface of the medium.

After incubating the seeds with disks, the zones of microbial growth inhibition were measured. Statistical processing of the results of the study was performed using classical methods of mathematical statistics and a

Microsoft Excel table processor.

3. STUDY RESULTS AND DISCUSSION

The average age of the students who participated in the study was 21 years old. They were mostly students of the Institute of Natural Sciences (36%, n = 99) and the Medical Institute (64%, n = 176). The majority of them were girls (68%, n = 187).

The total number of microorganisms on the palms and palmar part of the forearms of the males was 127±15 CFU/cm^2 and that of the females was 192±19 CFU/cm^2. Actinobacteria, staphylococci, streptococci, and corynebacteria were most often present (Figure 1). The number of corynebacteria on the skin of young boys was 1.5 times greater than that of girls.

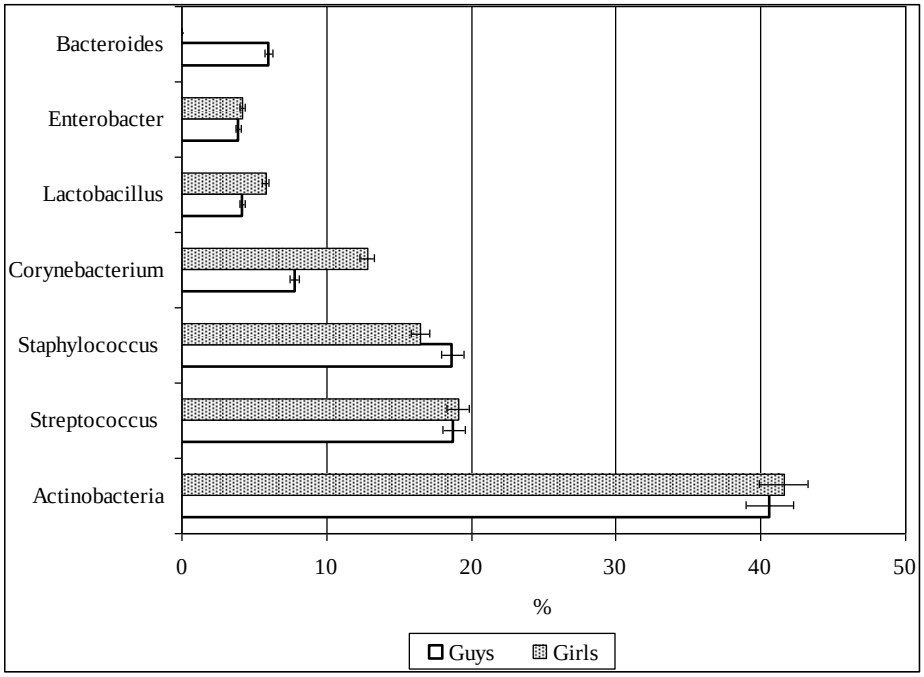

Figure 1 Gender analysis of bacterial diversity in the skin of guys and girls

Most often students used antibiotics for such diseases as colds, otitis media, diarrhea, and cystitis. Moreover, cystitis occurred 2.6 times more frequently in girls than in boys. Skin diseases were somewhat more frequent among girls. For the rest, the incidence among young men was higher than among girls (Figure 2).

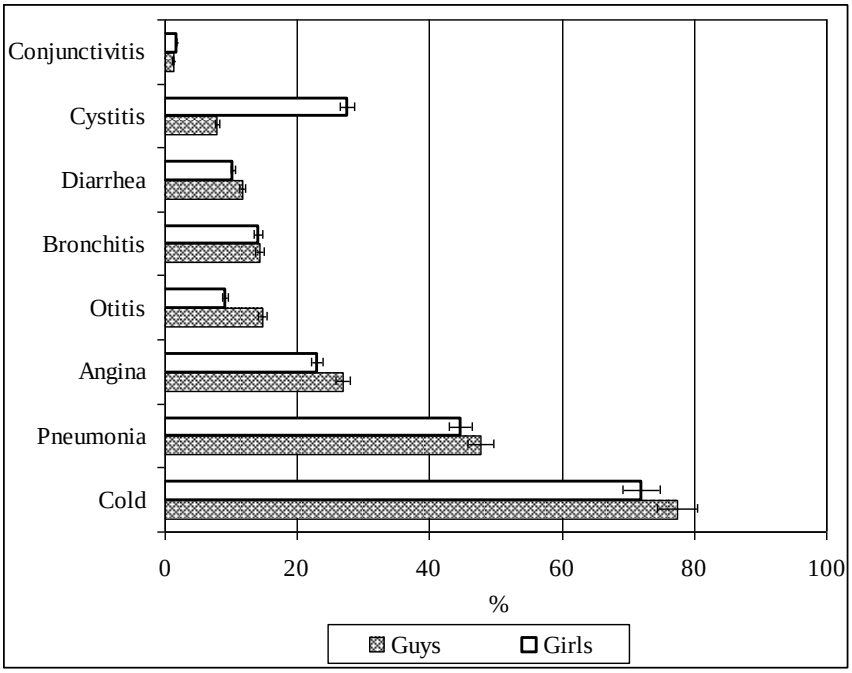

Figure 2 Comparative characteristics of the morbidity of guys and girls

Girls used antibiotics most frequently (13.8%). 55.1% of boys and 41.5% of girls used antibiotics infrequently. Only 2% of the students never used antibiotics (Figure 3).

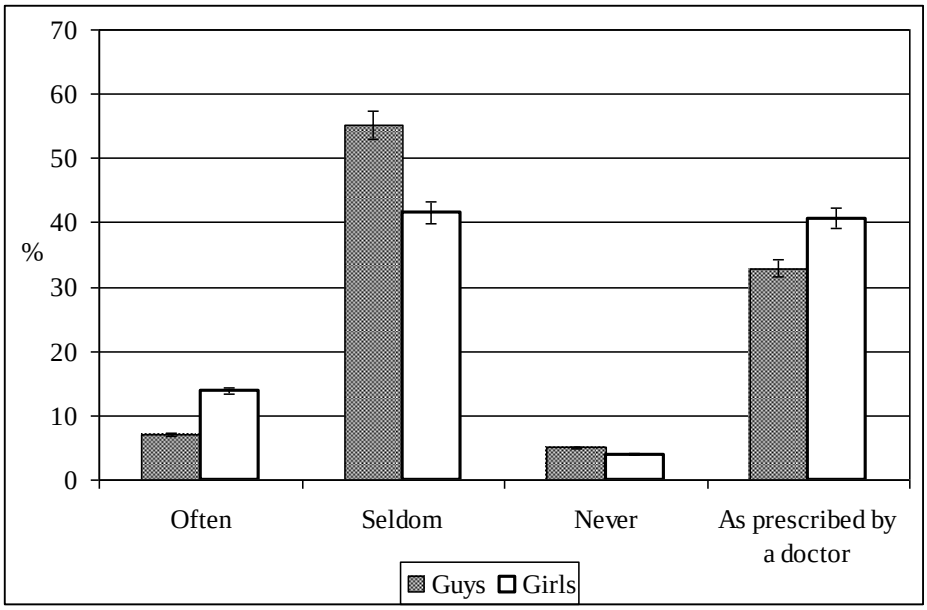

Figure 3 Gender analysis of antibiotic use by students

Most students received a prescription for antibiotics (82.4% girls and 69.9% boys). At the same time, young males were twice as likely to use antibiotics on their own (Figure 4).

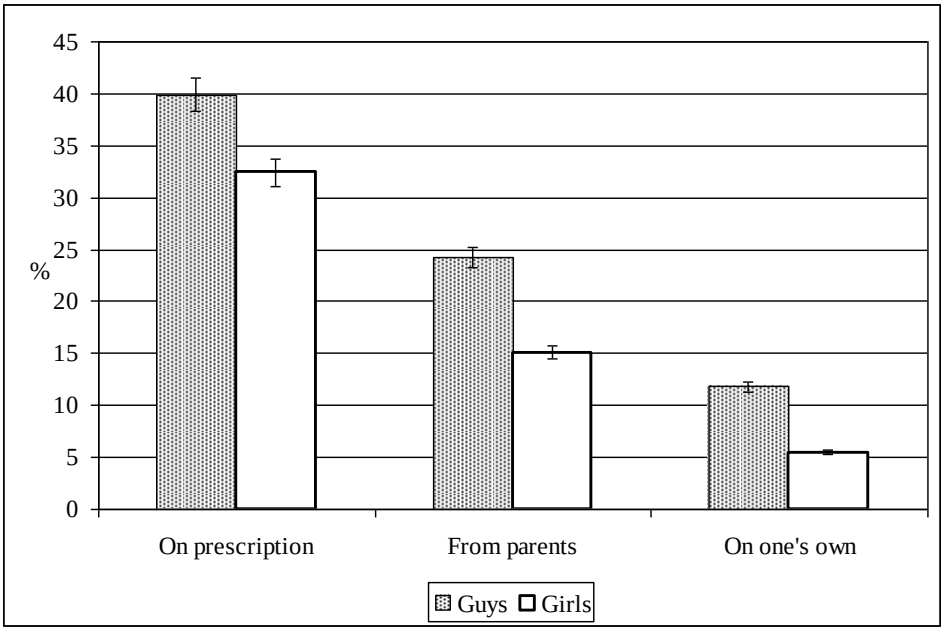

Figure 4 Comparative analysis of antibiotic prescriptions

The most frequently used antibiotics by students were levomycetin, tetracycline, furazolidone, and ampicillin (Figure 5).

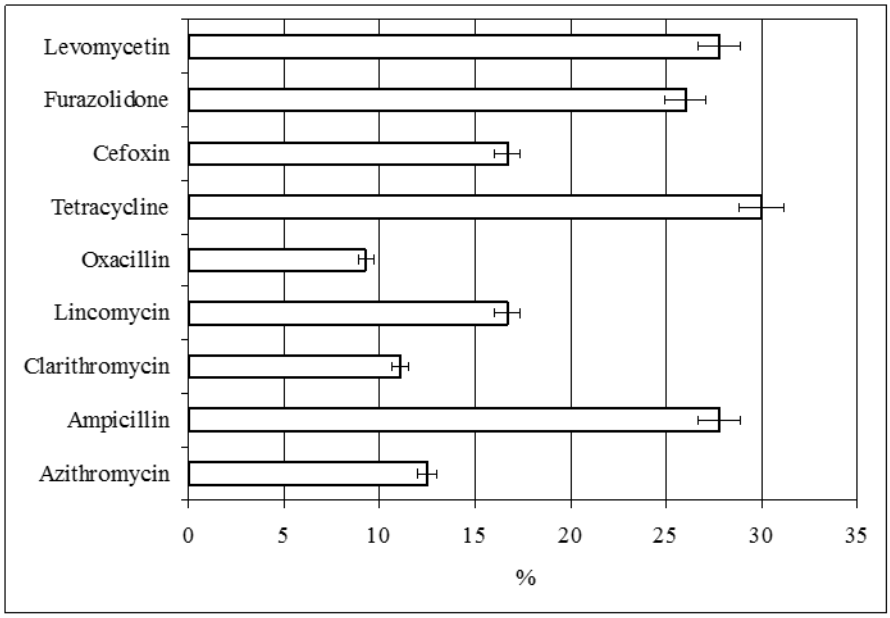

Figure 5 The highest-priority antibiotics among students

For the most part, students adhered to the full course of antibiotic treatment (65% of males and 74.7% of females). The course of antibiotic treatment was discontinued after 2-3 days by 18.9% of the males and 11.4% of the females. Girls were somewhat more responsible for antibiotic treatment (Figure 6).

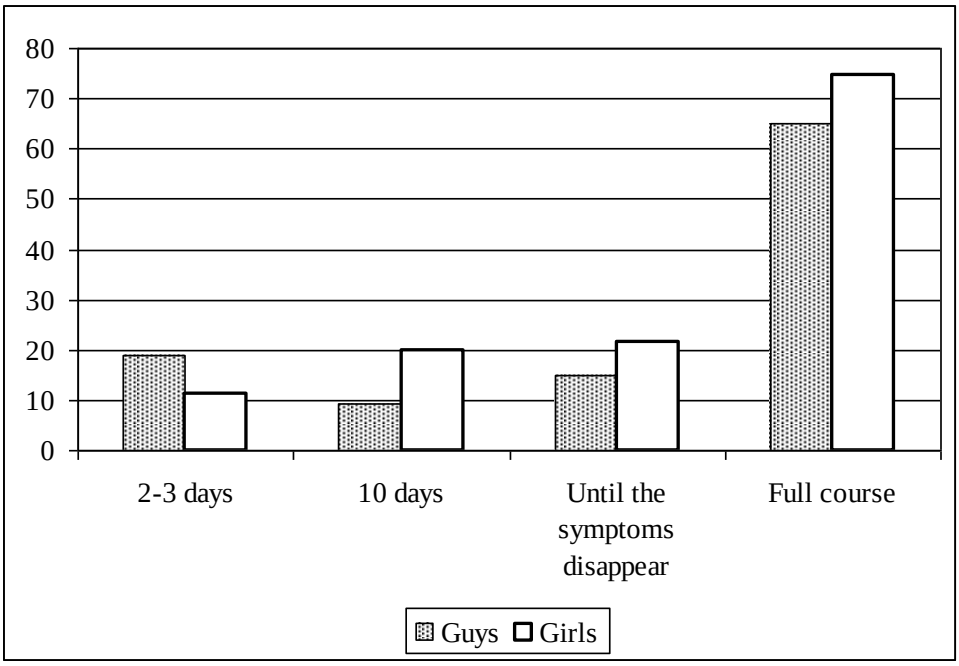

Figure 6 Results of antibiotic use

The results of diffusion tests showed multi-resistance and gender differences in the resistance of skin microorganisms to antibiotics. Moreover, girls had significantly lower levels of microbial resistance to some antibiotics than boys (Figures 7 and 8). Microorganisms showed the greatest resistance to lincomycin (71.4% in boys and 45.3% in girls), phosphomycin (68.57% in boys and 53.85% in girls), clarithromycin (60% in boys and 50.4% in girls) oleandomycin (51.43% in boys and 16.2% in girls), benzylpenicillin (51.41% in boys and 42.2% in girls), doxycycline (40% in boys and 29.1% in girls), tetracycline (22.86% in boys and 23.0% in girls) and other antibiotics.

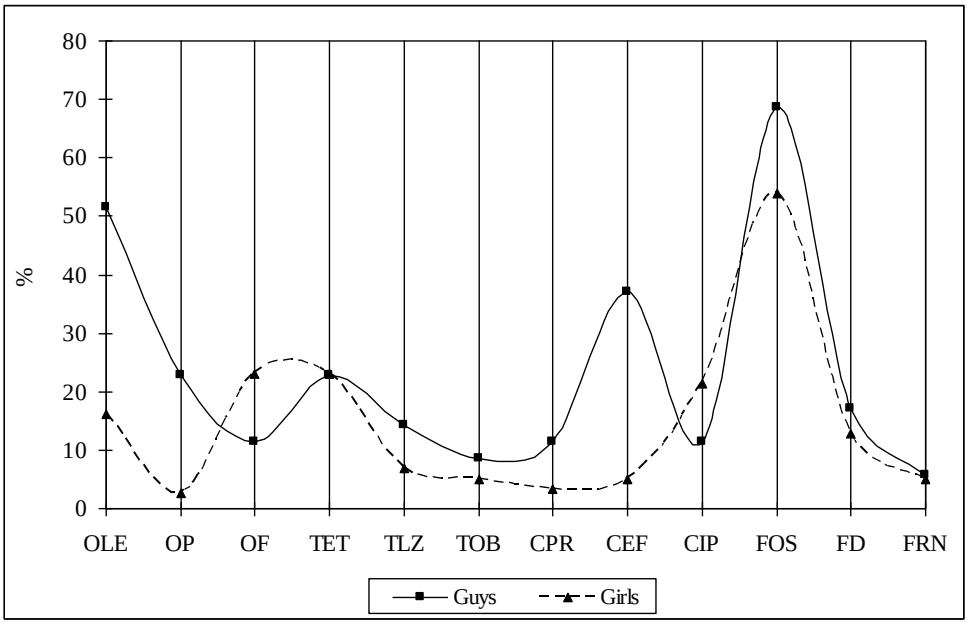

Figure 7 Gender-specific features of skin microflora resistance to antibiotics

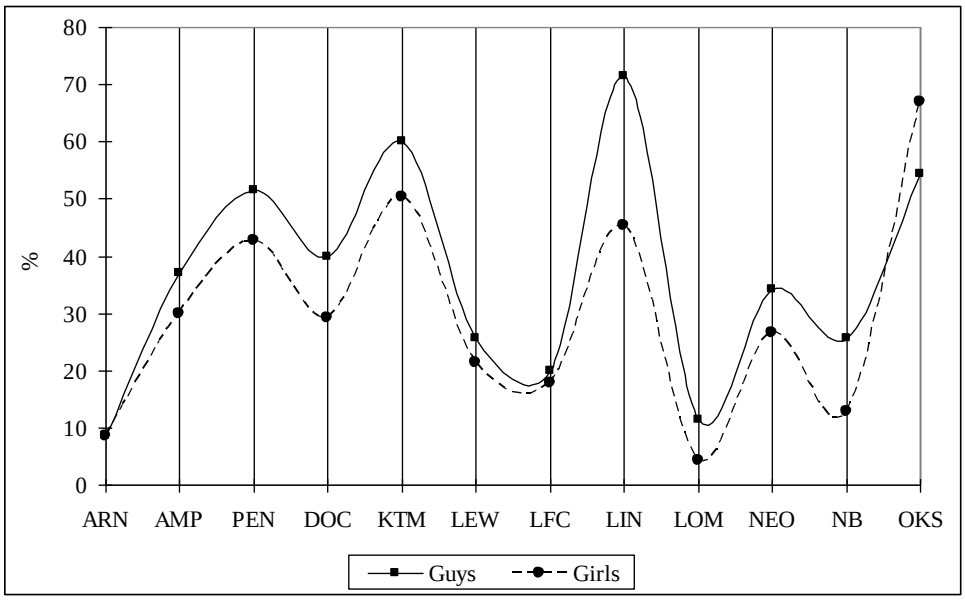

Figure 8 Gender differences in antibiotic resistance of skin microflora

For girls, the most effective antibiotics were optoquine, tobramycin, cefoperazone, furazolidone, and lomefloxacin. For young men, only furazolidone was the most effective antibiotic.

4. Conclusion

Actinobacteria, Streptococcus, Staphylococcus, Corynebacterium, Lactobacillus, and Enterobacter were present on the skin of the palms and palmar part of the forearm in all students.

Gender differences in the number of microorganisms were revealed. There were 51.2% more microorganisms on the skin of girls than on the skin of boys. The number of Corynebacteria on the skin of boys was 1.6 times greater, and the number of Enterobacter on the skin of girls was 1.3 times greater.

The most frequent use of antibiotics by students was for illnesses such as colds, otitis media diarrhea, and cystitis. Cystitis in girls was 2.6 times more common than in boys.

Girls used antibiotics most frequently (63%), while boys used antibiotics 1.6 times less frequently. Only 2% of students never used antibiotics. Girls more often (82.4%) received a prescription for antibiotics than boys (69.9%). Young men were twice as likely to use antibiotics on their own.

Diffusion test results showed multi-resistance and gender differences in skin microbial resistance to antibiotics. Microorganisms showed the greatest resistance to lincomycin (71.4% in boys and 45.3% in girls), phosphomycin (68.57% in boys and 53.85% in girls), clarithromycin (60% in boys and 50, 4% in girls), oleandomycin (51.43% in boys and 16.2% in girls), benzylpenicillin (51.41% in boys and 42.2% in girls), doxycycline (40% in boys and 29.1% in girls), and tetracycline (22.86% in boys and 23.0% in girls).

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