[Short title + Author Name - P&H title] 11 (2021) 429–435

Contents lists available at ScienceDirect

African Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/afjem

Demographics and clinical characteristics of hospitalised patients under investigation for COVID-19 with an initial negative SARS-CoV-2 PCR test result

D.J. van Hoving [a,*], N. Hattingh [b], S.K. Pillay [b], T. Lockey [b], D.J. McAlpine [b], K. Nieuwenhuys [b], E. Erasmus [a,b]

[a] Division of Emergency Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa
[b] Emergency Centre, Khayelitsha Hospital, Cape Town, South Africa

ARTICLE INFO

Keywords:
COVID-19
South Africa
Emergency
District
Negative

ABSTRACT

Background: The COVID-19 pandemic is placing abnormally high and ongoing demands on healthcare systems. Little is known about the full effect of the COVID-19 pandemic on diseases other than COVID-19 in the South African setting.

Objective: To describe a cohort of hospitalised patients under investigation for SARS-CoV-2 that initially tested negative.

Methods: Consecutive patients hospitalised at Khayelitsha Hospital from April to June 2020, whose initial polymerase chain reaction test for SARS-CoV-2 was negative were included. Patient demographics, clinical characteristics, ICD-10 (International Statistical Classification of Diseases and Related Health Problems 10th Revision) diagnosis, referral to tertiary level facilities and ICU, and all-cause in-hospital mortality were collected. The 90-day re-test rate was determined and comparisons were made using the χ^2-test and the independent samples median test.

Results: Overall, 261 patients were included: median age 39.8 years, 55.6% female ($n = 145$). Frequent comorbidities included HIV (41.4%), hypertension (26.4%), and previous or current tuberculosis (24.1%). Nine (3.7%) patients were admitted to ICU and 38 (15.6%) patients died. Ninety-three patients (35.6%) were re-tested and 21 (22.6%) were positive for SARS-CoV-2. The top primary diagnoses related to respiratory diseases ($n = 82$, 33.6%), and infectious and parasitic diseases ($n = 62$, 25.4%). Thirty-five (14.3%) had a COVID-19 diagnostic code assigned (26 without microbiological confirmation) and 43 (16.5%) had tuberculosis. Older age ($p = 0.001$), chronic renal impairment ($p = 0.03$) and referral to higher level of care (all $p < 0.001$; ICU p = 0.03) were more frequent in those that died.

Conclusion: Patients with tuberculosis and other diseases are still presenting to emergency centres with symptoms that may be attributable to SARS-CoV-2 and requiring admission. Extreme vigilance will be necessary to diagnosis and treat tuberculosis and other diseases as we emerge from the COVID-19 pandemic.

African relevance

- Patients whose initial PCR test result for SARS-CoV-2 were negative, had a reasonable positive re-test rate
- A substantial underlying disease burden exists in those requiring testing for SARS-CoV-2
- Extreme vigilance is necessary to diagnosis and treat tuberculosis and other diseases during the COVID-19 pandemic

Introduction

The onset of the pandemic caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2), posed significant challenges to healthcare operations and systems across the world. Pandemics place abnormally high and ongoing demands on health systems that necessitate healthcare facilities to develop plans to redistribute resources [1–3]. Diagnostic, therapeutic, and preventive interventions are expected to be

* Corresponding author.
E-mail address: nvhoving@sun.ac.za (D.J. van Hoving).

https://doi.org/10.1016/j.afjem.2021.09.002
Received 15 January 2021; Received in revised form 21 June 2021; Accepted 16 September 2021
Available online 27 September 2021

scarce [4], whilst acute care services still need to be delivered at an acceptable standard.

Healthcare utilisation changes during infectious disease outbreaks. Historically, infectious disease epidemics and pandemics have resulted in an unprecedented fall in the number of emergency centre visits. In 2015, the MERS (Middle East Respiratory Syndrome) epidemic resulted in a 30% reduction in emergency centre visits across Korea [5], while emergency centre visits halved at the height of the SARS (Severe Acute Respiratory Syndrome) epidemic in Taiwan in 2003 [6]. During the early phases of the coronavirus (COVID-19) pandemic, a reduction in emergency centre numbers occurred across the globe in both adults and children [7–9]. A trend witnessed in the US indicated that as the number of patients hospitalised with COVID-19 increased, the number of emergency centre visits for other medical conditions rapidly decreased [9]. In the same manner, the COVID-19 pandemic triggered an unprecedented decline in hospital admissions and treatment for all subtypes of acute coronary syndromes in Austria [10], whereas patients with ST-elevation myocardial infarction had noticeable delays in seeking medical care in Hong Kong; some did not seek medical attention at all [11]. High acuity patients requiring medical intervention were also not presenting to US hospitals with subsequent reports of increased out-of-hospital cardiac arrests [12]. On the other hand, a higher acuity of disease with a concomitant higher frequency of admissions in those patients that did present to hospital was witnessed in South Africa [7,8].

The response to an infectious disease outbreak can have unprecedented and catastrophic repercussions on other healthcare-related aspects; the 2014-2015 Ebola outbreak in West Africa being a good example [1]. Although Ebola is associated with a high mortality rate, reduced access to healthcare increased the number of deaths caused by malaria, tuberculosis and HIV/AIDS [1]. The transmission and subsequent mortality rate resulting from these three diseases likely surpassed that of Ebola itself in Liberia, Guinea and Sierra Leone. A combination of factors is to be considered and include poor utilisation of healthcare services due to the fear of nosocomial transmission, limited routine health services (e.g. childhood vaccinations, obstetric care, screening for sexually transmitted infections) and the increased burden of the Ebola outbreak on the healthcare system. The deaths of healthcare workers further crippled the already overburdened healthcare system [1]. In 2014 and 2015, Ebola claimed more than 11,000 lives across the three West African countries [13], whereas tuberculosis-related deaths in 2014 alone numbered 11,900 [14]. In rural Guinea, outpatient visits fell by 40% and subsequently the diagnosis rate of tuberculosis decreased by 53% [15]. Furthermore, the mortality rate for tuberculosis doubled in Guinea [14]. Many of the tuberculosis-related deaths may have been prevented if routine tuberculosis treatment programs and prevention efforts were not compromised [14].

The disruption of prevention and control programs during the Ebola outbreak also affected measles vaccination coverage rates with a consequent high measles incidence until two years after the end of the outbreak [15]. Similarly, access to ante- and post-natal care also decreased by 18% and 22% respectively, with a concomitant 11% decrease in deliveries at healthcare facilities. The collateral damage thereof was a 30% rise in maternal deaths and a 24% increase in neonatal deaths [16].

The increased prevalence of COVID-19 during the pandemic could also result in cognitive errors in diagnosis. The delayed diagnosis of COVID-19 may result in unnecessary transmission to others, but as important is that other treatable diagnoses may be missed due to over-diagnosing of COVID-19 [17–19]. The rising number of people infected with COVID-19, combined with the oversaturation of the lay-media and academia, may lead clinicians to miss other respiratory infections such as tuberculosis and pneumonia [18,19]. Another example is the misinterpretation of chest discomfort and dyspnoea as being related to COVID-19 rather than myocardial ischaemia [10].

The COVID-19 pandemic is likely to negatively affect prevention and control measures, as well as the diagnosis and treatment of various diseases across the globe. Strict instructions to stay home as well as the fear of nosocomial infection may prevent or lead to deferral of care resulting in fewer patients presenting with acute and time-sensitive diagnoses. The reduction in acute medical, surgical and paediatric emergencies presenting to hospitals are of concern for an increase in downstream morbidity or mortality [2]. Little is known about the full effect of the COVID-19 pandemic on diseases other than COVID-19 in the South African setting. The objective of the study was to describe a cohort of hospitalised patients under investigation for SARS-CoV-2 that initially tested negative.

Methods

A retrospective cohort study was done.

Khayelitsha Hospital is a 300-bed hospital situated in the expansive township of Khayelitsha, Cape Town. It serves a health district with a population of more than 390,000 (2011) [20], although current estimates are that this figure is now around 1.2 million due to the influx of people from adjacent provinces for better living, employment and access to healthcare [21]. The majority of people residing in Khayelitsha are predominantly Black African (99%) with significant levels of unemployment (38%) [20]. There is a tremendous burden of disease related to HIV, tuberculosis and interpersonal violence [22]. Khayelitsha Hospital provides inpatient services such as surgical, medical, paediatric and obstetrics [23]. It houses a large emergency centre, which is 30% larger than that of a standard district hospital emergency centre [23]. All patients sick enough to be hospitalised are admitted via the emergency centre. The annual emergency centre volume ranges between 36,000 and 42,000 patients, with an admission rate of about 40% for adults and 60% in children. The in-hospital mortality rate is around 2.5%.

The first detected case of COVID-19 in South Africa occurred on 05 March 2020 [24], and the first patient investigated for COVID-19 at Khayelitsha Hospital was tested on 27 March 2020.

A database of all patients investigated for SARS-CoV-2 in the emergency centre of Khayelitsha Hospital was kept. Emergency centre clinicians completed an online form when a patient was tested for SARS-CoV-2. The variables included the patient's name, home address, work address, hospital folder number, date of birth, gender, whether the patient was a staff member and whether the patient was admitted. An electronic timestamp was automatically added when the form was submitted. Test results were followed up and communicated to the patients. Testing criteria followed the prescribed guideline from the National Department of Health and the National Institute for Communicable Diseases of the National Health Laboratory Services (Appendix A, Table B.1) [25]. Testing by means of a SARS-CoV-2 polymerase chain reaction (PCR) test was accessible for all patients meeting the testing criteria, however the public health sector soon experienced substantial testing backlogs and subsequent prolonged turnover times following the acceleration phase of the epidemic. The Western Cape therefore initiated a risk-adjusted testing strategy in June 2020 restricting testing to high-risk symptomatic individuals living within the Cape Town Metropolitan area (Appendix A, Table B.1) [26].

All consecutive patients (regardless of age) attending the emergency centre over a three-month period (1 April–30 June 2020) who were investigated for SARS-CoV-2 were eligible for inclusion. Patients who required hospitalisation and who had an initial negative oropharyngeal or nasopharyngeal PCR result were included. Patients with missing folders were excluded.

Data were collected by the investigators after an extract of the electronic database was obtained. Additional variables were obtained from electronic patient discharge summaries of in-hospital specialities. Variables included age, gender, comorbidities, HIV-status, CD4 cell count in HIV-positive patients, referred to tertiary level facilities, admitted to intensive care unit, discharge diagnosis and all-cause in-hospital mortality. Patient discharge diagnoses were determined from completed ICD-10 codes (International Statistical Classification of

Diseases and Related Health Problems, 10th revision). Data from the initial and subsequent PCR tests results were accessed via the National Health Laboratory Service (NHLS) web view. All results within 90 days of the original test result were included. NHLS data were double checked using patient name and date of birth to include results from all public health facilities that the patient may have attended. CD4 cell count was used if the test was performed during the admission or within three months prior to the admission.

Data were collected by two independent trained abstractors and differences were resolved by discussion.

Incomplete data points were excluded from the analysis. Summary statistics were used to describe all variables. Categorical data were summarised using frequency counts and percentages, and distributions of variables are presented as two-way tables or bar charts. Continuous variables (age and process times) are presented as medians with quartiles. The relationship between categorical variables was determined with the χ^2 test or the Fisher's exact test, and continuous variables were compared with the independent samples median test. A 5% significance level was used, and data were analysed using SPSS Statistics (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp).

Results

Overall, 6743 patients visited the emergency centre during the study period, of which 4796 (71.1%) were admitted. This is substantially less than emergency centre visits during similar periods in 2019 ($n = 10{,}245$; admitted $n = 5623$ (54.9%)). A total of 272 patients met the inclusion criteria of which 11 (4.0%) were due to missing folders; 261 patients were thus included in the analysis.

The median age of participants was 39.8 years, mostly consisting of females ($n = 145$, 55.6%) and adults ($n = 206$, 78.9%). The most frequent comorbidity was being HIV-positive ($n = 108$, 41.4%), followed by hypertension ($n = 69$, 26.4%) and previous or current tuberculosis ($n = 63$, 24.1%). Only nine (3.4%) were admitted to the intensive care unit (Table 1). Ninety-two of the HIV-positive patients had a CD4 cell count done within three months of the admission date; the median (25th–75th percentile) was 98.0 (49.8–242.3) cells/mm^3. The all-cause in-hospital mortality was 15.6% ($n = 38$).

A total of 130 retests were done on 93 (35.6%) patients within 90 days of the initial test done on admission (re-tested once $n = 68$; re-tested twice $n = 14$; re-tested three times $n = 10$; re-tested four times n = 1). Twenty-one (22.6%) of repeat-tested patients had a subsequent positive SARS-CoV-2 result, of which 14 were during the index admission (seven within 7 days of the initial swab and 11 within 14 days of the initial swab). Overall, 11 (11.8%) were positive within 7 days of the previous test result (not necessarily during the index admission) and 14 (15.1%) within 14 days.

The top three diagnostic categories were respiratory diseases ($n = 82$, 33.6%), infectious and parasitic diseases ($n = 62$, 25.4%), and diseases of the circulatory system ($n = 21$, 8.6%) (Table 2).

Thirty-five patients (14.3%) had a diagnostic code for COVID-19 (primary diagnosis $n = 29$, 11.9%); only nine of the 35 patients (25.8%) had a microbiological confirmation of SARS-CoV-2 (four patients had a positive test result during admission but no diagnostic code related to COVID-19 were entered; 13/39 (33.3%) had microbiological confirmation). The remainder was diagnosed by the in-hospital specialities utilizing clinical and radiological information. A further breakdown of the top three diagnostic categories are available in Table 3.

Diseases of the respiratory system remained the top diagnostic category in patients that were referred to higher level of care ($n = 15$, 36.6%), admitted to an intensive care unit (n = 6, 66.7%), or died (n = 5, 23.8%) (Table 4). The diagnostic categories per age group are presented in Appendix A (Table B.2).

The primary diagnostic category was not significantly different between patients who died and those that survived (Table 5). Older age ($p = 0.001$), chronic renal impairment ($p = 0.03$) and referral to higher level of care (all $p < 0.001$; ICU p = 0.03) were more frequent in those that died.

Discussion

This study reports the demographics and clinical characteristics of

Table 1
Demographics, comorbidities and referral to higher level of care in admitted patients whose initial SARS-CoV-2 test was negative.

	n (%) Unless otherwise specified
Age (years)	
Median (Q1-Q3)[a]	39.8 (26.8-57.9)
Gender	
Male	116 (44.4)
Female	145 (55.6)
Comorbidities	
HIV[b] positive[c]	108 (41.4)
Hypertension[d]	69 (26.4)
Previous or current tuberculosis on presentation[d]	63 (24.1)
Diabetes mellitus[d]	50 (19.2)
Chronic renal impairment[d]	20 (7.7)
Chronic obstructive pulmonary disease[d]	11 (4.2)
Ischaemic heart disease[d]	7 (2.7)
Other	109 (41.8)
Referred to higher level of care	
All	41 (15.7)
Intensive care unit	9 (3.4)

[a] 25th percentile–75th percentile.
[b] Human immunodeficiency virus.
[c] Unknown = 20.
[d] Unknown = 18.

Table 2
Diagnostic categories of admitted patients whose initial SARS-CoV-2 test was negative.

Diagnostic category (ICD-10[a] chapter)	≤12 years, n (%)	Adult, n (%)	All, n (%)
I Certain infectious and parasitic diseases	9 (16.4)	53 (28.0)	62 (25.4)
II Neoplasms	0 (0)	6 (3.2)	6 (2.5)
III Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	0 (0)	3 (1.6)	3 (1.2)
IV Endocrine, nutritional and metabolic diseases	2 (3.6)	8 (4.2)	10 (4.1)
V Mental and behavioural disorders	0 (0)	7 (3.7)	7 (2.9)
VI Diseases of the nervous system	1 (1.8)	3 (1.6)	4 (1.6)
IX Diseases of the circulatory system	0 (0)	21 (11.1)	21 (8.6)
X Diseases of the respiratory system	37 (67.3)	45 (23.8)	82 (33.6)
XI Diseases of the digestive system	0 (0)	2 (1.1)	2 (0.8)
XII Diseases of the skin and subcutaneous tissue	1 (1.8)	1 (0.5)	2 (0.8)
XIII Diseases of the musculoskeletal system and connective tissue	0 (0)	2 (1.1)	2 (0.8)
XIV Diseases of the genitourinary system	0 (0)	9 (4.8)	9 (3.7)
XVI Certain conditions originating in the perinatal period	4 (7.3)	0 (0)	4 (1.6)
XVIII Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	0 (0)	1 (0.5)	1 (0.4)
XXII Codes for special purposes	1 (1.8)	28 (14.8)	29 (11.9)
Total[b]	55 (100)	189 (100)	244 (100)

[a] International Statistical Classification of Diseases and Related Health Problems, 10th revision.
[b] Excluded due to missing diagnostic codes, $n = 17$.

Table 3
Breakdown of top three diagnostic categories of admitted patients whose initial SARS-CoV-2 test result was negative.

	≤12 years, n	Adult, n	All, n
Diseases of the respiratory system	37	45	82
Influenza and pneumonia	6	31	37
Bacterial pneumonia	2	11	13
Viral pneumonia	2	4	6
Pneumonia in parasitic diseases	0	1	1
Pneumonia, unspecified	2	15	17
Acute lower respiratory infections	30	2	32
Acute bronchiolitis due to respiratory syncytial virus	2	0	2
Acute bronchiolitis due to rhinovirus	2	0	2
Acute bronchiolitis unspecified	4	0	4
Unspecified	22	2	24
Chronic lower respiratory diseases	1	8	9
Acute upper respiratory infections	3	0	3
Other diseases of pleura	1	0	1
Certain infectious and parasitic diseases	9	53	62
Tuberculosis	2	41	43
Pulmonary tuberculosis	2	23	25
Extra-pulmonary, disseminated & miliary tuberculosis	0	10	10
Not specified	0	8	8
Human immunodeficiency virus [HIV] disease	0	8	8
Intestinal infectious diseases	4	2	6
Other bacterial diseases	3	2	5
Diseases of the circulatory system	0	21	21
Hypertensive diseases	0	5	5
Pulmonary heart disease and diseases of pulmonary circulation	0	2	2
Chronic rheumatic heart diseases	0	1	1
Other forms of heart disease	0	13	13

Table 4
Diagnostic categories of admitted patients whose initial SARS-CoV-2 test was negative and who subsequently were referred to higher level of care, admitted to an intensive care unit, and who died.

Diagnostic category (ICD-10[a] chapter)	Referred to tertiary hospital	ICU admission	Died
	n (%)	n (%)	n (%)
I Certain infectious and parasitic diseases	3 (7.3)	0 (0)	3 (14.3)
II Neoplasms	0 (0)	0 (0)	1 (4.8)
III Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	1 (2.4)	0 (0)	1 (4.8)
IV Endocrine, nutritional and metabolic diseases	1 (2.4)	0 (0)	0 (0)
V Mental and behavioural disorders	1 (2.4)	0 (0)	1 (4.8)
IX Diseases of the circulatory system	6 (14.6)	0 (0)	1 (4.8)
X Diseases of the respiratory system	15 (36.6)	6 (66.7)	5 (23.8)
XI Diseases of the digestive system	1 (2.4)	0 (0)	1 (4.8)
XIII Diseases of the musculoskeletal system and connective tissue	1 (2.4)	0 (0)	0 (0)
XIV Diseases of the genitourinary system	3 (7.3)	0 (0)	2 (9.5)
XVI Certain conditions originating in the perinatal period	1 (2.4)	1 (11.1)	0 (0)
XVIII Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	0 (0)	0 (0)	1 (4.8)
XXII Codes for special purposes	8 (19.5)	2 (22.2)	5 (23.8)

[a] International Statistical Classification of Diseases and Related Health Problems, 10th revision.

Table 5
Comparison of demographics and clinical characteristics between patients who died and those who did not.

n (%), unless otherwise stipulated	Alive ($n = 223$)	Died (n = 38)	*p*-Value
Age (years)			
Median (Q1-Q3)[a]	36.6 (14.1–57.3)	49.9 (40.0–64.9)	0.001
Gender			
Male	100 (44.8)	16 (42.1)	0.75
Female	123 (55.2)	22 (57.9)	
Comorbidities			
HIV[b] positive	87 (39.0)	21 (55.3)	0.06
Hypertension	58 (26.5)	11 (45.8)	0.046
Previous or current tuberculosis at admission	53 (24.2)	10 (40.0)	0.09
Diabetes mellitus	41 (18.7)	9 (37.5)	0.06
Chronic renal impairment	15 (6.8)	5 (20.8)	0.034
Chronic obstructive pulmonary disease	11 (5.0)	0 (0)	0.61
Ischaemic heart disease	6 (2.7)	1 (4.2)	0.52
Other	94 (42.2)	15 (39.5)	0.76
Referred to higher level of care			
All	29 (13.0)	12 (57.1)	<0.001
Intensive care unit	6 (2.7)	3 (14.3)	0.03
Primary diagnostic category			
Infectious and parasitic diseases	58 (26.0)	3 (14.3)	0.24
Diseases of the circulatory system	21 (9.4)	1 (4.8)	0.70
Diseases of the respiratory system	78 (35.0)	5 (23.8)	0.30
Codes for special purposes (COVID-19)	24 (10.8)	5 (23.8)	0.09

[a] 25th percentile–75th percentile.
[b] Human immunodeficiency virus.

patients who warranted admission based on their clinical status and whose initial SARS-CoV-2 PCR test result was negative. Almost 40% were retested within 90 days and 8% had a subsequent positive result (6% during the index admission). HIV and hypertension were frequent comorbidities, while diseases related to the respiratory system (34%) was the most frequent primary diagnosis. Older age, chronic renal impairment and referral to higher level of care were more frequent in those that died.

Overall positivity among repeat-tested patients was 23%. This is substantially lower than found in a US-based laboratory study where 40% of repeat-tested patients were positive [27]. The interpretation of a positive PCR test after a previous negative result in the absence of SARS CoV-2 infection is rather complex. It could simply be that the initial test was a false negative or that the retest had been contaminated [28]. Inappropriate timing of sample collection in relation to illness onset and deficiency in sampling technique are the most frequent reasons for false-negative results [29]. Also to consider is that a positive PCR test does not imply SARS-CoV-2 viability and infectivity, as the detection of viral-RNA is possible long after the infectious virus has been eradicated [28].

The study demonstrates the underlying disease burden in those meeting criteria for admission and also requiring testing for SARS-CoV-2. The prevalence of comorbidities in those with an initial negative SARS-CoV-2 test was rather high (HIV-positive 41.4%, hypertension 26.4%, previous or current tuberculosis 24.1%, diabetes mellitus 19.2%). The prevalence of HIV is similar to a previous study which described a prevalence of 38.4% in patients managed in the resuscitation area of Khayelitsha Hospital's emergency centre [30]. On the other hand, the prevalence of hypertension is less than previously recorded in the urban black population of Cape Town (26.4% versus 35.6%) [31], whereas the diabetes prevalence is higher (19.2% versus 13.1%) [32]. The high tuberculosis prevalence is also a reflection of the ongoing burden of tuberculosis in the local setting. This is expected to increase similarly to the post-Ebola rise in tuberculosis cases [33]. Tuberculosis screening programmes was temporarily suspended during the national COVID-19 lockdown and a 48% decrease in the number of tuberculosis-

related tests (sputum TB PCR (Xpert)) volumes occurred [34]. This reduction in test volume corresponded to a 33% decline in the number of positive tests for tuberculosis [34].

The main primary diagnosis related to diseases of the respiratory system (33.6%). This should be expected as the testing criteria for SARS-CoV-2 is mainly focused on the respiratory system. Respiratory pathogens were unfortunately not routinely tested for, but in an Italian study the most common pathogens detected in patients tested for SARS-CoV-2 were influenza A (22.2%), influenza B (9.5%) and rhinovirus/enterovirus (8.7%) [35]. It is not surprising that 17% of the patients in our study had a new diagnosis of tuberculosis (Table 3). This is somewhat higher than a recent study in Khayelitsha where 13.5% of patients managed in the resuscitation area had tuberculosis [30].

The all-cause in-hospital mortality was around 16%. This is substantially higher than the 2018 mortality rate for Khayelitsha Hospital (2.5%) [36]. It is also higher than the mortality (5%) in patients with diabetic emergencies managed in Khayelitsha Hospital (personal communication: N Lotter), and the mortality rate in HIV-positive patients investigated for tuberculosis at Khayelitsha Hospital (7%) [37]. However, the mortality rate is similar than non-trauma adults (17%) from the same hospital [30]. Death was not associated with the primary diagnosis or HIV-positive status, but rather with older age and comorbidities including chronic renal insufficiency.

The results of the study are limited by the retrospective nature of the design. Bias related to the retrospective nature of the study has been lessened using a standardised data collection tool and that all data were independently double-checked. Still, we cannot ensure that all patients tested in the emergency centre were included on the electronic database. This was also a single-centre study at a district-level facility and care must be taken to apply the results in different settings. Four percent of eligible patients were excluded due to missing folder numbers and the results could have shifted in any direction if these patients were included. Lastly, diagnostic codes completed by in-hospital disciplines were used and may have introduced bias from either an inaccurate diagnosis or erroneous selection of diagnostic codes. We did not attempt to quantify this.

This study demonstrates that patients with tuberculosis and other diseases are still presenting to emergency centres with symptoms that may be attributable to SARS-CoV-2 and requiring admission. Prior study has shown that testing and diagnosis of tuberculosis has decreased during the current pandemic. Extreme vigilance will be necessary to diagnosis and treat tuberculosis and other diseases as we emerge from the COVID-19 pandemic.

Dissemination of results

Results from this study were shared with staff members at the emergency centre of Khayelitsha hospital through an informal presentation.

Authors' contribution

Authors contributed as follow to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content: DJvH contributed 35%; EE 15%; and NH, KSP, TL DJM and KN contributed 10% each. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

Declaration of competing interest

The authors declared no conflicts of interest.

Appendix A

Table B.1
Qualifying criteria for COVID-19 testing in the Western Cape over the study period.

Release date	Clinical and epidemiological criteria for person under investigation for SARS-CoV-2[a]
10 March 2020[b]	1) Acute respiratory illness with sudden onset of at least one of the following irrespective of admission status: - cough - sore throat - shortness of breath - fever [≥ 38 °C (measured) or history of fever (subjective)] AND 2) In the 14 days prior to onset of symptoms, met at least one of the following: - Were in close contact with a confirmed or probable case of SARS-CoV-2 infection - Had a history of travel to areas with local transmission of SARS-CoV-2 - Worked in, or attended a health care facility where patients with SARS-CoV-2 infections were being treated - Admitted with severe pneumonia of unknown aetiology
3 June 2020[c]	Person who has COVID-19 symptoms and at least one of the following: - Admitted to hospital - >55 years - Any age with ≥1 of the following conditions: o Diabetes, hypertension or heart disease on treatment o Cancer on treatment o Tuberculosis on treatment o HIV[d] with poor adherence to antiretroviral therapy o Chronic lung disease on treatment - Healthcare worker - Living in a care or old age home

[a] Severe acute respiratory syndrome coronavirus.
[b] National testing criteria.
[c] Testing criteria for Cape Town Metropolitan area.
[d] Human immunodeficiency virus.

Table B.2
Diagnostic categories per age group of admitted patients whose initial SARS-CoV-2 test was negative and who subsequently were referred to higher level of care, admitted to an intensive care unit, and who died.

Diagnostic category (ICD-10[a] chapter)	Referred to tertiary hospital			ICU admission			Died		
	≤12 years, n (%)	Adult, n (%)	All, n (%)	≤12 years, n (%)	Adult, n (%)	All, n (%)	≤12 years, n (%)	Adult, n (%)	All, n (%)
I Certain infectious and parasitic diseases	1 (10.0)	2 (6.5)	3 (7.3)	0 (0)	0 (0)	0 (0)	1 (100)	2 (10.0)	3 (14.3)
II Neoplasms	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5.0)	1 (4.8)
III Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	0 (0)	1 (3.2)	1 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5.0)	1 (4.8)
IV Endocrine, nutritional and metabolic diseases	1 (10.0)	0 (0)	1 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
V Mental and behavioural disorders	0 (0)	1 (3.2)	1 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	1 (4.8)
IX Diseases of the circulatory system	0 (0)	6 (19.4)	6 (14.6)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5.0)	1 (4.8)
X Diseases of the respiratory system	7 (70.0)	8 (25.8)	15 (36.6)	3 (75)	3 (60)	6 (66.7)	0 (0)	5 (25.0)	5 (23.8)
XI Diseases of the digestive system	0 (0)	1 (3.2)	1 (2.49)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	1 (4.8)
XIII Diseases of the musculoskeletal system and connective tissue	0 (0)	1 (3.2)	1 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
XIV Diseases of the genitourinary system	0 (0)	3 (9.7)	3 (7.3)	0 (0)	0 (0)	0 (0)	0 (0)	2 (10)	2 (9.5)
XVI Certain conditions originating in the perinatal period	1 (10.0)	0 (0)	1 (2.4)	1 (25.0)	0 (0)	1 (11.1)	0 (0)	0 (0)	0 (0)
XVIII Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5.0)	1 (4.8)
XXII Codes for special purposes	0 (0)	8 (25.8)	8 (19.5)	0 (0)	2 (40)	2 (22.2)	0 (0)	5 (25.0)	5 (23.8)
Total	10 (100)	31 (100)	41 (100)	4 (100)	5 (100)	9 (100)	1 (100)	20 (100)	21 (100)

References

[1] Parpia AS, Ndeffo-Mbah ML, Wenzel NS, Galvani AP. Effects of response to 2014–2015 Ebola outbreak on deaths from malaria, HIV/AIDS, and tuberculosis, West Africa. Emerg Infect Dis 2016;22:433–41. https://doi.org/10.3201/eid2203.150977.

[2] Walker LE, Heaton HA, Monroe RJ, Reichard RR, Kendall M, Mullan AF, et al. Impact of the SARS-CoV-2 pandemic on emergency department presentations in an integrated health system. Mayo Clin Proc 2020;95:2395–407. https://doi.org/10.1016/j.mayocp.2020.09.

3. Furstenburg PP, Mukonkole SN, Kibamba CN, Kuiler A, Ngemntu N, Lahri S, et al. Emergency Centre reorganization in preparation to the COVID-19 pandemic: a district hospital's dynamic adaptation response. Afr J Prim Heal Care Fam Med 2020;12:a2514. https://doi.org/10.4102/phcfm.v12i1.2514.

[4] Emanuel EJ, Persad G, Upshur R, Thome B, Parker M, Glickman A, et al. Fair allocation of scarce medical resources in the time of Covid-19. N Engl J Med 2020;382:2049–55. https://doi.org/10.1056/nejmsb2005114.

5. Lee SY, Khang YH, Lim HK. Impact of the 2015 Middle East respiratory syndrome outbreak on emergency care utilization and mortality in South Korea. Yonsei Med J 2019;60:796–803. https://doi.org/10.3349/ymj.2019.60.8.796.

[6] Huang H-H, Yen DH-T, Kao W-F, Wang L-M, Huang C-I, Lee C-H. Declining emergency department visits and costs during the severe acute respiratory syndrome (SARS) outbreak. J Formos Med Assoc 2006;105:31–7. https://doi.org/10.1016/S1726-4901(09)70146-7.

[7] Hendrikse C, Parak M, van Hoving DJ. A descriptive analysis of the effect of the national COVID-19 lockdown on the workload and case mix of patients presenting to a district-level emergency Centre in Cape Town, South Africa. S Afr Med J 2020;110:1113–8. https://doi.org/10.7196/SAMJ.2020.v110i11.15028.

8. Akuaake LM, Hendrikse C, Spittal G, Evans K, van Hoving DJ. Cross-sectional study of paediatric case mix presenting to an emergency Centre in Cape Town, South Africa, during COVID-19. BMJ Paediatr Open 2020;4:e000801. https://doi.org/10.1136/bmjpo-2020-000801.

9. Hartnett KP, Kite-Powell A, DeVies J, Coletta MA, Boehmer TK, Adjemian J, et al. Impact of the COVID-19 pandemic on emergency department visits - United States, January 1, 2019-May 30, 2020. MMWR Morb Mortal Wkly Rep 2020;69:699–704. https://doi.org/10.15585/mmwr.mm6923e1.

[10] Metzler B, Siostrzonek P, Binder RK, Bauer A, Reinstadler SJ. Decline of acute coronary syndrome admissions in Austria since the outbreak of COVID-19: the pandemic response causes cardiac collateral damage. Eur Heart J 2020;41:1852–3. https://doi.org/10.1093/eurheartj/ehaa314.

11. Tam C-CF, Cheung K-S, Lam S, Wong A, Yung A, Sze M, et al. Impact of coronavirus disease 2019 (COVID-19) outbreak on ST-segment–elevation myocardial infarction care in Hong Kong, China. Circ Cardiovasc Qual Outcomes 2020;13:e006631. https://doi.org/10.1161/CIRCOUTCOMES.120.006631.

12. Wong LE, Hawkins J, Langness S, Murrell K, Iris P, Sammann A. Where are all the patients? Addressing Covid-19 fear to encourage sick patients to seek emergency care. NEJM catalyst innovations in care delivery. https://catalyst.nejm.org/doi/full/10.1056/CAT.20.0193. [Accessed 30 November 2020].

13. Centers for Disease Control and Prevention. 2014-2016 Ebola outbreak in West Africa. Atlanta: Centers for Disease Control and Prevention. https://www.cdc.gov/vhf/ebola/history/2014-2016-outbreak/index.html. [Accessed 11 October 2020].

[14] Ansumana R, Keitell S, Roberts GMT, Ntoumi F, Petersen E, Ippolito G, et al. Impact of infectious disease epidemics on tuberculosis diagnostic, management, and prevention services: experiences and lessons from the 2014–2015 Ebola virus disease outbreak in West Africa. Int J Infect Dis 2017;56:101–4. https://doi.org/10.1016/j.ijid.2016.10.010.

[15] Leuenberger D, Hebelamou J, Strahm S, De Rekeneire N, Balestre E, Wandeler G, et al. Impact of the Ebola epidemic on general and HIV care in Macenta, Forest Guinea, 2014. AIDS 2015;29:1883–7. https://doi.org/10.1097/QAD.0000000000000784.

16. Jones S, Ahmed C. Exploring the impact of the Ebola outbreak on routine maternal health services in Sierra Leone. London: VSO International; 2015.. https://www.vsointernational.org/sites/default/files/VSOSierroaLeone-ImpactofEbola.pdf.

17. Romano PS. Coronavirus disease 2019 (COVID-19) and diagnostic error. Rockville: Patient Safety Network. https://psnet.ahrq.gov/primer/coronavirus-disease-2019-covid-19-and-diagnostic-error#3. [Accessed 11 October 2020].

[18] Gandhi TK, Singh H. Reducing the risk of diagnostic error in the COVID-19 era. J Hosp Med 2020;15:363–6. https://doi.org/10.1056/nejmcp2009249.

19. DiMaria CN, Lee B, Fischer R, Eiger G. Cognitive bias in the COVID-19 pandemic. Cureus 2020;12:e9019. https://doi.org/10.7759/cureus.9019.

20. Statistics South Africa. Khayelitsha. Pretoria: Statistics South Africa; 2011. http://www.statssa.gov.za/?page_id=4286&id=328.

21. Khayelitsha Development Forum. Khayelitsha statistics. Cape Town: Khayelitsha Development Forum; 2011. http://kdfholdings.co.za/about/khayelitsha-statistics/.

22. Hunter LD, Lahri S, van Hoving DJ. Case mix of patients managed in the resuscitation area of a district-level public hospital in Cape Town. Afr J Emerg Med 2017;7:19–23. https://doi.org/10.1016/j.afjem.2017.01.001.

23. Western Cape Government. Eco-friendly Khayelitsha Hospital. Cape Town: Western Cape Government; 2014. http://www.westerncape.gov.za/general-publication/eco-friendly-khayelitsha-hospital.

24. South African Government News Agency. President Ramaphosa announces a nationwide lockdown. Pretoria: SAnews; 2020. https://www.sanews.gov.za/south-africa/president-ramaphosa-announces-nationwide-lockdown.

25. National Institute for Communicable Diseases, National Department of Health. Coronavirus disease 2019 (COVID-19) caused by a Novel Coronavirus (SARS-CoV-2) - Guidelines for case-finding, diagnosis, management and public health response in South Africa. Johannesburg: National Institute for Communicable Diseases. https://www.nhls.ac.za/wp-content/uploads/2020/03/NICD_DoH-COVID-19-Guidelines-10March2020_final.pdf. [Accessed 11 October 2020].

26. Western Cape Government. Statement by premier Alan Winde - our testing strategy is focused on saving lives. Cape Town: Western Cape Government; 2020. https://coronavirus.westerncape.gov.za/news/statement-premier-alan-winde-our-testing-strategy-focused-saving-lives.

27. Green DA, Zucker J, Westblade LF, Whittier S, Rennert H, Velu P, et al. Clinical performance of SARS-CoV-2 molecular tests. J Clin Microbiol 2020;58:e00995-20. https://doi.org/10.1128/JCM.00995-20.
28. Alvarez-Moreno CA, Rodríguez-Morales AJ. Testing dilemmas: post negative, positive SARS-CoV-2 RT-PCR – is it a reinfection? Travel Med Infect Dis 2020;35:101743. https://doi.org/10.1016/j.tmaid.2020.101743.
[29] Sethuraman N, Jeremiah SS, Ryo A. Interpreting diagnostic tests for SARS-CoV-2. JAMA 2020;323:2249–51. https://doi.org/10.1001/jama.2020.8259.
30. Swarts L, Lahri S, van Hoving DJ. The burden of HIV and tuberculosis on the resuscitation area of an urban district-level hospital in Cape Town. Afr J Emerg Med 2020. https://doi.org/10.1016/j.afjem.2020.09.016.
31. Peer N, Steyn K, Lombard C, Gwebushe N, Levitt N. A high burden of hypertension in the urban black population of Cape Town: the cardiovascular risk in black South Africans (CRIBSA) study. PLoS One 2013;8:e78567. https://doi.org/10.1371/journal.pone.0078567.
32. Peer N, Steyn K, Lombard C, Lambert EV, Vythilingum B, Levitt NS. Rising diabetes prevalence among urban-dwelling black South Africans. PLoS One 2012;7:e43336. https://doi.org/10.1371/journal.pone.0043336.
33. Bah OM, Kamara HB, Bhat P, Harries AD, Owiti P, Katta J, et al. The influence of the Ebola outbreak on presumptive and active tuberculosis in Bombali District, Sierra Leone. Public Health Action 2017;7(Suppl 1):S3–9. https://doi.org/10.5588/pha.16.0093.
34. National Institute for Communicable Diseases. Impact of COVID-19 intervention on TB testing in South Africa. Johannesburg: National Institute for Communicable Diseases; 2020. https://www.nicd.ac.za/wp-content/uploads/2020/05/Impact-of-Covid-19-interventions-on-TB-testing-in-South-Africa-10-May-2020.pdf.
35. Bordi L, Nicastri E, Scorzolini L, Di Caro A, Capobianchi MR, Castilletti C, et al. Differential diagnosis of illness in patients under investigation for the novel coronavirus (SARS-CoV-2), Italy, February 2020. Eurosurveillance 2020;25:2000170. https://doi.org/10.2807/1560-7917.ES.2020.25.8.2000170.
36. Parliamentary Monitoring Group. Khayelitsha Hospital challenges and successes. Cape Town: Parliament of South Africa; 2018. https://pmg.org.za/committee-meeting/27112/.
[37] Van Hoving DJ, Kenge AP, Maartens G, Meintjes G. Point-of-care ultrasound predictors for the diagnosis of tuberculosis in HIV-positive patients presenting to an emergency center. J Acquir Immune Defic Syndr 2020;83:415–23. https://doi.org/10.1097/QAI.0000000000002279.