

## Allergic Reactions to Antibiotics in the Population of Boys and Girls Aged 15 Years Old in the Tuzla Canton of Bosnia And Herzegovina

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### Abstract

Hypersensitivity reactions can occur in any mode of application and to almost all antibiotics. The purpose of the study was to determine which groups of antibiotics most often cause allergic reactions, and to determine statistically significant differences in the occurrence of allergic reactions to antibiotics between boys and girls of the same age, whether there are differences in the occurrence of allergic reactions between respondents in urban and rural areas. The sample consists of 1605 respondents, the sample was randomly selected and stratified by sex, and all data were processed in the statistical program. The results of the research show that 9,1 % of the total population of boys and girls aged 15 from the Tuzla canton is allergic to some type of antibiotic. The percentage of allergic reactions in the total population of 15-year-old boys and girls from the suburbs is slightly higher than among peers in urban areas, but the differences are not statistically significant. The percentage of allergic reactions in the population of 15 years of rural area is 8.62%. A higher rate of allergic reactions was recorded in the group of boys from urban and rural areas. Macrolide allergies were found only in group of boys in rural areas. This study confirmed the most common allergies to penicillin antibiotics and revealed differences in the occurrence of allergic reactions between girls and boys.

**Keywords:** allergies; antibiotics; male and female population; urban and suburban areas;

### I. INTRODUCTION

Except the pharmacological effect, drugs can cause a number of side effects. These adverse drug reactions are divided into two basic groups - type A and type B. The most common are type A reactions (80%). They can occur in any person and are the result of drug overdoses, drug side effects, or drug interactions.

Type B reactions occur in 20% of cases and are not related to the pharmacological action of the drug. These reactions include allergies (hypersensitivity) to the drug, and their development involves immune mechanisms, and non-immune hypersensitivity, which includes pseudoallergic reactions, reactions related to changes in metabolism or enzyme deficiency, and drug intolerance [1,2]. Symptoms appear minutes to hours after taking the medicine.

In mild allergic reactions, it is necessary to discontinue the antibiotic that caused the allergic reaction and replace it with another group of antibiotics. But, if the allergic reaction is extremely strong, then, in addition to the abolition of that antibiotic, the treatment of allergic manifestations caused by the antibiotic must also be carried out.

Sensitization to the drug occurs more often after topical application (on the skin or mucous membranes), and less often after oral application. The anaphylactic reaction is more common after parenteral application (penicillin). The risk of developing allergies increases with prolonged use of high doses as well as due to frequent use of the same drug. Drug allergies are less common in infants and young children than in adults, and allergic skin reactions are significantly more common in women [3].

Drug allergies can be divided according to the time interval between the drug taken and the reactions that occur. We divide them into early reactions that occur within one hour and are mediated by IgE antibodies. Late reactions occur after several hours or days. Late reactions represent a heterogeneous group of reactions, often with the appearance of cutaneous manifestations, and are mediated by IgG, IgM antibodies, Th1 and Th2 lymphocytes, cytotoxic lymphocytes, chemokines, and other effector cells [4]. If the reaction occurs within one hour of drug application (regardless of the route of application), there is a significantly higher risk of anaphylaxis when re-application the same drug [5]. Penicillin allergies are associated with IgE, i.e. an antibody found in the body that mediates allergic reactions. When penicillin, which can cause an allergic reaction, is taken into the body, the immune system produces IgE. IgE then travels through the body and binds to a type of

allergic cell called mast cells. IgE sits on the surface of mast cells and waits. When a person gets the medicine again, they may have a reaction and this sudden reaction may include anaphylaxis [6].

Reactions that are not mediated by IgE antibodies usually appear after 6 hours of drug application (delayed reactions) or a few days after discontinuation of the drug, eg ampicillin allergy usually manifests after 7-10 days from the start of treatment, and often 1-3 days after discontinuation of treatment [7].

Penicillin cause very little direct toxicity. The most common side effects to penicillin are hypersensitivity reactions, and at the same time, of the drugs in general, penicillin most commonly cause hypersensitivity reactions. Immunogenic properties are associated with  $\beta$ -lactam ring cleavage and by forming of penicilloyl formation which is a major determinant of immunogenicity.

Of the amount of penicillin applicated for therapeutic purposes, about 5% is covalently bound to individual serum amino acids. Under physiological conditions, the beta-lactam ring opens, creating an amide bond between the carboxy group of the penicillin molecule and the amino group of the protein. In this way, a penicilloyl conjugate is formed, which is also called the major allergic determinant of penicillin. Of the total protein-bound penicillin in the body, 80-95% is metabolized in this way. It is important that this reaction is the same for all penicillin (natural and semi-synthetic). Therefore, the penicilloyl group is the major determinant of all penicillin, regardless of the structure of the side chain. It is important to note here that penicillin is metabolized in other ways as well. These metabolites are produced in small amounts and are therefore called minor allergic determinants. Although they are produced in small quantities, they are often responsible for the development of very serious allergic reactions in the body.

Hypersensitivity reactions can occur with any type of application and to any type of penicillin, and their total frequency ranges from 0.7-10%. There is cross-sensitivity among different types of penicillin, as they all contain a penicillin nucleus built of a four-membered beta lactam and a five-membered thiazolidine ring. The cephalosporin nucleus is sufficiently different from the penicillin nucleus, so some people with penicillin allergy, tolerate cephalosporin, well and may receive cephalosporin therapy for susceptible agents. The frequency of cross-allergy between these two groups of beta-lactam antibiotics ranges between 5-10%. However, it is considered that patients with anaphylaxis to penicillin should not receive cephalosporin. Although allergic reactions to penicillin are common, according to some reference sources, in only 10% of cases will there be a recurrent allergic reaction with the next application of penicillin. However, for people with a history of allergic reactions to penicillin, another type of antibiotic with a similar antimicrobial spectrum is recommended. Different forms of hypersensitivity reactions are possible: maculopapular rash, nettle rash, fever, bronchospasm, vasculitis, serum sickness, exofoliative dermatitis, Stevens-Johnson syndrome, and anaphylaxis. The most severe symptoms are anaphylaxis, which can be fatal (anaphylactic shock, angioneurotic edema), and the frequency of this allergic reaction ranges between 0.004-0.04%. Anaphylactic shock occurs a few minutes after penicillin application. Allergic reactions are less common with oral application of the drug and more common with topical or intramuscular application of procaine-benzylpenicillin [8]. The incidence of rash of allergic genesis, of all penicillin, is most common to ampicillin (9%), and occurs in patients with viral infection, especially infectious mononucleosis in the form of maculopapular rash, who due to non-recognition of the disease and wrongly given ampicillin to treat angina present in mononucleosis. It is considered to be a toxic, not a real allergic reaction.

Due to the possibility of a severe allergic reaction after topical application, topical preparations of penicillin are not produced, and topical application of penicillin to the skin and mucous membranes and inhalation of aerosols is considered a professional error.

Risk factors for the occurrence of allergies to antibiotics are the occurrence of allergies in the immediate family, the dose of the drug, the length of treatment and the method of administration. Eg. anaphylaxis is more common with parenteral versus oral application. Symptoms of anaphylaxis may include: itching, hives (raised spots on the skin that are extremely itchy), swelling of the lips, face and / or throat-angioedema, shortness of breath, vomiting, diarrhea, symptoms of low blood pressure (dizziness, fainting) [6].

Sulpha allergy is a term used to describe the side effects caused by sulfonamides, a group of drugs that includes both antibiotics and non-antibiotics. It is believed that all sulfonamide drugs can cause allergies, but this is not entirely true. Antibiotic sulfonamides (used to treat bacterial infections) are more likely to trigger an allergic reaction than non-antibiotics. These reactions occur in only 3% of patients. People who metabolize the drug slowly or have a suppressed immune system (such as organ transplant recipients and people with HIV / AIDS) have a higher risk of sulfa allergies. Symptoms of sulfa allergy usually include the appearance of a widespread rash, photosensitivity. In severe cases, the onset of the rash may be accompanied with edema of the face, hands, feet and tongue (known as angioedema), Stevens-Johnson syndrome [2,9].

Any patient who has had a systemic reaction should be hospitalized or at least observed for 12-24 hours. If only a skin rash has appeared, it is enough to take antihistamine tablets. If a severe allergic reaction occurs, a doctor's examination and observation of the patient is required.<sup>7</sup>

*Desensitization to antibiotics*

By methods of rapid and slow oral and intravenous desensitization, it is possible to achieve transient tolerance in patients allergic to antibiotics and some other drugs. Desensitization is recommended in cases where there is no alternative drug and treatment is necessary with the same drug. In vitro and in vivo tests are important to determine allergies. Desensitization can be risky for the patient, so it should be performed by specially trained staff in emergency care facilities.

History and skin tests are the basis for determining the type of hypersensitivity, antigen identification, and are more reliable than in vitro tests. They are usually performed between the 3rd week and the 3rd month of the side effect. Skin tests represent an important finding for antigen identification and are better indicators of early-type IgE antibody-mediated hypersensitivity than in vitro tests, and are also cheaper [7]. For type I hypersensitivity reactions, a prick test is used and, if negative, and intradermal test.

To avoid errors in the interpretation of the test, it should be checked that the patient has not used some medications such as antihistamines, corticosteroids, antidepressants as they may affect the test result. Positive (histamine) and negative (saline) controls should be applied simultaneously. The test is read after 15-20 minutes. The test is positive if the urticaria diameter is 3mm larger than the negative control. A negative skin test has a high predictive value (99%) that the patient is not allergic to penicillin [7].

If the patient has a history of severe reactions, reagents should be diluted 100-fold for the primary sample. If the puncture test is negative, intracutaneous tests may be performed. If the skin test result is positive, treatment of patients with penicillin may cause an anaphylactic reaction. If the test results are negative, a serious reaction is unlikely but not ruled out. Although skin tests for penicillin do not cause de novo hypersensitivity, patients are tested immediately before starting penicillin therapy.

Only 10-20% of patients who respond to penicillin show positive skin tests. For many drugs (including cephalosporins), the samples are unreliable, and since they only diagnose IgE-mediated allergies, they do not allow us to predict the development of core rash, hemolytic anemia, or nephritis. When an allergy to a particular drug is confirmed, after obtaining the written consent of the patient or parent (in the case of children), accelerated desensitization to penicillin or other beta lactam orally or intravenously is applied, gradually doubling the dose at regular intervals. Drug desensitization - mainly penicillin, began to be used since 1946 [10].

Following the introduction of cephalosporin to treat infections, cross-reactions were often present (5-15% of cases). Namely, cephalosporine and penicillin contain the same beta lactam ring, and these preparations before 1980, also contained traces of penicillin. Newer generations of cephalosporine (III-IV) are less likely to give cross-reactions (1-3%) and are more often associated with side chains [11]. Patients allergic to cephalosporine, if they have a negative skin test for penicillin, can be treated with it. Aztreonam (monobactam) does not cross-react with beta-lactams (except rarely cephalosporine), and carbapenem like imipenem rarely cross-react with penicillin.

When using other antibiotics such as macrolides, tetracyclines, and aminoglycosides in case of early hypersensitivity (IgE antibody-mediated) as well, desensitization is recommended if the skin tests are positive. Unfortunately, since no antigenic determinants are known, the drug itself should be applied at the appropriate diluted concentration. For the diagnosis of hypersensitivity to these antibiotics, skin tests are less sensitive and specific than testing with beta-lactam antibiotics.

*Association of allergic reactions with antibiotic therapy in early childhood*

Doctors have found that multiple groups of antibiotics increase the risk of allergies, and that it is greatest in those in the penicillin group. If a child takes an antibiotic in the first year, he has a 20 percent higher risk of developing asthma, just like if he was born by caesarean section. Microbiologist Brett Finaly says rural life and breastfeeding reduce the risk of developing asthma by 20 percent. He led a study that back in 2015 found that four types of bacteria in a child's gut can reduce the risk of developing asthma. Allergic protection begins in the mother's womb, and in the first 100 days of life, the intestinal microbiome affects the immune response that causes or protects against asthma. Which side will prevail depends largely on how we promote a healthy intestinal flora. A Finnish study published in the journal *The Lancet* found that the incidence of atopic dermatitis was 50 percent lower in children whose mothers took the probiotic *Lactobacillus rhamnosus* during pregnancy. The protective effect was also visible seven years after birth [12]. U.S. physicians and the study's author, pediatric gastroenterologist at the Uniformed Services University in Maryland, Dr. Cade Nyland, found that there was a higher risk in later childhood of food allergies, asthma, or skin dermatitis in babies receiving penicillin [13].

They found that antibiotics are not only associated with an increased risk of allergic disease, but that there is also an increased risk of more groups of antibiotics, "said Nyland, adding that unnecessary and excessive prescribing of antibiotics for viral infections dramatically increases the risk of developing allergies later age. In this study, doctors reviewed the medical records of about 800,000 children born between 2001 and

2013, and then examined which of them was prescribed penicillin in the first six months of life. They then compared the data with children who were later diagnosed with some of the allergies: such as food allergy, anaphylaxis, asthma, atopic dermatitis, allergic rhinitis, allergic conjunctivitis or contact dermatitis. They found that antibiotics increased the risk of allergic disease, with it being lowest in children receiving sulfonamides and highest in those receiving some of the penicillin antibiotics. Due to the use of antibiotics, the risk for food allergies increased by 8 percent, and for the development of asthma by as much as 47 percent. However, this study is not complete. Namely, it has only been proven that there is a connection, but not that it is certainly a cause-and-effect relationship between antibiotics and allergies. NYU Langone allergist and immunologist Dr Purvi Parik says the link could be linked to our microbiome, especially in the gut, which plays a big role in the immune system, because antibiotics not only kill the bacteria that cause the infection, also kill "good" Bacteria that protect us from the development of allergic or autoimmune diseases. Also emphasizes that this research could be useful in terms of further confirming what we know about the use of antibiotics and changes in the microflora of the body [13].

Gary Huffnagle, a professor of Internal Medicine, Microbiology and Immunology at the University of Michigan, says that the increasing use of antibiotics may be responsible for the rise in allergies and asthma in the world, which are really dangerous for us. His research team offered the first experimental evidence that a disorder of the intestinal flora can cause allergic reactions and asthma. In the last 20 years, asthma in the world has increased by 160%. Currently, 25% of children in America suffer from asthma, in England - 30%, in Croatia about 10% and this number is constantly growing. Getting to the cause of the rise in asthma and allergies is not easy. Experts blame the polluted environment, unhealthy food, and even a change in hygiene habits. But some experts have long included antibiotics among the causes. Prof. Gary Huffnagle points out that the connection between allergies and antibiotics is obvious. Wherever the use of antibiotics has increased, the number of people with asthma and allergies has also increased. In countries where antibiotic use is not widespread, asthma and allergies are rare [14].

New research in Berlin has confirmed that the rise in asthma and allergies in Western countries is proportional to the rise in antibiotic use. So, if a child needs an antibiotic for a bacterial infection, it should not be avoided for fear of an allergic disease. But prescribing antibiotics should not be overdone when they are not absolutely necessary, especially for viruses or colds, as they can cause long-term consequences and develop resistance due to overuse.

## **II. EXAMINEES AND METHOD**

### **2.1 Sample of respondents**

The sample of examinees for this research consists of a group of boys and girls, primary and secondary school students from the Tuzla Canton at the age of 15. The sample was collected from January 1, 2018 to May 30, 2019. It consists of a total of 1605 respondents, of which 574 respondents are from rural areas (226 boys and 348 girls), 665 respondents from urban schools (357 boys and 308 girls) and 366 respondents from suburban schools (116 boys and 250 girls). The sample of respondents was divided into two groups:

1. Experimental group: boys aged 15 years from the Tuzla Canton.
2. Control group: 15-year-old girls from the Tuzla Canton.

### **2.2. Data collection method**

Subjects were selected by random sampling. The research was conducted voluntarily. The questionnaire was submitted to schools with the previously obtained consent of the Ministry of Education and Science of Tuzla Canton (Number: 10 / 1-38-3462 / 19), and for the accuracy of the data, it was filled out by the parents or guardians of the examinees. The age of the respondents is from 14.6 to 15.5 years. The survey questionnaire consisted of several questions, such as: the exact age of the respondents, whether the antibiotic was ever used in therapy, what type of antibiotic was most often used, the length of therapy, whether there are allergies to antibiotics and which, whether antibiotics are used only with a doctor's recommendation, do they follow the instructions for use, especially when it comes to regular use and duration of therapy, do they always feel better after antibiotic therapy and what is the most common type of prescribed therapy - topical, per os or parenteral.

### **2.3. Data processing method**

After data collection, the division into gender categories and data collection area was performed, and then for each sex certain age categories and settlements were calculated basic statistical parameters and statistical significance ( $\chi^2$ -test hi-square), between the compared categories of respondents. All data were processed in Microsoft Office Excel 2013 and SPSS 21 statistics, and presented in Microsoft Office Word 2013. The first part of statistical data processing consisted of analysis of the sample by groups, which are expressed in the form of tables and graphs. Testing of the selected data was performed by chi-square test. Significance of the

association was determined by chi-square test at a significance level of 0.05. The null hypothesis can be accepted if the value of  $p > 0.05$ , ie. there is no statistically significant correlation between the tested data. Measurements were performed with a contingency coefficient (phi-coefficient) and a Cramer coefficient at the significance level of 0.05. The correlation was measured by the Pearson correlation coefficient, at the significance level of 0.05. In the end, all the obtained results are presented in tables and graphs.

### III. RESULTS

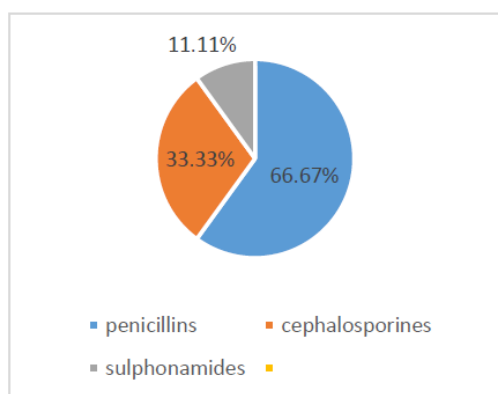
This study examined the occurrence of allergic reactions to antibiotics in the 15-year-old population, as well as to which group of antibiotics these allergies most commonly occur.

The percentage of occurrence of allergic reactions to antibiotics in the population of boys and girls aged 15 from the area of the city of Tuzla are shown in Table 1 and Graphs 1-3.

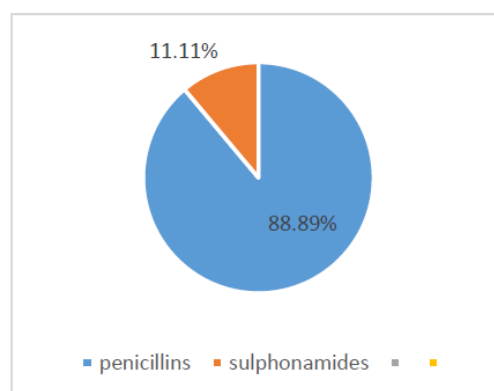
The results of the research show that 7.21% of the total population of boys and girls aged 15 from the area of the city of Tuzla is allergic to some type of antibiotic. Of these, 5.8% are allergic to penicillin antibiotics, 1% are allergic to cephalosporine and 0.8% are sulfa allergy.

**Table 1.** Percentage of occurrence of allergic reactions to certain classes of antibiotics in the population of 15 years from the area of the city of Tuzla

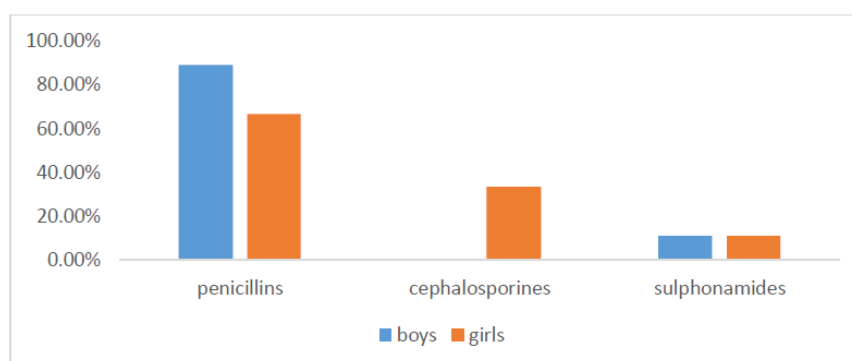
	Allergies to antibiotics		Allergies to penicillins	Allergies to cephalosporines	Allergies to sulphonamides	Allergies to macrolides
	yes	no				
Boys	27 (8,18%)	303 (91,82%)	24 (88,89%)	-	3 (11,11%)	-
Girls	18 (6,12%)	276 (93,88%)	12 (66,67%)	6 (33,33%)	2 (11,11%)	-
<b>Total</b>	<b>45 (7,21%)</b>	<b>579 (92,79%)</b>	<b>36 (5,8%)</b>	<b>6 (1%)</b>	<b>5 (0,8%)</b>	-



**Figure 1.** Percentage of allergic reactions in a group of 15-year-old girls



**Figure 2.** Percentage of allergic reactions in a group of 15-year-old boys



**Figure 3.** Differences in the occurrence of allergic reactions to antibiotics between boys and girls aged 15 from the city of Tuzla

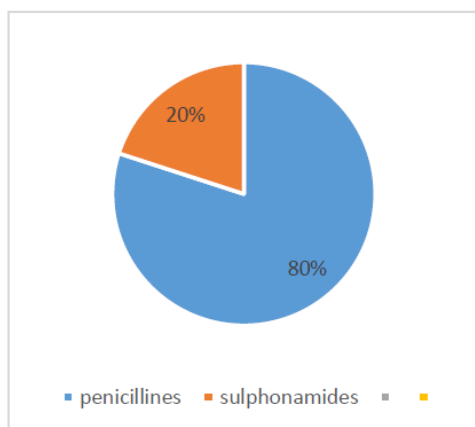
***Allergic Reactions To Antibiotics In The Population Of Boys And Girls Aged 15 Years Old In ..***

The percentage of occurrence of allergic reactions to antibiotics in the population of boys and girls aged 15 years in the suburbs is shown in Table 2 and Graphs 4-6.

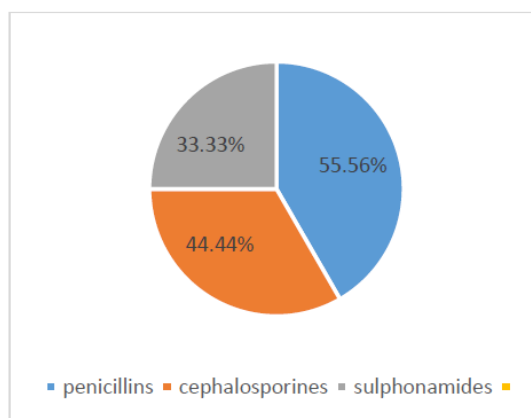
The percentage of allergic reactions in the total population of boys and girls aged 15 from suburban settlements is 12.8%. 8.5% of this population is allergic to penicillin, 3.3% are allergic to cephalosporin and 3.6% to sulfonamides. It can be noticed here that allergies to sulfonamides are higher in the group of girls (33.33%) than in the group of boys.

**Table 2.** Percentage of occurrence of allergic reactions to certain classes of antibiotics in the population of 15 years in suburban area

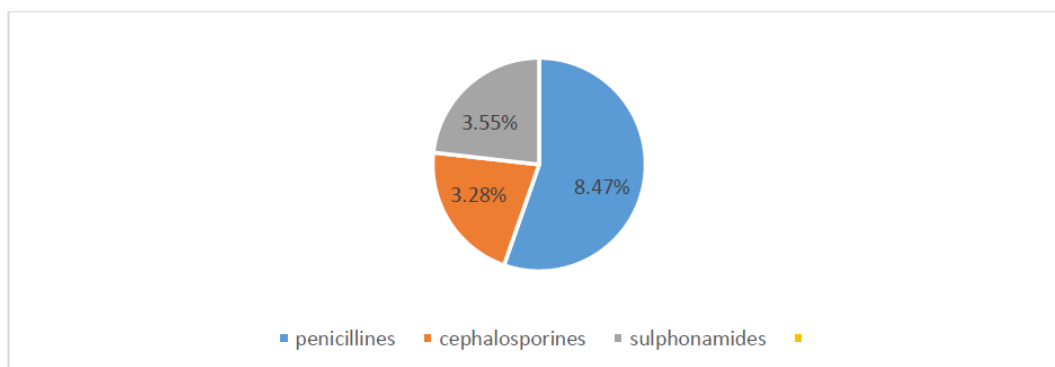
	Allergies to antibiotics		Allergies to penicillines	Allergies to cephalosporines	Allergies to sulphonamides
	yes	no			
Boys	20 (17,24%)	96 (82,76%)	16 (80%)	-	4 (20 %)
Girls	27 (10,8 %)	223 (89,2%)	15 (55,56%)	12 (44,44%)	9 (33,33%)
<b>Totale</b>	<b>47 (12,84%)</b>	<b>87,16%</b>	<b>31 (8,5%)</b>	<b>12 (3,3%)</b>	<b>13 (3,6%)</b>



**Figure 4.** Percentage of allergic reactions to antibiotics in the 15-year-old boy population.



**Figure 5.** Percentage of allergic reactions to antibiotics in the 15-year-old girl population



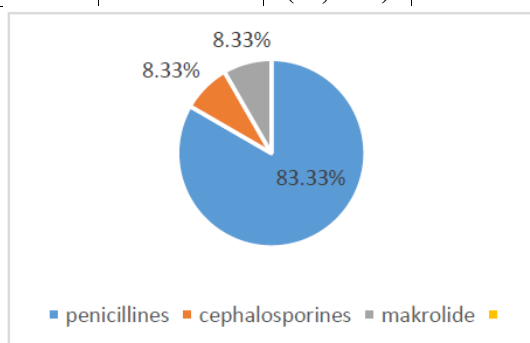
**Figure 6.** Percentage of allergic reactions to certain classes of antibiotics in the population of boys and girls aged 15 in the suburbs

The percentage of occurrence of allergic reactions to antibiotics in the population of boys and girls aged 15 years in rural areas is shown in Table 3 and Charts 7-9. The table shows that 8.6% of the rural population is allergic to some type of antibiotic. The most common are allergies to penicillin (6.8% of this population is allergic to penicillin antibiotics).

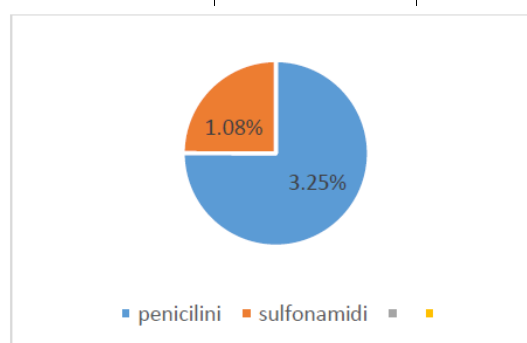
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**Table 3.** Percentage of occurrence of allergic reactions to certain classes of antibiotics in the population of 15 years from rural area

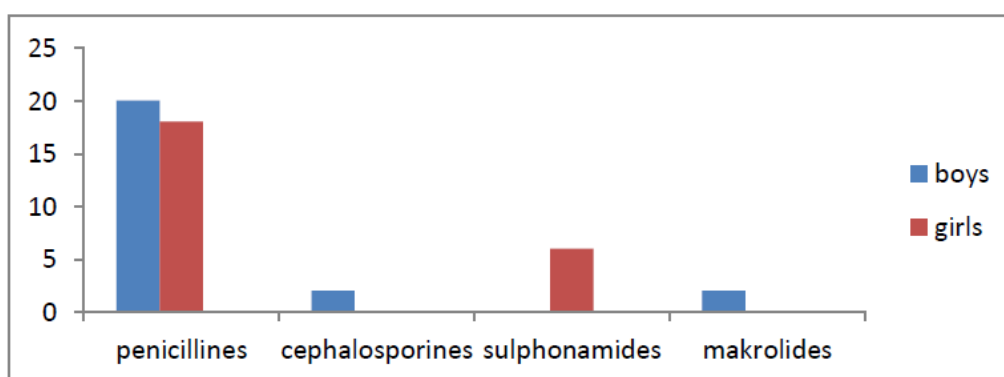
	Allergies to antibiotics		Allergies to penicillines	Allergies to cephalosporines	Allergies to sulphonamides	Allergies to macrolides
	yes	no				
Boys	24(10,71%)	200 (89,29%)	20 (83,33%)	2(8,33%)	-	2 (8,33%)
Girls	24 (7,27%)	309 (93,63%)	18 (75%)	-	6 (25%)	-
<b>Totale</b>	<b>48 (8,62%)</b>	<b>509 (91,38%)</b>	<b>38 (6,86%)</b>	<b>2 (0,36%)</b>	<b>6 (1,08%)</b>	<b>2 (0,36%)</b>



**Figure 7.** Percentage of allergic reactions to reactions to antibiotics in the 15-year-old boy



**Figure 8.** Percentage of allergic reactions to antibiotics in the 15-year-old girl

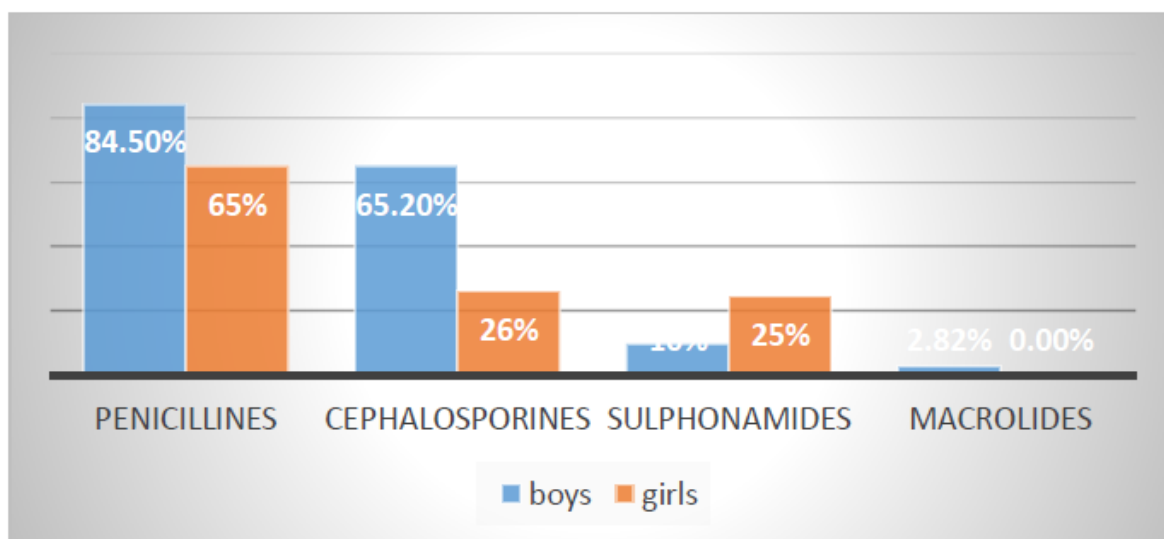


**Figure 9.** Differences in the occurrence of allergic reactions to antibiotics between boys and girls aged 8 from the area of the city of Tuzla

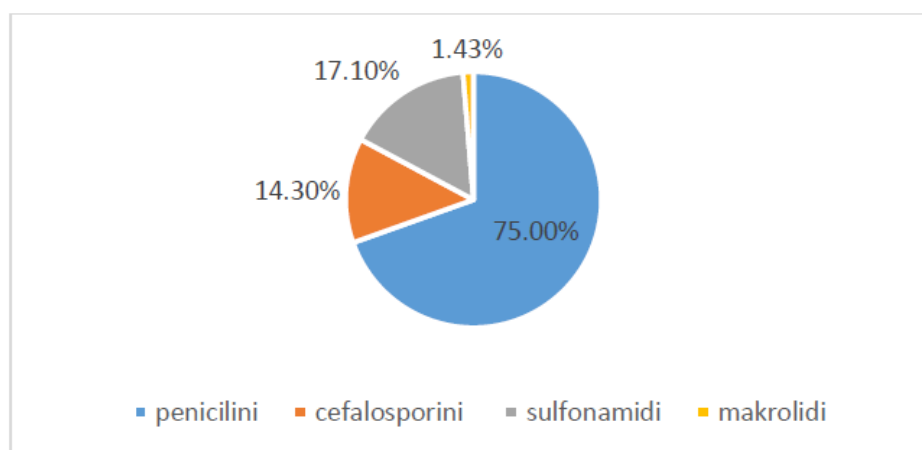
Table 4 shows data on the occurrence of allergic reactions in the total sample of boys and girls in Tuzla Canton.

**Table 4.** Percentage of occurrence of allergic reactions to certain classes of antibiotics in the population of 15 years from Tuzla canton

	Allergies to antibiotics		Allergies to penicillines	Allergies to cephalosporines	Allergies to sulphonamides	Allergies to macrolides
	yes	no				
Boys	71(10,6%)	599 (89,4%)	60 (84,5%)	2 (2,8%)	7 (9,8%)	2 (2,82%)
Girls	69 (7,9%)	805 (92,1%)	45 (65,2%)	18 (26,1%)	17 (24,6%)	-
<b>Totale</b>	<b>140 (9,1%)</b>	<b>1404 (91%)</b>	<b>105 (6,8%)</b>	<b>20 (1,3%)</b>	<b>24 (1,6%)</b>	<b>2 (0,13%)</b>



**Figure 10.** Differences in the occurrence of allergic reactions to antibiotics between boys and girls aged 15 from Tuzla canton



**Figure 10.** Percentage of allergic reactions to certain classes of antibiotics in the population of 15 years of Tuzla Canton

Table 5 shows statistically significant differences in the occurrence of allergic reactions between the observed groups of respondents in Tuzla Canton, calculated by the chi-square test. No statistically significant differences were found in any of the examined categories.

**Table 5.** Differences in the occurrence of allergic reactions to antibiotics between the observed groups of subjects

Compared categories	N	df	Phi value	Cramer's value	Contingency coefficient	Pearson Chi-Square	Sig. (p)
All Boys-Girls aged 15 years.	1544	1	0,047	0,047	0,047	3,359	0,067
City-Village	1544	1	-0,011	0,011	0,011	0,170	0,680
Boys from the city-Boys from the village	670	1	0,003	0,003	0,003	0,005	0,944
Girls from the city-Girls from the village	874	1	-0,018	0,018	0,018	0,282	0,595



#### IV. DISCUSSION

The results of the research (Table 1) show that 7.21% of the total population of boys and girls aged 15 in the area of the city of Tuzla is allergic to some kind of antibiotic. Of these, 5.77% are allergic to penicillin antibiotics, 0.96% are allergic to cephalosporins and 0.8% are sulfa allergy. In the group of boys, this procedure is higher than in the group of girls and amounts to 8.18%, but this difference between the observed groups is not statistically significant. Also, the data show that no cases of cephalosporin allergy were recorded in the group of boys, while the procedure of sulfonamide allergy was the same in the both observed group of these populations. Allergies to macrolides were not reported in any of the observed groups.

The percentage of allergic reactions in the total population of boys and girls aged 15 from suburban area (Table 2) is 12.84% and is slightly higher than among peers in the urban area, but these differences are not statistically significant. In group of boys in the suburbs, as in boys in the city, there is a slightly higher percentage of allergic reactions to antibiotics compared to the group of girls and it amounts to 17.24%. And in the population of 15 years from the suburbs, the largest percentage are allergies to penicillins 8.5%, followed by sulfonamides 3.6% and cephalosporins 3.3%. Allergies to sulfonamides are higher in the group of girls (33.3%) than in the group of boys. Macrolide allergies were not reported in any of the observed groups.

The results of the research show that the percentage of allergic reactions in the population of 15 years from rural area (Table 3) is 8.62% and a higher percentage of allergic reactions (10.71%) is found in the group of boys as is the case with the comparison of populations of 15 years-village. Even in this population, the differences between the group of boys and girls are not statistically significant. Allergies to penicillin antibiotics (6.86%), followed by sulfonamides (1.08%) and cephalosporins (0.36%) are also most common in this population. Here, unlike the 15-year-old population in the city and suburbs, allergies to macrolides also occur and make up only 0.36%. total population, and were recorded only in the group of boys.

#### V. CONCLUSION

Research has confirmed that the most common allergies to antibiotics, are allergies to penicillins. Namely, the largest percentage of allergic reactions are reactions to penicillin in the group of boys and in the group of girls aged 15 in urban, suburban and rural areas. It is interesting to emphasize, that the greater the percentage of allergic reactions to antibiotics always present in the group of boys. It is also interesting that allergies to macrolide antibiotics were not found in any of the examined categories except in the group of boys from rural areas and they make up only 0.36% of all allergic reactions. Antibiotic allergies are in most cases present in suburban and rural settlements compared to urban ones. Future research may focus on the reasons and factors that use the occurrence of different degrees of allergic reactions to certain groups of antibiotics between male and female populations. It can also be examined, why there are differences in the occurrence of allergic reactions between examinees of urban and suburban areas.

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