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Chest radiographs may assist in predicting the outcome in the early phase of Covid-19. UK district general hospital experience of Covid-19 first wave

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ABSTRACT

Objectives: Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2) has caused enormous strain on health-care systems worldwide. Early recognition of prognostic markers and appropriate management of patients with coronavirus disease 2019 (Covid-19) remains a major global health concern, particularly when resources are limited. We undertook a study to see if basic tests can inform frontline clinicians of disease trajectory in individual patients with COVID-19.

Methods: We retrospectively assessed characteristics of the first 50 consecutive patients admitted to district general hospital in the United Kingdom with positive SARS-Cov-2 RNA swabs.

Results: Our patient cohort shared broad similarities with previously published data on comorbidities and presenting features. We have found that chest radiographic assessment differed between survivors and non-survivors. Air space shadowing in middle zones were more prevalent in non-survivors (73.3% vs. 35.5% [p = 0.027]). Chest radiograph severity score was also found to be higher in non-survivors compared to survivors (3 vs. 1.5 [p = 0.007]).

Conclusions: In this small retrospective study, our results suggest features of chest radiographs at presentation may provide a helpful tool for prognostication. In environments with constrained computed tomography (CT) imaging with serial chest radiographs could be a cost-effective tool in the assessment of Covid-19 patients.

1. Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a positive-stranded RNA virus first identified in November 2019 as causing pneumonia in a cluster of patients in Wuhan, China [1]. It has since developed rapidly into a global emergency, straining healthcare capacity worldwide. At the time of writing, there are estimated to be over twenty-nine million global infections with growing mortality [2]. The effects of this disease have been widespread, affecting the mental and physical well-being of communities in every country, leading to widespread behavioral and social changes [3].

Retrospective studies have identified several comorbidities and clinical characteristics as risk factors for poor outcomes [4–6], which, at the time of writing, have primarily been identified in countries with early onset of pandemic. The preliminary reports from UK suggest that disease course and associated risk factors are not uniform. It has become clear that epidemiology, pathology, and outcomes may vary between countries depending on lifestyle, ethnicity, and healthcare system resources [7]. There is therefore a pressing need to publish available data on the features of those patients who are admitted to hospital with Covid-19 in different countries.

Identification of Covid-19 has primarily been carried out by viral RNA detection. However, these methods do not provide insight into the severity of infection. Computed tomography

(CT), lung pathology, and biomarkers have all been suggested to provide concurrent diagnostic and risk stratification assistance [8]. The application of CT to disease staging is now in worldwide use where it is available; however, chest radiography is a simpler, cheaper, more widely available resource. We are not aware of any studies comparing the effectiveness or value when comparing CT to chest radiographs in assessing Covid-19 patients.

In early March, district general hospitals in the UK were dealing with first wave of patients with Covid-19 – the unknown clinical entity when no diagnostic clear pathways and treatment regime were available for routine use. We therefore designed a study to characterize outcomes and disease course of the first 50 patients who had detectable viral RNA on reverse transcriptase-polymerase (RT-PCR) nasopharyngeal swabs at our center in the United Kingdom.

2. Patients and methods

2.1. Study population, setting, and data collection

We collected retrospective, observational data on a consecutive series of 50 patients with laboratory-confirmed Covid-19 infection, admitted to St Peter's Hospital (SPH), a part of the Ashford and St Peter's Hospitals NHS Foundation Trust, Surrey, England, UK. This District General Hospital provides urgent

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and routine health-care services for the area with approximately 400,000 population in counties bordering the south-western London metropolitan area and the region westward. We included data on mortality for patients aged >18 to leave a cohort of 49 individuals. Included patients were admitted between the 10 and 25 of March. The 30-day outcome of last included patient was therefore 25 April.

Laboratory confirmation of infection was defined by a reverse-transcriptase-polymerase chain (RT-PCR) reaction assay of a nasopharyngeal swab (NPS). The data for patients with a detectable RT-PCR for SARS Coronavirus-2 were obtained from the SPH Public Health England (PHE) Clinical Characterization Protocol-UK trial database PHE. This database of the first 50 patients was cross-referenced with an internal database from the Infectious Diseases Department to double-check the inclusion of the first 50 consecutive confirmed cases at our hospital. Clinical characteristics were collected from electronic records and scanned paper documentation. No specific work-up protocol was used as all laboratory tests, radiographic, and other imaging were performed at the discretion of the attending physician.

This study was designed by a physician-led executive committee and has approval of the relevant audit and research and development team at Ashford and St Peter's Hospital Foundation Trust. Ethical approval was provided by the Ashford & St Peter's Hospital Research and Development department.

2.2. Specimen collection and testing

Clinical specimens for Covid-19 diagnostic testing were taken according to PHE guidance [new onset cough or fever (temperature >37.8°C) in patients who may need admission or inpatients developing these similar symptoms]. Local guidance to aid emergency department and medical clinicians recommended considering admission for high-risk patients (e. g. underlying cardiorespiratory comorbidities, immunosuppression, active cancer, etc.) or low-risk patients with severe symptoms (e.g. hypoxemia, severe dyspnea, tachypnea, etc.).

2.3. Clinical assessment summary

The date of admission, baseline characteristics, and past medical history were obtained from Evolve (Kainos Evolve Ltd. 2011, Northern Ireland, UK) or Metavision (iMD-Soft, United States) – intensive care electronic records. The treatment details were obtained from emergency department clerking proformas within the emergency department and ward drug charts. Vital Pac (System C Healthcare Ltd., England, UK) was used for vital signs and hemodynamic parameters. Data for blood test and microbiology results were obtained from the ICE software (ICE Health Sytems, Canada). Mortality, discharge data, and 30-day outcome from index admission were obtained from Evolve.

2.4. Radiographic assessment

All hospital radiographic imaging (CT, CXR, MRI, and echocardiography) is automatically stored in the Intellispace PACS (Phillips, Netherlands) software system. For this study, we have obtained and analyzed chest radiographs taken on admission. We have excluded patients who had a positive swab taken >10 days from admission. Each radiograph was assessed for the presence of airspace shadowing and/or consolidation. The distribution of radiographic changes was described in terms of zonality (upper, middle, and lower zones) and laterality (right or left). A severity index was then determined for each study as previously outlined by Wong et al. [9]. A score of 0–4 was assigned to each lung depending on the percentage of involvement of each hemithorax by airspace shadowing and/or consolidation (0 = no involvement; 1 = <25%; 2 = 25–50%; 3 = 50–75%; 4 = >75% involvement). The scores for each lung were then summed to produce the final severity score with maximum score of 8. The presence of pleural fluid and other miscellaneous findings (e.g. cardiomegaly, fibrosis, pleural plaques, etc.) was also recorded.

The blind assessment and scoring of radiographs were performed off-line by a group of three experienced radiology doctors who scored independently each radiographic image. Where disagreement was identified independent adjudicator radiologist with a specialist interest in thoracic imaging was recruited to make a final determination.

2.5. Statistical analysis

The data were divided into two groups – survivors and non-survivors. Descriptive statistics were used in summarizing data from all groups; values are reported as medians with interquartile ranges or means with standard deviations. Between group comparisons were made using Student's t-test or Mann-Whitney test as appropriate. Analysis was performed with statistical software SPSS version 25 (IBM).

3. Results

Fifty consecutive patients were assessed, and their demographic characteristics are presented in Table 1. The mean age at admission was 65.2 years; patients who did not survive at 30 days were significantly older (75 ± 10.9 vs. 60.2 ± 21.2 $p < 0.01$). There were more females in our sample (55%), the average BMI was 27.7 ± 5.4. There was high prevalence of Caucasians in our cohort of patients.

Comorbidities are displayed in Table 2. There was a high prevalence of cardiovascular disease including hypertension (56.3%), ischemic heart disease (14.6%), and congestive cardiac failure (12.5%).

Table 3 displays common symptoms reported by patients during their presentation. The most common presenting complaints were cough and dyspnea.

Table 4 displays the radiological features at presentation. There were broad similarities between survivors and non-survivors at 30 days. The presence of mid-zone air space shadowing was the main differentiating factor and was more prevalent in non-survivors (73.3% vs. 35.5% [$p = 0.027$]). The median Wong score on admission chest x-ray was higher in non-survivors (3.0 vs. 1.5 [$p = 0.007$]).

Table 5 displays the laboratory findings at presentation. Inflammatory markers were similar between survivors and non-survivors. Albumin at presentation was lower in non-survivors (39 ± 5.8 vs. 42 ± 3.5 [$p = 0.028$]).

Table 1. Demographics.

	Full cohort (n = 50)	Alive at 30 d (n = 33)	Dead at 30 d (n = 17)	P-value
Gender (male − %)	44.0	48.5	35.3	0.548
Age (y), mean ± SD, range	65.2 ± 19.6 (15–94)	60.2 ± 21.2 (15–94)	75.0 ± 10.9 (55–94)	0.010
Height (m), mean ± SD	1.71 ± 0.11	1.72 ± 0.11	1.70 ± 0.12	0.525
Weight (kg), mean ± SD	82.0 ± 20.0	85.3 ± 20.9	75.9 ± 17.3	0.160
Body Mass Index (kg/m^2), mean ± SD	27.7 ± 5.4	28.5 ± 5.7	26.3 ± 4.7	0.216
Ethnicity (n,%)				
White British	33 (66.0%)	23 (20.5%)	10 (62.5%)	
White Other	1 (2.0%)	0 (0%)	1 (6.3%)	
Other	6 (12.0%)	3 (10.7%)	3 (18.8%)	
Pakistani	2 (4.0%)	2 (7.1%)	0 (0%)	
Indian	1 (2.0%)	0 (0%)	1 (6.3%)	

Table 2. Comorbidities.

	Full cohort (n = 50)	Alive at 30 d (n = 33)	Dead at 30 d (n = 17)
Diabetes (%) (n = 47)	17/47(36.2%)	9/31 (29.0%)	8/16 (50.0%)
Hypertension (%) (n = 48)	27/48 (56.3%)	15/31 (48.4%)	12/17 (70.6%)
Ischemic Heart disease (%) (n = 48)	7/48 (14.6%)	3/31 (9.7%)	4/17 (23.5%)
Heart failure (%) (n = 48)	6/48 (12.5%)	2/31 (6.5%)	4/17 (23.5%)
Active malignancy (%) (n = 48)	4/48 (8.3%)	1/31 (3.2%)	3/17 (17.6%)
Atrial fibrillation (%) (n = 48)	7/48 (14.6%)	4/31 (12.9%)	3/17 (17.6%)
Chronic kidney (%) (n = 48)	5/48 (10.4%)	3/31 (9.7%)	2/17 (11.8%)
Respiratory disease (%) (n = 48)	17/48 (35.4%)	12/31(38.7%)	5/17 (29.4%)

Table 3. Presenting complaints.

	Full cohort (n = 50)	Alive at 30 d (n = 33)	Dead at 30 d (n = 17)
Cough (%) (n = 37)	20/37 (54.1%)	15/25 (60.0%)	5/12 (41.7%)
Dyspnea (%) (n = 37)	20/37 (54.1%)	13/25 (52.0%)	7/12 (58.3%)
Fever (%) (n = 37)	18/37 (48.6%)	14/25 (56.0%)	4/12 (33.3%)
Chest pain (%) (n = 37)	15/37 (40.5%)	10/25 (40.0%)	5/12 (41.7%)
Nausea/Vomiting (%) (n = 37)	4/37 (10.8%)	3/25 (12.0%)	1/12 (8.3%)
Abdominal pain (%) (n = 37)	2/37 (5.4%)	2/25 (8.0%)	0/12 (0%)

Table 4. Radiological features.

	Full cohort (n = 50)	Alive at 30 d (n = 33)	Dead at 30 d (n = 17)	P-value
Normal chest x-ray (n = 46)	3/46 (6.5%)	3/31 (9.7%)	0/15 (0%)	0.541
Consolidation (n = 46)	3/46 (6.5%)	3/31 (9.7%)	0/15 (0%)	0.541
Airspace shadow (n = 46)	37/46 (80.4%)	24/31 (52.2%)	13/15 (86.7%)	0.696
Right side airspace shadow (n = 46)	29/46 (63.0%)	17/31 (54.8%)	12/15 (80.0%)	0.117
Left side airspace shadow (n = 46)	31/46 (67.4%)	19/31 (61.3%)	12/15 (80.0%)	0.317
Upper Zone airspace shadow (n = 46)	1/46 (2.2%)	0/31 (0%)	1/15 (6.7%)	0.326
Mid Zone airspace shadow (n = 46)	22/46 (47.8%)	11/31 (35.5%)	11/15 (73.3%)	0.027
Lower Zone airspace shadow (n = 46)	34/46 (73.4%)	22/31 (71.0%)	12/15 (80.0%)	0.723
Pleural effusion (n = 46)	4/46 (8.7%)	2/31 (6.5%)	2/15 (13.3%)	0.587
R pleural effusion (n = 46)	2/46 (4.3%)	1/31 (3.2%)	1/15 (0.67%)	1.00
L pleural effusion (n = 46)	2/46 (4.3%)	1/31 (3.2%)	1/15 (0.67%)	1.00
Wong score (n = 46)	2 (0–6)	1.5 (0–4)	3.0 (0–6)	0.007

Table 5. Laboratory variables at presentation.

	All (n = 50)	Survivors (n = 33)	Non-survivors (n = 13)	P-value
White cell count (n = 46) (10^9/L)	7.5 ± 4.9	6.9 ± 5.66	7.9 ± 3.38	0.508
Neutrophils (n = 46) (10^9/L)	5.8 ± 4.46	5.8 ± 4.934	6.3 ± 3.52	0.575
Lymphocytes (n = 46) (10^9/L)	0.9 ± 0.71	1 ± 0.78	0.8 ± 0.54	0.14
Neutrophil:Lymphocyte (n = 46)	6.9 ± 8.8	6.1 ± 5.1	8.5 ± 12.7	0.305
C-reactive Protein (n = 46) (mg/L)	67.5 ± 102.7	79.0 ± 79.41	54.0 ± 113.5	0.542
Albumin (n = 28) (g/L)	41 ± 7.3	42 ± 3.5	39 ± 5.8	0.028

In 18 patients who had serial chest radiographs, 12 (80%) patients had a lowest lymphocyte count within 48 hours of the highest Wong score. In 10 (66%) patients, the lowest lymphocyte count was within 24 hours of the peak Wong score. Highest neutrophil-to-lymphocyte ratio (NLR) also occurred within 48 hours of the most severe Wong score in 10 (66%).

4. Discussion

In summary, this was a retrospective study which identified chest radiography as potentially correlated to patient outcome in a small consecutive series of patients from the early phase of the Covid 19 pandemic.

Largely, our findings are in keeping with reports from other countries and preliminary data from the UK. This includes the profile of comorbidities and the prodromic features of Covid-19 patients [10]. Our data confirmed importance of age, but we did not observe significant difference in BMI or gender.

In keeping with published data, patients with COVID-19 infection requiring hospital admission appeared to have high prevalence of hypertension and diabetes in our cohort. The prevalence of preexisting respiratory conditions was not particularly high; however, a non-significant rise in the number of COPD patients affected by COVID-19 was noted (12.5%) in comparison to recently published data (2%) [11].

Simple and broadly available radiographic assessment at presentation indicated that the presence of mid-zone airspace shadowing was more prevalent in non-survivors than survivors (73.3% vs. 35.5%). This is likely to reflect both the variation in the severity of pulmonary infection between individuals and different phase of disease progression given those patients present at different times of their infection.

In 18 patients, who had prolonged admission and underwent serial chest radiographs, we have noticed that increase in 'Wong' score was associated with profound lymphopenia and high NLR (neutrophil-lymphocyte ratio). Previous studies have indicated that lymphopenia may predict disease severity in COVID-19 infection [12]. In a more recent study, COVID-19 patients were seen to have CD8+ cell aberrant activation and dysregulation which may be implicated in its pathogenesis, although the true mechanism for lymphopenia in these patients remains elusive [13].

Our study provides insight into the background of Covid-19 patients and clinical presentation of these patients at a district general hospital in the United Kingdom. This was a pragmatic design and is a reflection of the multiteam approach and adaptive nature of combining frontline work as Covid-19 response with research and audit activities.

The role of cost-effective imaging modalities is likely to play an important part in resource-limited settings. We believe this data provides some insight into the importance of non-CT imaging in the context of a global pandemic. Other forms of non-CT imaging, such as pulmonary/cardiac ultrasound have also been suggested to have been used in a similar vein [14].

5. Conclusion

In conclusion,this was a retrospective, descriptive study on the baseline characteristics and clinical course of the first 50 patients who were admitted to a single center in the United Kingdom with Covid-19.

All inferences from our data should firmly be placed within the context of its small sample size and these findings should be viewed as preliminary, which is a key limitation of this work. One of the main obstacles for in-depth study of such correlations was that there were fewer chest radiographs on the individual patients in comparison to the number of serial (almost daily) blood tests they underwent. However, this reflects the usual clinical care that most clinicians would adopt in these circumstances and is likely to differ from studies undertaken for purely research purposes.

Our investigation suggests the presence of mid-zone shadowing on chest radiographs is an effective tool in identifying patients most at risk of poor outcomes; therefore, it may be a useful tool in triaging patients presenting with Covid-19. These findings will be particularly useful in regions with limited resources. As the global burden of infection shifts from industrialized to developing nations, the availability of resources in patients' work-up will inevitably be limited. Low-cost diagnostic tools, such as chest radiographs, are widely available and can back up confident management plan in any health-care setting. This work will therefore be of direct importance and relevance to health-care professionals working within these contexts.

Author contributions

Max Berrill: Conceptualization, methodology, investigation, project administration, curation, supervision, writing – original draft, writing – review. Jola Karaj: conceptualization, investigation, writing – review. Georgiana Zamfir: conceptualization, investigation, writing – review. Jordan Coleman: investigation. Felicity Saltissi: investigation, conceptualization, writing – review. Rachel Mason: investigation. Saeed Akbar: investigation. Frances Sheehan – conceptualization, investigation, writing – review. Kanchan Dhamija: conceptualization, investigation, writing – review. Aigul Baltabaeva: conceptualization, methodology, investigation, writing – review. Sujoy Saikia: conceptualization, methodology, project administration, supervision

Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

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