

# Prevalence of Antibiotic use in Patients with COVID-19 in a Local Hospital in Kosovo: A Retrospective Descriptive Study

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Throughout the COVID-19 pandemic, there has been a notable escalation in the administration of antibiotics among hospitalized individuals on a global scale. This trend holds the potential to exacerbate the prevailing issue of antibiotic resistance on a worldwide level. The overarching purpose of this paper was to analyze the use of antibiotics in patients hospitalized with COVID-19 at a local hospital in a city of Kosovo during the period October 2020 to January 2021. The work retrospectively analyzes the data of patients treated with COVID-19 at a Local Hospital in a city of Kosovo in the internal ward and included 300 patients, where the health records of hospitalized patients were used. Based on the collected data, it appears that the most used empiric antibiotic in the ward was Levofloxacin and Ceftriaxone, the duration of the use of antibiotics per day was different in patients hospitalized with COVID-19, starting with Levofloxacin that was given every 24 hours, Imipenem every 12 hours and Ceftriaxone every 8 hours. Reasons for the use of antibiotics were: Disease burden, markers of inflammation, and radiological changes. According to the age group, the most infected group included the age between 51-70 years old with 44% and the smallest percentage was of the age group between 91-100 years old with 2%. The escalation in antibiotic usage among hospitalized patients during the pandemic has also impacted our nation, Kosovo, where such medications were consistently prescribed since the onset of the pandemic. Our observations reveal that Imipenem, Levofloxacin, and Ceftriaxone emerged as the most frequently utilized antibiotics.

**Keywords:** Antibiotics; COVID 19; ICU; Patients Resistance.

The use of antibiotics of hospitalized patients during the pandemic has increased all over the world and has caused resistance to them to be considered as the main global health challenge<sup>1</sup>. In several nations, the use of antibiotics was overspread in the early stages of the COVID-19 pandemic. According to a recent meta-analysis, during the first six months of the pandemic, 74.6% of the patients with COVID-19 had antibiotic

prescriptions written for them<sup>2</sup>. This could be explained by the fact that COVID-19 shares many clinical signs, including fever, tiredness, and cough, with bacterial pneumonia. Doctors typically administer empiric or preventative antibiotics to patients when these disease diagnoses cannot be made with sufficient precision. Antibiotics are massively prescribed due to the lack of knowledge about the viruses causing the disease and the lack

of guidelines for its management. In the early days of the pandemic, a study published in March 2020 showed antibiotic prescriptions for 95% of cases<sup>3</sup>. Over 70% of patients, primarily those with broad-spectrum infections, were estimated by systematic reviews, to have received antibacterial therapy. Over-prescription of antibiotics is likely due to the fear of bacterial co-infections of the respiratory tract<sup>4</sup>. There are not many studies assessing how empirical antibiotic use affects clinical outcomes in COVID-19 patients who don't have a bacterial infection<sup>5</sup>. While some studies have reported on the use of antimicrobials, their significance, and the potential for inappropriate or indiscriminate use, particularly when combined with broad-spectrum antibiotics, that are not adequately taken into account. In the 71% of patients in a research done by Chen *et al.* received antibiotic treatment; of these, 25% received single antibiotic therapy and 45% received combination medication. The cephalosporin, quinolone, carbapenem, and tetracycline classes of antibiotics were the most commonly used ones<sup>6</sup>. Additionally, a different study found that the three most commonly used antibiotics during the pandemic were azithromycin (18%), ceftriaxone (25%) and moxifloxacin (64%)<sup>7</sup>. Taking into consideration all these data collected around the world with the overuse of the antibiotics and its huge impact on the resistance of the antibiotics, it is still necessary to properly evaluate the impact of antibiotic use in COVID-19 patients on a larger scale, with as much participation from other nations as possible.

## MATERIAL AND METHODS

This investigation constitutes a retrospective observational analysis conducted within a regional hospital situated in Kosovo. Encompassing patients admitted due to COVID-19 infection exhibiting a spectrum of symptom severity from mild to severe, the study involved the enrollment of 300 individuals. The cohort comprised patients hospitalized between October 2020 and January 2021. Exclusion criteria were applied to patients who tested positive for COVID-19 but were not subsequently admitted to the hospital.

### Data collection and analysis

The demographic data underwent

meticulous scrutiny. Initially, age was scrutinized as a potential determinant, delineating the populace into five distinct cohorts: individuals aged 20 to 30 years, 31 to 50 years, 51 to 70 years, 71 to 90 years, and a final cohort spanning from 91 to 100 years. Subsequently, an array of variables including comorbidities, smoking status, and vaccination history were scrutinized. Following this, a comprehensive dataset on antibiotic utilization was amassed, elucidating the rationale behind antibiotic selection, a detail expounded upon within the results section. This dataset encompassed pertinent laboratory parameters including C-reactive protein, total leukocyte count, and neutrophil count, each categorized as elevated, diminished, or within normal limits. Conclusively, an exhaustive compilation of antibiotic regimens administered for empirical therapy was undertaken, culminating in the identification of the most frequently employed antibiotic. The ensuing findings are succinctly articulated through numerical representations and percentage distributions across all graphical and tabular presentations.

### Ethical approval

The number approved for permission by the Ethical Council of the Chamber of Pharmacists of Kosovo is 77/ 14/03/2023!

## RESULTS

### Demographic characteristics of the patients

Initially, we analyzed the demographic features of the patients. Out of 300 patients in total, the majority were male with 60% while female with 40% (Figure 1 A). While we were interested to see the ages which were affected the most, we divided them into groups as shown on the Figure 1 B, and accordingly, most of the patients were between the age group of 51 to 70 years old with 44% followed by those between 71 to 90 years old with total 117 patients (39%).

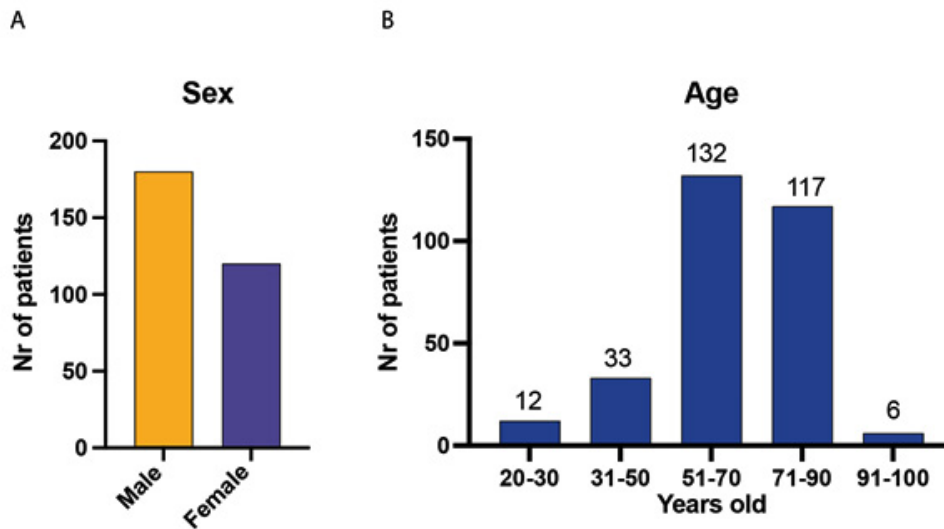
### Diagnosis of the disease and other parameters correlated to it

Furthermore, we have checked the methods by which the disease was diagnosed, whether it is by investigating the clinical symptoms or by performing Real Time-Polymerase Chain Reaction (RT-PCR) test or using both ways of diagnosis. Indeed, most of the cases were confirmed only by the clinical appearance of the

disease, with 204 patients diagnosed this way, while only a small portion, with 5% were diagnosed using both, clinical symptoms and PCR test (Figure 2 A). Moreover, we were interested to know if these patients received the anti-COVID-19 vaccine, and as expected more than the half, 84% respectively, were vaccinated (Figure 2 B).

Moreover, recognizing that a significant portion of the patient cohort comprised individuals of middle age and considering the multi-organ impact of COVID-19 beyond the respiratory system, our aim was to assess the presence of comorbidities potentially prolonging infection

duration and exacerbating prognostic outcomes. Notably, our observations revealed a prevalence of additional diseases among the patients, including but not limited to diabetes, arterial hypertension (AHT), cardiac ailments, renal dysfunction, malignancies, pulmonary disorders, epilepsy, and dementia. Among these, arterial hypertension emerged as the most prevalent comorbidity, affecting 132 patients, constituting 44% of the cohort, followed by diabetes affecting 81 patients, accounting for 27% (refer to Figure 2C). Subsequently, considering the primary impact of smoking on pulmonary health and its relevance to



**Fig. 1.** The demographic data of the patients with COVID-19. A- The graph showing the number of the patients depending on the sex. B- The age of the patients divided five groups starting from: 20 to 30 years old, 31 to 50 years old, 51 to 70 years, 71 to 90 years old and the final group from 91 to 100 years old

**Table 1.** The laboratory parameters used as a guide for antibiotic prescription (\* For 126 patients the values were missing)

	CRP*		Leukocytes		Neutrophiles	
	Nr.	%	Nr.	%	Nr.	%
Normal	6	2	153	51	3	1
High	168	56	147	49	297	99
Low	/	/	/	/	/	/

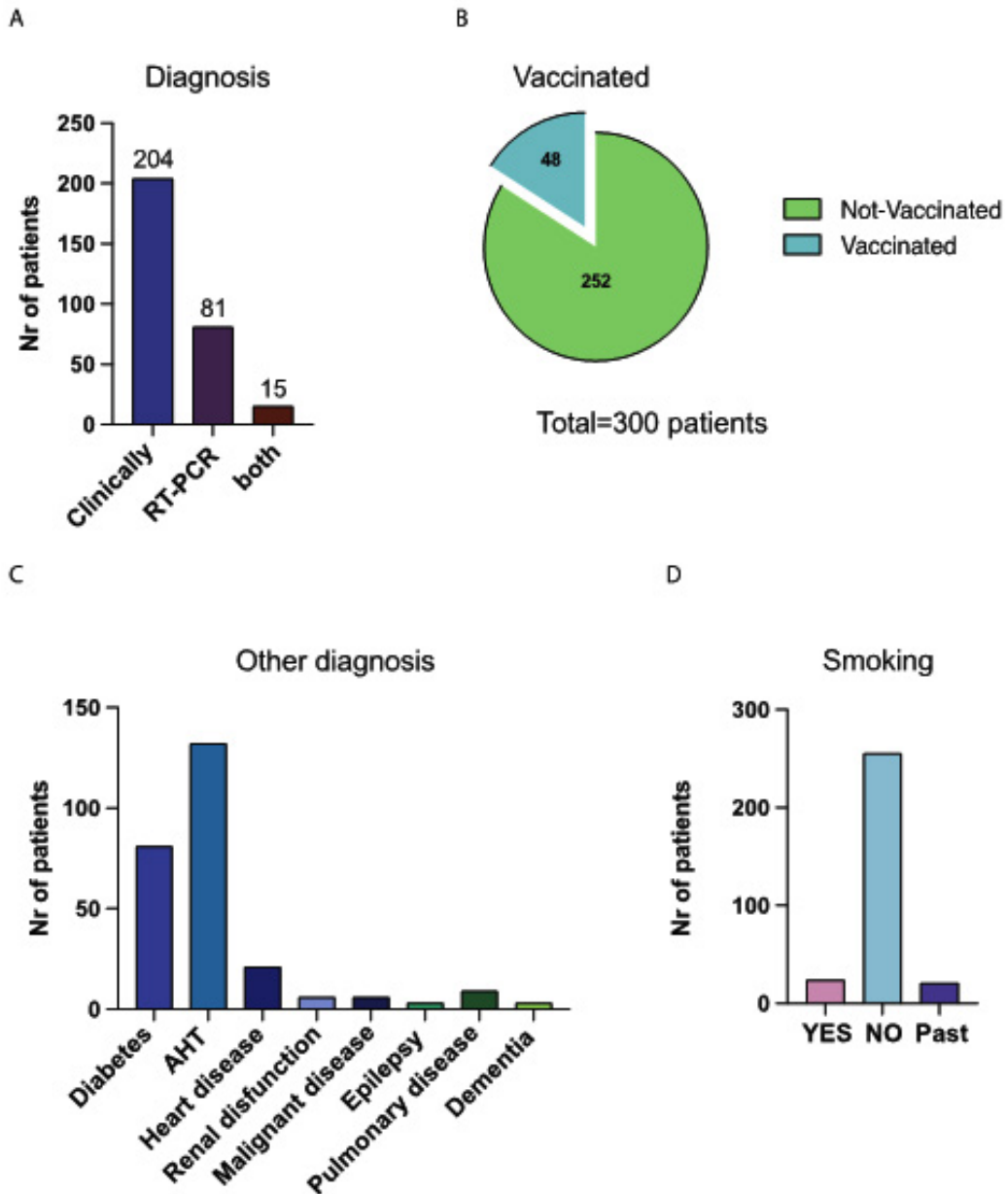
**Table 2.** The antibiotics used in all the patients with COVID-19 and their frequencies

Antibiotics	Levofloxacin	Ceftriaxone	Imipenem
Usage	Once per day Every 24 h	Three times per day Every 8 h	Twice per day Every 12 h

COVID-19 infection, we examined the smoking status of patients to ascertain its potential influence on disease severity. Surprisingly, the majority of patients were non-smokers, comprising 85% of the cohort, while a mere 7% had a history of smoking but had ceased prior to contracting the disease (refer to Figure 2D).

**Antibiotics used to treat the COVID-19 patients**

Subsequently, our investigation focused in the utilization of antibiotics. Initial scrutiny of patient health records revealed several indications for antibiotic administration, encompassing the severity of the disease, levels of inflammation biomarkers, and discernible alterations noted by



**Fig. 2.** Diagnosis and co-morbidities of patients. A- The graph shows the method by which the patients were diagnosed. B- A representing graph of the patients who were vaccinated or not. C- Patients with COVID-19 had other co-morbidities such as: Diabetes, Arterial Hypertension (AHT), Heart disease, Renal disfunction, Malignant disease, Epilepsy, Pulmonary disease and Dementia. D- Last graph shows the patients who were smokers during the time of the hospitalization, those who did not smoke and those who were smokers in the past

clinicians through radiologic imaging. Our analysis identified three primary parameters indicative of inflammation based on laboratory findings: C-reactive protein (CRP), total leukocyte count, and neutrophil count. Notably, CRP data were unavailable for 42% of patients, with the remaining exhibiting predominantly elevated levels (56%), while a mere 2% presented within the normal range. Conversely, leukocyte counts were elevated in 49% of patients and within normal limits in 51%. Neutrophil counts, however, were elevated in 297 patients, representing 99% of the cohort, while only 1% demonstrated a normal count (refer to Table 1). Given the established association between heightened white blood cell counts and infectious states, the widespread prescription of antibiotics to hospitalized patients is explicable. Indeed, all hospitalized patients included in the study received antibiotic treatment, with empiric regimens featuring prominently, including Levofloxacin, Ceftriaxone, and Imipenem, as illustrated in Table 2.

## DISCUSSION

The use of antibiotics during the pandemic in hospitalized patients has increased worldwide. In most of the countries, including Kosovo, it was a common protocol to be followed. However, despite being widely used in all the hospitals, some of the records are missing, especially regarding the vaccination status, the blood culture reports, laboratory analysis of the markers and also the specific doses and uses of antibiotics. From the data that we collected from the patients that were hospitalized with COVID-19, it turns out that 60% were men, while 40% were women. All were admitted to the ward, while there were none in the intensive and joint care, according to the age group the most affected age group was 51-70 years old with 44% and with the smallest percentage was the age group between 91-100 years old with only 2%.

Out of 300 patients, 261 of them had co-morbidities. Among them the most frequent was Arterial Hypertension which corresponds to 50,6%, followed by Diabetes with 31% of patients and others such as heart and pulmonary disease, renal dysfunction, malignant disease, epilepsy and dementia. Similarly, other groups reported that patients, especially of older ages were followed

by other co-morbidities which further contributed to the severity of the COVID-19<sup>8</sup>. The burden of COVID-19 was even heavier when accompanied with other diseases, this was also documented in other studies. In China, 75% of the patients with COVID-19 who were in critical condition or even died had other co-morbidities, more precisely diabetes and cardiac disease<sup>9</sup>. Hence, having other diseases had further worsen the symptoms of COVID-19 which made is obvious for the physicians to diagnose the patients. In fact, in our study we have observed that most of the patients, 204 out of 300, who were admitted in the hospital ward were diagnosed by clinical appearance of the diseases rather than running a RT-PCR test. Another interesting finding during our research, was that most of the patients who were admitted to the hospital with symptoms were not immunized against COVID-19, 84% of the patients to be precise. This further hampered the management of the disease.

Another interesting factor which led to a number of studies, is smoking. Considering the known impact of smoking in the lungs and also knowing that the main target of the COVID-19 was lungs, it raised questions among scientist whether smokers would have more severe outcomes during the pandemic times or not. Indeed, there is a plethora of studies out there, which might have raised confusion about the smoking. However, most of them are supported evidences that more smokers were admitted to the hospitals compared to non-smokers and most of them had severe symptoms of COVID-19<sup>10-13</sup>. Surprisingly, in our case 85% of the patients were non-smokers. Hence, this made COVID-19 a not so easy problem to solve.

In fact, even the treatment was a challenge. Considering antibiotics as a powerful use in the world of infections, they were one of the main tools used to fight the symptoms of COVID-19. In our case, antibiotics were used based on clinical appearance and the severity of the disease, the values of the inflammation biomarkers and according to the changes the doctors noticed based on the radiologic images. Considering the role of white blood cells in inflammation and infection, especially that of the neutrophils and also the significant increase of CRP<sup>14-16</sup>, it was the most common laboratory exam performed on patients

with COVID-19. Indeed, in our case, 99% of the patients had high number of neutrophils and 56% of the data collected included high levels of CRP. To be more precise we have to emphasize that the data for 126 patients concerning CRP analyses were missing. Considering these data, it might explain the use of antibiotics by the view of physicians. Indeed, all of the patients conducted in the study, which were hospitalized, were prescribed antibiotics. Since the illness was relatively new and there were no established protocols for treating its symptoms, the majority of hospitalized patients worldwide used antibiotics frequently<sup>17</sup>. In our case all of the hospitalized COVID-19 patients were prescribed antibiotics, the most common being Levofloxacin, Ceftriaxone and Imipenem. However, different studies have concluded that the use of antibiotics were not necessary at all<sup>4,17</sup><sup>18</sup>. In fact, in a meta-analyses study conducted by Lansbury *et al.*, it was shown that only a small group of patients had bacterial co-infections which does not justify the use of antibiotics<sup>19</sup>.

Despite subsequent considerations indicating that the administration of antibiotics may not have been warranted and, indeed, could have exacerbated the issue of antibiotic resistance, their usage was deemed imperative. Given the absence of a definitive protocol and the necessity to correlate symptoms with the clinical presentation of the disease alongside laboratory findings, physicians found themselves navigating a precarious path where antibiotics appeared as the only viable recourse for patient management.

Taken together, these findings pile up the evidences on the use of antibiotics during the COVID-19 pandemic, however further deeper studies should be conducted in order to better evaluate the impact it had on antibiotic resistance.

## CONCLUSION

After an unstoppable work, based on the results collected from this research, we saw an increase in the use of antibiotics, during the COVID-19 pandemic, by patients hospitalized in our country, Kosovo, mainly in the Ferizaj General Hospital, where the use of antibiotics was administered from the very beginning of the pandemic. We found that in these patients hospitalized in the internal ward there was

a use of antibiotics such as Imipenem, and Meropenem, Levofloxacin, Ceftriaxone which were administered for different durations. The knowledge about the virus and the lack of guidelines for its management, from our results, it is noted that the guideline for the use of antibiotics was higher from the side of the hospitals other than from the primary care. Also, the reasons for the use of antibiotics by the patients were: Disease weight, inflammatory laboratory markers, radiological changes. Most of the respondents in this research were part of the group age that included the older age, where it was proven that most of the patients besides the COVID-19 disease, also had concomitant diseases. We also note that the number of recovered patients was greater than the number of deaths and transferred to the University Clinical Center.

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### Conflict of Interest

The authors declare no conflict of interest.

### Authors' Contribution

F,A, A, H, M,A, G, H (Conceptualization, formal analysis, data curation, supervision, writing original draft, review, and editing). (Investigation, patient administration, software, visualization, validation, review, and editing). All authors declared that they contributed to this article and that they have read and approved the final manuscript.

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