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Antibiotic resistance of vaginal infection-causing bacteria in the municipality of Korça, Albania

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Abstract

Women's health is of particular importance across the globe. Women serve as the forerunners of entire generations which is a convincing factor why the health of their reproductive organs requires adequate attention to combat vaginal infections, which are the most prevalent of all. Dozens of microorganisms inhabit the vagina, turning it into a complex environment, with some of these posing a risk to women's health. The objective of this study is to evaluate the antibiotic resistance of bacterial vaginosis based on its prevalence. The study was conducted from January 2017 to December 2021 at the Microbiologic/Bacteriologic Laboratory of the Regional Directorate of Health in Korça. A total of 3175 women aged 14 to 45, and older, participated in the study. The method employed to assess antibiotic resistance of the most prevalent bacterial infections was the disc diffusion method (a modified version of the Kirby-Bauer method). Consequently, some 2174 women out of a total of 3175, or 67.62% of women resulted having positive vaginal cultures. The highest frequency of infection was observed among women aged 45 years or younger, followed by those aged 36-45 and 26-35. Conversely, a low frequency of infection was noted among those aged 1 to 14. *Escherichia coli* emerged as the most prevalent bacteria, followed by *Staphylococcus spp.* Among the most tested antibiotics, pathogenic bacteria exhibited one-fold, two-fold, and multi-fold resistances. However, following the Covid-19 pandemic in 2021, *E. coli* exhibited increased resistance to Azithromycin, which was widely administered during the pandemic. We conclude that in order to mitigate antibiotic resistance and enhance the efficacy of treatment for vaginal infections, it is imperative to alter antibiotic treatment protocols.

Keywords: antibiotic resistance, vaginal infection, *Staphylococcus* spp., *E coli.*

1. Introduction

The vaginal ecosystem is complex harboring a multitude of microorganisms. This unique environment undergoes significant changes throughout life, from birth to puberty, which persist during and after menopause. Women are more susceptible to urinary and vaginal infections due to anatomical and functional proximity to the anal canal and a short urethra (Onderdonk et al., 2016; Wilson, 2009). The vaginal environment changes in response to practices such as washing, dressing, contraceptive use, sexual activity, and illnesses. Additionally, it is influenced by factors such as age, smoking habits, alcohol consumption, increased number of sexual partners, menopausal status, use of hormonal contraception, and the presence of acute and chronic infections (Pal, 2007; Cherpes et al., 2008). Bacterial vaginosis was first reported by Gardner and Dukes in 1955 (Scott et al., 1987; Holst et al., 1987).

Therefore, bacterial vaginosis stands as the primary cause of vaginitis. Typically, it is associated with preterm labor, premature rupture of membranes, spontaneous abortion, chorioamnionitis, cervicitis, endometritis, urinary tract infections, cervical intraepithelial neoplasia, pelvic inflammatory disease (PID), and the delivery of low-birth-weight infants (Donati et al., 2010; Wilson, 2009).

Indeed, studies investigating the prevalence of vaginal infections in our country, especially those linked to antibiotic sensitivity, are limited. However, based on prior research, more than 2.6 million cases of antibiotic-resistant bacterial infections and 44,000 associated deaths are reported annually (CDC, 2013; Javed et al., 2018). Presently, the proliferation of bacterial resistance to antibiotics is a matter of concern, which has become increasingly prevalent. This has led to the emergence of the concept of "superbacteria," a term used for pathogenic bacterial strains responsible for causing fatalities worldwide each year (Van de Wijgert et al., 2017; Jespers et al., 2014; Gajdacs, 2019).

Today, there is discussion about an increase in resistance to several drugs targeting pathogens such as Staphylococcus aureus, Escherichia coli, or Pseudomonas aeruginosa (Tumuhamye et al., 2021; Srinivasan et al., 2008; Demba et al., 2005). Antibiotic resistance depends on various factors, which can differ from one location to another (Gajdacs, 2019; Tumuhamye et al., 2021). This resistance arises due to several reasons, including climate and geographic conditions, treatment methods, and indiscriminate usage (as observed during Covid-19) (Tumuhamye et al., 2021; Shrivastava et al., 2018; Brocklehurst et al., 2013).

In light of this, antibiograms are deemed essential not only before initiating antibiotic therapy ,but also after treatment. The goal of this approach is to determine which antibiotics are effective against the pathogenic bacteria, thereby aiding healthcare professionals in creating a database for short-term antibiotic treatment, even in cases where conducting an antibiogram is not seen as feasible (Brocklehurst et al., 2013; Gajdacs, 2019).

Therefore, the primary objective of our study is to evaluate the antibiotic resistance of bacterial microorganisms and dynamically monitor the frequency and spread of vaginal infections over time, considering factors such as age, settlement, and their development.

The study timelines spans from January 2017 to December 2021, and the data were collected from the Regional Directorate of Health in Korça. During this period, 3175 patients presented themselves to the institution's laboratory environment for testing for vaginal infections.

Secretions from vaginal swabs were inoculated into a medium that promotes pathogenic growth, and only 2147 cases, or 68% of the samples, tested positive for vaginal infection. Among the positive results, bacterial vaginosis caused by E. coli, Staphylococcus spp., and Staphylococcus aureus was identified. Subsequently, an antibiogram was conducted for these positive samples to determine the most effective antibiotic treatment for patients with vaginal infections.

2. Materials and Methods

2.1. Study period

The materials used in this study comprised vaginal swab samples obtained from female patients between January 2017 and December 2021. These samples were collected from Regional Korça Hospital in collaboration with the Regional Directorate of Health, Municipality of Korça. Additionally, tampons were utilized as part of the sampling process.

2.2. Sample collection

The vaginal swab samples obtained from patients were subjected to microbiological examination to assess their content. Each sample was coded prior to analysis, with the sample number corresponding to its respective Petri dish. The evaluation of samples was conducted according to the Amsel Clinical Criteria, which categorizes samples as either positive or negative (Amsel et al., 1983)

2.3. Laboratory processing for bacterial identification and isolation

The material was inoculated onto blood agar media. Following inoculation, the Petri dishes were placed in a thermostat and incubated at an optimal temperature for growth, typically 37°C, for a period of 24 hours. After the incubation period, an evaluation of the morphology, color, and aroma of the colonies grown on the media was conducted. These characteristics aided in determining the type of microorganism present.

2.4. Antibiogram

An antibiogram was ustilized to determine the sensitivity of microorganisms to antibiotics. Initially, Mueller Hinton agar media was prepared, followed by inoculation of pathogens. Discs saturated with antibiotics were then placed on the agar using the Disk Diffusion technique by Kirby-Bauer. Subsequently, the Petri dishes were incubated, and the antibiogram was read and interpreted (Bauer et al., 1959; Kirby et al., 1956).
Within 15 minutes of inoculating bacterial colonies, antibiotic discs were placed on the agar using sterile forceps. The discs were spaced equally apart from each other, and light pressure was applied to ensure optimal contact of each disc with the media. In 2017 and 2018, only five antibiotic discs were used: ampicillin, Bactrim, cephalosporin, gentamicin, and tetracycline. However, in 2019, a total of 12 antibiotics were utilized. Tetracycline and cephalosporin were excluded in 2019, while nine additional antibiotics were added: amikacin, amoxicillin, azithromycin, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, cefuroxime, and erythromycin.

2.5. Yielding results

After the incubation period, the bacterial colonies were measured, evaluated, and their resistance or sensitivity to antibiotics was interpreted. This was done over the course of the five-year study using tables containing standard values in the SPSS software program.

3. Results and Disscusions

3.1. Frequency of vaginal infections transmission based upon years, residence and age.

During the period from January 2017 to December 2021, a total of 3175 samples were analyzed at the Regional Directorate of Health in Korça (DRSHK), collected from the vaginal tracts of patients in the Korça municipality. Throughout the study period, 2147 samples tested positive, accounting for 68% of the cases. (See Table no.1).

Table 1. Frequency and dynamics of vaginal infections transmission across the years, based upon residence and age.

Characteristics		**Years** (*positive cases*)					**Total**	**Frequency (%)**
Years		**2017**	**2018**	**2019**	**2020**	**2021**		
Bacteria		557	437	385	551	217	**2147**	100%
Residence	***Urban***	481	363	322	446	179	**1791**	0.83%
	Rural	76	74	63	105	38	**356**	0.17%
Age	***0-14 years***	21	13	13	22	9	**78**	0.36%
	15-25 years	76	57	47	84	25	**289**	13.46%
	26-35 years	112	77	68	131	48	**436**	20.30%
	36-45 years	92	57	64	91	32	**336**	15.64%
	46> years	256	233	193	223	103	**1008**	46.94%

In Table 1 and Figure 1, it is evident that the highest incidence of vaginal infection spread was recorded in 2017 and 2020, at 25.04% and 25.66%, respectively. In contrast, the incidence was lower in 2018 at 20.35% and even lower in 2019 at 10.10%. The decrease in infections, particularly in 2020, and the increase in 2021, can be attributed in part to the COVID-19 pandemic, during which laboratories were primarily focused on patients with COVID-19.

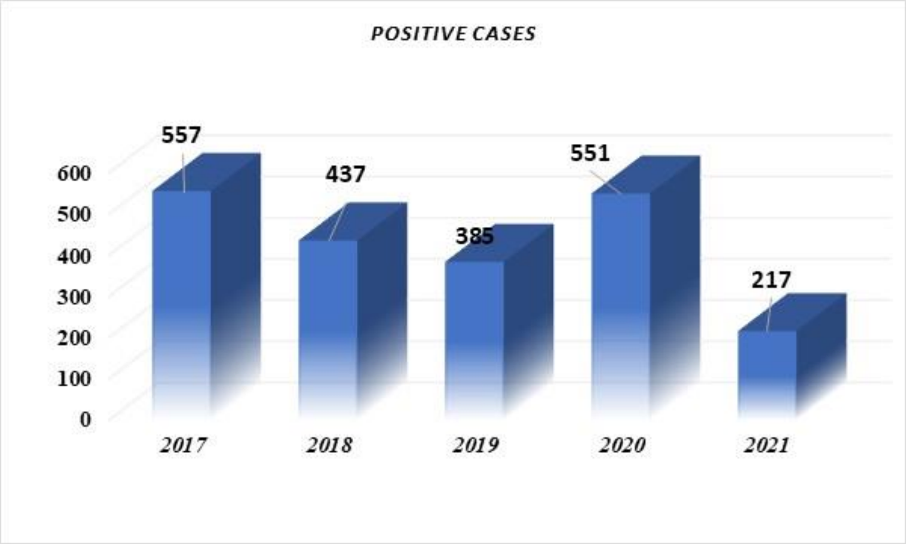

Figure 1. Dynamic spread of vaginal infections during the years of the study

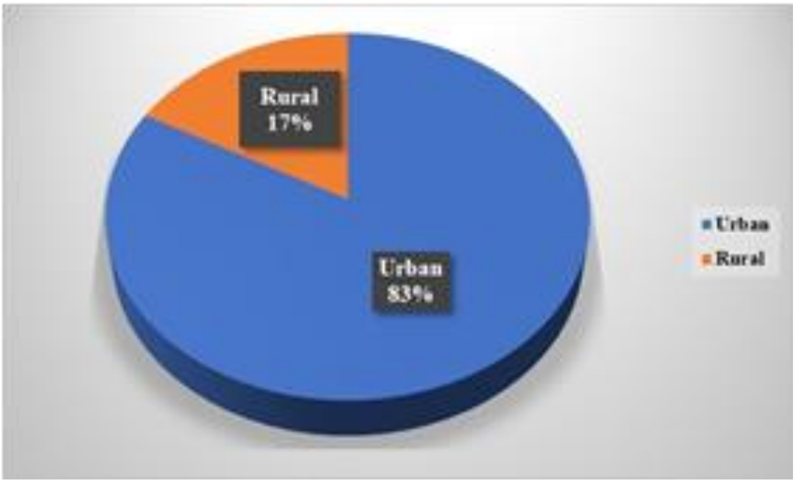

Figure 2. Relationships between demographic characteristics and vaginal infections transmission

In Table 1 and Figure 2, it is evident that the majority of analyzed samples with bacterial presence originate from urban zones. Out of 4127 (83%), 873 (17%) cases were in rural zones. It's important to note that significant demographic changes have occurred in our country since 1990, with a notable increase in population in urban zones.

Similar studies have been conducted to explore the relationship between residence and vaginal infections. For example, a study conducted in Ismailia, Egypt, from January to July 2012 (Baraia et al., 2015) found that females living in urban zones had a 42.5% prevalence of vaginal infections, compared to 57.5% in rural zones. However, in contrast to our study, it is evident that positive cases of vaginal infections prevail in rural zones. Similarly, results from Brazil for the period of September 2013 to January 2013 (Marconi et al., 2015) revealed a significant difference, with 93% of females affected by vaginal infections residing in urban zones, compared to only 7% in rural zones. These findings suggest that residence may not have a crucial impact on the prevalence of vaginal infections.

From Table 1 and Figure 3, it is apparent that the presence of vaginal infection is notably higher in females aged ≥ 46. Out of 5000 positive cases studied, 2563 were in females aged 46 or older. In contrast, females aged 26-35 had three times fewer infections, with only 782 positive cases, and a similar trend was observed for females aged 36-45, with 737 cases.

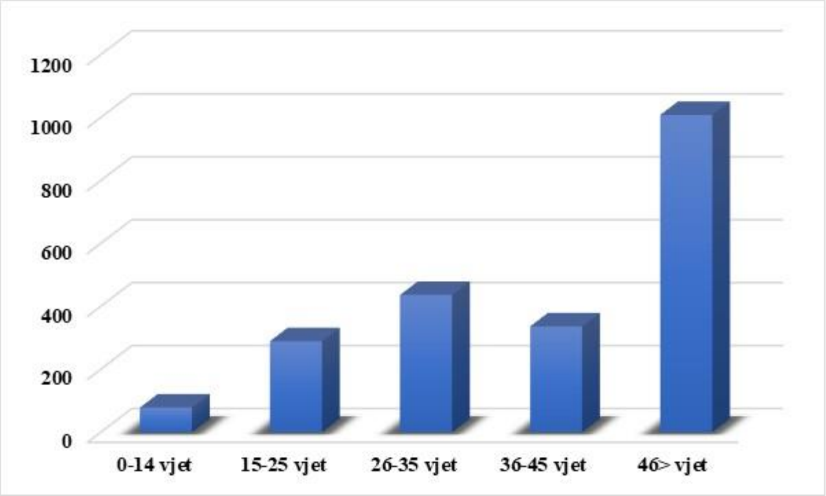

Figure 3. The dynamics of the transmission of vaginal infections based on age groups

Figure 3 graphically depicts the dynamics of vaginal infection spread based on age. It is evident that age is a significant factor that impacts the presence of vaginal infections in females. There is a small number of patients affected by infections considered between the ages of 0-14 years old. Thus, as females age increases, the likelihood of being affected by vaginal infections also increases (Chi-square; $\chi 2=47.214$, $p<0.05$).

Garba et al. (2014) in Nigeria found that vaginal infections were widespread between ages 26 – 30, at approximately 35.8%, and less prevalent in females aged 40, at around 10.5%. According to Erikson et al. (2011), in different time periods in Finland, the most affected ages by bacterial vaginosis have varied. From 1983 to 2008, the most affected age group by vaginal infection has been dynamic, not constant. In 1983, females aged 50 were predominantly affected by vaginal infections. In 1988, females aged 55 were predominantly affected as well. Meanwhile, in 2003 and 2008, another conclusion was drawn, indicating that females aged 35 were mostly affected. In all of the afore-mentioned studies, it is evident that vaginal infections vary across different age groups in different countries (Garba et al., 2014; Van de Wijgert et al., 2017; Tolosa et al., 2006; Jespers et al., 2014; Erikson et al., 2011). This variation may be attributed to differences in standards of living and information about vaginal infections affecting females. Globally, the overall prevalence of BV was over 29.2% among women aged 14–49 years (Van de Wijgert et al., 2017). In white women, the prevalence of BV was 23%, whereas in Mexican Americans, it was 32% (Tolosa et al., 2006). In African-American women, the prevalence of BV was approximately 51%, which is alarmingly high. In sub-Saharan Africa, the prevalence of BV was 50% (Jespers et al., 2014).

Out of the 2147 cases that tested positive, samples collected from patients in DRSHK revealed the presence of both Gram-positive and Gram-negative bacteria. Among them, 49% were identified as Gram-positive (1053 cases), and 51% were identified as Gram-negative (1094 cases) isolated from vaginal secretions.

According to Table 2, the results indicated the dominance of Gram-negative bacteria over Gram-positive ones. Similar findings were observed in other studies conducted in India and Finland, where Erikson et al. (2011) concluded that Gram-negative bacteria were more prevalent than Gram-positive ones (Erikson et al., 2011; Ghiasi et al., 2014). The findings of the current study were also consistent with studies conducted in India, such as those by Nahar et al. (2016) reporting S. aureus (41.07%) dominance, Krauss-Silva et al. (2014) in Addis Ababa reporting E. coli (41%) prevalence, and Bitew et al. (2017) reporting K. pneumoniae (30.5%) prevalence. Similar trends were observed in studies conducted in Belgium (Donders et al., 2002) and America (Krauss-Silva et al., 2014).

Table 2. Dynamic of Gram+ and Gram- spread, and the frequency of transmission in % during years of study 2017 – 2021

Years	**2017**		**2018**		**2019**		**2020**		**2021**	
Bacteria	Bacterial spread	Frequency in %	Bacterial spread	Frequency in %	Bacterial spread	Frequency in %	Bacterial spread	Frequency in %	Bacterial spread	Frequency in %
Gram+	348	62.48%	253	57.67%	177	46.22%	300	48.00%	85	38.99%
Gram-	209	37.52%	184	42.33%	206	53.78%	225	52.00%	132	61.01%
Total	557	100%	437	100%	383	100%	525	100%	217	100%

The prevalent bacteria identified in bacterial infections during the analysis of 2147 positive samples from January 2017 to December 2021 were *Staphylococcus spp, Staphylococcus aureus, E. coli, Klebsiella spp, Pseudomonas aeruginosa, and Streptococcus haemolysis.*

Table 3. Transmission dynamics of bacterial strains during 2017 – 2021

Year	***Staphylococcus spp+***	***Staphylococcs aureus+***	***Streptococcus haemolysis+***	***E. coli-***	***Proteus spp-***	***Klebsiella spp-***	***Pseudomonas aeruginosa-***
2017	314	34	0	178	26	4	0
2018	249	4	0	155	18	11	0
2019	175	2	0	182	16	4	4
2020	221	9	0	305	14	5	1
2021	83	1	1	119	11	2	0
Total	**1042**	**50**	**1**	**939**	**85**	**26**	**5**

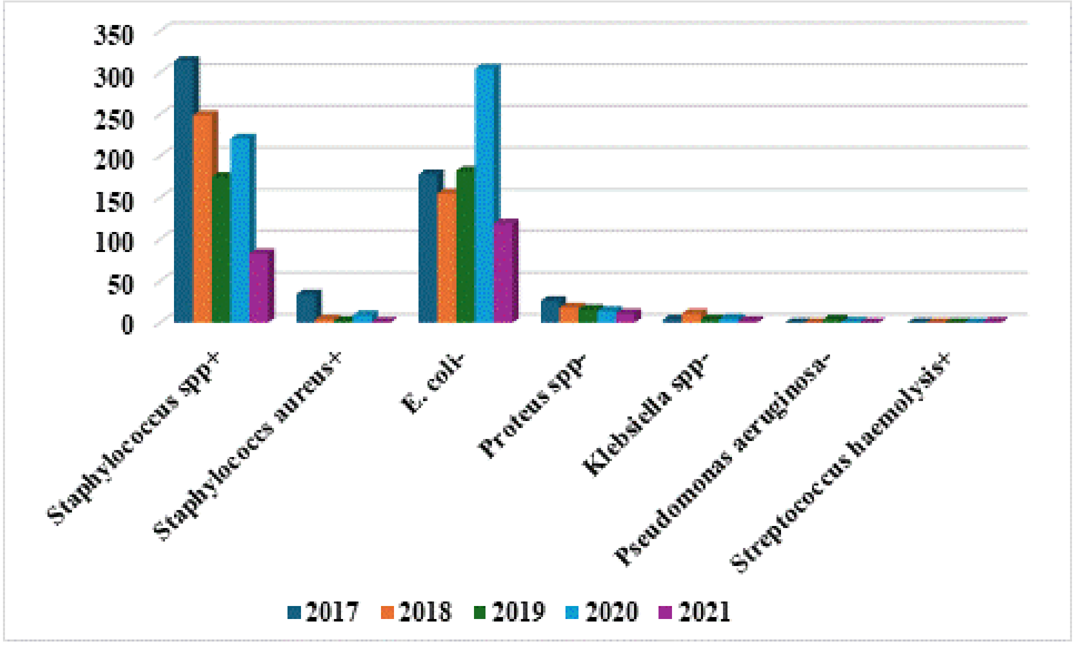

Figure 4. Transmission dynamics of bacterial strains during 2017 – 2021

It is evident from the above graphical display that *Staphylococcus spp* is prevelant, accounting for 48.53% of cases, followed by E. coli at 43.73%. The least prevalent ones were *Klebsiella* at 1.21%, *Pseudomonas aeruginosa* at 0.23%, and *Streptococcus haemolysis* at 0.04% of cases.
In two different studies conducted in Northern India and Nigeria, it was evident that the most prevalent bacteria were *Staphylococcus aureus* and *E. coli* (Sood et al., 2018; Edet *et al.*, 2017).

3.2. Antibiotic resistance

During the study period from January 2017 until December 2021 at DRSHK, 2147 cases that resulted positive for vaginal infection were tested for their sensitivity to different antibiotics. In this study, seven types of microorganisms were reviewed for resistance, namely: *Staphylococcus spp, Staphylococcus aureus, E. coli, Proteus spp, Klebsiella spp, Pseudomonas aeruginosa, and Streptococcus haemolysis.*

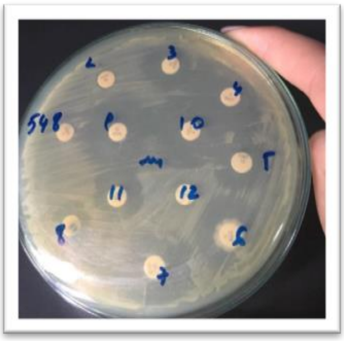

Figure 5. Antibiogram for *E. Coli*, discs with antibiotics

Table 4. Sensibility and resistance of *E. Coli* during 2017 - 2021

	E. coli									
	2017		**2018**		**2019**		**2020**		**2021**	
	S	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**
Augmentin	116	37	48	107	80	97	279	23	109	10
Ampicillin	16	136	27	125	81	93	182	118	73	46
Gentamicin	88	56	105	43	114	57	254	49	96	23
Ciprofloxacin	47	77	59	84	144	30	259	43	100	19
Amikacin	22	134	26	121	54	115	114	185	29	89
Ceftriaxone	-	-	-	-	71	106	172	130	48	71
Ceftazidime	-	-	-	-	56	118	176	128	49	69
Norfloxacin	-	-	-	-	82	86	205	95	66	53
Cefuroxime	-	-	-	-	136	42	215	88	77	41
Azithromycin	-	-	-	-	136	36	234	64	98	21
Bactrim	-	-	-	-	126	45	248	55	81	37
Cefoxitin	-	-	-	-	46	128	150	148	57	62

It is evident, based on Table 4, that during the study period from January 2017 to December 2018 in the DRSHK laboratory, five antibiotics were used to test *E. coli* resistance against them. The first five antibiotics used were Augmentin, ampicillin, gentamicin, ciprofloxacin, and amikacin. Meanwhile, from December 2019 to December 2021 in the DRSHK laboratory, 12 antibiotics were tested to analyze bacterial resistance, namely: ampicillin, bactrim, gentamicin, amikacin, amoxicillin, azithromycin, ceftotaxime, cefoxitin, ceftazidime, ceftriaxone, cefuroxime, and erythromycin.

As noted in Table 5 and Figure 6, *E. coli* was resistant to Augmentin in the years 2018 and 2019 with 69% and 53% resistance, respectively. However, the usage of other antibiotics caused a decrease in resistance in 2020 and 2021.

Table 5. Antibiotic resistance of *E. coli* during 2017 – 2021

	Augmentin	**Ampicillin**	**Ceftazidime**	**Azithromycin**	**Cefoxitin**	**Amikacin**
2017	20%	76%	0%	0%	0%	75%
2018	69%	81%	0%	0%	0%	78%
2019	53%	51%	65%	20%	70%	63%
2020	0.80%	39%	42%	21%	49%	60%
2021	0.90%	37%	58%	18%	52%	75%

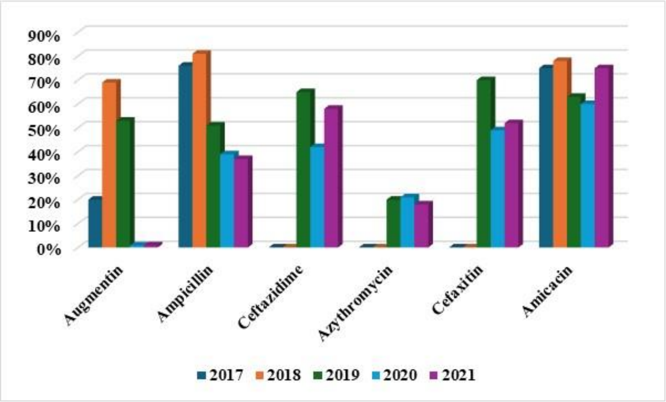

Figure 6. Antibiogram susceptibility pattern of *E.coli* in percentage during 2017-2021

The same trend has been evident for ampicillin. However, in 2019, 2020, and 2021, the usage of Ceftazidime and Cefoxitin proved to be ineffective as *E. coli* demonstrated resistance to them. Similarly, amikacin was found to be ineffective for usage as *E. coli* displayed resistance throughout the years, affecting 60% to 78% of cases.

Table 5 highlights that E. coli is exhibiting increased resistance to several antibiotics, not only single-fold resistance but also two-fold, three-fold, and multi-fold resistances. This heightened resistance may stem from various factors, including the increased use of these antibiotics without prescription or consultation with a healthcare provider, lack of antibiogram testing, issues with drug quality, unnecessary usage, and their application in animal products.

Similar results were observed in other studies. Bitew et al. (2022) concluded that E. coli was the predominant isolated bacteria and exhibited resistance to erythromycin (95.5%), trimethoprim/sulfamethoxazole (91.3%), and ceftriaxone (63.6%). Additional findings echoed these results concerning E. coli resistance, as seen in studies conducted in Bahir Dar (Mulu et al., 2015), India (Akram et al., 2005), and Portugal (Linhares et al., 2013).

Table 6. Antibiotic resistance of *Staphylococcus aureus* during 2017-2021

Staphylococcus aureus										
	2017		2018		2019		2020		2021	
Antibiotic	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**
Augmentin	6	19	1	2	1	1	9		1	
Ampicillin	5	22	1	3		1	6	3	1	
Gentamicin	20	7	2	1	1		8	1	1	
Ciprofloxacin	5	21		1	2		8	1		
Amikacin	3	25		3	2		9		1	
Ceftriaxone						2		8		1
Ceftazidime					1	1	7	2		
Norfloxacin						1		9	1	
Cefuroxime					2		9		1	
Azithromycin					2		9		1	
Bactrim							8	1	1	
Cefoxitin							8	1	1	

In Table 6, it is evident that *S. aureus* exhibited resistance to augmentin, ampicillin, ciprofloxacin, and amikacin in 2017 and 2018. In 2019 and 2020, *S. aureus* showed resistance to ceftazidime and norfloxacin in 100% of the cases.

Similarly, Bitew et al. (2021) found that *S. aureus* displayed resistance to erythromycin (69.8%), trimethoprim/sulfamethoxazole (53.5%), and amoxicillin (39.5%). However, despite this resistance, S. aureus was susceptible to ciprofloxacin (93%), gentamicin (93%), cefoxitin (90.7%), tobramycin (83.7%), and clindamycin (81.4%). These findings were consistent with previous reports in Ethiopia and abroad (Howe et al., 2019).

As noted in Table 7 and Figure 7, *Staphylococcus spp.* exhibited resistance to augmentin, ampicillin, and ciprofloxacin in 2017 and 2018, with rates of 69% and 53%, respectively. Additionally, throughout all the study years, *Staphylococcus spp.* displayed resistance to amikacin. Only three antibiotics were found to be sensitive to *Staphylococcus spp.:* cefuroxime, azithromycin, and bactrim.

Table 7. Antibiotic resistance of *Staphylococcus spp.* during 2017-2021

Staphylococcus spp.										
	2017		2018		2019		2020		2021	
Antibiotic	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**
Augmentin	63	185	77	165	80	83	193	26	74	9
Ampicillin	24	233	44	197	95	63	140	80	50	33
Gentamicin	162	102	158	75	81	84	167	52	64	18
Ciprofloxacin	64	178	81	142	130	34	165	53	64	19
Amikacin	17	280	29	215	41	127	70	147	20	62
Ceftriaxone	-	-	-	-	35	132	66	154	15	67
Ceftazidime	-	-	-	-	30	139	92	125	31	52
Norfloxacin	-	-	-	-	77	87	120	97	51	32
Cefuroxime	-	-	-	-	129	40	165	55	64	19
Azithromycin	-	-	-	-	142	23	159	60	68	15
Bactrim	-	-	-	-	92	66	148	70	53	30
Cefoxitin	-	-	-	-	35	127	95	121	34	49

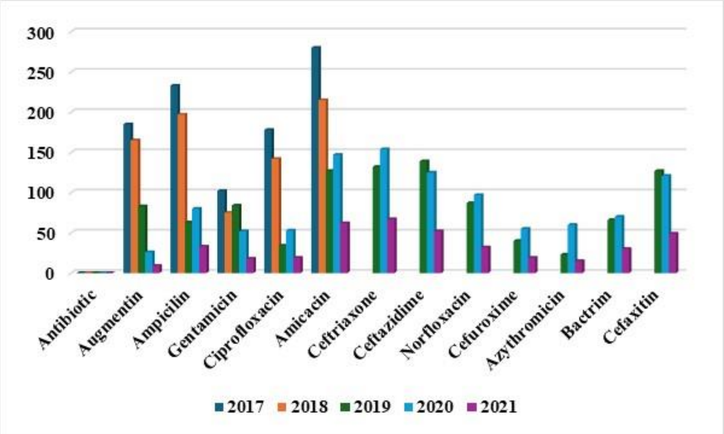

Figure 7. Antibiogram susceptibility pattern of *Staphylococcus spp.* in percentage during 2017-2021

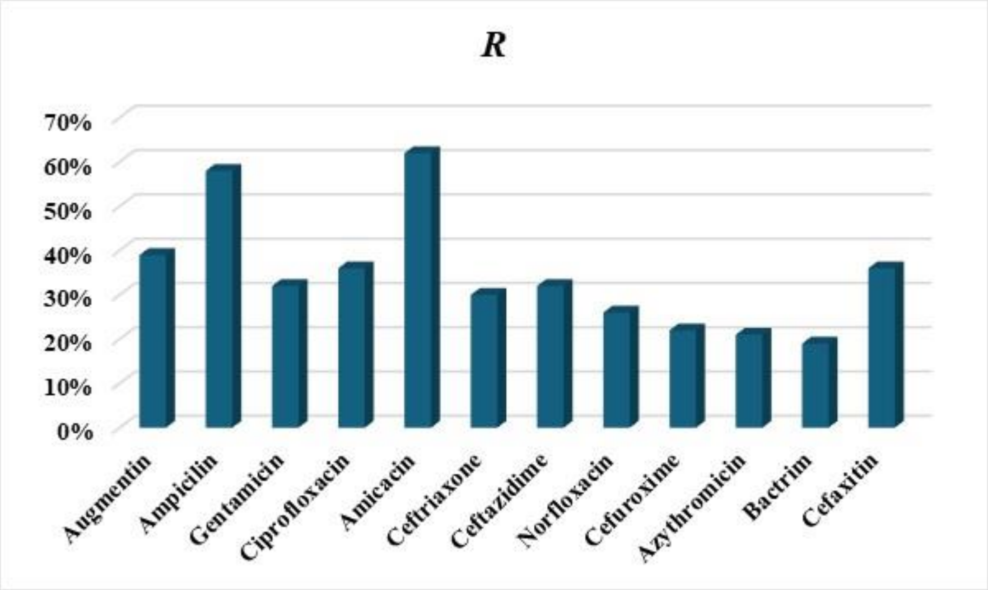

Figure 8. Bacterial resistance to 12 antibiotics used during the 5 years of study

As universally agreed, multidrug-resistant bacteria have surged dramatically over the past two decades, while the number of pharmaceutical companies developing new antimicrobial agents has declined (Nasim et al., 2019). Consequently, antibiotic-resistant bacteria, particularly following the Covid-19 pandemic, have emerged as one of the most pressing health challenges and a cause for alarm among world health leaders, especially in resource-limited countries like Albania (Venter et al., 2015).

This finding aligns with studies conducted in Addis Ababa (41.5%) according to Bitew et al. (2017), Kenya (43.1%) (Nzomo et al., 2013), and Nigeria (33%) (Javed et al., 2019; Aduloju et al., 2019).

Gram-negative bacteria have demonstrated greater resistance to most antibiotics compared to Gram-positive bacteria, attributed to the tougher biological structure of Gram-negative bacteria, which acts as a permeability barrier and facilitates drug efflux pumps (Venter et al., 2015). Generally, antibiotic-resistant bacteria employ various mechanisms such as physically removing the drug from the cell, modifying the target site, and altering the folic acid synthesis pathway to counteract the inhibitory effects of drugs (Bitew et al., 2021; Odonkor et al., 2011).

The rise of pathogenic resistant strains poses serious health concerns as antibiotics become less effective (Venter et al., 2015). The World Health Organization has indicated that there are currently insufficient novel antimicrobial drugs available. This suggests that soon there may not be enough new tools to combat these new strains of 'superbacteria' – pathogens that do not respond to traditional treatments (Shrivastava et al., 2018; CDC, 2013).

4. Conclusions

According to the results from 2017 to 2021, it is evident that *E. coli* was the most prevalent bacterium in vaginal infections.

During 2020, and partly in 2021, the Covid-19 pandemic resulted in a reduction in the analysis of bacterial infections and antibiograms.

Furthermore, the lack of coordination between private laboratories and the National Microbiology Institute has hindered the collection of accurate statistics and trends regarding cases of vaginal infections. As a result, there is a lack of reliable data on the number of cases and the number of antibiograms conducted during these years in the municipality of Korça.

Strains of *E. coli, S. aureus,* and *Staphylococcus spp.* have exhibited resistance at various levels, including one-fold, two-fold, and multi-fold resistance.

Increased awareness regarding the rising resistance of *E. coli* in vaginal infections is essential. Additionally, healthcare providers should adhere to guidelines for antibiotic treatment, utilize antibiograms when necessary and upon prescription, and avoid empiric treatment whenever possible.

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