

Increased Severe Adverse Outcomes and Decreased Emergency Room Visits for Pyelonephritis: First Report of Collateral Damage during COVID-19 Pandemic in Urology

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Keywords

Outcome · Morbidity · Side effect · Coronavirus · SARS-CoV-2 · 2019-nCoV · Urinary infection · Pyelonephritis

Abstract

Purpose: The coronavirus disease 2019 (COVID-19) pandemic is disrupting urology health-care worldwide. Reduced emergency room visits resulting in adverse outcomes have most recently been reported in pediatrics and cardiology. We aimed to compare patients with emergency room visits for pyelonephritis in 2019 (pre-COVID-19 era) and within the first wave of pandemic in 2020 (COVID-19 era) with regard to the number of visits and severe adverse disease outcomes. **Methods:** We performed a retrospective multicentre study comparing characteristics and outcomes of patients with pyelonephritis, excluding patients with hydronephrosis due to stone disease, in 10 urology departments in Germany during a 1-month time frame in March and April in each 2019 and

2020. **Results:** The number of emergency room visits for pyelonephritis in the COVID-19 era was lower (44 patients, 37.0%) than in the pre-COVID-19 era (76 patients, 63.0%), reduction rate: 42.1% ($p = 0.003$). Severe adverse disease outcome was more frequent in the COVID-19 era (9/44 patients, 20.5%) than in the pre-COVID-19 era (5/76 patients, 6.6%, $p = 0.046$). In detail, 7 versus 3 patients needed monitoring (15.9 vs. 3.9%), 2 versus no patients needed intensive-care treatment (4.5 vs. 0%), 2 versus no patients needed drain placement (4.5 vs. 0%), 2 versus no patients had a nephrectomy (4.5 vs. 0%), and 2 versus 1 patient died (4.5 vs. 1.3%). **Conclusion:** This report of collateral damage during COVID-19 showed that emergency room visits were decreased, and severe adverse disease outcomes were increased for patients with pyelonephritis in the COVID-19 era. Health authorities should set up information campaign programs actively encouraging patients to utilize emergency room services in case of severe symptoms specifically during the actual second wave of pandemic.

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic is disrupting urology health-care worldwide [1]. Surgical and oncological care in urology is prioritized and carried out according to local infection load, and resources aiming to minimize harm to non-COVID-19-related health care in urology [2, 3]. To this end, the European Association of Urology has adapted their comprehensive guidelines to the COVID-19 era, with recommendations tiered for 4 levels of priority: low, intermediate, high, and emergency [4]. Similarly, the German urological community revealed recommendations for the treatment of emergency patients [5]. Concerning the management of urological emergency conditions, pathways for urosepsis, urinary retention, and gross hematuria have been proposed [6].

Recent correspondences outline that patients' emergency room visits are remarkably reduced during COVID-19 time compared to similar time periods in 2019 [7]. Patients' reticence for accessing emergency health care is caused by fear of acquiring SARS-CoV-2 in the hospital environment, uncertainty of the availability of health-care services, and social responsibility for using resources in times of scarcity [8]. Concerning urological emergencies, timely emergency room visit of patients is particularly relevant for urosepsis due to its high mortality rate of 18–28% [9]. We observed in our daily clinical urology practice that patients with pyelonephritis most recently presented both in fewer numbers and with increased disease severity. Pyelonephritis is a condition that can lead to urosepsis and usually develops slowly presenting with dysuria and/or increasing flank pain and/or fever. Due to these disease characteristics, pyelonephritis qualifies as suitable indicator disease for generating the hypothesis of fewer and delayed patient visits to the emergency room leading to increased severe adverse disease outcomes. To this date, few clinical data on emergency room visits of urology patients during COVID-19 [10] and no clinical data on adverse outcomes of non-COVID-19-related health care in urology exist. To investigate this recent observation, we performed a multi-centre retrospective study to compare patients with emergency room visits for pyelonephritis in 2019 (non-COVID-19 era) and 2020 (COVID-19 era) with regard to the number of visits and severe adverse disease outcomes.

Patients and Methods

Study Population

We performed a retrospective data analysis from 120 patients treated for pyelonephritis at 10 urology departments in Germany.

Patients were selected as having pyelonephritis according to the ICD code of the patient file and clinical symptoms. Patients with acute obstructive uropathy due to a ureteral stone were not included. Patients with antecedent DJ-insertion and readmission because of Pyelonephritis were defined as reflux-pyelonephritis patients.

The first group consisted of consecutive patients who searched urological help due to pyelonephritis between March 12 and April 12, 2019. This time span was defined as pre-COVID-19 era. The second group consisted of consecutive patients with a first consultation between March 12 and April 12, 2020, starting from the beginning of COVID-19 pandemic in Germany (COVID-19 era). All patients presented as emergency patients. The local Ethics Board approved this study.

Measures

Demographical information about age and gender, as well as date of consultation, date of discharge, date of first symptom presentation, previous antibiotic therapy, and prior DJ-insertion due to ureteral stones, was collected. Duration of hospitalization was computed. Additionally laboratory and clinical parameter were evaluated: C-reactive protein (CRP) (mg/L), leukocyte count (number/ μ L), and fever ($^{\circ}$ C). We focused on 5 outcome parameters: first need of monitoring/intermediate care unit, second need of intensive care, third need of drain placement for abscess, fourth nephrectomy, and finally death. The appearance of any of these outcomes was defined as adverse outcome of pyelonephritis.

Statistical Analyses

Descriptive statistic was used for patients' characteristics. Patients were stratified according to treatment era (COVID-19 vs. pre-COVID-19 era) (Table 1) and according to outcome (adverse vs. mild outcome) (Table 2).

Stacked columns were used to depict numbers of inpatients and outpatients (Fig. 1a) as well as proportion of patients with adverse versus mild outcome of pyelonephritis (Fig. 1b), stratified according to the treatment time, COVID-19 versus the pre-COVID-19 era. Boxplots were fitted to depict distributions of leucocytes and CRP counts, stratified according to COVID-19- versus pre-COVID-19-era patients (Fig. 2). All statistical analyses were performed using RStudio v0.98.953 (R Project for Statistical Computing, www.R-project.org).

Results

Overall, 120 patients out of 10 urological departments were included. The number of emergency room visits for pyelonephritis in the COVID-19 era was lower (44 patients, 37.0%) than in the pre-COVID-19 era (76 patients, 63.0%) ($p = 0.003$). Figure 1a depicts the resulting reduction rate of 42.1% of emergency room visits during COVID-19 era. Patients' emergency room visits per center were decreased during COVID-19 era (median 4 [IQR]) compared to pre-COVID-19 era (median 7 [IQR], $p = 0.0001$). Thirty-three (27.5%) patients were treated as outpatients (30.3 vs. 22.7%, $p = 0.5$) and 87 (72.5%) pa-

Table 1. Patients' characteristics

	Overall	Patients with pyelonephritis in the non-COVID era	Patients with pyelonephritis in the COVID era	<i>p</i> value
<i>N</i> (%)	120 (100)	76 (63.0)	44 (37.0)	
Age, median (IQR)	33 (21–51)	31 (21–51)	37 (21–50)	0.9
Gender, <i>n</i> (%)				
Female	98 (81.7)	65 (85.6)	33 (75)	0.4
Male	22 (18.3)	11 (14.5)	11 (25)	
Hospitalization, <i>n</i> (%)				
Inpatients	87 (72.5)	53 (69.7)	34 (77.3)	0.5
Outpatients	33 (27.5)	23 (30.3)	10 (22.7)	
Hospitalization, days, median (IQR)	4 (0–6)	4 (0–5.2)	4 (2–8.6)	0.5
Temperature at presentation, °C, median (IQR)	37.8 (37.0–38.7)	37.7 (37.0–38.5)	38.2 (37.0–38.8)	0.4
CRP at presentation, mg/L, median (IQR)	74 (23–190)	74 (23–194)	83 (25–172)	0.9
Leukocytes at presentation, /L, median (IQR)	12.9 (9.7–16)	11.8 (9.3–15.3)	13.7 (10.2–17.8)	0.0450
Antibiotics prior presentation, <i>n</i> (%)				
Yes	39 (32.5)	23 (30.3)	16 (36.4)	0.5
No	56 (46.7)	32 (42.1)	24 (54.5)	
NA	6 (5)	5 (6.6)	1 (2.3)	
Severe outcome of pyelonephritis, <i>n</i> (%)				
Yes	14 (11.7)	5 (6.6)	9 (20.5)	0.0469
No	106 (88.3)	71 (93.4)	35 (79.5)	
Monitoring/Intermediate care unit, <i>n</i> (%)				
Yes	10 (8.3)	3 (3.9)	7 (15.9)	0.0521
No	110 (91.7)	73 (96.1)	37 (84.1)	
Intensive-care unit, <i>n</i> (%)				
Yes	2 (1.7)	0 (0)	2 (4.5)	0.3
No	118 (98.3)	76 (100)	42 (95.5)	
CT intervention, <i>n</i> (%)				
Yes	2 (1.7)	0 (0)	2 (4.5)	0.1
No	117 (98.3)	75 (100)	42 (95.5)	
Nephrectomy, <i>n</i> (%)				
Yes	3 (2.5)	1 (1.3)	2 (4.5)	0.6
No	117 (97.5)	75 (98.7)	42 (95.5)	
Death, <i>n</i> (%)				
Yes	2 (1.7)	1 (1.3)	1 (2.3)	0.9
No	118 (98.3)	75 (98.7)	43 (97.7)	

CRP, C-reactive protein; COVID-19, coronavirus disease 2019.

tients were treated as inpatients (69.7 vs. 77.3%, $p = 0.5$) during the COVID versus pre-COVID-19 era.

Median age of all patients was 31 years (IQR 21–51). Patients in the pre-COVID-19 era were 31-years (21–51) old versus 37 (21–50) in the COVID-19 era, $p = 0.9$. Most patients were female (81.7 vs. 18.3%) with no statistically significant difference between COVID-19 and pre-COVID-19 era (85.6 vs. 75.0%, $p = 0.4$). Median duration of hospitalization was overall 4 days (0–6) and 4 (0–5.2) versus 4 (2–8.6), $p = 0.5$ days (COVID-19 vs. pre-COVID-19 era). The median temperature of patients was 37.8°C (37.0–38.7) without significant difference between CO-

VID-19 versus pre-COVID-19-era patients (37.7°C [37.0–38.5] versus 38.2°C [37.0–38.8], $p = 0.4$). Figure 2 shows that inflammatory blood values were higher in patients treated in the COVID-19 era compared to laboratory results in patients in the pre-COVID-19 era (leukocytes 13.7 vs. 11.8/ μ L, $p = 0.045$ and CRP: 83 vs. 74 mg/L, $p = 0.9$). None of the patients had a proven COVID-19 infection.

Overall 14 patients (11.7%) presented at least one of the above defined adverse outcome factors. Figure 1b shows that adverse outcome was more frequent in patients in the COVID-19 era (9/44 patients, 20.5%) than in the pre-COVID-19 era (5/76 patients, 6.6%, $p = 0.046$). In

Table 2. Patients' characteristics stratified according to severe and mild outcome of pyelonephritis

	Overall	Patients with mild outcome of pyelonephritis	Patients with severe outcome of pyelonephritis	<i>p</i> value
<i>N</i> (%)	120 (100)	106 (88.3)	14 (11.7)	
Age, years, median (IQR)	33 (21–51)	32 (21–51)	35 (21–50)	0.9
Gender, <i>n</i> (%)				
Female	98 (81.7)	87 (82.1)	11 (78.6)	1
Male	22 (18.3)	19 (17.9)	3 (21.4)	
Hospitalization, days, median (IQR)	4 (0–6)	4 (0–5)	7.5 (6–11)	<0.001
Temperature at presentation, °C, median (IQR)	37.8 (37.0–38.7)	37.7 (37.0–38.7)	38.2 (37.0–38.9)	0.6
CRP at presentation, mg/L, median (IQR)	74 (23–190)	60 (22–168)	237 (120–380)	0.001
Leukocytes at presentation, /L, median (IQR)	12.9 (9.7–16)	12.2 (9.7–15.3)	17 (13.8–23.3)	0.01
Antibiotics prior presentation, <i>n</i> (%)				
Yes	39 (32.5)	34 (32.1)	5 (35.7)	0.6
No	56 (46.7)	50 (47.2)	6 (42.9)	
na	6 (5)	6 (5.7)	0 (0)	
Prior DJ-Insertion/reflux pyelonephritis, <i>n</i> (%)				
Yes	11 (9.2)	11 (10.4)	0 (0)	0.09
No	73 (60.8)	62 (58.5)	11 (78.6)	
na	17 (14.2)	17 (16)	0 (0)	
Time of presentation, <i>n</i> (%)				
Non-COVID era	76 (63.3)	71 (67)	5 (35.7)	0.047
COVID era	44 (36.7)	35 (33)	9 (64.3)	

CRP, C-reactive protein; COVID-19, coronavirus disease 2019.

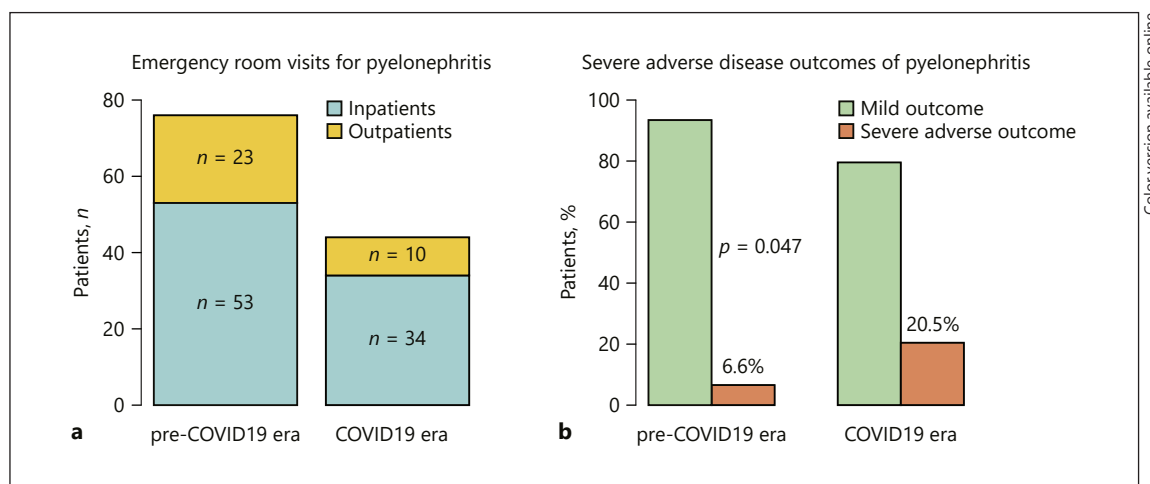


Fig. 1. a Depicts numbers of patients emergency room visits for pyelonephritis resulting in inpatient and outpatient treatments, stratified according to the treatment time, pre-COVID-19 era versus COVID-19 era. **b** Depicts proportions of patients with mild versus severe adverse outcomes of pyelonephritis, stratified according to the treatment time, pre-COVID-19 era versus COVID-19 era. COVID-19, coronavirus disease 2019.

detail, 7 versus 3 patients needed monitoring (15.9 vs. 3.9%), 2 versus no patients needed intensive-care treatment (4.5 vs. 0%), 2 versus no patients had a drain placement for abscess (4.5 vs. 0%), 2 versus no patients had a

nephrectomy (4.5 vs. 0%), and 2 versus 1 patient died (4.5 vs. 1.3%) (Table 1).

Patients with adverse outcome of pyelonephritis (14/120 = 11.7%) were not significantly older (32 vs. 35

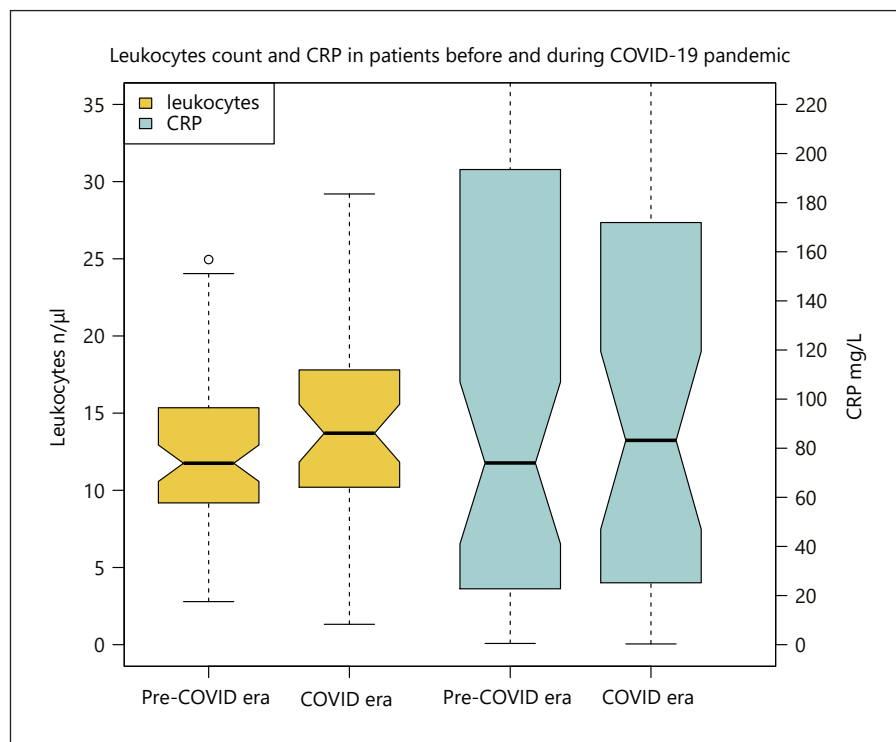


Fig. 2. Leukocytes count and CRP in patients with pyelonephritis stratified according to time of treatment (pre-COVID vs. COVID era). CRP, C-reactive protein. COVID-19, coronavirus disease 2019.

years; $p = 0.9$), had no higher temperature at presentation (37.7 vs. 38.2°C ; $p = 0.6$), and did not differ in terms of gender (female 82.1 vs. 78.6%) (Table 2). Proportion of patients with prior antibiotic therapy (32.1 vs. 35.7% ; $p = 0.6$) or prior DJ-Insertion (10.4 vs. 0%) was not statistically different between patients with mild versus adverse outcome of pyelonephritis. In contrast, patients with adverse outcome of pyelonephritis had a longer hospital stay (7.5 vs. 4 days; $p < 0.001$), a higher CRP at presentation (237 vs. 60 mg/L; $p = 0.001$) and a higher leukocyte count (17 vs. 12.3 μL ; $p = 0.01$).

Discussion

In this multicentre retrospective study, we found a significant reduction of 42% of emergency room visits of patients for pyelonephritis during the COVID-19 era compared to pre-COVID-19 era. Vice versa, adverse outcomes including monitoring, intensive-care treatment, drain placement for abscess, nephrectomy, and death were more frequent in the COVID-19 era (combined adverse outcome rate: 20.5%) compared to the pre-COVID-19 era (6.6%, $p = 0.045$).

To our best knowledge, this study is one of the first reports of clinical data on adverse disease outcomes in

urology during COVID-19 pandemic. Currently, remarkable feats are undertaken to deliver optimal urology care during COVID-19 [11]. However, until a vaccine is found [12], the burden of surgical and oncological urology care that we are facing ahead is enormous and adverse outcomes due to delay in diagnosis and treatment are most likely to occur [13, 14]. While prioritization of urology care is directly in our hands, other collateral effects of the pandemic like delayed emergency room visits are not.

Our observation of fewer emergency room visits during COVID-19 for pyelonephritis is generally in line with data from Italy, Portugal, and China that showed a decrease ranging from 38 to 88% [7, 8, 15–18]. In Austria, a relative reduction of 39.4% in admissions for acute coronary syndrome has been reported during COVID-19 era which was theoretically estimated to an increase of 110 deaths [19].

Although we did not directly prove delayed access to emergency care in our cohort of patients, we assume a link between decreased emergency room visits and increased severe adverse outcomes during the COVID-19 era. Since pyelonephritis is a disease that can develop and deteriorate slowly over a period of days, we assume that patients in the COVID-19 era presented to the emergency room with significant delay, which might have led to

increased adverse outcomes. In fact, leukocyte counts were significantly higher in our study patients in the COVID-19 era than in the non-COVID-19 era. The symptom of fever in patients with pyelonephritis is also a cardinal symptom of SARS-CoV-2 infection. Indeed, patients with fever and respiratory symptoms were in Germany advised as a first action to stay at home and contact the local health authority by phone for further instructions and triage. On the other hand, we do not assume that care delivery in the German urology departments has negatively impacted patient outcomes since the health-care system in Germany has not experienced capacity pressure thus far.

Consequently, actively encouraging patients to visit the emergency room in case of a real emergency during COVID-19 era is the call-to-action derived from our study, especially in times where infection rate is rising again. Patients' barrier-free access to early telemedicine video-consultation might be another option to optimize triage and ensure timely emergency room visits [20].

Our study has important strengths. Most importantly, we report important clinical data of adverse disease outcomes in urology during COVID-19 pandemic. In this regard, timely adverse outcome reporting of collateral damages during the pandemic is of utmost importance since adjustments in clinical care can be made in time to reduce collateral damage and maintain optimal patient outcomes. Moreover, the multicentre study design reflects a true representation of patients with pyelonephritis in Germany, a country severely affected by COVID-19. Finally, clinically relevant severe adverse outcomes were measured as outcome parameter and were more frequent in the COVID-19 era. Limitations include those inherent to the retrospective study design. Furthermore, patient flow and access to emergency room might differ between health-care systems.

Conclusion

Emergency room visits were decreased, and severe adverse disease outcomes were increased for patients with pyelonephritis in the COVID-19 era. Health authorities

should set up information campaign programs actively encouraging patients to utilize emergency room services in case of severe symptoms.

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Statement of Ethics

Ethical approval was waived by the local Ethics Committee of University Mainz in view of the retrospective nature of the study and all the procedures being performed were part of the routine care. Therefore, we did not get an approval reference number.

Conflict of Interest Statement

The authors have no potential conflicts of interest.

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The authors did not receive any funding.

Author Contributions

H. Borgmann: project development, data collection or management, data analysis, and manuscript writing/editing. J.P. Struck: data collection or management and manuscript writing/editing. A. Matigk: data collection or management and manuscript writing/editing. M. Wenzel: data collection or management and manuscript writing/editing. A. Pilatz: data collection or management and manuscript writing/editing. J. Kranz: data collection or management and manuscript writing/editing. R. Weiten: data collection or management and manuscript writing/editing. N. von Landenberg: data collection or management and manuscript writing/editing. P.J. Spachmann: data collection or management and manuscript writing/editing. C. Aksoy: data collection or management and manuscript writing/editing. A. Haferkamp: data collection or management and manuscript writing/editing. K. Boehm: project development, data collection or management, data analysis, and manuscript writing/editing. All authors read and approved the final version of the manuscript.

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