Original Article

Development of a preoperative Early Warning Scoring System to identify highly suspect COVID-19 patients

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Abstract

Background and Aims: The coronavirus disease 2019 (COVID-19) is spreading at an unprecedented speed. Lack of resources to test every patient scheduled for surgery and false negative test results contribute to considerable stress to anesthesiologists, along with health risks to both caregivers and other patients. The study aimed to develop an early warning screening tool to rapidly detect 'highly suspect' among the patients scheduled for surgery.

Methods: Review of literature was conducted using terms 'coronavirus' OR 'nCoV 2019' OR 'SARS-CoV-2' OR 'COVID-19' AND 'clinical characteristics' in PUBMED and MedRxiv. Suitable articles were analysed for symptoms and investigations commonly found in COVID-19 patients. Additionally, COVID-19 patient's symptomatology and investigation profiles were obtained through a survey from 20 COVID-19 facilities in India. Based on literature evidence and the survey information, an Early Warning Scoring System was developed.

Results: Literature search yielded 3737 publications, of which 195 were considered relevant. Of these 195 studies, those already included in the meta-analyses were not considered for independent assessment. Based on the combined data from meta-analyses and survey, risk factors of COVID-19 disease identified were as follows: history of exposure, fever, cough, myalgias, lymphocytopaenia, elevated C-reactive protein (CRP)/lactate dehydrogenase (LDH) and radiographic infiltrates.

Conclusion: Development of this Early Warning Scoring System for preoperative screening of patients may help in identifying 'highly suspect' COVID-19 patients, alerting the physician and other healthcare workers on the need for adequate personal protection and also to implement necessary measures to prevent cross infection and contamination during the perioperative period.

Keywords: Coronavirus, cough, COVID-19, humans, India, myalgia, prevalence, risk factors

Introduction

The coronavirus disease 2019 (COVID-19) caused by the Severe Acute Respiratory Syndrome novel Corona Virus 2 (SARS-nCoV-2) is spreading across the world at an unprecedented speed. The disease is increasingly reported in India based mainly on active surveillance and self-reporting whereas countries such as Italy, United Kingdom (UK) and United States of America (USA) are in the community transmission phase of the disease. The disease is contagious,

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spreads through droplets, airborne transmission and fomites. The virus can survive on a variety of surfaces for prolonged durations. Human-to-human transmission occurs not only in close personal contacts but also among the larger community.

Many asymptomatic COVID-19 patients and those with mild symptoms may potentially spread the disease.[1] Therefore, unless everyone scheduled for surgery is tested for COVID-19 disease, the risk of inadvertent transfer of infection to healthcare workers (HCW), patients and their attenders remains high. Currently, the diagnosis is dependent on quantitative Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) of respiratory secretions to detect the SARS-nCoV-2 nucleic acid.[2] The Indian Council of Medical Research (ICMR) for COVID-19 advocates testing of all symptomatic individuals and asymptomatic direct and high-risk contacts of a confirmed case between day 5 and day 10 of coming into contact.[3] Though the MOHFW has put in case definitions for suspect, probable and confirmed cases[4] however, at the time of submission of this manuscript, ICMR does not recommend routine preoperative COVID-19 testing in all patients scheduled for surgery. The results of RT-PCR are influenced by faulty collection techniques, a low viral load in the window period and low sensitivity of RT-PCR (59–71%).[5] The time lag between sample collection and obtaining the results (minimum 2–4 h) limits the use of routine preoperative COVID-19 testing in patients scheduled for emergent procedures. Insufficient test kits make it difficult to screen all the patients. However, operating an undetected COVID-19 patient risks HCWs contracting the disease, subsequent loss of manpower and closure of the healthcare facility. Pooled sampling by RT-PCR may help to identify such patients in the preoperative period.

Though Chest Computed Tomography (CCT) is more sensitive than RT-PCR, it may generate false positives in cases of non-COVID-19 pneumonia.[6] Moreover, routine CCT is economically not feasible and risky as this involves movement of the suspected patient across several corridors to the radiology suite. Treating every patient as possible COVID-19 is also not economically feasible. A high index of suspicion based on history, clinical evaluation and available investigations appears to be the only way to minimise transmission from undetected COVID-19 patients.

The aim was to develop a multi-parametric screening tool for rapid preoperative identification of 'highly suspect' COVID-19 patients. In view of recent ICMR guidelines, this screening tool is also expected to contribute to better triaging of such patients and help in rational use of Personal Protective Equipment (PPE).

Methods

Ten countries (Belgium, China, France, Germany, Iran, Italy, Spain, Turkey, UK, USA) with high prevalence of COVID-19 were identified using the data from 'covidworldometers'.[7] A search (until 26th April 2020) was made in PubMed and MedRxiv, to identify studies reporting COVID-19 characteristics from these countries with the focus on clinical symptoms, signs, laboratory and imaging results.

The following terms 'Coronavirus' or 'nCoV 2019' or 'SARS-CoV-2' or 'COVID-19' and 'Clinical Characteristics' were used for the literature search. From the manuscripts accessed, those related to (a) epidemiological aspects of the disease (b) presenting features (c) laboratory and radiographic findings and (d) the presence of any underlying chronic health conditions were included for data extraction and analysis. The studies considered for the development of this EWSS included meta-analyses, systematic reviews, observational studies and case series. The narrative reviews, case reports and editorials were excluded. To maintain heterogeneity of the clinical spectrum and reduce the regional bias, an attempt was made to include the characteristic presenting features from studies covering all the global regions. Due to lack of published data from India, a survey was conducted to collect such information about the Indian COVID-19 patients from the physicians working at 20 COVID-19 facilities in India.

The development of Early Warning Scoring System (EWSS) was based on the analysis of the collected evidence from literature and survey findings. A plan was made to study the epidemiological characteristics, clinical features and investigations of patients with COVID-19 disease. It was decided that the presence of these characteristics with a higher prevalence in multiple studies will be given higher scores, and those with lower prevalence in fewer studies will be given lower scores.

As part of the methodology, the data from meta-analyses from China and systematic reviews, case series published from non-Chinese COVID-19 patients were analysed. The symptoms and the investigations so analysed, were subcategorised into major and minor criteria, based on the prevalence rates reported in the meta-analyses and survey findings. It was planned that a maximum score of 5 will be assigned to each of the main clinical characteristics of COVID-19 disease in the EWSS. Domestic travel to areas of high COVID-19 prevalence within India and HCW attending to COVID-19 patients/suspects would be assigned 5 points if such exposure history was present within past 14 days. Secondary contacts and COVID-19 RT-PCR tested negative patients would be assigned 3 points if such history was obtained within 14 days.

If a symptom or an investigation was reported by 2 meta-analyses with a prevalence of >40%, it was considered a major

criterion (2 points for each major criterion). When the reported prevalence was less than this, it was considered a minor criterion (1 point for each minor criterion). The survey data complimented the major criteria if the symptom or investigation was reported by more than 10 centres with prevalence from 25% to 100%. Based on the data from meta-analyses and survey findings, 5 points were assigned for the presence of strongly suggestive features on imaging [chest radiograph (CXR) or CCT] since the reported prevalence was >40% from at least 2 meta-analyses. A ceiling on the score to a maximum of 5 was put to each essential characteristics for the purpose of preparing this scoring system.

Since male gender,[8-12] age >60 years,[12] and presence of co-morbidities[13-16] (hypertension, diabetes mellitus, ischaemic heart disease, chronic obstructive pulmonary disease, bronchial asthma, heart failure, obesity, hypercholesterolemia, and malignancy) have been found to increase susceptibility for acquiring COVID-19, 1 point was assigned for the presence of each of these associated risk factors subject to a maximum score of 2. A lesser score was assigned as these factors increased the predisposition but were not essential characteristics.

The scoring was designed with the understanding that higher the number of essential characteristics, larger the suspicion for COVID-19. Therefore, a score of up to 10 signifies the presence of one or two essential characteristics, hence, low suspicion. A score of 11–15 signifies the presence of at least three essential characteristics or two essential characteristics along with associated risk factors, hence, high suspicion. A score of 16 or greater signifies the presence of all 4 essential characteristics or at least 3 essential characteristics along with associated risk factors, hence, very high suspicion.

Results

Literature search yielded 3737 publications, of which 195 studies were considered relevant. Of these 195 studies, those included in the meta-analyses were not considered for independent assessment. Most of the systematic reviews and meta-analyses were from China or included studies [Tables 1 and 2] related to Chinese population.[8-13] Limited data were available from non-Chinese population [Table 3].[14-20] There was only one study from India as on 20th May 2020.[21]

These revealed that the COVID-19 manifestations involve four essential characteristics (a) history of exposure to a known COVID-19 source, (b) clinical spectrum of symptoms and signs (c) derangement in investigations and (d) chest infiltrates on imaging in moderate to severe disease. The evidence from these meta-analyses[8-12] and the survey findings suggests that all four characteristics have a high correlation index for the development of the disease. Hence, a maximum score of 5 was assigned to each of these characteristics in the EWSS.

The data from Chinese population [Table 1] revealed the following: Two meta-analyses found that 5.6–11.9% of the patients were asymptomatic at the time of testing.[10,13] Fever, cough and myalgia were the most common manifestations in mild to moderate disease.[9,10.12,13] Dyspnea[11,12] was the only symptom associated with both severe disease [pooled odd ratio (pOR) 3.70, 95%; Confidence Interval (CI) 1.83 –7.46] and ICU admission (pOR 6.55, 95% CI 4.28– 10.0).[22] Less common manifestations included expectoration, fatigue, diarrhoea, headache, hemoptysis, sore throat, anorexia, chest tightness/chest pain, dizziness, rhinorrhoea, nausea, vomiting, nasal congestion, pharyngalgia, shivering/chills and abdominal pain.[9-13]

Studies from non-Chinese origin showed that fever, cough, fatigue, dyspnoea/shortness of breath were the major clinical manifestations.[14-20] Presence of pharyngodynia (12.4%), nasal congestion (3.7%) and rhinorrhoea (4%) in confirmed COVID-19 patients was found in one systematic review published from.[17] A total of nine patients (five of Chinese origin) from Bolivia[19] who had travelled to France presented with predominant symptoms of cough and fever. Of the 28 hospitalised COVID-19 patients, prevalence of cough and sore throat was 28.6% each, fever, myalgia, headache (25% each).[18] Diarrhoea was an infrequent symptom (10.7%).[18] In a study from New York, the commonest presenting symptoms of COVID-19 patients were found to be cough (79.4%), fever (77.1%), dyspnoea (56.5%), myalgia (23.8%), diarrhoea (23.7%), nausea and vomiting (19.1).[14] A case series from Seattle reported shortness of breath with cough (88%) followed by fever as main clinical presentations.[15] Based on anecdotal evidence gathered from around the world Ministry of Health and Family Welfare, Government of India and American academy of otolaryngology-head and neck surgery proposed anosmia, dysgeusia and ageusia to be added to the list of screening tools for COVID-19 infection.[4,17,23]

The information from the Survey conducted in India obtained from the participating physicians working in 20 COVID-19 facilities (1 primary, 7 secondary, 12 tertiary), with a cumulative experience of managing 2716 COVID-19 patients revealed the following: predominantly observed clinical symptoms (>25% patients at a COVID-19 facility) were fever (14 facilities), cough (16 facilities), myalgia (11 facility) and dyspnoea (6 facilities). Other manifestations were expectoration, dyspnoea, chills/shivering, chest pain/chest tightness, hemoptysis, nasal congestion/rhinorrhoea,

sore throat, headache/dizziness, diarrhoea, nausea/vomiting, abdominal pain, anorexia and pharyngalgia. Eleven out of 20 facilities noted dyspnoea in only severe diseases. Of 2716 COVID-19 patients, 158 were admitted to ICU and 45 underwent surgery. Many contacts of these COVID-19 positive patients were completely asymptomatic and did not realise they were infected with SARS-nCoV-2.

The data of laboratory investigations [Table 2] involving Chinese population from six meta-analyses[7-12] showed lymphocytopenia (43.1–64.5%), elevated Erythrocyte Sedimentation Rate [(ESR), 41.8–65.6%] and deranged acute phase reactants in COVID-19 disease CRP (44.3–73.6%) and LDH (28.3–57.0%). Lymphocytosis, leucocytosis/leukocytopenia, neutrophilia/neutropenia, thrombocytopenia, elevated D-dimer levels, increased serum bilirubin/alanine transferase/aspartate transferase, increased serum creatinine, elevated procalcitonin, high troponin I and elevated serum ferritin were reported less frequently.[8-13] A systematic review of 27 studies comprising of 656 patients reported decreased albumin levels in 75.8% of COVID-19 positive patients. (95% CI 30.5–100.0%).[12]

Study from USA reported lymphocytopenia in 18 out of 24 patients (75%)[14] and from Korea reported increased CRP in 11/27 (40.7%) patients and increased LDH in 11/26 (42.3) patients.[18]

From the survey conducted in India, the predominant laboratory derangements (>25% patients at a COVID-19 facility) were lymphocytopenia (14 facilities), elevated CRP (10 facilities) and elevated LDH (10 facilities). Other laboratory derangements such as lymphocytosis, leucocytosis/leukocytopenia, neutrophilia/neutropenia, thrombocytopenia, elevated erythrocyte sedimentation rate, elevated D-dimer levels, increased serum bilirubin/alanine transferase/aspartate transferase, hypoalbuminemia, increased serum creatinine, elevated procalcitonin, increased creatinine kinase were reported to have a lower prevalence.

The prevalence of bilateral pneumonia on CXR was 72.9%[12] while CCT showed unilateral or bilateral pneumonia with a prevalence of 72.9–92.6%.[8,10,13]The CCT was highly sensitive in diagnosing pneumonia.[5,6] The common patterns on CCT were ground glass opacity, bilateral patchy shadowing or multiple lobular and subsegmental areas of consolidation.[6] Meta-analyses [Table 2] reported abnormal CCT prevalence ranging from 75.7–96.6% in COVID-19 patients.[8,10,13] In studies involving non-Chinese population, a comparable prevalence of bilateral pneumonia ranging from 50 to 75.7% was observed with CCT.[17,18] Evidence of pneumonia on CCT was observed in most admitted patients (78.6%) though only 27.3% of them required oxygen supplementation and most of them were able to carry out their routine activities ('walking pneumonia').[18] A high incidence of infiltrates (75.3% and 96%, respectively) and ground glass opacities (21%) was observed in patients at admission to ICU.[14,15] It was observed that nearly all (95.9%) patients with COVID-19 had signs of pneumonia on CCT while only 26.4% patients in the non-COVID-19 group had such abnormalities on CCT.[24] Predominant ground glass opacities mixed with consolidations (with both peripheral and central distributions) on CCT were reported with a C-index of 0.9 in COVID-19 pneumonia.[22] Chest infiltrates were the predominant radiological findings (>25% patients at a COVID-19 facility) in 13 facilities in the survey.

Various meta-analyses[9,10,12,17]and case series[14-16]have reported a higher prevalence in male gender ranging from 55.9 to 82%. The age at presentation to hospital ranging from 36 to 57 years,[9,13.17] with median age at presentation to ICU and non-ICU to be 62.4 and 46.0 years, respectively.[11] Median/mean age of patients admitted to ICU as per the data from Italy, Korea, New York and Seattle was 63,40, 62.2, 64 ± 18 years, respectively.[14-16,18] Higher morbidity and oxygen requirement was observed in older patients.[16] Significant number (36.8%) of hospitalised patients had comorbidities.[12] Hypertension,[12,14,17] diabetes mellitus,[12,15,17] coronary artery disease,[14,17] chronic obstructive pulmonary disease (COPD),[17] bronchial asthma,[14,15] chronic kidney disease,[15,16] chronic liver disease,[16] hypercholesterolaemia,[16] obesity[14] and malignancy[16] were predictive of increased risk and severity of the disease.

Survey results showed that male gender constituted >25% of patients in 17 facilities, age ≥60 years and other comorbidities (HT, diabetes mellitus, ischaemic heart disease, chronic obstructive pulmonary disease, bronchial asthma, heart failure, kidney or liver diseases, hypercholesterolaemia, obesity, and malignancy, immunocompromising conditions) were observed in 10 facilities each.

Discussion

Considering the magnitude, virulence and spread of the disease, it was decided to develop a reliable and inexpensive screening tool (EWSS) based on the current evidence.

Exposure to a known COVID-19 source is essential for the development of the disease. The median incubation period is estimated to be 5 days with a range of 2–14 days. Hence, exposure history specifically includes past 14 days in the EWSS.[25] Though WHO[26] and ICMR advocate PCR testing of all primary contacts of a COVID-19 patient, it is possible that domestic travellers to high prevalence areas within India and HCWs in contact with suspect/positive COVID-19 patients can be infected with SARS-nCoV-2. This population has a higher chance of acquiring COVID-19 due to high R_0 factor.[27] Hence, such exposure

Table 1: Symptomatology of COVID-19 disease

Author Country Study Type Journal	Sun *et al.*[8] China Meta-analysis J Med Virol	Li *et al.*[9] China Meta-analysis J Med Virol.	Zhu *et al.*[10] China Meta-analysis J Med Virol.	Jain *et al.*[11] UK Meta-analysis MedRxiv	Morales *et al.*[12] USA Meta-analysis Travel Med Infect Dis.	Fu *et al.*[13] China Meta-analysis J Infect.
Study period	February 20, 2020	December 2019 to February 2020	1st January 2020 to 28 February 2020	December 2019 to 5th March 2020	1st January 2020 to 23rd February 2020	24th January 2020 to 28th February 2020
Number of patients	50466	1994	3062	1813	2874	3600
Number of studies included	10	10	30	7	19	43
Mean Age in years (95% CI)	NA	NA	NA	NA	51.97 (95% CI 46.06-57.89)	NA
Males % (95% CI)	NA	60	56.9	ICU 67.2 Non ICU 57.1	Male 55.9% (51.6-60.1%)	NA
Fever % (95% CI)	89.1 (0.818-0.945)	88.5	80.4 (73.0%-86.9)	ICU 62.9 Non ICU 49.7	Total 88.7 (84.5-92.9) Adult 92.8 (89.4-96.2) Children 43.9 (28.2-59.6)	83.3 (78.4-87.7)
Cough % (95% CI)	72.2 (0.657-0.782)	68.6	63.1 (57.9-68.2)	ICU 67.2 Non ICU 67.1	57.6 (40.8-74.4) Adult 63.4 (48.0-78.8) Children 22.0 (0.0-52.9)	60.3 (54.5-66.3)
Muscle soreness/fatigue % (95% CI)	42.5 (0.213-0.652).	35.8 Myalgia and fatigue combined	Fatigue 46 (38.2-54) Muscle soreness 33 (26.0-40.5)		29.4 (19.8-39.0)	Fatigue 38.0 (29.8-46.5) Mylagia 28.5 (21.2-36.2)
Dyspnoea % (95% CI)	NA	21.9	33.9 (24.2-44.3)	ICU 61.2 Non ICU 10.2	45.6 (10.9-80.4)	24.9 (16.6-34.4)
Expectoration % (95% CI)	NA	28.2	41.89 (33.9-50)	ICU 28.4 Non ICU 33.1	28.5 (10.8-46.3)	26.9 (18.3-36.4)
Chills	NA	NA	NA	NA	NA	15.0 (0.3-41.4)
Chest pain % (95% CI)	NA	NA	28.3 (1.0-72.9)	NA	NA	14.9 (4.9-28.4)
Chest tightness % (95% CI)	NA	NA	35.7 (23.2-49,3)	NA	NA	NA
Hemoptysis % (95% CI)	NA	NA	NA	NA	NA	2.0 (0.0-11.4)
Sore throat % (95% CI)	NA	NA	NA	NA	11.0 (2.8-19.2)	12.3 (8.5-16.5)
Nasal congestion % (95% CI)	NA	NA	33	NA	NA	1.8 (0.4-3.9)
Headache or dizziness % (95% CI)	NA	12.1%	15.4 (11.6-19.6)	ICU 9.5 Non ICU 13.0	8.0 (5.7-10.2)	14.0 (9.9-18.6)
Dizziness % (95% CI)	NA	NA	NA	NA	NA	7.6 (0.0-23.5)
Diarrhoea % (95% CI)	NA	4.8	12.9 (89.9-17.4)	ICU 8.6 Non-ICU 4.0	6.1 (2.4-9.7)	8.4 (4.8-12.6)
Nausea and vomiting % (95% CI)	NA	3.9	10.2 (5.4-16.3)	NA	NA	3.6 (1.0-7.4)
Abdominal pain % (95% CI)	NA	NA	4.4 (2.5-6.9)	NA	NA	NA
Anorexia % (95% CI)	NA	NA	38.8 (14,1-67.1)	NA	NA	NA
Rhinorrhea % (95% CI)	NA	NA	NA	NA	NA	3.5 (0.5-7.4)
Pharyngalgia% (95% CI)	NA	NA	13.1 (7.4-20.3)	NA	NA	NA
Shivering % (95% CI)	NA	NA	10.9 (5.8-17.4)	NA	NA	NA
No obvious symptoms % (95% CI)	NA	NA	11.9 (2.9-25.8)	NA	NA	5.6 (1.4-11.6)

NA=Not available; ICU=Intensive Care Units

history was assigned 5 points. Secondary contacts and COVID-19 RT-PCR tested negative patients (possible false negative results) may have contracted SARS-nCoV-2 but the relative probability is less. Hence such history was assigned 3 points.

Angiotensin converting enzyme-2 (ACE-2), identified as a functional receptor for SARS-nCoV-2 is expressed in nasal mucosa, bronchus, lung, oesophagus, stomach, intestine, heart, kidney and urinary bladder making these organs vulnerable to SARS-nCoV-2. Primary viral replication occurs in mucosal epithelium of nasal

Table 2: Laboratory Investigations and Imaging Findings of COVID-19 patients

Author Country Study Type Journal	Sun *et al.*[8] China meta-analysis J Med Virol	Li *et al.*[9] China meta-analysis J Med Virol.	Zhu *et al.*[10] China meta-analysis J Med Virol.	Jain *et al.*[11] UK meta-analysis MedRxiv	Morales *et al.*[12] USA meta-analysis Travel Med Infect Dis.	Fu*et al.*[13]China meta-analysis J Infect.
Study period	February 20, 2020	December 2019 to February 2020	1st January 2020-28 February 2020	December 2019-5th March 2020	1st January 2020-23rd February 2020	24th January 2020-28th February 2020
Number of patients	50.466	1994	3062	1813	2874	3600
Number of studies included	10	10	30	7	19	43
Lymphocytopenia % (95% CI)	NA	(64.5%)	56.5 (46.5-66.4)		43.1 (18.9-67.3)	57.4 (44.8-69.5)
Lymphocytosis	NA	NA	NA	NA		8.2 (0.5-21.1)
Leucocytosis % (95% CI)			12.6 (8.4-17.4)		16.8 (5.5-28.0)	9.8 (5.1-15.5)
Leukocytopenia % (95% CI)		(29.4%)	69.7 normal (62.8-76.2)		18.7 (8.5-28.8)	20.1 (15.5-27.2)
Neutrophilia % (95% CI)	NA	NA	NA	NA	NA	25.9 (18.6-33.9)
Neutropenia % (95% CI)	NA	NA	NA	NA	NA	3.6 (0.0-12.5)
Thrombocytopenia % (95% CI)	NA	NA	NA	NA	NA	11.4 (5.5-18.7)
Hypoalbuminemia %	NA	NA	NA	NA	75.8 (30.5-100.0)	NA
Abnormal liver function % (95% CI)	NA	NA	29.0 (17.5-42.1)	NA	10.7 (0.0-25.1)	NA
Abnormal renal function % (95% CI)	NA	NA	25.5 (5.6-53.5)	NA	4.5 (1.0-8.0)	NA
Increased serum bilirubin % (95% CI)	NA	NA	NA	NA	NA	14.3 (3.1-30.5)
Increased alanine transferase % (95% CI)	NA	NA	NA	NA	24.1 (13.5-34.6)	14.2 (4.6-27.1)
Increased aspartate transferase % (95% CI)	NA	NA	NA	NA	33.3 (26.3-40.4)	18.6 (8.5-31.1)
Increased serum creatinine % (95% CI)	NA	NA	NA	NA		3.1 (0.0-18.0)
Increased creatinine kinase % (95% CI)	NA	NA	NA	NA	21.3 (3.2-39.4)	10.8 (3.1-21.5)
Increase of lactic dehydrogenase	NA	28.3%	NA	NA	57.0 (38.0-76.0)	51.6 (31.4-71.7)
Elevated D–dimer% (95% CI)	NA	NA	37.2 (17.7-59.1)	NA	NA	29.3 (4.8-61.6)
Elevated ESR % (95% CI)	NA	NA	65.6 (36.8-89.3)	NA	41.8 (0.0-92.8)	NA
Elevated C–reactive protein % (95% CI)	NA	44.3%	73.6 (66.1-80.4)	NA	58.3 (21.8-94.7)	68.6 (58.2-78.2)
High procalcitonin % (95% CI)	NA	NA	17.5 (7.8-29.9)	NA	NA	NA
Abnormal CXR/CCT % (95% CI)	Abnormal CCT	NA	Abnormal CCT	NA	Abnormal CXR	Abnormal CCT
Unilateral pneumonia % (95% CI)	NA	NA	25.8 (15.6-37.4)	NA	25.0 (5.2-44.8)	25.3 (11.8-41.4)
Bilateral pneumonia % (95% CI)	96.6% (0.921, 0.993)	NA	75.7 (65.7-84.5)	NA	72.9 (58.6-87.1)	25.3 (11.8-41.4)
Ground glass opacity % (95% CI)	NA	NA	NA	NA	68.5 (51.8-85.2)	80.0 (67.3-90.4)
Fibrous stripes % (95% CI)	NA	NA	NA	NA	NA	25.9 (2.9-59.8)
Solid nodules % (95% CI)	NA	NA	NA	NA	NA	20.7 (5.7-41.1)
≤3 affected lobes % (95% CI)	NA	NA	NA	NA	NA	38.9 (25.3-53.4)
>3 affected lobes % (95% CI)	NA	NA	NA	NA	NA	57.3 (42.6-71.4)
Normal imaging % (95% CI)	NA	NA	NA	NA	NA	27.3 (0.0-76.8)

NA=Not available; ESR=Erythrocyte Sedimentation Rate; CXR=Chest X-ray; CCT=Chest Computer Tomogram

cavity with further multiplication in lower respiratory tract mucosa, giving rise to features of mild viremia (80.9%); manifesting as cough, fever and myalgia.[28] Hence, these were included as major criteria in the EWSS [Table 4]. Mild viremia may also manifest in other ways which are included as minor criteria. Dyspnea and hypoxemia are major manifestation of severe COVID-19 due to development of pneumonia.[11,12] They are mainly seen in severely sick patients who need admission to intensive care unit.[11,12] They were excluded from EWSS as primary aim was to identify highly suspect COVID-19 patients who don't present with symptomatic influenza like illness (ILI) or Severe Acute Respiratory Infection (SARI).

The data compiled from Integrated Health Information Platform (IHIP)/Integrated Disease Surveillance Programme (IDSP) portal case investigation forms, from 15,366 COVID-19 patients reported fever (27%) and cough (21%) as the major presenting symptoms.[4]

Reduced lymphocyte count, elevated CRP or LDH[8-16,28] were frequently observed in COVID-19 patients and hence were considered major criteria in the EWSS. Non-specific markers [Table 2] may result from either cytokine storm in response to the infection or multi-organ involvement by the virus and hence were considered minor criteria.[8-16,28]

Table 3: Symptomatology, Laboratory Investigations and Imaging Findings of COVID-19 patients from non-Chinese populations

Author Date Country Study	Goyal *et al.*[14] 05th March to 27th March 2020 New York, USA Correspondence	Bhatraju *et al.*[15] 24th February to 09th March 2020 Seattle, USA Correspondence	Grasselli G *et al.*[16], 20th February to 18th March 2020 Lombardy, Italy Observational Study	Kim *et al.*[18] February 2020 Korea Original Article	Escalera-Antezana *et al.*[19] March 2020 Bolivia Original Article	Lescure *et al.*[20] Jan 24 to Jan 29, 2020 France Observational Study	Gupta *et al.*[21] First February 2020 to 19th March 2020. New Delhi, India Observational Study
Number of patients	393	24	1591	28	12	5	21
Age in years	62.2 (48.6-73.7) median (IQR)	64±18 (mean±SD)	63 (56-70) median (IQR)	42.6±13.4	39.0 (IQR 25.3-43)	47 (31-80)	40.3 (16-73)
Number of male patients (%)	238 (60.6)	15 (63)	1304 (82)	15 (53.6%)	6 (50.0%)	3	14 (66.7)
Obesity (%)	136/380 (35.8)	NA	NA	5 (17.9)	NA	NA	NA
Diabetes Mellitus	99 (25.2)	14 (58%)	180 (17)	2 (7.1)	NA	NA	14.2
Hypertension	197 (50.1)	NA	509 (49)	0	1	1	23.8
Cardiovascular disease (includes cardiomyopathy and heart failure)	NA	NA	223 (21)	0	NA	NA	NA
Coronary artery disease	54 (13.7)	NA	NA	0	NA	NA	NA
Hypercholesterolemia	NA	NA	188 (18)	0	NA	NA	NA
Chronic obstructive pulmonary disease	20 (5.1)	1 (4%)	42 (4)	0	NA	NA	NA
Chronic kidney disease	NA	5 (21%)	36 (3)	0	NA	NA	NA
Chronic liver disease	NA	NA	28 (3)	1 (3.6)	NA	NA	NA
Bronchial asthma	49 (12.5)	3 (14%)	NA	1 (3.6)	NA	NA	NA
Ischaemic stroke	NA	2 (8%)	NA	NA	NA	NA	NA
Obstructive sleep apnea	NA	5 (21%)	NA	NA	NA	NA	4.7%
Human immunodeficiency virus	NA	1 (4%)	NA	0	NA	NA	NA
Malignancy (includes active neoplasia and neoplasia in remission)	NA	NA	81 (8)	1 (3.6)	NA	NA	NA
Fever (%)	77.1	12 (50%)	NA	7 (25.0)	9	3	42.9%
Cough (%)	79.4	21 (88%)	NA	8 (28.6)	9	4	42.9%
Malaise/Myalgia	NA	NA	NA	NA	4	NA	NA
Expectoration (%)	NA	10 (42%)	NA	6 (21.4)		NA	NA
dyspnea (%)	56.5	21 (88%)	NA	1 (3.6)	1	1	4.8%
Chills (95% CI)	NA	NA	NA	NA	NA	NA	NA
Chest pain (95% CI)	NA	NA	NA	NA	NA	NA	NA
Hemoptysis (95% CI)	NA	NA	NA	NA	NA	NA	NA
Sore throat (%)	NA	2 (8%)	NA	8 (28.6)	5	NA	23.8
Nasal congestion (95% CI)	NA	NA	NA	NA	NA	NA	NA
Myalgias %	23.8	NA	NA	7 (25.0)	5	NA	NA
headache (%)	NA	2 (8%)	NA	7 (25.0)	NA	NA	13.6%
Dizziness % (95% CI)	NA	NA	NA	NA	NA	NA	NA
Diarrhoea % (%)	23.7	NA	NA	3 (10.7)	2	1	NA

Contd...

Table 3: Contd...

Author Date Country Study	Goyal *et al.*[14] 05th March to 27th March 2020 New York, USA Correspondence	Bhatraju *et al.*[15] 24th February to 09th March 2020 Seattle, USA Correspondence	Grasselli G *et al.*[16], 20th February to 18th March 2020 Lombardy, Italy Observational Study	Kim *et al.*[18] February 2020 Korea Original Article	Escalera-Antezana *et al.*[19] March 2020 Bolivia Original Article	Lescure *et al.*[20] Jan 24 to Jan 29, 2020 France Observational Study	Gupta *et al.*[21] First February 2020 to 19th March 2020. New Delhi, India Observational Study
nausea and vomiting (%)	19.1	NA	NA	NA	1	NA	NA
Abdominal pain % (95% CI)	NA	NA	NA	1 (3.6)	2	NA	NA
Anorexia % (95% CI)	NA	NA	NA	NA	NA	NA	NA
Rhinorrhea (%)	NA	4 (17%)	NA	2 (7.1)	NA	NA	NA
Pharyngalgia % (95% CI)	NA	NA	NA	NA	NA	NA	NA
shivering % (95% CI)	NA	NA	NA	NA	NA	NA	NA
No obvious symptoms % (95% CI)	NA	NA	NA	NA	NA	NA	NA
Lymphopenia (%)	90.0	1 (4%)	NA	7 (25.0)	NA	3/4	NA
Increased CRP	NA	NA	NA	11/27 (40.7)	NA	1	NA
Increased LDH	NA	NA	NA	11/26 (42.3)	NA	NA	NA
Thrombocytopenia %	27%	NA	NA	15 (53.6)	NA	0	NA
History of Travel to country where Covid-19 is endemic within previous 3 months	NA	0	NA	NA	5	5	13 (61.9%)
Known sick contact	NA	13 (54)	NA		7		NA
Chest radiography (CXR)	NA	23 (96%)	NA	Unilateral 7 (25.0) Bilateral 6 (21.4)	NA	2	NA
Chest computed tomography (CCT)	NA	5 (21)	NA	Unilateral 8/18 (44.4) Bilateral 8/18 (44.4)	NA	NA	NA

Table 4: COVID-19 SCORE
Preoperative Early Warning Screening Score for COVID-19 patients scheduled for surgery

	Clinical Characteristics	Points
A	**Exposure**	
	1. H/o domestic travel to an area of high prevalence of COVID-19 disease within 14 days OR 2. Healthcare worker dealing with COVID-19 or suspect cases not meeting the current guidelines on mandatory testing, of the Ministry of Health and Family Welfare, GOI, scheduled for surgery.	5 (if answer is yes to any one or multiple questions)
	Secondary contacts of COVID-19 patients during quarantine period	3
	False negative results in suspects within 14 days of RT PCR COVID testing	
B	**Symptoms**	
	Major Criteria: Fever (axillary temperature >100° F or >37.8° C) Cough Myalgia	3 (If 2 or more present)
	Minor Criteria: Expectoration, dyspnoea, chills, chest pain, chest tightness, hemoptysis, nasal congestion, anosmia, dysgeusia, ageusia, sore throat, headache or dizziness, diarrhoea, nausea and vomiting, abdominal pain, anorexia, rhinorrhoea, pharyngalgia, shivering	2 (If 2 or more present)
C	**Laboratory Investigations**	
	Major Criteria: Lymphocytopenia Elevated C-reactive protein Increased lactate dehydrogenase	3 (If 2 or more present)
	Minor Criteria: Neutrophil to lymphocyte ratio (NLR), hypoalbuminemia, lymphocytosis, leucocytosis, leukocytopenia, neutrophilia, neutropenia, thrombocytopenia, elevated erythrocyte sedimentation rate, elevated serum ferritin, elevated troponin I, elevated D-dimer levels, increased serum bilirubin, increased alanine transferase, increased aspartate transferase, increased serum creatinine, elevated procalcitonin, increased creatinine kinase	2 (If 2 or more present)
D	**Imaging**	
	CXR or CT chest suggestive of pneumonia	5
E	**Associated risk factors**	
	Age ≥60 years, male gender, hypertension, diabetes mellitus, ischemic heart disease, chronic obstructive pulmonary disease, bronchial asthma, heart failure, hypercholesterolemia, obesity and malignancy	2 Maximum (1 each for presence of any factor)

Exposure, symptoms, laboratory investigations, imaging are assigned a maximum of 5 points while as associated risk factors receive a maximum of 2 points. Wherever only one symptom/sign or laboratory investigation is present score should be considered as Zero. **Very High risk=16-22; High Risk=11-15; Low Risk=1 to 10**

SARS-nCoV-2 induced lung injuries manifest on CXR/CCT as fibrous stripes, solid nodules and patchy ground-glass opacities.[5,6] The findings were a major component of our EWSS as they were observed with high prevalence even in asymptomatic to severe COVID-19 patients.

Among the possible associated risk factors, the preponderance of SARS-nCoV-2 infection among male population is attributed to their relative lack of innate and adaptive immunity as compared to female gender by X-chromosome and sex hormones.[29] Similarly, age ≥60 years[9-12] and comorbidities[14-16] have been known to decrease the viral clearance, thus increase the host's susceptibility for contracting the virus.[8]

The information from the survey findings from the questionnaires [Table 5] complemented the evidences in classifying the criteria and assignment of scores for EWSS. In allotting the scores, the prevalence of various features (exposure history, major and minor criteria for symptoms and laboratory investigations, radiological evidence and associated risk factors) reported from the COVID-19 facilities [Table 6] were considered.

A multi-parameter screening tool used similar parameters as used in our study but was proposed for outpatient screening for COVID-19.[24] In a previous prediction model, the presence of symptoms, laboratory investigations and characteristic imaging findings correlated with the diagnosis of COVID-19 pneumonia with high predictive performance (C-index 0.81-1).[22] Although the aim of our EWSS was to identify COVID-19 suspects, a similar model aimed to predict the occurrence of critical illness confirmed the presence of increased lactate dehydrogenase, infiltrates on chest imaging and the presence of comorbidities similar to our EWSS.[30]

The advantage of our EWSS over these prediction models[22,24,30] is that it involves the evidences from both the Chinese and non-Chinese population. The information obtained by the survey of the attending physicians of COVID-19 facilities in India, strengthens the applicability

Table 5: Survey questionnaire

1.Type of the hospital:

Primary /secondary / tertiary healthcare centre

2. Is it a declared COVID centre by the central/state government?

Yes	No

3. Number of COVID-19 positive patients so far

4. Number of COVID-19 positive patients in ICU

5. Number of COVID-19 positive patients operated so far

6. COVID-19 patients with history of travel within 14 days to a location where there is transmission of COVID-19 or close contact with a confirmed or suspected case?

≤ 25%,	25 -50%.	51-75%,	76-100%

7. COVID-19 patients with no history of exposure

≤ 25%,	25 -50%.	51-75%,	76-100%

8. Healthcare worker managing a patient with acute respiratory symptom or fever in the last 14 days and admitted with suspected COVID-19 infection

≤ 25%,	25 -50%.	51-75%,	76-100%

9. Common clinical presentation of COVID-19 positive patients (tick the presentations)

a) Fever

≤ 25%,	25 -50%.	51-75%,	76-100%

b) Cough

≤ 25%,	25 -50%.	51-75%,	76-100%

c) Muscle pain

≤ 25%,	25 -50%.	51-75%,	76-100%

d) Dyspnoea

≤ 25%,	25 -50%.	51-75%,	76-100%

e) Was dyspnoea seen in severe disease only

Yes	No

f) Expectoration, chills, chest pain/tightness, haemoptysis, nasal congestion, sore throat, headache/dizziness, diarrhoea, nausea/vomiting, abdominal pain, Anorexia, rhinorrhoea, pharyngalgia, shivering

≤ 25%,	25 -50%.	51-75%,	76-100%

g) Any other presentation

≤ 25%,	25 -50%.	51-75%,	76-100%

Contd...

Table 5: Contd....

10. Laboratory investigations

a) Lymphocytopaenia

≤ 25%,	25 -50%.	51-75%,	76-100%

b) Elevated C-reactive protein

≤ 25%,	25 -50%.	51-75%,	76-100%

c) Elevated lactate dehydrogenase

≤ 25%,	25 -50%.	51-75%,	76-100%

d) Elevated neutrophil to lymphocyte ratio (NLR)

≤ 25%,	25 -50%.	51-75%,	76-100%

e) Hypoalbuminaemia

≤ 25%,	25 -50%.	51-75%,	76-100%

f) Lymphocytosis, leucocytosis/leukocytopaenia, neutrophilia/neutropaenia, thrombocytopaenia, elevations in erythrocyte sedimentation rate / D-dimer levels / serum bilirubin / alanine transferase / aspartate transferase / serum creatinine / procalcitonin / creatinine kinase.

≤ 25%,	25 -50%.	51-75%,	76-100%

11. Imaging: Infiltrates on chest X-ray or CT scan

≤ 25%,	25 -50%.	51-75%,	76-100%

12. Associated conditions:

a) Males

≤ 25%,	25 -50%.	51-75%,	76-100%

b) Age 60 years and above

≤ 25%,	25 -50%	51-75%	76-100%

c) Co-morbidities: Hypertension, diabetes mellitus, chronic obstructive pulmonary disease, bronchial asthma, ischaemic heart disease, heart failure, kidney or liver disease, hypercholesterolaemia, obesity, malignancy, steroid use, cerebrovascular disease, immunocompromising conditions

≤ 25%,	25 -50%.	51-75%,	76-100%

8. Any COVID-19 positive patient presented in critically ill state (septic shock, multi-organ dysfunction or failure, life threatening malignancy, etc)

≤ 25%,	25 -50%.	51-75%,	76-100%

of EWSS in Indian conditions.

This screening tool can complement the results of RT-PCR, enhancing the overall diagnostic sensitivity for COVID-19. The score is expected to be useful until a rapid, reliable point-of-care laboratory test for COVID-19 becomes available for all patients.

Our study has few limitations. Most of the meta-analyses had significant heterogeneity and too many outcomes were studied without sub-group analysis. One of the meta-anaylses included is in preprint stage (MedRxiv) and may undergo changes after peer review.[11] The scoring system developed from the current literature may need to be revised based on further evidences, in future. Some of the studies were included in more than one metaanalysis. This may have led to duplication of some data. An attempt was made to overcome this limitation by considering the data from the systematic trials and case series from non-Chinese COVID-19 patients for 'development of EWSS'. There is a possibility of community transmission of the COVID-19 disease

in future. Hence, the criteria for domestic travel in the scoring system may have to be modified as more evidence emerges. The results from the meta-analysis were analysed mainly for development of EWSS. However, the results of the survey helped to gather information about the clinical characteristic of COVID-19 patients in India, and hence complemented the results from the meta-analysis. However, as the input obtained from our survey was based on the memory recall of the treating physician without precise epidemiological backup at the time of survey it could not be used to devise an EWSS score based on logistic regression analysis. An attempt will be made by the authors to overcome this limitation by a prospective multicentric study in the Indian scenario.

Minor symptoms as dysgeusia and anosmia which may help in early diagnosis were not included in survey questionnaire and may have been missed on reporting by the physicians from the participating COVID-19 facilities.

This is the first of the EWSS, which is proposed in the study and is currently being prospectively validated by a multicentre study (with proper audit from high prevalence COVID-19 facilities in India) and may undergo modifications as new evidences emerge. More details about the clinical characteristics are needed to identify the asymptomatic COVID-19 patients who are presenting for elective or emergency surgical procedures.

Conclusion

A novel easy-to-apply EWSS has been developed based on a combination of exposure risk, symptomatology, laboratory parameters, imaging characteristics and associated risk factors. As a preoperative screening tool, EWSS can help in identifying 'high suspect' COVID-19 patients. This will allow the healthcare workers to take adequate personal protection and also implement necessary measures to prevent

Table 6: Survey data of common clinical presentation of COVID-19 patients

	<25	25-50	51-75	76-100	Unable to comment
Exposure					
History of travel within 14 days to a location where there is transmission of COVID-19 or close contact with a confirmed or suspected case or cluster phenomenon?	2	5	10	3	-
Symptoms					
Fever	5	4	4	6	1
Cough	2	4	9	3	2
Muscle pain	9	6	1	4	
Dyspnea	13	3	1	2	1
Was dyspnea seen in severe disease only	Y	N	Cant say	-	-
	11	6	3		
Expectoration, chills, chest pain/tightness, hemoptysis, nasal congestion, sore throat, headache/dizziness, diarrhoea, nausea/vomiting, abdominal pain, anorexia, rhinorrhoea, pharyngalgia, shivering	11	5	3	1	-
Any other presentation	16	1	-	-	3
Laboratory investigations					
Lymphocytopenia	5	9	2	3	1
Elevated C-reactive protein	9	7	-	3	1
Increased lactate dehydrogenase	10	8	2		
Altered Neutrophil to lymphocyte ratio (NLR)	12	5	2		1
Hypoalbuminemia	16	3	1	-	1
Lymphocytosis, leucocytosis/leukocytopenia, neutrophilia/neutopenia, thrombocytopenia , elevated erythrocyte sedimentation rate/D-dimer levels/serum bilirubin/alanine transferase/aspartate transferase/serum creatinine/procalcitonin/creatinine kinase	12	6	1	-	1
Imaging					
Infiltrates on chest X ray or CT scan	7	8	1	4	-
Associated conditions					
Male gender	3	3	11	3	-
Age 60 years or above	10	5	4	1	-
Hypertension/Diabetes Mellitus/Chronic Obstructive Pulmonary Disease/ Bronchial Asthma/Ischemic Heart Disease, Heart Failure/Kidney or Liver disease/Hypercholesterolemia/Obesity/Malignancy/Steriod use/ immunocompromised conditions/Cerebrovascular disease	10	5	3	2	-
Any COVID-19 positive patient presenting with critically ill features (septic shock/multi-organ dysfunction or failure/life threatening malignancy, etc)	17	3	-	-	-

cross infection and contamination during the perioperative period.

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Conflicts of interest

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