Case Report

COVID-19 situation in Baden-Württemberg, Germany: Preliminary case series study during the first wave

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Abstract

The present case series study presents the preliminary data of 347 of severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) positively tested patients in the Mittelbaden hospital, Baden-Baden Bühl, Germany, during the period from March to June 2020. Among the 347 patients, 55% were males. The mean age-wise was 52.5±20.2 years in the overall cohort and 78.9±11.1 years in fatal outcome cases. A total of 120/347 patients (34.6%) required hospitalization, but only 36/347 (10.37%) cases required intensive care. The overall fatality rate was 6.6% (23/347), of which 12 patients were from the intensive care unit. The most frequent clinical symptoms observed were cough (62.5%), hyperthermia (47.8%), rhinorrhea (25.1%), sore throat (23.1%), dyspnea (22.8%), and headache (19.3%). Laboratory data analysis showed no specific findings, but severe laboratory disturbances could predict critical illness. A higher risk of severe illness or lethal outcome in elderly patients with several comorbidities was the most frequent. The fight against COVID-19 infection in Germany seems to be more successful during the first wave than in other countries. The improvement of the healthcare system against infectious outbreaks depends directly on the analysis of regional factors.

Keywords: Coronavirus, SARS-CoV-2, COVID-19, symptoms, death rate, laboratory findings

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Introduction

An outbreak of unknown etiology pneumonia emerged in China in December 2019, and the number of initial cases was linked to a Huanan Seafood Market in Wuhan city **(De Salazar et al., 2020, Hsu et al., 2020, WHO, 2020c)**. Thereafter, on 11 February 2020, the World Health Organization (WHO) and the International Committee on Taxonomy of viruses announced the official name of the new disease as coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) **(WHO, 2020b)**.

Following the virus outbreaks and spread worldwide, the WHO classified the epidemic situation as pandemic on 11 March 2020. According to the WHO Situation Report of 28 June 2020, the number of positively confirmed cases of COVID-19 infection was 9.843.073 worldwide and the number of COVID-19 associated death cases was 495.760 in 215 countries and territories **(WHO, 2020a)**. While the pathogenesis and etiology of SARS-CoV-2 infection are still not completely known, it has been observed that it is genetically similar to SARS-CoV and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) viruses **(Leung, 2020)**.

The SARS-CoV-2, taxonomically, is the part of the SARS-related coronaviruses that belongs to the subgenus *Sarbecovirus*, a subdivision of the genus *Betacoronavirus*, an enveloped positive-strand RNA virus isolated from the bat. Other *Betacoronaviruses* that caused epidemics over the last two decades in Asia are SARS-CoV in 2002–2003 in China and MERS-CoV in 2012–2013 in Saudi Arabia **(Rodriguez-Morales et al., 2020)**. Close contacts are considered the most common way of transmitting SARS-CoV-2 from human to human. The viral RNA was also detected in stool samples, gastrointestinal tract tissues, saliva, urine, tears and conjunctival secretions **(Wang et al., 2020)**.

Four common human coronaviruses (HKU1, NL63, OC43 and E229) were known to cause 10–20% of respiratory infections worldwide and are present in all continents. Mortality is poorly assessed, but studies have shown as many asymptomatic carriers as symptomatic patients, which poses a significant challenge to infectious control **(Roussel et al., 2020; Yuen et al., 2020).** The basic reproductive number (R0) of SARS-CoV-2 has been estimated in different clinical research data from 2,68 to 3,77, resulting in an epidemic doubling time of about 6 days **(Li et al., 2020; Wang et al., 2020; Yuen et al., 2020).** The COVID-19 produces an acute viral infection in humans with a median incubation period of three days **(Wang et al., 2020)**.

According to literature data, clinical and laboratory manifestations of COVID-19 are non-specific. They range from mild to moderate infection course, with more systematic symptoms and severe radiological abnormalities seen in older patients **(Yuen et al., 2020).** The variation of case-fatality rate (from less than 1% to more than 30%) and clinical symptoms distribution in existing publications **(Lai et al., 2020; Li et al., 2020; Onder et al., 2020; Roussel et al., 2020)** requires thorough data analysis with knowledge of differences and particularities of national healthcare systems in different regions and countries.

This study aimed at describing the cohort of COVID-19 positively tested patients during the first wave in the hospital of Mittelbaden, at Baden Baden, Germany, in the period of the infectious outbreak during three months between March and June 2020 to assess the situation during the first wave of SARS-CoV-2 pandemic.

Preliminary case series study during the first wave

The current study is a case series study with the retrospective cohort of patients who tested positive for SARS-CoV-2 in Mittelbaden (KMB) hospital at Baden-Baden, in the epidemics outbreak period from March to June 2020. The Baden-Baden city is located in Southwest Germany in the federal state of Baden-Württemberg, close to the France and Switzerland border with 55123 population.

Regional medical healthcare service is located on the KMB clinic chain and includes ten hospitals in Baden-Baden, Rastatt, and Bühl city areas. After the WHO announcement of the COVID-19 pandemic situation, the COVID-19 out-patient admission in-patient department and intensive care unit (ICU) were created to help manage COVID-19 positively tested patients in the clinic. From 1 March until the end of June 2020, around 6000 tests for SARS-CoV-2 were performed in KMB.

The samples from nasopharyngeal and oropharyngeal swabs were investigated using real-time PCR. All COVID-19 positively tested patients (n=347) were included in the study cohort. For each participant, data was collected directly from the medical records of demographic data, medical interview, clinical symptoms, laboratory findings, X-ray and computer tomography results, and treatment outcomes. Statistical analysis was performed using StatSoft Statistica 8.0 (USA). We analyzed the routinely collected data with no additional harm or intervention to patients during this study. The database was anonymized, with strict access to the data only for researchers of this particular study. No ethical approval was required. However, the consent of the patients was sought.

A total of 347 SARS-CoV-2 positively tested patients were included in the current study, out of which 55% (191/347) were males. The mean age was 52.5±20.2 overall. However, it was 67.8±17.8 and 67±13.8 years in the hospitalized and ICU patients, respectively. The mean age among the fatal outcome cases was 78.9±11.1 years. The vast majority of patients, 227 (65.4%), required no treatment, but the home quarantine was recommended for two weeks. A total of 120 cases (34.6%) were hospitalized based on clinical and laboratory parameters. However, 36 (10.4%) of all positively tested cases representing 30% of in-patients, required intensive care.

The mean duration of hospitalization was 12.5±11 days (range 1-62). We found that 11.4% of cases from the study cohort required additional hospital visits because of symptoms deterioration or the appearance of new symptoms. By exploring anamnesis data, we found that 209 cases (60%) had known contact with COVID-19 positive person or visit of an epidemiologically high-risk region. On the other hand, 23 patients (6.6%) did not report any contacts with potentially COVID-19 positive person or a recent trip. The mean duration of the potential contact to the appearance COVID-19 symptoms was 7.8±4.8 (range 1-21) days. In our study cohort, the overall fatality rate was 6.6% (23 cases), all were from in-patients. The fatality rate of the ICU-patients was 12/36 (33.3%). A total of 6 patients from ICU were transported to other clinics due to ICU overload. **Figure 1** shows the frequencies of hospitalization, ICU admissions, and the patient's death rate recruited in the study.

Patients showed a non-specific clinical picture of COVID-19 (**Table 1**) correlated with previous literature data **(Li et al., 2020, Rodriguez-Morales et al., 2020, Wang et al., 2020)**. The most frequently reported symptom was cough in 127 patients (62.5%), predominantly non-productive (91.7% of cases). Hyperthermia was reported in 166 (47.8%) patients, while rhinorrhea and sore throat were found in 87 (25.1%) and 80 (23.1%) patients, respectively. A total of 67 (19.3%) patients presented with headaches, and 79 (22.8%) patients had breathing problems. The breathing disturbances were classified as light breathing disturbance in the form of initial respiratory problems in 55.7% (n=44/79) and severe dyspnea in 44.3% (n=35/79) of patients. In the patients who required intensive care, the

initial dyspnea number was high (44.4%, n=16). Interestingly, in the first part of the study period, we observed a higher number of in-patient admissions because of respiratory disturbances; however, there was a rise in dehydration-associated symptoms (syncopal episodes, disorientation) during the second part of the study (i.e., mid-march). The detailed list of clinical symptoms in the study cohort is shown in **Table 1**.

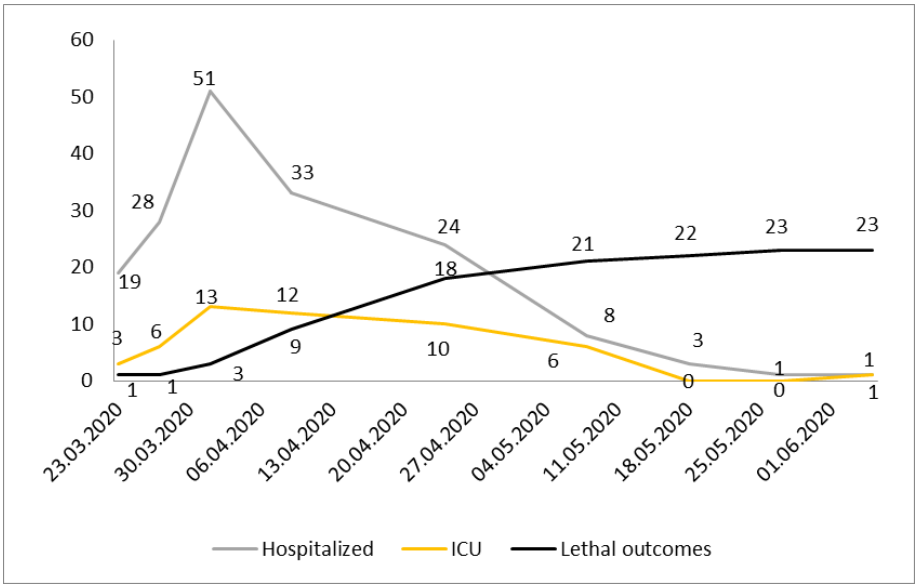

Figure 1. Diagram of general and ICU hospitalization and mortality rate in Mittelbaden hospital at Baden-Baden, Germany, during March and June 2020

Table 1. Clinical symptoms of COVID-19 patients in Mittelbaden hospital at Baden-Baden, Germany between March and June 2020.

Clinical symptom	No. (347)	%
Cough	217	62.5
Body temperature increase	166	47.8
Rhinorrhea	87	25.1
Sore throat	80	23.1
Breathing disturbances	79	22.8
Headache	67	19.3
Muscle/Joints pain	62	17.9
General weakness	46	13.3
Nausea/vomiting	43	12.4
Dehydration and neurological symptoms (syncope, disorientation)	35	10.1
Diarrhea	33	9.5
Loss of appetite	19	5.5
Chills	17	4.9
Abdominal pain	14	4
Taste/smell disturbance	11	3.2
Night sweats	5	1.4
Back pain	2	0.6
Dysuria/Hematuria	3	0.8
Fear of death	2	0.6
Hoarseness	1	0.3
Just "Common cold"	13	3.7
No symptoms	16	4.6

Analysis of the clinical background could give us an understanding of COVID-19 risk stratification. In the current study, cohort comorbidities were found in 137 patients (39.5%), predominantly in the in-patients group. One disease comorbid was reported in 45 patients (32.9% of comorbidities), two comorbidities were found in 34 cases (24.8%), three or more comorbidities were seen in 58 patients (42.3%). In ICU, 17 patients (47.2%) had three and more underlying diseases (Table 2). Analysis of the data on comorbidities in the current study revealed no special phenotype is predicting COVID-19 severe prognosis. However, we found that having three or more underlying comorbidities could be a predictor of the severe or critical course of COVID-19 infection. Our findings showed no specific laboratory signs for COVID-19 infection.

Multiple laboratory disturbances in complete blood count and biochemical analysis could be potential evidence of multi-organ damage in COVID-19 patients **(Table 3)**. On the other hand, ICU-patients had more severe laboratory disturbances. This could be attributed to the higher grade of systemic inflammation and more severe body metabolism disturbance and the higher prevalence of comorbidities in these patients.

However, the analysis revealed no significant difference in patients' laboratory findings in general and ICU cohorts ($p>0.05$). Pulmonary X-ray or computer tomography were performed in 57 patients (17 in ICU and 40 other patients). In 48 (84.2%) cases, lung tissue abnormalities were found, among them 16 cases (94.1%) of ICU patients. In nine patients (15.8%), no X-ray signs

of lung damage were found despite a positive coronavirus SARS-CoV-2 RNA test.

Table 2. Comorbidities of COVID-19 in-patients in Mittelbaden hospital at Baden-Baden, Germany between March and June 2020.

Nosology	No. (137)	%
Arterial hypertension	59	43.1
Respiratory pathology	33	24.1
Heart arrhythmias	29	21.2
Diabetes mellitus	27	19.7
Cerebrovascular disorders	26	19.0
Coronary heart disease	16	11.7
Obesity	15	10.9
Hypothyroidism	14	10.2
Arteriosclerosis and aneurisms	13	9.5
Malignancies	13	9.5
Chronic renal insufficiency	12	8.8
Asthma	11	8.0
Chronic heart insufficiency	9	6.6
Dementia, Parkinson disease, Schizophrenia	8	5.8
Vertebral fractures	7	5.1
Obstructive sleep apnea	7	5.1
Surgical interventions < 1 month	6	4.4
Urogenital infections	6	4.4
Inflammatory colon diseases	6	4.4
Heart valve pathology	6	4.4
Depression	5	3.6
Rheumatoid pathology	4	2.9
Pulmonary embolism	2	1.5
Other	10	7.3

Statement of principal findings

Despite the relatively similar characters of COVID-19 infection for the vast majority of infected cases, this nosology is considered potentially threatening. Literature reported different numbers of the fatality rate in different regions **(Lai et al., 2020, Onder et al., 2020)**. Because of the non-specific clinical and laboratory findings, it is challenging to create a typical COVID-19 patient profile. We found a slight predominance of COVID-19 in males (55%). The risk of a heavy course and poor prognosis is increased at the age of 52.5 (overall cohort group) to 78.9 years (the group of cases with lethal outcomes). This finding corresponds to previous literature data **(Li et al., 2020, Rodriguez-Morales et al., 2020)**.

Most of the patients did not require hospitalization, 10.4% of all patients in the study cohort required intensive care (30% of in-patient cases), and the prediction of critical COVID-19 illness is the key point of the diagnostic process. Our results and literature data indicated that comorbidities (3 and more), initial severe lymphopenia, LDH, and C-reactive protein increase, and CT of pulmonary parenchymal damage could potentially be used to predict severe illness course and require close monitoring for about two weeks. But we should keep in mind the possible secondary bacterial infection, especially for ICU patients under mechanical ventilation. The lung CT is considered an important method to diagnose COVID-19 pneumonia and control treatment success. This because there was no bacteriological alternative to existing COVID-19 tests and a wide spectrum of the clinical course of this infection (from asymptomatic to acute respiratory distress syndrome)

In the current study cohort, the fatality rate is estimated to be higher than the global COVID-19 fatality rate (6.6% vs. 5.0%), and that in Germany as a whole (4.6%) according to the WHO Situation Report **(WHO, 2020a)**. That could be explained by the proximity of borders and the easier accessibility of infection from the high-risk regions. The increase of fatality rate in hospitalized (17.5%) and ICU (33.3%) patients requires the focus of primary medical resources for supporting the hospital level of COVID-19 management. Nevertheless, the fatality rate of coronavirus SARS-CoV-2 infection seems to be less than those of SARS-CoV (over 10%) and MERS-CoV (over 35%) **(Li et al., 2020)**.

It is worth mentioning that 2,6 million people die annually from respiratory infections, excluding tuberculosis **(Roussel et al., 2020)**. We have to be careful with the interpretation of results while COVID-19 is a new infection, and all the effects are still being observed and researched. The current study's general tendencies correspond to other studies that more severe laboratory disturbances could correlate with more severe courses of COVID-19, ICU requirement, and poor prognosis. Despite all the European Union and Germany preventive measures, it could not avoid COVID-19 infection spread.

Epidemic management depends on many biological and logistic factors and directly impacts the medical and organizational measures. This study's findings help understand the extent and burden of COVID-19 infection outbreak in the area of Baden-Baden city, compared to the epidemiological situation in other regions, and to optimize the healthcare work system.

Table 3. Laboratory findings of COVID-19 patients in Mittelbaden hospital at Baden-Baden, Germany, between March and June 2020.

Laboratory finding[1]	No. (147)[2]	%	ICU patients (n=36)	%
C-reactive protein increase (>0,5 mg/dl)	126	85.1	36	100
LDH increase (>225 U/l)	105	71.4	30	83.3
Lymphopenia (AD-Lymph <25%)	100	68.0	30	83.3
MDRD decrease (<90 ml/min)	88	59.9	27	75.0
Segmental cells increase (AD-Seg >70%)	79	53.7	28	77.8
Hyponatremia (<135 mmol/l)	63	42.9	20	55.6
Procalcitonin increase (>0,5 ng/ml)	62	42.2	20	55.6
ASAT increase (>50 U/l)	48	32.7	18	50.0
CK increase (>174 U/l)	47	32.0	17	47.2
Granulocyte Index increase (AD-IG >0,5%)	39	26.5	18	50.0
Hyperuricemia (Urea>50 mg/dl)	38	25.9	16	44.4
Creatinine increase (>1,1 mg/dl)	36	24.3	11	30.6
Thrombocytopenia (<150.000/µl)	35	23.8	15	41.7
Erythrocytopenia (<4,2 mln/ µl)	31	21.1	6	16.7
GGT increase (>66 U/l)	27	18.4	8	22.2
Anemia (Hb<12 g/dl)	26	17.7	4	11.1
Uric acid increase (>7,2 mg/dl)	26	17.7	6	16.7
ALAT increase (>50 U/l)	26	17.6	7	19.4
Monocytosis, % (AD-Mono>12%)	22	14.9	2	5.6
Leukopenia (<4000/µl)	16	10.9	2	5.6
Leukocytosis (>10000/µl)	14	9.5	7	19.4
Segmental cells decrease (AD-Seg <50%)	10	6.8	-	-
SO2 for ICU patients on admission, %± SD			83.6±11.2	

[1]Only laboratory data on the patient's admission day are put in.

[2]Laboratory analyses were performed for all in-patients but not for all out-patients.

Strengths and weaknesses of the study

The study was performed on a large group (n=374) of patients and included all the positive cases from March to June 2020 in KMB. Our study is also subject to some limitations. First, there were difficulties in assessing the diagnostic power of existing diagnostic tools (PCR, Immunoglobulin tests, computer tomography) to diagnose COVID-19 infection. Second, a part of ICU-patients (n=6) was transferred to other hospitals and the outcomes of treatment were not included in the study cohort. However, a dramatic impact on the treatment results is not expected. However, our results are in concordance with previous data **(Lai et al., 2020, Leung, 2020, Rodriguez-Morales et al., 2020)**, confirming existing opinions about the non-specific clinical and laboratory character of the COVID-19 respiratory infectious process.

Conclusions, unanswered questions, and future research

This study provides an opportunity for assessment and a better understanding of the characteristics of COVID-19 infection in KMB, which is essential to improve and rationalize the medical healthcare structure. However, we note that SARS-CoV-2 is a new infection and requires future analyses of the epidemiology, preventive measures, treatment, and diagnosis of SARS-CoV-2 during the second wave.

Additional Article Information

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