Infection and Drug Resistance

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ORIGINAL RESEARCH

COVID-19 and Severe Acute Respiratory Infections: Monitoring Trends in 421 German Hospitals During the First Four Pandemic Waves

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Introduction: Reliable surveillance systems to monitor trends of COVID-19 case numbers and the associated healthcare burden play a central role in efficient pandemic management. In Germany, the federal government agency Robert-Koch-Institute uses an ICD-code-based inpatient surveillance system, ICOSARI, to assess temporal trends of severe acute respiratory infection (SARI) and COVID-19 hospitalization numbers. In a similar approach, we present a large-scale analysis covering four pandemic waves derived from the Initiative of Quality Medicine (IQM), a German-wide network of acute care hospitals.

Methods: Routine data from 421 hospitals for the years 2019–2021 with a "pre-pandemic" period (01–01-2019 to 03–03-2020) and a "pandemic" period (04–03-2020 to 31–12-2021) was analysed. SARI cases were defined by ICD-codes J09-J22 and COVID-19 by ICD-codes U07.1 and U07.2. The following outcomes were analysed: intensive care treatment, mechanical ventilation, in-hospital mortality.

Results: Over 1.1 million cases of SARI and COVID-19 were identified. Patients with COVID-19 and additional codes for SARI were at higher risk for adverse outcomes when compared to non-COVID SARI and COVID-19 without any coding for SARI. During the pandemic period, non-COVID SARI cases were associated with 28%, 23% and 27% higher odds for intensive care treatment, mechanical ventilation and in-hospital mortality, respectively, compared to pre-pandemic SARI.

Conclusion: The nationwide IQM network could serve as an excellent data source to enhance COVID-19 and SARI surveillance in view of the ongoing pandemic. Future developments of COVID-19/SARI case numbers and associated outcomes should be closely monitored to identify specific trends, especially considering novel virus variants.

Keywords: initiative of quality medicine, Germany, COVID-19, SARI, inpatient, hospital network

Introduction

Close monitoring of temporal trends with respect to, eg, case numbers, intensive care (ICU) capacities and mortality in the inpatient sector represents an integral part of pandemic control, as the ongoing COVID-19 pandemic still poses a major burden for health-care systems worldwide. The importance of leveraging existing national surveillance systems for respiratory diseases has been emphasized by the World Health Organization (WHO) and European Centre for Disease Prevention and Control (ECDC)[1–3] as it is crucial to additionally monitor trends of other circulating pathogens (eg, influenza). With regard to the inpatient sector, the ECDC recommends surveillance for severe acute respiratory infections (SARI) to meet this need.[3] A SARI surveillance system (ICOSARI) based on ICD-10-codes (International Statistical Classification of Diseases and Related Health Problems, Version 10) using routine data of the Helios hospital network

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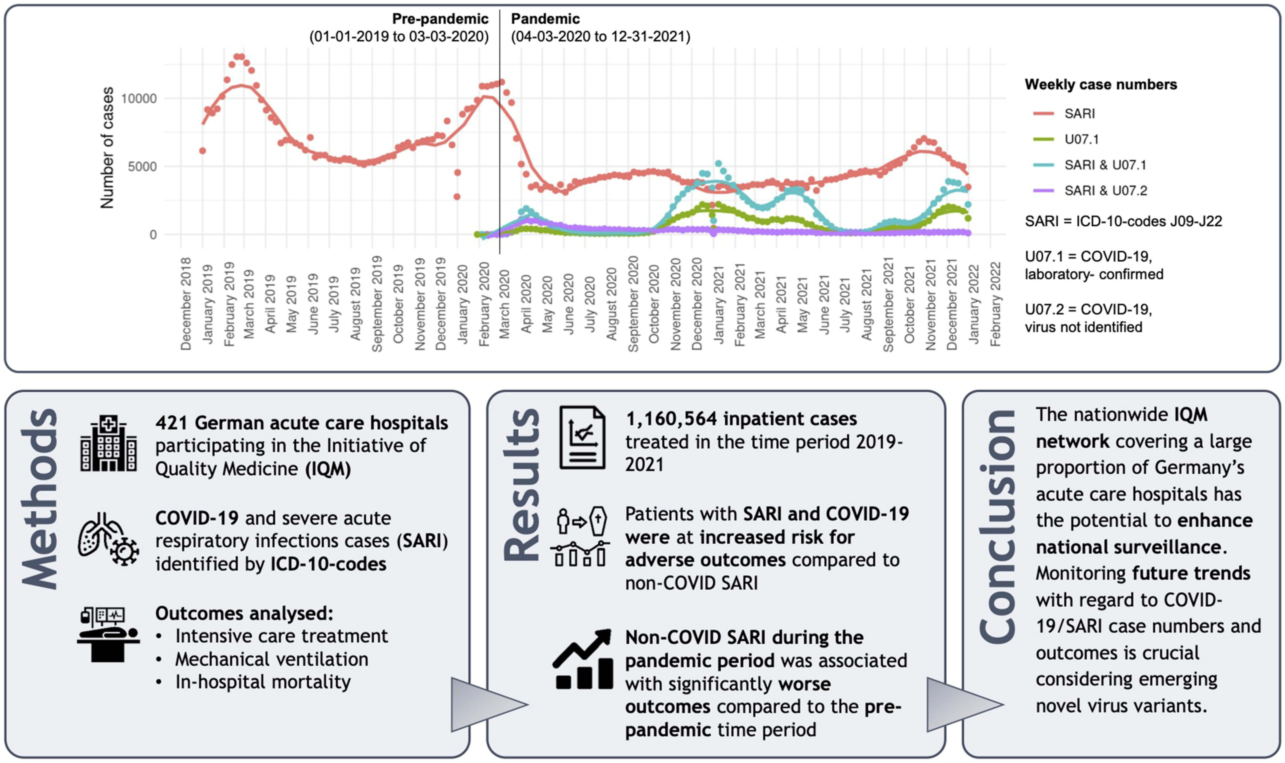
Graphical Abstract



was established in Germany in 2017.[4] ICOSARI data of 71 German hospitals is continuously analysed and reported by the federal government agency Robert-Koch-Institute (RKI) as part of the national pandemic monitoring program.[5]

Within the German health-care system, inpatient care is provided by around 1900 hospitals run by the state, local authorities, non-profit organisations and private providers.[6] Quality assurance is regulated by law and overseen by the Federal Joint Committee (G-BA), which in turn is supported by the independent Institute for Quality and Efficiency in Health Care (IQWiG) and the independent Institute for Quality and Transparency in the Health Care System (IQTIG).[6] In addition to statutory quality assurance, more than 500 hospitals in Germany and Switzerland are voluntarily organised in the "Initiative of Quality Medicine" (*IQM, Berlin, Germany*).[7] Utilizing a large-scale administrative dataset derived from the IQM, we conducted an extended analysis of SARI and COVID-19 cases covering four pandemic waves to report on patient characteristics and respective outcomes and compare pre-pandemic with pandemic time periods.

Methods

Within the IQM, member hospitals provide anonymized routine data semi-annually to a central data evaluation centre (*3M Health Information Systems, Berlin, Germany*) where quality indicators are calculated and made publicly available.[8,9] For this analysis, administrative data of 421 German hospitals between 2019 and 2021 (full inpatient treatment only) was retrospectively analysed. The periods 01–01-2019 to 03–03-2020 and 04–03-2020 to 31–12-2021 were defined as "pre-pandemic" and "pandemic", respectively. To account for potential differences with regard to the dominating SARS-CoV-2 variant, we defined time periods for Wildtype, Alpha and Delta dominance (according to data by RKI)[10] and performed subgroup analyses (Table S1a–c).

Present COVID-19 was identified by ICD-10-codes U07.1 (PCR-confirmed SARS-CoV-2 infection) and U07.2 (suspected COVID-19, virus not identified) as main or secondary diagnosis. Additionally, we identified SARI cases by ICD-10-codes J09-J22 in accordance with common methods of SARI surveillance in Germany.[4] Four groups were defined consecutively:

SARI without any concomitant coding for COVID-19 (hereafter referred to as "SARI"), proven COVID-19 (U07.1) and SARI with concomitant COVID-19 codes (SARI&U07.1; SARI&U07.2). The following outcomes and treatments were analysed utilizing the Operation and Procedure Classification System (OPS): ICU treatment (OPS-codes 8–980/d/f, 8–70x, 8–711/2/3/4/8, 8–721.1/2/3, 8–97a/b), mechanical ventilation (duration of ventilation >0 h), in-hospital mortality.

For the description of patient characteristics, we employed logistic regression for binary variables and linear regression for numeric variables. For the comparison of outcomes in the different cohorts, we used logistic regression with a logit link function.

The analysis was carried out according to the principles outlined in the Declaration of Helsinki. Given the retrospective evaluation of anonymized data, patient informed consent has not been obtained and ethics committee approval was determined not to be required in accordance with German law [Professional Code for Physicians (Saxony) §15]. Within the IQM network, data security is ensured by local data protection authorities of all member hospitals.

Results

A total of 1,160,564 cases fulfilling the above-mentioned definition of SARI or COVID-19 (or both) in the period 2019–2021 were included in the analysis. Temporal trends and weekly case numbers are depicted in the graphical abstract. The four COVID-19 waves present themselves in peaks of U07.1 and SARI&U07.1 cases. Case numbers of SARI&U07.1 were higher in comparison to U07.1 suggesting a considerable proportion of severe disease courses among hospitalized patients. A considerable number of SARI&U07.2 cases was only present during the first wave. There was no peak of SARI cases in the winter period 2020/2021, but a small peak in fall/winter of 2021 where case numbers remained significantly lower as compared to the winter periods of 2018/2019 and 2019/2020 due to enhanced hygiene measures adopted by the German federal government during the fourth wave.[11]

Case numbers of SARI decreased markedly in 2020 and 2021 (Table 1). Mean age was significantly lower in the U07.1 group and significantly higher in SARI&U07.1 and SARI&U07.2 groups compared with SARI. Male gender was more frequent only in the U07.1 group. Of note, COVID-19 patients hospitalized during the Wildtype period were older in comparison to Alpha and Delta (Table S1a-c). Compared to SARI, U07.1 cases had lower odds for all outcomes of interest, whereas significantly higher odds were observed for SARI&U07.1, but not SARI&U07.2 (Table 1). This applied

Table 1 Case Numbers, Patient Characteristics and Outcomes in SARI and COVID-19 Patients

	SARI	U07.1	P-value	SARI & U07.1	P-value	SARI & U07.2	P-value
Case numbers							
2019	391,890	0	n/a	0	n/a	0	n/a
2020	283,566	21,704	n/a	47,621	n/a	20,657	n/a
2021	234,414	48,613	n/a	103,085	n/a	9014	n/a
Total	**909,870**	**70,317**	**n/a**	**150,706**	**n/a**	**29,671**	**n/a**
Age							
Mean (SD)	64.5 ±26.8	59.9 ±24.9	<0.01	67.5 ±17.1	<0.01	69.3 ±20.9	<0.01
≤59 years	27.0% (245,329)	41.7% (29,319)	<0.01	30.5% (45,974)	<0.01	22.6% (6701)	<0.01
60–69 years	15.1% (136,968)	13.0% (9155)	<0.01	18.2% (27,481)	<0.01	15.9% (4717)	<0.01
70–79 years	22.5% (205,068)	16.9% (11,853)	<0.01	21.1% (31,818)	<0.01	22.5% (6666)	0.77
≥80 years	35.4% (322,505)	28.4% (19,990)	<0.01	30.1% (45,433)	<0.01	39.1% (11,587)	<0.01

(*Continued*)

Table 1 (Continued).

	SARI	U07.1	P-value	SARI & U07.1	P-value	SARI & U07.2	P-value
Sex*							
Male	41.9% (381,571)	55.7% (39,186)		42.8% (64,474)		40.7% (12,079)	
Female	58.1% (528,225)	44.3% (31,128)	<0.01	57.2% (86,228)	<0.01	59.3% (17,589)	<0.01
	SARI	**U07.1**	**Odds ratio (95% CI); P-value**	**SARI & U07.1**	**Odds ratio (95% CI); P-value**	**SARI & U07.2**	**Odds ratio (95% CI); P-value**
Intensive care treatment							
	24.5% (223,003)	6.3% (4444)	0.23 (0.22–0.24); <0.001	30.1% (45,363)	1.37 (1.35–1.38); <0.001	23.1% (6858)	0.87 (0.84–0.89); <0.001
Mechanical ventilation							
	17.0% (154,564)	2.3% (1621)	0.13 (0.12–0.13); <0.001	22.6% (34,131)	1.47 (1.45–1.49); <0.001	15.4% (4584)	0.85 (0.82–0.87); <0.001
In-hospital mortality							
	13.6% (123,490)	6.0% (4207)	0.47 (0.46–0.49); <0.001	22.6% (34,085)	1.96 (1.93–1.99); <0.001	14.9% (4413)	1.03 (0.99–1.06); 0.119

Notes: Patient characteristics, treatments and outcomes are compared between SARI and the other three cohorts (U07.1; SARI & U07.1; SARI & U07.2). For comparison of patient characteristics, we employed logistic regression for binary variables and linear regression for numeric variables. Comparison of treatments and outcomes (intensive care, mechanical ventilation, in-hospital mortality) was performed via logistic regression, adjusted for age, sex and date to account for yearly seasonal trends. *There were few cases with missing information for sex or with indication of sex other than male/female. Exact numbers are: 74 (SARI); 3 (U07.1); 4 (SARI & U07.1); 3 (SARI & U07.2). U07.1: COVID-19, virus identified. U07.2: suspected COVID-19, virus not identified.
Abbreviation: SARI, Severe acute respiratory infections.

to the total cohort as well as the three sub-cohorts considering the dominating virus variant. In-hospital mortality rates for U07.1/SARI&U07.1 were highest during the Wildtype period, followed by Delta (Table S1a-c).

Comparing SARI cases without any additional coding for COVID-19 in the pre-pandemic and pandemic periods, we found a slightly different age and gender distribution. Interestingly, SARI (excluding COVID-19) during the pandemic period was associated with significantly worse outcomes compared to pre-pandemic times (Table S2).

Discussion

In this analysis of claims data derived from 421 German acute care hospitals, which represents to the best of our knowledge the largest German dataset of COVID-19 and SARI inpatients yet analysed, we highlight the following main findings: COVID-19 patients with concomitant SARI compared to SARI not caused by SARS-CoV-2 were at a markedly increased risk for adverse outcomes independent of the dominating virus variant. Comparing the pandemic to the pre-pandemic period, non-COVID SARI was associated with significantly worse outcomes during the pandemic, for example with a 27% higher in-hospital mortality risk. Mean age was higher in the "pandemic" group, albeit the observed difference was only small with questionable clinical relevance (63.9 vs 65.2 years; $P < 0.01$). Patients' restraint to enter the healthcare system during the pandemic which consecutively would lead to delayed treatment and increased case severity or, on the other hand, limited treatment, and ICU capacities due to the high burden of COVID-19 could have possibly influenced outcomes of non-COVID SARI patients. This contrasts observations made for the first year of the pandemic where a reduced in-hospital mortality risk was reported for patients with respiratory diseases after excluding SARS-CoV-2 cases.[12] It may also be assumed, that SARI patients indeed suffered a SARS-CoV-2 infection in their domestic environment but were hospitalized at a time when the virus could no longer be detected by PCR. In this context, a possible selection bias must be mentioned as a limitation, as unequal time periods with clearly different monthly case numbers were analysed (Table S2). The reduced overall SARI case numbers during the pandemic period might have led to a larger relative share of more severe cases which required hospitalization. However, this trend requires close future monitoring.

As mentioned before, real-world comprehensive SARI surveillance is of uttermost importance in the light of the ongoing pandemic and is established in several European countries including Germany.[13–16] Routine data fully based on ICD-codes should be considered a reliable data source to serve this purpose as has also been stated by authors of a previous study focusing on emergency department attendees in Germany.[17] Monitoring timely trends of COVID-19 and SARI cases can also facilitate the assessment of SARS-CoV-2-related disease severity, which was just recently proposed by members of this author group.[18] This is especially important with regard to possible future virus variants.

As a limitation it must be noted that the IQM administrative dataset contains no information with regard to patients' vaccination status and this influencing variable could therefore not be considered separately in this analysis.

Conclusion

Quickly available standardized routine data of the IQM network comprising COVID-19, SARI and ICU cases provide an excellent basis for monitoring trends and enhance nationwide surveillance and pandemic management. This data source comprising a large amount of acute care hospitals has the potential to supplement the existing ICOSARI network in Germany due to the extended coverage.

Abbreviations

CI, Confidence interval; COVID-19, Coronavirus disease 2019; ECDC, European Centre for Disease Prevention and Control; ICD-10, International Statistical Classification of Diseases and Related Health Problems Version 10; ICOSARI, ICD-code-based SARI surveillance system in Germany; ICU, Intensive care unit; IQM, Initiative of Quality Medicine; OPS, Operation and Procedure Classification System; OR, Odds Ratio; PCR, Polymerase chain reaction; RKI, Robert-Koch-Institute; SARI, Severe acute respiratory infection(s); SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

Data Sharing Statement

The data that support the findings of this study are not publicly available as they contain information that could compromise the privacy of research participants but are available from the IQM network (info@initiative-qualitaetsmedizin.de) upon reasonable request.

Ethics Approval and Consent to Participate

The analysis was carried out according to the principles outlined in the Declaration of Helsinki. Given the retrospective evaluation of anonymized data, patient informed consent has not been obtained and ethics committee approval was determined not to be required in accordance with German law [Professional Code for Physicians (Saxony) §15].

Consent for Publication

All authors gave final approval for publication.

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Author Contributions

JL is the first author of this manuscript. RK is senior author of this manuscript and the corresponding author. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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We declare no conflicts of interest associated with this publication.

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