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ORIGINAL ARTICLE

Microbiological profile of multidrug resistant bacteria before and during COVID-19 in CHU Mohammed VI

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ABSTRACT

Background and Objectives: A new type of corona virus has caused Corona virus disease-19 and, subsequently, a global pandemic. All individuals are prone to the disease, so drastic measures were taken to prevent its spread. This study aimed to evaluate the impact of COVID-19 on the progression of the antimicrobial resistance rate by comparing two periods: before and during COVID-19.

Materials and Methods: We used a cross-sectional design to investigate the Antimicrobial Resistance (AMR) rate before (03/2019 to 03/2020) and during COVID-19 (03/2020 to 03/2021) in a University Hospital in Marrakech. The data were analyzed using SPSS Version 25.0.

Results: Among the 7106 specimens, there was a significant increase in the multidrug-resistant bacterial from 27.38% to 35.87% during COVID-19 ($p<0.001$), particularly in blood culture, cerebrospinal fluid, catheter, and pus. However, there was a non-significant change in puncture fluid, expectoration, protected distal sampling, joint fluid, stool culture, and genital sampling. A decrease in Multidrug-resistant bacteria (MDRB) was observed only in cytobacteriological urine tests ($p<0.05$). According to species, there was an increase in extended-spectrum beta-lactamase-producing Enterobacteriaceae, carbapenem-resistant Enterobacteriaceae, and methicillin-resistant *Staphylococcus aureus*.

Conclusion: In our study, it is particularly noticeable that the MDRB has increased. These results highlight the importance that the pandemic has not been able to slow the progression.

Keywords: Multidrug resistant bacteria; Antimicrobial resistance; Rate; Corona virus disease-19; Microbiological profile

INTRODUCTION

Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is a new member of enveloped RNA β-coronavirus (1), which causes severe pneumonia with clinical symptoms different from known coronaviruses, such as SARS-CoV and MERS-CoV (2). Along with flu-like symptoms induced by the dis-

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ease, many people developed multiple organ failure and severe respiratory complications, sometimes followed by death (3). The SARS-CoV-2 infection constitutes a public health threat worldwide as it is highly contagious (4). Everybody is susceptible to the disease, mainly transmitted through close contact and respiratory droplets (5). Therefore, immediate and numerous measures have been recommended to reduce the transmissions, such as distancing, using facemasks, frequent handwashing, and covering the mouth and nose when sneezing and coughing. Since its first detection, the infection and mortality rates of the SARS-CoV-2 have far exceeded that of any other common flu (6). The World Health Organization and the Centers for Disease Control and Prevention recommended refraining from traveling to high-risk, heavily affected areas and avoiding close and unprotected contact with people with severe respiratory infections and domestic and wild animals (7).

The coinfection of the SARS-CoV-2 with other microorganisms, such as viruses, bacteria, and fungi, is a significant factor in COVID-19. It can raise the difficulties of diagnosis, treatment, and prognosis and even increase the disease symptoms and mortality (8). Many trials and investigations indicate a strong relationship between other viruses, bacteria, fungi, and SARS-CoV-2 (9). Clinically, differentiating between isolated COVID-19-related viral infection and possible added bacterial or fungal infection is challenging. Secondary bacterial infections from COVID-19 cases in Wuhan were reported in 15% of hospitalized patients and higher among the non-survivor group than survivors (50% versus 1%) (10). In the more detailed COVID-19 data, information on the frequency, nature, and susceptibility profiles of secondarily infecting pathogens remains limited (11). In the context of COVID-19, we are witnessing increased multidrug-resistant bacterial (MDRB) infections in our hospitals. Preliminary studies and evidence from high-burden COVID-19 areas suggest that superinfections are common, particularly in severe cases. Almost all SARS-CoV-2 severe cases result in pneumonia with the inflamed alveolar space, resulting in an ideal environment for microbial growth (12). The presence of secondary bacterial infections in patients infected with SARS-CoV-2 complicates treatment and prognosis (13). Control standards were used for nosocomial infections to be prevented, such as the proper distribution of equipment, triage strategy, congestion reduction, environmental health reorganization, and standard precautions such as safe injections, handwashing, and personal protective equipment (14). The unsuccessfully treated antimicrobial resistance-induced (AMR) infections worldwide claim the lives of at least 700,000 people annually. They are predicted to be associated with the deaths of 10 million per year by 2050, with a cost of US$100 trillion to the global economy due to loss of productivity (15). More than 2.8 million MDRB infections occur annually in the USA, causing at least 35000 deaths and $20 billion in healthcare expenditures (16). A Moroccan study showed that MDRB infection is a significant health problem and is responsible for higher morbidity and mortality, longer duration of mechanical ventilation, and more extended intensive care unit (ICU) stay (17). In acute care environments, the long-term propagation of AMR due to increased patient exposure to inappropriately used antimicrobials remains a possible consequence of the COVID-19 pandemic and an issue of concern. Still, the wide-ranging impacts of the pandemic on social and healthcare systems need to be highlighted, and data to be gathered to update and upgrade national strategies that address the long-term challenges of AMR while maintaining access to effective drugs. This current COVID-19 pandemic will hopefully lead to ongoing and improved infection prevention and control (IPC) practices globally in healthcare facilities and the community. We aimed to evaluate the impact of COVID-19 on the progression of the AMR rate by comparing two periods: before and during COVID-19.

MATERIALS AND METHODS

Study design and setting. This study used data from a microbiology laboratory and was an observational, descriptive, and retrospective analysis. We used a cross-sectional design to investigate the AMR rate before and during the COVID-19 outbreak in the University Hospital Center (CHU) Mohammed VI of Marrakech-Morocco-North Africa, a third resort healthcare public establishment. It comprises four hospitals with a complete range of specialized disciplines, a haemato-oncology center, and a mother-child hospital. It has a capacity of 1548 beds and provides care to the whole population of Marrakech-Safi and the southern regions, with approximately 57,096 admissions per year.

Sample size and sampling. The study sample was all data relating to the MDRB strains isolated from blood culture, cerebrospinal fluid, puncture fluid, cytobacteriological urine test, expectoration, protected distal sampling, joint fluid, catheter, stool culture, genital sampling, and pus of patients hospitalized in the different departments of the CHU during the study period, and without age restriction. The study period was 12 months before COVID-19 (03/03/2019 to 03/03/2020): Group A and 12 months during COVID-19 (03/03/2020 to 03/03/2021): Group B.

Minister of Health of Morocco, 2020. Available at:
https://www.sante.gov.ma/Pages/communiqu%C3%A9s.aspx?communiqueID=355 (Accessible 03/09/2023) (18).

Measurement. Blood samples were collected in BD BACTEC® vials (Becton Dickinson, USA) and were processed by the BD BACTEC™ FX-400 (Becton Dickinson Diagnostics, Sparks, USA) automated system according to the manufacturer's recommendations. The positive samples underwent a Gram staining procedure for all specimens and were sub-cultured on appropriate media. MALDI-TOF mass spectrometry and B.D. Phoenix M50™ system were used for identification and antimicrobial susceptibility testing of isolates. The results were interpreted following the guidelines of the French Society for Microbiology Antibiogram Committee and the European Committee on Antimicrobial Susceptibility Testing (CA-SFM/EUCAST). The MDR bacterial strains included extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBLE), carbapenem-resistant Enterobacteriaceae (CRE), methicillin-resistant *Staphylococcus aureus* (MRSA), multidrug-resistant *Acinetobacter baumannii* (ABMR), and multidrug-resistant *Pseudomonas aeruginosa* (PAMR).

Data collection and data analysis. First, the data was collected on Microsoft Excel 2007 and then analyzed on IBM SPSS Statistics for Windows, Version 25.0. (IBM Corp., Armonk, N.Y., USA). Percentage, frequency, and confidence interval were used to describe the AMR rates before and during the COVID-19 outbreak. Percentage change [(new value − old value)/old value) * 100] was used to describe changes in the AMR rates in MDR bacterial strains and total samples. Pearson's chi-square test was used to compare the AMR rates, and the significance level was set at <0.05.

RESULTS

We received 7106 specimens from several departments of the University Hospital. Most specimens were received from the pediatric department (31%), and the rest from the ICU, chirurgical departments, and medical departments with 29%, 25%, and 14%, respectively. The total number of MDRB was higher in Group A (3663 cases) compared to Group B (3443 cases). There was a significant increase in the MDRB in the total number of specimens from 1003 (27.38%) in Group A to 1235 (35.87%) in Group B with a p-value< 0.001. This increase was mainly observed in blood culture, cerebrospinal fluid, pus, and catheter. In blood culture, there were 448 cases (13.01%) of MDRB in Group B and only 293 (7.99%) in Group A. In cerebrospinal fluid, there were only 4 cases (0.11%) in Group A compared to 23 (0.67%) MDRB in Group B with a p-value of 0.006 for both cerebrospinal fluid and blood culture. For catheter, the number of MDRB passed from 49 (1.34%) to 71 (2.06%) and the pus from 308 (8.41%) to 372 (10.81%), with p < 0. 011. There was a non-significant increase in cases of puncture fluids, expectoration, protected distal sampling, and stool culture. However, a significant decrease in MDRB was observed only in cytobacteriological urine tests (p<0.05). Although there was a decrease in MDRB cases in joint fluid and genital sampling in Group B compared to Group A, the changes were not statistically significant (Table 1).

According to species, there was a significant increase in ESBLE and/or CRE, MRSA, and total species (p<0.05). ESBLE and/or CRE passed from 774 cases (21.13%) to 951 (27.62%), and MRSA from 42 (1.15%) to 66 (1.92%) with a p-value < 0.001. However, for ABMR and PAMR, the changes were not statistically significant, with p-values of 0.94 and 0.56, respectively (Table 2). The percentage of the germs found in the different specimens are summarized in Table 3.

DISCUSSION

The COVID-19 pandemic has undoubtedly altered the lives of individuals, communities, and societies worldwide. So far, the most insightful response to the disease has been the isolation, diagnosis, and care for all cases, including those with mild symptoms, to reduce transmission successfully. Larry Kerr has

Table 1. The distribution of MDRB according to specimens before and during COVID-19

Variable	Time				Percentage Change	p value
	The twelve months before COVID-19: Group A (N =3663)		The twelve months during COVID-19: Group B (N=3443)			
	n (%)	95% confidence interval	n (%)	95% confidence interval		
Blood culture	293 (7.99)	7.12 -8.88	448 (13.01)	11.89-14.14	62.83	0.006
Cerebrospinal fluid	4 (0.11)	0.00 - 0.22	23 (0.67)	0.40-0.94	509.09	0.006
Joint fluid	1 (0.03)	0.000-0.08	0 (0.00)	0.00-0.09	-100	0.398
Puncture fluid	16 (0.44)	0.22-0.65	19 (0.55)	0.30-0.80	25	0.667
Cytobacteriological urine test	268 (7.32)	6.47-8.16	226 (6.56)	5.74-7.39	-10.38	0.027
Expectoration	2 (0.06)	0.00-0.13	5 (0.15)	0.02-0.27	150	0.706
Protected distal sampling	50 (1.37)	0.99-1.74	63 (1.83)	1.38-2.28	33.58	0.068
Stool culture	4 (0.11)	0.00- 0.22	4 (0.12)	0.00- 0.23	9.09	0.123
Catheter	49 (1.34)	0.97-1.71	71 (2.06)	1.59-2.54	53.73	0.001
Pus	308 (8.41)	7.51-9.31	372 (10.81)	9.77- 11.84	28.54	0.011
Genital sampling	8 (0.22)	0.07- 0.37	4 (0.12)	0.00- 0.23	-45.45	0.744
Total specimens	1003 (27.4)	25.94- 28.83	1235 (35.9)	34.27-37.47	31.02	<0.001

Table 2. The MDR bacterial strains isolated before and during COVID-19

Variable	Time				Percentage Change	p value
	The twelve months before COVID-19: Group A (N =3663)		The twelve months during COVID-19: Group B (N=3443)			
	n (%)	95% confidence interval	n (%)	95% confidence interval		
ABMR	179 (4.89)	4.19-5.59	205 (5.95)	5.16-6.75	21.68	0.94
PAMR	8 (0.22)	0.07-0.37	13 (0.38)	0.17- 0.58	72.73	0.56
ESBL and/or CRE	774 (21.13)	19.81-22.45	951 (27.62)	26.13-29.12	30.71	<0.001
MRSA	42 (1.15)	0.80-1.49	66 (1.92)	1.46- 2.38	66.96	<0.001
Total	1003 (27.38)	25.94-28.83	1235 (35.87)	34.27-37.47	31.01	<0.001

N: total effective; n: positive effective; ABMR: multidrug-resistant *Acinetobacter baumannii*; PAMR: multidrug-resistant *Pseudomonas aeruginosa*; ELSE: extended-spectrum beta-lactamase-producing Enterobacteriaceae; CRE: carbapenem-resistant Enterobacteriaceae; MRSA: methicillin-resistant *Staphylococcus aureus*

recently compared the AMR pandemic to a "multitude of small fires that are much less visible than the single massive firestorm that is the COVID-19 pandemic" (19). In our study, it is particularly noticeable that the MDRB has globally increased. Although experts have expressed concern about the link between COVID-19 and AMR (20-24), current studies have presented widely conflicting results. Several studies from Germany, Italy, and the US have reported a rising trend of infections with the acquisition of MDRB during the COVID-19 pandemic (25-28). However, other studies, particularly from France and Spain, did not show increased infections with MDRB (29-33). Fattorini et al. (34) concluded that only 1.3% of 522 COVID-19 patients in ICUs and seemingly no COVID-19 patients in other units developed a healthcare-associated superinfection with AMR bacteria. These differing experiences may be attributed to the impact of previous antibiotic prescribing and IPC practices leading to varying background AMR prevalence, namely in healthcare facilities in different countries (24). Still, the remaining issue is whether the AMR situation will exacerbate or improve due to the current COVID-19 pandemic (22). This is proof

Table 3. The Percentage of Germs in the Specimens

		Group A		Group B	
Sample	**GERMS**	**Total**	**%MDRB**	**Total**	**%MDRB**
Blood culture	AB	53	79,2	79	78,5
	PA	7	14,3	36	2,8
	EB	390	61,0	516	70,5
	SA	101	11,9	106	19,8
Cerebrospinal fluid	AB	3	33,3	3	66,7
	PA	6	0,0	2	0,0
	EB	9	22,2	29	72,4
	SA	5	20,0	10	0,0
Joint fluid	AB	0	0,0	0	0,0
	PA	0	0,0	0	0,0
	EB	1	0,0	0	0,0
	SA	8	12,5	6	0,0
Puncture fluid	AB	2	50,0	5	60,0
	PA	10	0,0	12	0,0
	EB	79	17,7	81	19,8
	SA	10	10,0	7	0,0
Cytobacteriological	AB	19	78,9	33	87,9
urine test	PA	41	2,4	48	4,2
	EB	1328	19,0	896	21,4
	SA	32	0,0	25	12,0
Expectoration	AB	0	0,0	1	0,0
	PA	6	0,0	7	0,0
	EB	4	50,0	10	40,0
	SA	0	0,0	1	100,0
Protected distal	AB	28	89,3	22	100,0
sampling	PA	25	0,0	29	6,9
	EB	61	39,3	66	54,5
	SA	29	3,4	21	14,3
Stool culture	AB	0	0,0	0	0,0
	PA	1	0,0	2	0,0
	EB	30	13,3	10	40,0
	SA	0	0,0	0	0,0
Catheter	AB	9	77,8	15	80,0
	PA	12	0,0	5	0,0
	EB	73	54,8	66	83,3
	SA	18	11,1	16	25,0
Pus	AB	98	86,7	88	84,1
	PA	160	3,8	195	4,1
	EB	690	28,0	723	35,4
	SA	288	8,3	256	13,3
Genital sampling	AB	3	100,0	1	100,0
	PA	0	0,0	2	0,0
	EB	24	20,8	10	30,0
	SA	0	0,0	3	0,0

MDRB: multidrug-resistant bacterial; AB: *Acinetobacter baumannii*; PA: *Pseudomonas aeruginosa;* EB: Enterobacteriaceae; SA: *Staphylococcus aureus*

that unless instant gathered data are available, the impact of the COVID-19 pandemic on AMR will remain unclear in the coming months or even years.

Overall, COVID-19 should lead to a decline in resistance rates observed in many countries due to extensive measures such as distancing, wearing face masks, frequent handwashing, and covering the mouth and nose when coughing and sneezing. However, on a global level, changes in AMR rates will not necessarily be uniform. In more developed countries, resistance rates will likely decrease. However, in many other countries, such as Morocco, where this study was carried out, too many factors combine to lead to poor controls on the progression of AMR (e.g., poor sanitary conditions, poverty, lack of housing) (22). Moreover, a study conducted in Morocco showed that MDRB infection is a significant health problem and is responsible for higher morbidity and mortality, longer duration of mechanical ventilation, and prolonged ICU stay (17). In such countries, we might see even more propagation of resistant bacteria if economies and governance deteriorate further (35).

In our study, the number of MDRB increased in total specimens, especially blood culture, cerebrospinal fluid, catheter, and pus. The AMR rates were significant ($p<0.05$) for MRSA, ESBLE, and/or CRE. Despite the surge in cases of puncture fluid, expectoration, protected distal sampling, and stool culture, the changes were not statistically significant ($p>0.05$). Restricted access to health services during the pandemic is causing discontinuation of treatments, such as for tuberculosis and human immunodeficiency virus, which could also result in selection for drug resistance. Likewise, disruption to vaccination services can lead to a higher risk of infection and, subsequently, overuse of antimicrobials (11). A further looming threat is the extensive use of biocidal agents for personal and environmental disinfection, including in non-health-care settings. Low-level exposure to biocidal agents can select for drug-resistant strains and increase the risk of cross-resistance to antibiotics, particularly those that treat Gram-negative bacteria (36, 37).

In our study, however, a significant decrease in AMR was observed only in cytobacteriological urine tests ($p<0.05$). Although there was a decrease in MDRB cases in joint fluid and genital sampling in Group B compared to Group A, the changes were not statistically significant ($p>0.05$). Several factors may explain the decrease in AMR, such as fewer

emergency and planned hospital admissions (38, 39), including chronically ill patients (e.g., oncology patients, diabetic patients, transplant patients), resulting in fewer antibiotic prescriptions—self-quarantine of COVID-19 patients with exaggerated standard precautions, e.g., increased hand hygiene. Also, there has been a significant decrease in international air travel, resulting in a decreased risk of global dissemination of AMR bacteria and genes from highly endemic regions (24). In hospitals, examples of bacteria that are common pathogens that frequently spread include MRSA and vancomycin-resistant Enterococcus (24). These bacteria mainly spread via either direct person-to-person transmission or the hands of medical and nursing staff and contaminated surfaces in healthcare facilities. Improved cleaning of frequently touched surfaces, rigorous hand hygiene, and better adherence to ICP should decrease bacterial spread within and among healthcare settings (40, 41). According to Collihnon and Beggs (34), handwashing practices in Africa have improved noticeably since the outbreak of COVID-19, with access to more handwashing stations in community centers, schools, markets, bus terminals, and other public spaces in urban and rural areas. Disease transmission is highly linked to prolonged physical proximity. Higher population density and crowded living conditions are additional factors that mediate AMR transmission, even in the pre-COVID-19 era. Countries with less crowded households and lower population density had fewer AMR infections and AMR-related deaths (36-41). Two types of procedures were used to prevent infections originating in hospitals: routine care practices like handwashing, which are used on all patients in appropriate circumstances, and more intensive isolation precautions, mainly when patients are suspected of having particular infections (42).

During the pandemic, we need to combine our efforts to prevent and control AMR and ensure the effectiveness of antimicrobials via four measures. The first measure is to provide targeted training for health workers to enhance clinical skills and improve critical competencies, including better use of antibiotics. The second point is to avoid disrupting essential health services, including antiretroviral and tuberculosis drugs and vaccines. The third measure is to show the utmost caution in using biocides for disinfection and to prioritize biocidal agents with or without a low selection pressure for antibiotic resistance. Lastly, research must become an essential part of studying new antibiotics.

Our study was among the first ones that compared the two periods before and during COVID-19. However, it has limitations: a limited number of samples were analyzed, the hospital hospitalized mostly people with COVID-19 during the pandemic, proved by molecular biology (PCR), and there needed to be more information and communication with other departments. Therefore, it took much work to provide more comparisons and more results.

CONCLUSION

In our study, it is particularly noticeable that the MDRB has increased. Despite the hygiene measures undertaken during COVID-19, the MDRB has remained the same. We notice a progression of a silent pandemic of antibiotic resistance that will hereafter threaten humanity. These results highlight the importance that the pandemic has not been able to slow the progression.

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