



Article Trends in Bacterial and Candida Infections Before and Throughout the COVID-19 Pandemic

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Abstract: The COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)virus, resulted in significant global health consequences. The interventions introduced to limit the spread of the virus had a significant impact on the course of the pandemic, but they might also involve other pathogens besides SARS-CoV-2. This study investigates the epidemiological variations for major bacterial and common fungal pathogens represented by Candida species infection in Qatar through retrospective hospital records. Retrospective data were collected on all bacterial and Candida infections from Hamad General Hospital between January 2019 and December 2021. Statistical analyses were performed using R (Version 4.1.0). Infection count comparisons were performed using chi-square goodness of fit tests. Differences in patient numbers were tested with one-way ANOVA followed by post hoc Tukey HSD. The number of infections and measures were correlated using Spearman rank correlation. The significance level was set at 0.05, and where applicable, the Holm-Bonferroni method was used to correct for multiple testing. The general trend for bacterial and Candida infections showed a significant decrease (p < 0.05) following the imposed restrictions and increases during restriction lifting periods. The number of bacterial infections correlated with the number of international visitors ($\rho = 0.61$, p < 0.01), while the number of Candida infections correlated with hospital admissions of COVID-19 patients ($\rho = 0.59$, p = 0.013). The results provide a general overview of the infection trends in Qatar during the COVID-19 pandemic and illustrate some of the pandemic interventions' effects on bacterial and Candida infections. However, further research is needed to better understand the underlying trend dynamics.

Keywords: bacteria; COVID-19; hospital; Candida; Qatar

1. Introduction

In March 2020, the World Health Organization (WHO) declared COVID-19 diseases caused by SARS-CoV-2 as a global pandemic. By the following month, more than 800,000 deaths were reported worldwide [1]. Although COVID-19 is a viral infection caused by the SARS-CoV-2 virus, associated direct and secondary pathology and the healthcare system, disruptions significantly impacted other acute and chronic infections and non-communicable diseases [2–5]. The consequences of the COVID-19 pandemic cannot be overstated, spanning direct public health and extending beyond recorded morbidity and mortality to include devastating social and economic consequences [6]. For example, during the pandemic, there was a noticeable increase in antimicrobial consumption, particularly for hospitalized patients [2–9].



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Copyright: © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). Treatments for the COVID-19 disease, including antimicrobials, immune suppression such as steroids, and immune-modulating therapy, can influence the epidemiology of bacterial and fungal infections [10]. Several studies found changes in bacterial and fungal (most commonly *Candida* species) infection epidemiology, particularly among hospitalized patients [5,11,12]. Additionally, social distancing and the restrictions governments imposed to quell the spread of SARS-CoV-2 may have affected the spread of other pathogens as they depend on close contact for spread [13]. While epidemiological changes in hospitalized patients have been described, only a few studies investigated epidemiological changes in bacterial and fungal infections on a larger scale or in terms of community spread during the pandemic.

The COVID-19 pandemic has had a profound impact on healthcare systems worldwide, influencing the epidemiology of bacterial and fungal infections through multiple direct and indirect pathways. While this study focuses on trends observed in Qatar, similar patterns have been reported globally. For instance, in Italy, Deiana et al. [14] observed a rise in healthcare-associated infections (HAIs) during the pandemic, particularly in intensive care units (ICUs), where increased reliance on invasive devices and immunosuppressive therapies contributed to heightened risks. In England, Gerver et al. [10] identified an increase in fungal co-infections, including *Candida* species, among hospitalized COVID-19 patients, highlighting the burden of critical care interventions on infection dynamics. Expanding on such international comparisons enriches our understanding of how localized trends fit within broader global patterns,

Qatar is one of the Gulf countries in the Arabian Peninsula, with a population of about 3 million. The healthcare system is based on universal coverage, operated by Hamad Medical Corporation (HMC), which serves the entire population, making it ideal for country-wide epidemiological surveillance. In Qatar, the first COVID-19 case was reported on the 29 February 2020, while restrictions and measures were imposed on the 15 March 2020. Using data covering the pandemic between the 1 January 2019 and the 31 December 2021, this study aims to investigate epidemiological changes in bacterial and fungal infections, which are represented by Candida species, across the country against social interventions. The three-year study period spans approximately 15 months before the pandemic, and all the COVID-19 pandemic waves up to the lifting of social restrictions in the country.

2. Materials and Methods

2.1. Settings

Hamad Medical Corporation (HMC) is the primary healthcare provider in the country. HMC is composed of the medical city (which consists of 14 acute and specialized care hospitals with a total capacity of almost 2500 beds), three general hospitals, and a network of 29 primary healthcare centers (PHCCs) that serve the country's population of nearly three million (Figure S1) Through a major central facility and a few peripheral supporting ones, the microbiology division of the Department of Pathology and Laboratory Medicine handles all specimens for microbiological identification and reporting.

2.2. Specifications for Datasets and Resources

Retrospective data were collected on all bacterial and *Candida* infections from the HMC central laboratory between 1 January 2019 and 31 December 2021. The microbial identification at HMC was mainly made using matrix- assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS), Brucker, Germany and BD PHOENIX M50, Version 2.75. Automated Microbiology System, US. The three-year study period includes the period of almost 15 months (1 January 2019–14 March 2020) before the first pandemic restrictions and the period following, which consists of the first restrictions period (15 March 2020–14 June 2020), first gradual restriction lifting (15 June 2020–2 February 2021), second restrictions period (3 February 2021–27 May 2021), and second gradual restriction lifting (28 May 2021–31 December 2021).

The data included patient demographics, specimen type, collection date, location, and identified organism. The data were processed to keep the first episode per patient per 365 days, and an infection type was defined using the orderable name and specimen type/body site. Infection types were grouped into urinary tract infections (UTIs), respiratory tract (RTIs), sterile sites (including bacteremia), wound, skin and soft tissue infections (Wound/SSTI), eye, ear, gastrointestinal, and genital. An extra "other" category was added to cover cases where the infection type could not be determined or did not fall into any of the groups.

In addition to the infection data, several other datasets were used to support analysis. COVID-19 statistics were obtained from the Qatar Open Data Portal (https://www.data. gov.qa/; URL accessed on 8 June 2022, Figure S2). The dataset includes the number of daily new COVID-19 cases, deaths, and hospitalizations, as well as the number of patients in the hospital per day due to COVID-19. Additionally, the numbers of monthly incoming international travelers were collected from the Qatar Monthly Statistics Reports published by the Qatar Planning and Statistics Authority (QPSA; https://www.psa.gov.qa/; URL accessed on 8 June 2022, Figure S3). Lastly, mobility and COVID-19 restriction metrics were collected from both the Google COVID-19 Community Mobility Reports (https://www.google.com/covid19/mobility/; URL accessed on 8 June 2022, Figure S4) and the Oxford COVID-19 Government Response Tracker (OxCGRT; Figure S5) [15].

2.3. Statistical Analysis

All statistical analyses were performed using R (Version 4.1.0). Infection count comparisons were performed using chi-square goodness of fit tests. Differences in patient numbers were tested with one-way ANOVA followed by post hoc Tukey HSD. The number of infections and measures were correlated using Spearman rank correlation. The significance level was set at 0.05, and where applicable, the Holm–Bonferroni method was used to correct for multiple testing. Where sex was a factor in the analysis, only infections where sex was mentioned were used because five patients did not have a record of sex.

3. Results

3.1. Infections and Demographics

A summary of patients' demographics and sampling sites is outlined in Table 1. After removing duplicates, the total number of infection episodes was 69,493, with 98.8% bacterial and 1.2% Candida infections. More than half the infections were among females, and non-Qatari patients. Infection episodes were highest in the pre-restrictions period, then decreased during the first restrictions period, increased during the first lifting period, declined again during the second restrictions period, and rose again during the second lifting period (Table S1). Pairwise comparisons between the periods show statistically significant differences between all pairs for bacterial infections (p < 0.01). Similarly, the differences between the periods of Candida species infections were significant, except between the first gradual lifting and second restrictions period (Figure 1).

Table 1. Demographic summary.

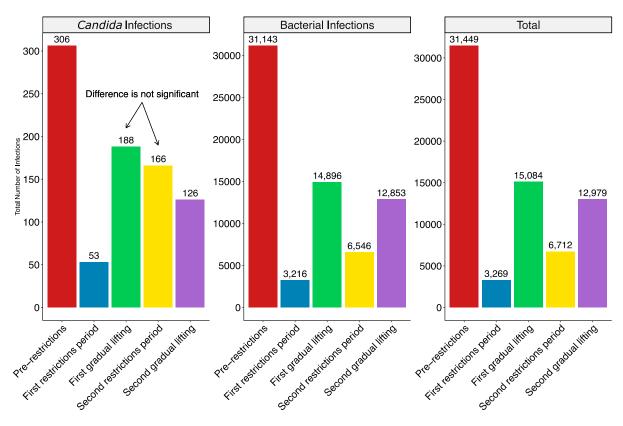
Characteristic	N = 69,493 ¹
Age	38 (25, 57)
Sex Female Male	38,511 (55%) 30,977 (45%)
Organism Bacteria Candida	68,654 (98.8%) 839 (1.2%)

Characteristic	N = 69,493 ¹	
Facility		
Medical City ²	41,102 (59%)	
Hospital	18,437 (27%)	
Other ³	465 (0.7%)	
РНСС	9489 (14%)	
COVID-19 Hospitalizations	824 (1.2%)	
Nationality		
Non-Qatari	50,193 (72%)	

19,299 (28%)

Table 1. Cont.

¹ Median (interquartile range); *n* (%). ² The medical city included Hamad General Hospital and 14 other specialized hospitals. ³ Other: includes facilities that do not fall into the other types.



Oatari

Figure 1. Number of infections stratified by period. Infection data were deduplicated to keep the first episode per patient per pathogen per 365 days. All pairwise comparisons of the number of infections were statistically significant (p < 0.01), except between the first gradual lifting and second restrictions period with Candida infections.

3.2. Age Distribution

Bacterial infections are most common in children ≤ 5 years of age, the middle age group of 30–40, and the elderly ≥ 60 . This trend was consistent throughout when stratified by COVID-19 periods (Figure 2). As for Candida infections, the distribution is less consistent. Infections were most common in the 20–30 years group pre-COVID-19 restrictions, then shifted toward ≥ 60 years old during the pandemic. Additionally, Candida infections were more common in females' pre-restrictions. However, they became more common in male patients after, as opposed to bacterial infections, which remain consistently more common in females (Figure S6).

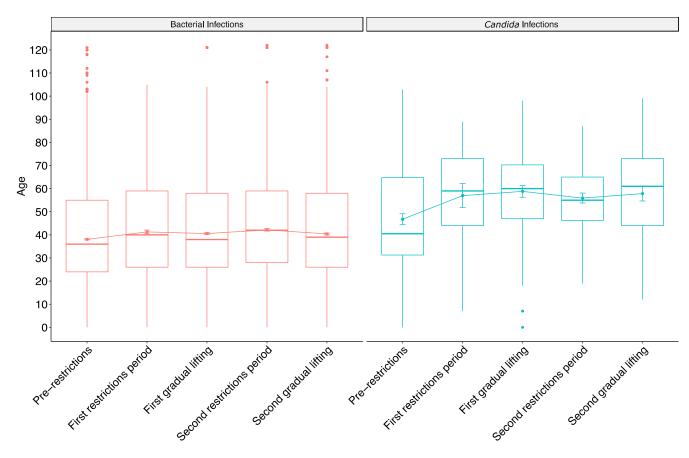


Figure 2. Age distribution box plot. The line shows the moving average age across the periods. The increase was significant in both cases (p < 0.01). The mean age increased from ~38 to ~42 for bacterial infections (p < 0.01) and from ~47 to ~58 for Candida infections. Fourteen records did not have an age.

The change in mean age for bacterial infections was statistically significant (p < 0.01) between pre-restrictions and all other periods, the first gradual lifting and second restrictions periods, and between the second restriction and second incremental lifting periods (Figure 2). Notably, the mean age increased throughout, except between the second restriction and gradual lifting periods, where it decreased (Table S2). As for Candida, the only significant differences were between pre-restrictions and the other periods (p < 0.01). The differences between the later periods were not significant. The increase in Candida infection means age was higher than with bacterial infections.

3.3. Infection Type Distribution

The distributions of infection types are shown in Figure 3. Bacterial UTIs are the most common throughout the period, followed by wound/SSTIs, RTIs, and sterile site infections. Despite the significant decrease in infection episodes following the pandemic, the overall distribution of bacterial infection categories remains consistent. Conversely, the distribution of Candida infections is not consistent. Pre-restrictions and wound/SSTIs were the most common, followed by sterile site infections. However, sterile site infections became more common during the pandemic. Stratifying by patients' sex, sterile site Candida infections were more common in males, and the number of female patients decreased during the pandemic (Figure S7).

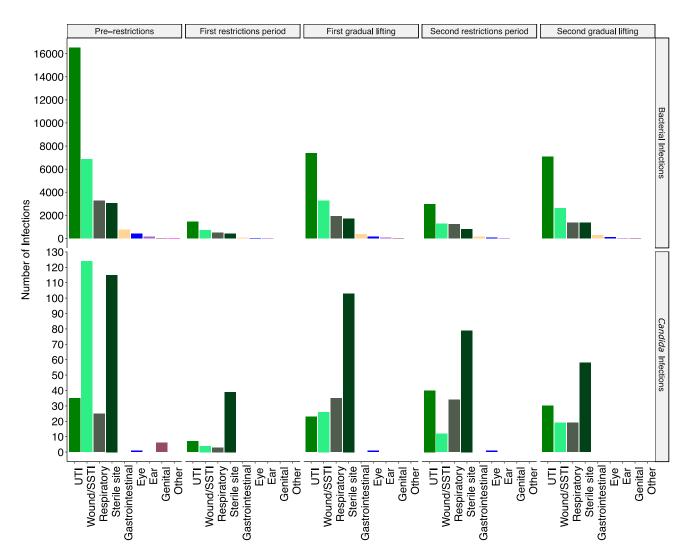


Figure 3. Number of infections stratified by type and COVID-19 period. The infection type was decided using the orderable name from the hospital and the sample type.

3.4. Association with COVID-19 Metrics

The number of days is not equal between the defined periods. Thus, the data were analyzed more using daily and monthly infections (Figure 4). The number of bacterial infections was lowest during both restriction periods, and there was a reduction in infections in August 2019. On the other hand, Candida shows the opposite trend, with peaks toward the end of the restriction periods.

These trends suggest a correlation between the number of infections and the COVID-19 pandemic measures and associated factors. A Spearman Rank correlation test shows that there is a moderate correlation between the number of incoming international travelers and bacterial infections ($\rho = 0.61$, p < 0.01; Figure S8), as well as moderate positive correlations between the number of Candida infections and both the Containment Health Index (an aggregate of containment and closure policies indices and health system policies; $\rho = 0.5$, p < 0.01) and the number of hospitalized COVID-19 patients ($\rho = 0.6$; p = 0.011; Figure S9).

Stratifying the number of infections by infection type shows an interesting trend with bacterial infections. Respiratory infections have an opposite trend to the overall number of infections, with peaks within restriction periods (Figure 5). This trend was correlated with the number of hospitalized COVID-19 patients ($\rho = 0.59$, p = 0.013).

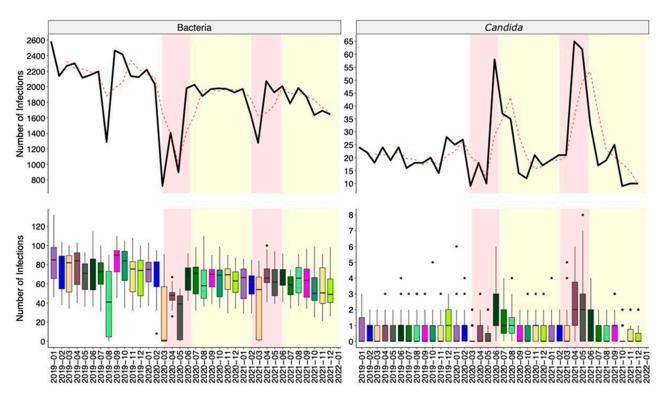


Figure 4. Daily and monthly bacterial and Candida infections. The top figures show the total infections per month, and the bottom figures are boxplots of the distribution of infections (number per day) each month. The dashed red lines in the top figures show the quarterly moving average. The red backgrounds show restriction periods, and the yellow backgrounds show periods of gradual lifting.

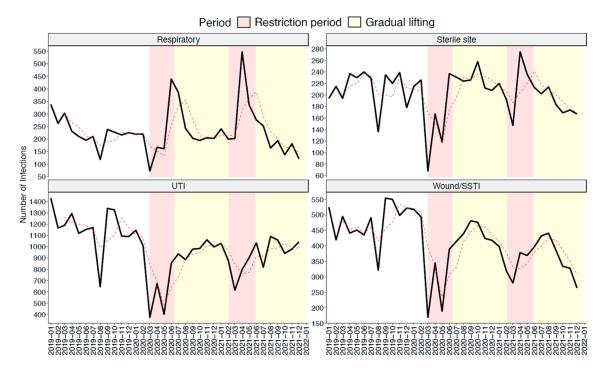
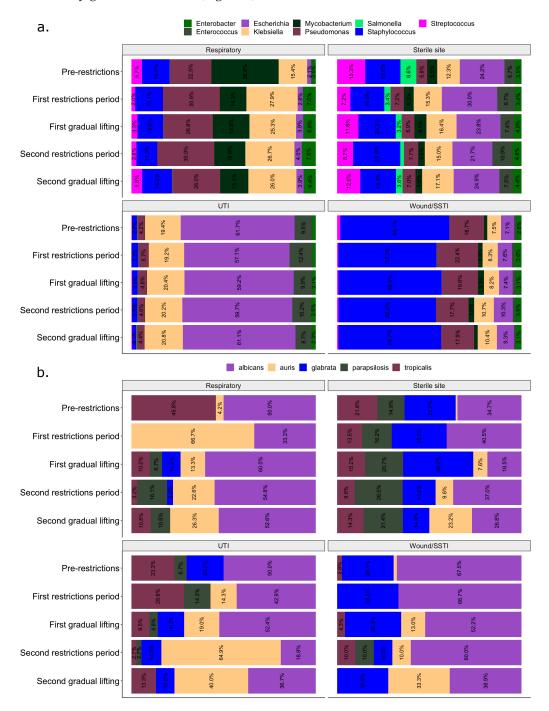
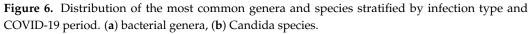


Figure 5. Monthly bacterial infections stratified by type. The dashed red lines show the quarterly moving average. The red backgrounds show restriction periods, and the yellow backgrounds show periods of gradual lifting.

3.5. Pathogens Diversity

At least 364 bacterial species from 125 genera caused bacterial infection episodes. The most common genera were Escherichia, Staphylococcus, Klebsiella, Pseudomonas, and Enterococcus. The distribution of these genera follows the same trend as the total number of infections (Figure 6). Notably, the proportion of Mycobacteria infections decreased significantly during the pandemic. As for Candida, the predominant species was albicans, followed by glabtara and auris (Figure 6).





4. Discussion

Several studies investigated the trends in co- and secondary bacterial infections in COVID-19 patients [10,11]. Other studies investigated COVID-19 and non-COVID-19 patients but focused on hospital-acquired infections (HAIs) [16-23]. These studies found an increase in the rate of HAIs during the COVID-19 pandemic, particularly in intensive care units (ICUs) and device-associated infections such as catheter-associated infections. The noticeable increase in HAIs has been implicated in increased pressure on healthcare facilities and disruption of routine practices. Interestingly, a study in Italy noted that while there was an increase in HAIs in internal medicine wards, which showed more patient pressure during the pandemic, long-term care wards showed a decrease [18]. The study's observed reduction in bacterial infections in long-term care units during the pandemic, despite increased hospital pressures, is intriguing and merits further investigation. This phenomenon might be linked to stringent infection control practices in such settings, including restricted visitation, heightened hygiene protocols, and focused resource allocation. These measures could have curbed bacterial transmission. Alternatively, the decline might indicate underdiagnosis or underreporting, possibly caused by limited healthcare access and diagnostic constraints during the pandemic. Whether this trend represents an isolated occurrence or reflects a global pattern remains uncertain. Comparative, cross-system analyses are essential to assess the broader relevance of these findings. Since most secondary and related pathology of COVID-19 were conducted at secondary care facilities, there is minor community-acquired infection (CAI) data and data related to the dynamics of the social restrictions. While the data in this study does not differentiate between HAIs and community-acquired infections (CAIs) since it included PHCCs and outpatient clinics, the study's strength is the inclusion of all infections across the healthcare network, which gives a better overview of national epidemiology. Most infections were bacterial at 98.8% compared to Candida at 1.2% (Table 1). Unlike other epidemiological and surveillance studies during the COVID-19 pandemic for primary and secondary infectious diseases, the mean young age of the cohort (38 years) reflects the represented country's young population [24]. While the gender ratio in Qatar's population is approximately 3:1 male-to-female, infections are more prevalent in females (https://www.psa.gov.qa/, URL accessed on 8 June 2022). This is likely because UTIs are the most common infections and have a higher incidence in females (Figure 3 and Figure S7) [25].

As for the changes through the COVID-19 pandemic, the results show that the total number of bacterial and Candida infection episodes decreased during both periods of social restriction and increased during the lifting of social constraints (Figure 1). This is obvious for bacterial infection episodes, which were statistically significant. The pattern is likely due to the lower exposure to communicable diseases and intensified awareness of infection prevention and control measures during the restriction periods or might be due to underreporting because of limited access to healthcare. There was also a pronounced bounce back of increased infection episodes following the second restrictions period compared to the first. This may be due to waning adherence to infection prevention and control measures of the pandemic. Moreover, infections during the evolving pandemic might be more common in COVID-19 patients than others, especially for long-term affected patients.

As for Candida species infection episodes, the pattern is different. During the first restriction period, a significant reduction in reported episodes was followed by a surge that persisted throughout, albeit less than before. Since invasive candidiasis is a recognized complication of COVID-19 disease and a significant cause of morbidity and mortality in patients admitted to critical care, it is plausible to extrapolate that patients admitted during the first pandemic wave with severe disease were admitted to ICU and subsequently developed severe invasive fungal infection [26,27]. This observation is supported by the dynamics of the pandemic time frame when the number of hospitalized COVID-19 patients peaked during the second restrictions period (Figure S2), as well as the significant shift in epidemiology when Candida species isolated from sterile sites, specifically bloodstream

infections replaced other categories throughout the epidemic (Figure 3). Furthermore, Candida infections are more common in older patients with chronic comorbidities in critical care settings [26]. As previously described, these mounting risk factors readily accumulate in patients with COVID-19 [26,27]. From the results, the shift in epidemiology was accompanied by a right shift in patient age not seen with bacterial infections, signifying older patients are more likely to be affected by Candida infection episodes (Figures 2 and 3). The observation that older adults were more susceptible to Candida infections during the pandemic aligns with existing evidence that chronic comorbidities significantly increase the risk of opportunistic fungal infections. Conditions such as diabetes [28], and cardiovascular diseases [29], prevalent in older populations, are known to weaken immune defenses, particularly in critical care settings. The intensive care setting introduces additional risk factors for *Candida* infections, including the use of broad-spectrum antibiotics, invasive procedures such as central venous catheters, and immune suppression therapies, which are commonly employed in managing critically ill patients. These factors create an environment conducive to fungal colonization and infection [30]. During the COVID-19 outbreak, the surge of critically ill patients requiring intensive care further amplified these risks. Many of these patients, particularly those with severe COVID-19, were subjected to prolonged mechanical ventilation, immune-modulating therapies, and high-dose corticosteroids, all of which have been associated with an increased incidence of invasive candidiasis [31]. The pandemic's impact on healthcare delivery, characterized by overburdened ICUs and prioritization of COVID-19 management, may have contributed to the increased susceptibility of older adults with chronic conditions to Candida infections. Additionally, delays in diagnosing and treating these infections due to the focus on managing COVID-19 patients could have intensified the observed trends.

The change in the influx of travelers and country population characteristics should be examined to explore other concomitant explanations for the noticeable shift in epidemiology for both bacterial and Candida infections. A sizable proportion of the country's population is immigrant workers from neighboring Asia, African, and Middle Eastern countries (88.4%) [24]. For instance, following the imposed travel and social restrictions in March 2020, bacterial respiratory infections were reduced significantly, and examined against the substantial reduction in the number of travelers and migrant workers coming into the country while the local population was static [32]. There was a moderate association between the number of bacterial infections and international travelers. On the other hand, Candida infections were associated with the number of hospitalized COVID-19 patients that peaked during the restriction periods, supporting the observation of increased infections in high-risk patients.

In addition to changes in the number of infections, a reduction in species diversity was observed. The most notable is the decrease in mycobacterial infections (Figure 6). This decrease may be due to a mixture of factors. For example, infection control and prevention measures, such as respiratory masks, social distancing, and restrictions, can affect infectivity since the pathogen relies on close contact. Secondly, a previous study showed that immigrant workers are Qatar's primary source of new tuberculosis infections [32]. Thus, travel restrictions may have reduced this route. Furthermore, even though the influence of current or previous TB infection or vaccination on the COVID-19 pandemic has been debated, no conclusive evidence was established of the direct impact of TB infection on COVID-19 disease. Still, indeed, from a global perspective, the pandemic has a negative impact on the propagation of the TB disease [33,34].

Lastly, for Candida species, the most notable change was with the rare but notorious species of Candida auris (Figure 6). The analysis revealed a noticeable shift in the diversity of Candida species during the pandemic, with Candida auris emerging more prominently. This species, known for its multidrug-resistant properties, became a significant concern during the pandemic period [35]. Candida auris presents unique challenges due to its high transmissibility, resistance to multiple antifungal agents, and persistence on environmental surfaces. These characteristics make eradication in healthcare settings exceptionally dif-

ficult. The pandemic's strain on healthcare systems, including overburdened ICUs and stretched infection control resources, likely contributed to the establishment and spread of this pathogen in vulnerable settings [35]. The pandemic environment, marked by increased use of corticosteroids, prolonged hospitalizations, and widespread antibiotic use, likely created favorable conditions for opportunistic infections like Candida auris. The shift in epidemiology toward more invasive Candida infections, particularly bloodstream infections, highlights the compounding effects of these risk factors [36]. Before the pandemic, Candida infections were predominantly caused by species like Candida albicans. However, the increased isolation of Candida auris during the pandemic period, replacing other less resistant species, underscores the pathogen's adaptability and the heightened risk profile of pandemic-era healthcare settings [37,38]. The first Candida auris case was reported in Qatar just before the pandemic in 2018 at a critical and unfortunate time [39]. Following being established in the healthcare facility, pandemic progression and associated critical care patients exposed to all highlighted risk factors contributed to this noticeable shift in epidemiology. To support that assumption, when a retrospective study of 36 cases of Candida auris fungemia was reviewed between 2018 and 2021, crossing the pandemic course, the majority occurred in patients who acquired long-term complications following primary COVID-19 infection [40].

Across the globe, the evolving COVID-19 pandemic changed the delivery of healthcare like never before, including epidemiology, clinical outcomes, and social and economic consequences. Examination of the effects of the pandemic interventions can prepare healthcare in all sectors for future events. The study showed a substantial reduction in bacterial and Candida infection following the first restriction, followed by a coordinated rise and fall for bacterial infections with subsequent restrictions but a persistent trend for Candida infections that shifted toward invasive disease. The trends correlated with the total number of hospitalized COVID-19 patients for Candida and the influx of international travelers for bacteria, suggesting the influence of the viral pandemic on other related infections and the influence of travel on the pandemic. While the study supplies a general overview of infection trends in the country, further research is needed to understand underlying trend dynamics better. For example, comparative studies to examine community as opposed to hospital infections or hospitalized versus non-hospitalized patients with or without COVID-19 disease will be of scientific value. Finally, exploring associated evolved microbiological and antimicrobial characteristics such as resistance will improve our understanding of the impact and sequelae of the pandemic.

The results herein provide a general overview of the infection trends in Qatar during the COVID-19 pandemic and illustrate some of the pandemic interventions' effects on bacterial and Candida infections. However, further research is needed to understand the underlying trend dynamics better.

5. Recommendations for Managing Bacterial and Fungal Infections in Future Pandemics

The findings of this study underscore the need for proactive strategies to manage bacterial and fungal infections during pandemics or global health crises. Strengthening infection prevention and control measures in healthcare settings is essential. This includes implementing stringent hygiene protocols, such as frequent surface disinfection, appropriate use of personal protective equipment (PPE), and regular hand hygiene practices. Additionally, routine environmental monitoring in critical areas, especially intensive care units (ICUs), is crucial for early detection and control of opportunistic pathogens like Candida auris.

Antimicrobial stewardship must be prioritized to mitigate the risks of resistance development during periods of increased antibiotic and antifungal usage. Healthcare systems should adopt tailored treatment guidelines focusing on targeted therapies for co-infections, avoiding the overuse of broad-spectrum agents. Simultaneously, protecting high-risk populations, including older adults and patients with chronic comorbidities, is vital. ICUs should be equipped with specialized teams and resources to manage invasive fungal and bacterial infections effectively. Targeted interventions for vulnerable groups can further minimize adverse outcomes.

Investments in diagnostic and surveillance capacities are equally critical. Rapid diagnostic tools should be widely available to enable the early identification of infections, including resistant strains. At the same time, integrated surveillance systems can track infection trends and pandemic metrics in real time. Such data can inform timely and effective interventions. Healthcare infrastructures must also be bolstered, with expanded ICU capacities and enhanced training programs for healthcare workers on infection prevention and management strategies during pandemics.

Finally, global collaboration is indispensable for addressing these challenges. Data sharing on infection trends and resistance patterns, along with the development of globally standardized protocols, can facilitate unified responses to bacterial and fungal infections during health emergencies. By adopting these measures, healthcare systems can mitigate the burden of secondary infections and improve outcomes during future pandemics.

6. Limitations of the Study

Perhaps the most important limitation of this study is that the study does not distinguish between community-acquired and hospital-acquired infections, which could affect the interpretation of the trends observed during different pandemic periods. In addition, changes in healthcare access and reporting standards during the pandemic may have affected the number of reported infection episodes, potentially leading to underreporting during restriction periods. Furthermore, the study's retrospective nature limits the ability to establish causal relationships. Lastly, the findings are based solely on data from Qatar, which may limit the generalizability of the results to other regions with different healthcare systems, population demographics, and pandemic responses. Finally, while this study provides an overview of infection trends during the pandemic, it does not explicitly analyze the potential impact of COVID-19 vaccination on bacterial and *Candida* infections. This represents an important area for further exploration, given the extensive global rollout of vaccines during this period.

Supplementary Materials: The following supporting information can be downloaded at https:// www.mdpi.com/article/10.3390/microbiolres15040166/s1, Table S1. Number of infections stratified by period, Table S2. Differences in the mean age between the COVID-19 periods, Figure S1. Map of Qatar with the facilities under Hamad Medical Corporation, Figure S2. Monthly COVID-19 Statistics, Figure S3. Monthly incoming international travelers, Figure S4. Google mobility indicators, Figure S5. OXFORD COVID-19 Government Response Tracker indices, Figure S6. Patient Age Distribution stratified by COVID-19 period, Figure S7. Number of infections stratified by type, COVID-19 period, and patient sex, Figure S8. Spearman Rank correlation plot for bacterial infections, Figure S9. Spearman Rank correlation plot for *Candida* infections.

Author Contributions: Conceptualization, N.O.E. and H.A.M.; data curation, G.W., E.I., and N.O.E.; writing—original draft preparation, H.A.M.; writing—review and editing, H.A., H.A.M., G.W., H.A.H., E.I., and N.O.E. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study and collaboration were approved by the Medical Research Centre (MRC) of Hamad Medical Corporation (HMC), which abides by local and international research standards (Protocol: MRC-02-21-949). The study also received approval from the Ethical Committee and Institution Review Board of the MRC after observing data management and sharing standards, including limited access to nominated primary investigators, data anonymity, and governance. All shared data had no traced patients' identification.

Informed Consent Statement: Not applicable.

Data Availability Statement: The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflicts of Interest: Authors Godwin Wilson, Hamad Abdel Hadi, Emad Ibrahim were employed by the company Hamad Medical Corporation. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

- 1. World Health Organization. Coronavirus Disease 2019 (COVID-19): Situation Report, 73. World Health Organization 2020. Available online: https://iris.who.int/handle/10665/331686 (accessed on 19 September 2024).
- 2. Santos, A.P.; Gonçalves, L.C.; Oliveira, A.C.C.; Queiroz, P.H.P.; Ito, C.R.M.; Santos, M.O.; Carneiro, L.C. Bacterial co-infection in patients with COVID-19 hospitalized (ICU and non-ICU): Review and meta-analysis. *Antibiotics* **2022**, *11*, 894. [CrossRef]
- 3. Kp, M.; Priyanka, M.; Ak, S.; Sb, S. Impact of COVID-19 pandemic on antimicrobial resistance and secondary microbial infections. *Int. J. Clin. Virol.* **2021**, *5*, 32–36. [CrossRef]
- Cultrera, R.; Barozzi, A.; Libanore, M.; Marangoni, E.; Pora, R.; Quarta, B.; Spadaro, S.; Ragazzi, R.; Marra, A.; Segala, D.; et al. Co-Infections in Critically Ill Patients with or without COVID-19: A Comparison of Clinical Microbial Culture Findings. *Int. J. Environ. Res. Public Health* 2021, 18, 4358. [CrossRef] [PubMed]
- Arastehfar, A.; Carvalho, A.; Hong Nguyen, M.; Hedayati, M.T.; Netea, M.G.; Perlin, D.S.; Hoenigl, M. COVID-19-Associated Candidiasis (CAC): An Underestimated Complication in the Absence of Immunological Predispositions? *J. Fungi* 2020, *6*, 211. [CrossRef] [PubMed]
- Sarkodie, S.A.; Owusu, P.A. Global assessment of environment, health and economic impact of the novel coronavirus (COVID-19). Environ. Dev. Sustain. 2021, 23, 5005–5015. [CrossRef]
- Kariyawasam, R.M.; Julien, D.A.; Jelinski, D.C.; Larose, S.L.; Rennert-May, E.; Conly, J.M.; Dingle, T.C.; Chen, J.Z.; Tyrrell, G.J.; Ronksley, P.E.; et al. Antimicrobial resistance (AMR) in COVID-19 patients: A systematic review and meta-analysis (November 2019–June 2021). Antimicrob. Resist. Infect Control 2022, 11, 45. [CrossRef]
- 8. Abu-Rub, L.I.; Abdelrahman, H.A.; Johar, A.R.A.; Alhussain, H.A.; Hadi, H.A.; Eltai, N.O. Antibiotics prescribing in intensive care settings during the covid-19 era: A systematic review. *Antibiotics* **2021**, *10*, 935. [CrossRef]
- 9. Al Mana, H.; Abdel Hadi, H.; Wilson, G.; Almaslamani, M.A.; Abu Jarir, S.H.; Ibrahim, E.; Eltai, N.O. Antimicrobial Resistance in Qatar: Prevalence and Trends before and Amidst the COVID-19 Pandemic. *Antibiotics* **2024**, *13*, 203. [CrossRef]
- Gerver, S.M.; Guy, R.; Wilson, K.; Thelwall, S.; Nsonwu, O.; Rooney, G.; Brown, C.S.; Muller-Pebody, B.; Hope, R.; Hall, V. National surveillance of bacterial and fungal coinfection and secondary infection in COVID-19 patients in England: Lessons from the first wave. *Clin. Microbiol. Infect.* 2021, 27, 1658–1665. [CrossRef]
- 11. Fattorini, L.; Creti, R.; Palma, C.; Pantosti, A. Bacterial coinfections in COVID-19: An underestimated adversary. *Ann. Ist. Super. Sanita* 2020, *56*, 359–364. [CrossRef]
- 12. Rangel, K.; Chagas, T.P.G.; De-Simone, S.G. *Acinetobacter baumannii* infections in times of the COVID-19 pandemic. *Pathogens* **2021**, 10, 1006. [CrossRef] [PubMed]
- 13. Boyer, C.B.; Rumpler, E.; Kissler, S.M.; Lipsitch, M. Infectious disease dynamics and restrictions on social gathering size. *Epidemics* **2022**, *40*, 100620. [CrossRef] [PubMed]
- Vicentini, C.; Russotto, A.; Bussolino, R.; Castagnotto, M.; Gastaldo, C.; Bresciano, L.; Bazzolo, S.; Gamba, D.; Corcione, S.; De Rosa, F.; et al. Impact of COVID-19 on healthcare-associated infections and antimicrobial use in Italy, 2022. *J. Hosp. Infect.* 2024, 149, 14–21. [CrossRef] [PubMed]
- Hale, T.; Angrist, N.; Goldszmidt, R.; Kira, B.; Petherick, A.; Phillips, T.; Webster, S.; Cameron-Blake, E.; Hallas, L.; Majumdar, S.; et al. A global panel database of pandemic policies (Oxford COVID-19 Government Response Tracker). *Nat. Hum. Behav.* 2021, *5*, 529–538. [CrossRef] [PubMed]
- 16. O'Toole, R.F. The interface between COVID-19 and bacterial healthcare-associated infections. *Clin. Microbiol. Infect.* **2021**, 27, 1772–1776. [CrossRef] [PubMed]
- Baker, M.A.; Sands, K.E.; Huang, S.S.; Kleinman, K.; Septimus, E.J.; Varma, N.; Blanchard, J.; Poland, R.; Coady, M.H.; Yokoe, D.S.; et al. The Impact of Coronavirus Disease 2019 (COVID-19) on Healthcare-Associated Infections. *Clin. Infect. Dis.* 2022, 74, 1748–1754. [CrossRef]
- Deiana, G.; Arghittu, A.; Gentili, D.; Dettori, M.; Palmieri, A.; Masia, M.D.; Azara, A.; Castiglia, P. Impact of the COVID-19 Pandemic on the Prevalence of HAIs and the Use of Antibiotics in an Italian University Hospital. *Healthcare* 2022, 10, 1597. [CrossRef]
- Gasch, O.; Badia-Cebada, L.; Carmezim, J.; Vaqué, M.; Pomar, V.; Moreno, E.; Marrón, A.; Jiménez-Martínez, E.; García-Quesada, M.J.; Garcia-Alarcón, X.; et al. Effects of the COVID-19 Pandemic on Incidence and Epidemiology of Catheter-Related Bacteremia, Spain. *Emerg. Infect. Dis.* 2022, *28*, 2181. [CrossRef]
- Parriott, A.M.; Kazerouni, N.N.; Epson, E.E. Association of the coronavirus disease 2019 (COVID-19) pandemic with the incidence of healthcare-associated infections in California hospitals. *Infect. Control Hosp. Epidemiol.* 2023, 44, 1429–1436. [CrossRef]
- Schwaber, M.J.; Lev, B.; Israeli, A.; Solter, E.; Smollan, G.; Rubinovitch, B.; Shalit, I.; Carmeli, Y.; the Israel Carbapenem-Resistant Enterobacteriaceae Working Group. Containment of a Country-wide Outbreak of Carbapenem-Resistant Klebsiella pneumoniae in Israeli Hospitals via a Nationally Implemented Intervention. *Clin. Infect. Dis.* 2011, *52*, 848–855. [CrossRef]

- Weiner-Lastinger, L.M.; Pattabiraman, V.; Konnor, R.Y.; Patel, P.R.; Wong, E.; Xu, S.Y.; Smith, B.; Edwards, J.R.; Dudeck, M.A. The impact of coronavirus disease 2019 (COVID-19) on healthcare-associated infections in 2020: A summary of data reported to the National Healthcare Safety Network. *Infect. Control Hosp. Epidemiol.* 2022, 43, 12–25. [CrossRef] [PubMed]
- Garcell, H.G.; Al-Ajmi, J.; Arias, A.V.; Abraham, J.C.; Felipe Garmendia, A.M.; Fernandez Hernandez, T.M. Impact of the COVID-19 pandemic on the incidence, etiology, and antimicrobial resistance of healthcare-associated infections in a critical care unit in Western Qatar. *Qatar Med. J.* 2023, 2023, 2. [CrossRef] [PubMed]
- 24. Qatar Population 2024. Available online: https://worldpopulationreview.com/countries/qatar (accessed on 19 September 2024).
- 25. Flores-Mireles, A.L.; Walker, J.N.; Caparon, M.; Hultgren, S.J. Urinary tract infections: Epidemiology, mechanisms of infection and treatment options. *Nat. Rev. Microbiol.* **2015**, *13*, 269–284. [CrossRef] [PubMed]
- Łagowski, D.; Gnat, S.; Nowakiewicz, A.; Barantsevich, N.; Barantsevich, E. Diagnosis and Treatment of Invasive Candidiasis. *Antibiotics* 2022, 11, 718. [CrossRef]
- Lortholary, O.; Renaudat, C.; Sitbon, K.; Madec, Y.; Denoeud-Ndam, L.; Wolff, M.; Fontanet, A.; Bretagne, S.; Dromer, F. Worrisome trends in incidence and mortality of candidemia in intensive care units (Paris area, 2002–2010). *Intensive Care Med.* 2014, 40, 1303–1312. [CrossRef]
- 28. Rodrigues, C.F.; Rodrigues, M.E.; Henriques, M. Candida sp. Infect. Patients Diabetes Mellitus. J. Clin. Med. 2019, 8, 76. [CrossRef]
- 29. Fuller, R.; Jacobs, S.E. Candida Infectious Endocarditis and Implantable Cardiac Device Infections. *Mycopathologia* **2023**, *188*, 893–905. [CrossRef]
- Thomas-Rüddel, D.O.; Schlattmann, P.; Pletz, M.; Kurzai, O.; Bloos, F. Risk Factors for Invasive Candida Infection in Critically III Patients: A Systematic Review and Meta-analysis. *Chest* 2022, *161*, 345–355. [CrossRef]
- Negm, E.M.; Mohamed, M.S.; Rabie, R.A.; Fouad, W.S.; Beniamen, A.; Mosallem, A.; Tawfik, A.E.; Salama, H.M. Fungal infection profile in critically ill COVID-19 patients: A prospective study at a large teaching hospital in a middle-income country. *BMC Infect. Dis.* 2023, 23, 246. [CrossRef]
- 32. AL-Suwaidi, Z. Tuberculosis in Qatar. Int. J. Mycobacteriol 2015, 4, 124. [CrossRef]
- Visca, D.; Ong, C.W.M.; Tiberi, S.; Centis, R.; D'Ambrosio, L.; Chen, B.; Mueller, J.; Mueller, P.; Duarte, R.; Dalcolmo, M.; et al. Tuberculosis and COVID-19 interaction: A review of biological, clinical and public health effects. *Pulmonology* 2021, 27, 151–165. [CrossRef] [PubMed]
- 34. McQuaid, C.F.; Vassall, A.; Cohen, T.; Fiekert, K.; White, R.G. The impact of COVID-19 on TB: A review of the data. *Int. J. Tuberc. Lung Dis.* **2021**, 25, 436–446. [CrossRef] [PubMed]
- 35. Forsberg, K.; Woodworth, K.; Walters, M.; Berkow, E.L.; Jackson, B.; Chiller, T.; Vallabhaneni, S. *Candida auris*: The recent emergence of a multidrug-resistant fungal pathogen. *Med. Mycol.* **2019**, *57*, 1–12. [CrossRef] [PubMed]
- 36. Schaefer, S.; Walits, E.; Thaler, K.; Patel, G. Impact of the COVID-19 Pandemic on *Candida auris* Infections: A Retrospective Analysis in an Academic Medical Center in New York City. *Open Forum Infect. Dis.* **2024**, *11*, ofae148. [CrossRef] [PubMed]
- Sears, D.; Schwartz, B.S. Candida auris: An emerging multidrug-resistant pathogen. Int. J. Infect. Dis. 2017, 63, 95–98. [CrossRef] [PubMed]
- Sanyaolu, A.; Okorie, C.; Marinkovic, A.; Abbasi, A.F.; Prakash, S.; Mangat, J.; Hosein, Z.; Haider, N.; Chan, J. Candida auris: An Overview of the Emerging Drug-Resistant Fungal Infection. Infect. Chemother. 2022, 54, 236. [CrossRef]
- Visan, F.; Al Ansari, N.; Al Wali, W.; Zakaria, A.; Al Hasanat, O.; Castro, J.; Hudaib, G.; Ummer, U.; Al Ajmi, J.; Asuncion, M.; et al. First *Candida auris* Outbreak Experience in a Tertiary-Care General Hospital in Qatar, 2019. *Infect. Control Hosp. Epidemiol.* 2020, 41, s235–s236. [CrossRef]
- 40. Koleri, J.; Petkar, H.M.; Hussam, H.A.; Muna, M.A. *Candida auris* Blood stream infection- a descriptive study from Qatar. *BMC Infect. Dis.* 2023, 23, 513. [CrossRef]

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