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RESEARCH ARTICLE

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INSIGHT OF THE 2019 NOVEL CORONAVIRUS: THE EPIDEMIC AND ITS CHALLENGES

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ABSTRACT

Objective: According to the world health organization, the novel coronavirus(2019-nCoV) is declared as a pandemic on 30th January 2020 and is considered to be highly contagious concerning the public health emergency of international concern (PHEIC). The novel coronavirus emerged as an outbreak in China which was followed by other 29 countries. The expansion of the novel human respiratory coronavirus known as SARS-COV-2[severe acute respiratory syndrome coronavirus2] COVID-2019[coronavirus disease 2019] has stressed towards its therapeutic needs to reduce and cease further progression of this pandemic. This review aims to provide a summary of clinical signs and symptoms of novel Betacoronavirus infection and to demonstrate its therapeutic conclusion for patients who may require antimicrobial treatment. **Methods:** From the present literature of microbiological infections, the article was reviewed and confirmed by 2019-nCoV[COVID-19] happened at the time of writing[13 February 2020]. Using the PubMed database and the Cochrane library literature study was carried out by using terms like “novelcoronavirus” or “2019-nCoV” or “The COVID-19”. **Results:** According to published manifestation, the majority of the cases were seen in males of age group ranging from 8-92. The endocrinal, Cardiovascular, digestive system and the diseases related to such systems were commonly reported. However, the chronic pulmonary disease (for example, COPD, bronchitis, and asthma) were astonishingly underreported. Moreover, a series of cases were reported with common signs and symptoms such as fever, dyspnoea, flanked by myalgia, cough, and fatigue. However, fever was noticed in all of the cases. The most commonly reported radiological features of 2019-nCoV noticed were bilateral ground-glass opacities, multiple bilateral lobular, and segmental areas of the lungs in the initial phase of the virus. **Conclusion:** Patients with positive coronavirus infection are mainly linked with respiratory disease and extrapulmonary signs and symptoms. However, there are fewer chances of pre-existing respiratory related concomitants.

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INTRODUCTION

In Wuhan (Hubei, China), a cluster of 27 pneumonia cases (including 7 severe cases) occurred from an unknown origin on 30 December 2019. The cases had been reported to the National Health Commission of China. Patients developed severe acute respiratory syndrome [SARS-COV-2] in the initial phase of this pneumonia. In some, patients even started developing acute respiratory distress syndrome. Real-time PCR (RT-PCR) and deep sequencing study of lower respiratory tract samples recognized a novel human coronavirus (nCoV), now termed as SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2). China reported with approximately 50,000 confirmed cases and the cases which started getting reported for the COVID-19 in other

countries were Canada, Australia, France, Vietnam, Germany, The United Arab Emirates (UAE), Finland, Italy, Thailand, Nepal, Republic of Korea, Cambodia, Sri Lanka, Spain, Sweden, India, the United States, Singapore, Malaysia, the Russian Federation, and the Philippines till the end of January 2020. The mortality rate was noticed at around 2% to 2.3%. Moreover, 71,350 cases were reported among 29 countries in five main continents on the 17 February 2020, according to ECDC and CDC surveillance. 1,775 mortalities were reported until then (N=1,770 in China, one in Japan, one in France, one in Hong Kong, one in Taiwan and one in the Philippines).

MATERIALS AND METHODS

Using the PubMed database and the Cochrane library literature study was carried out by using terms like “novelcoronavirus”

or “2019-nCoV” or ‘The COVID-19’. The comparison of studies regarding first outbreaks and findings was majorly done between November 30 2019 to February 13 2020. Seeing the nature of the review, no approval from the ethical committee was needed. Two investigators (SC and TL) performed the study. Identification (PubMed: 225, Cochrane: 0) of a total of 225 studies were done. Initially by title and abstract of these articles were reviewed by two investigators, later on in detail using a customized data abstraction form. If they showed an incorrect subject matter, duplications or review the studies were excluded. Review studies in English were only involved. 12 r full-text review studies were recognized as they confined original data.

RESULTS

Patients Characteristics: According to published manifestation, the majority of the cases were seen in males of age group ranging from 8-92. There were some cases which were reported in young people under 15 years. Prevalence of males and distribution of age, at the time of diagnosis, resemble those in Chinese epidemic even amongst the known infected subjects outside China. Although information about past medical conditions of corona positive patients was not available yet hypertension was reported in most of them as an underlined condition (Huang, 2019; Holshue, 2020; Lei, 2019; Rothe, 2019; Li, 2020; Zhu, 2019; Ren, 2002; Chen, 2019; Lui, 2020; Wang, 2019; Wang, 2019; Kim, 2019 and COVID-19, 2020) in approximately 80% and 31.2% respectively in the case series from Ren et al (Ren, 2020) and Wang et al. (2019) Diseases like cardiovascular and cerebrovascular(40%) were described in their population by Chen et al. (2019) Primarily, chronic liver disease was reported in their entire population (N=5) by Ren and colleagues. From the other cases of 2019-nCoV (Huang, 2018; Holshue, 2019; Lei, 2019; Rothe, 2019; Zhu, 2019; Chen, 2019 and Lui, 2020; Wang, 2019; Wang, 2020; Kim, 2020 and COVID-19, 2018) this feature differs so far. A rate of chronic obstructive pulmonary disease (COPD) of about 2% and 2.9%, respectively have been shown by Huang et al. and Wang et al. A rate of nearly 1% of respiratory system diseases, varied from an assessed COPD prevalence between 1.2-8.9% in diverse areas of China (Zhu, 2018), have been shown by Chen et al. (Chen, 2019). Moreover, bronchiectasis, interstitial lung diseases, previous smoking history, and asthma were underreported (Huang, 2020; Holshue, 2020; COVID-19; 2018). Huang and colleagues [9] noticed diabetes and represented the main comorbidity in their cohort (8; 20%). Therefore, diabetes was reported later on by other authors [11-12] in about 10% of subjects. Hypertriglyceridemia as the solitary of chronic illness was the first to report in the U.S. as the first case of 2019-nCoV by Holshue et al. [4] amongst the cases reported outside Asia. Whereas, the cases reported in Germany[6] were healthy overall.

Signs and Symptoms: Patients with the COVID-19 symptoms ranged from mild to severe. It takes around 2-4 days in a patient for the development of the symptoms after the exposure. Until 21 february 2020, 80000 cases were confirmed and most of the positive patients showed a history of close contact with epidemic area or with other confirmed cases. These patients in general showed respiratory signs and symptoms. In the cohort by Ren et al. (N=5; 100%) Dyspnoea was reported to be very common in some of the patients. The prime initial symptom indulged in the coronavirus fever, out

of which most of them showed higher temperature readings that progressed in several days which could not be lessened by routine antibiotics. Apart from these gastrointestinal symptoms such as nausea, vomiting, and diarrhea were also reported. Elevated troponin levels, myocarditis, myalgia, and diarrhea were amongst the other clinical symptoms which were detected at a lower frequency. Asymptomatic carriers need to be segregated from people suffering from SARS. In one of the studies, approximately 20% of patients seemed to have comorbidities primarily based on renal impairment, dysfunction of other organs, comorbid heart failure which is confirmed in patients with underlined cardiovascular diseases.

Chest radiographic abnormalities: Plain Chest radiography (CXR) or computed tomography (CT) should be undertaken for the suspected patients having breathing difficulties followed by a chest CT scan for the patients confined with severe lung difficulties. However, bilateral ground-glass opacities or subsegmental areas of consolidation with multiple bilateral lobules are reported as a main radiographic feature of the COVID-2019. Apart from this, multiple infiltrating shadows with ground-glass opacities of a single lobe or multiple lobes can be checked upon as a supplementary finding in the suspected patients. On recovery of the patient a fibrous strip may be seen in a radiograph. On the contrary patients with pleural effusions are hardly noticed, as lung consolidation may appear in severe cases. Huang et al., (2020), presented a case series of about 40 patients where findings of pneumonia had been reported when the patients had undergone a plain chest x-ray (CXR) or computed tomography (CT). Although, a plain chest x-ray (CXR) is considered as the first method of investigation, a computed tomography (CT) is employed to be one of the best methods to describe the extension and typology of lung parenchyma involvement to carry out infection control procedures (Lei, 2020).

LABORATORY FINDINGS

Hematological examination: In the initial stage reduction in the number of white blood cell count is commonly seen leading to leukopenia. Holshue et al. (Holshue, 2019) and Chen et al. reported thrombocytopenia but it was hardly mentioned in any other case series. However, extreme attention is needed when the absolute lymphocyte count is significantly reduced to $<0.8 \times 10^9/L$ or the CD4+ and CD8+ T-cell counts. It is generally suggested to keep an eye on blood count and re-check every 3 days. Muscle enzymes, liver enzymes, and myoglobin levels are increased in some patients. In some of the critical patients troponin and inflammatory conditions may also rise. Severe cases may illustrate high D-dimer levels and low blood lymphocyte count. However, up to 45% of severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) infections [17-18] low platelet count had been found. In early cases, muscle enzymes (for instance, a marginal increase in creatine-kinase or lactate-dehydrogenase) enzymes and hepatic abnormalities [for instance, a marginal increase in aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels] has been seen and reported (Table 1) [1, 4-15]. In the cohort study of Huang et al. most of the patients showed normal procalcitonin (PCT) levels in the initial stage of entry. However, abnormal C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were reported. Suspected patients reported PCT level of <0.1 ng/mL in about 69% of the cases.

Table 1. Showing number of suspected cases based on its region as of 13 Feb'20 as reported in the article

Authors name	Date	Continent	Country/state	No.	Age	Sex	Past medical history
COVID-19 national surveillance team	12 Feb'20	Oceania	Australia	14	45 (8–66)	11 males (67%)	N/A
Wang et al.[13]	9 feb'20	Asia	Shanghai, China	5	55(19-63)	3 males (75%)	Fatty liver (1 patient); no other medical history known
Lui et al. [11]	7 feb'20	Asia	Wuhan, Hubei, China	136	56 (20–83)	60 males (44.5%)	DM (10.4%), hypertension (9.6%), CD (7.2%), COPD (1.4%), malignancy (1.3%)
Kim et al.[14]	10 feb'20	Asia	Incheon, Korea	1	35	Female (N/A)	Obesity
Lei et al. [5]	1 Jan'20	Asia	Lanzhou, China	1	32	Female (N/A)	(N/A)
Wang et al.[12]	7 feb'20	Asia	Wuhan, Hubei,China	137	55 (22–92)	75 males (54.3%)	Hypertension (31.2%), CD (14.5%), DM (10.1%), malignancy (7.2%), COPD (2.9%), CKD (2.9%)
Holshue et al. [4]	31 Jan'20	America	SnohomishCounty, Washington	1	34	Male (100%)	Hypertriglyceridaemia
Chen et al.	30 Jan'20	Asia	Wuhan, china	98	55 (42– 67)	66 males (67%)	Cerebrovascular disease (40%), digestive system disease (10%), endocrine system disease (10%)
Rothe et al.[6]	30 Jan'20	Europe	Munich, Germany	4	35	Males (100%)	Healthy
Ren et al. [9]	11 Feb'20	Asia	Wuhan, china	5	52(41-65)	3 males (60%)	Chronic liver disease (100%), hypertension (80%)

Table 2. Showing clinical signs and symptoms, laboratory findings and its treatment modality

Authors name	Signs and symptoms	Symptoms at entry	Abnormal laboratory findings	Abnormalities at CXR	Ward of entry	Treatment	Outcome
COVID-19 national surveillance team	Fever and/or chills (93%)	Cough (73%)	N/A	Pneumonia	Internal medicine, ICU	N/A	Favorable
Wang et al. [13]	Fever (100%), rhonchi (100%)	Cough, dizziness, fatigue	Lymphopenia (25%)	Ground-glass opacities and consolidations, bilateral or mono lateral	Internal medicine	Lopinavir/ ritonavir, Shufeng Jiedu capsule, Arbidol (umifenovir)	Favorable
Lui et al. [11]	Fever (81.8%)	Cough (48%), myalgia or fatigue (32.1%), heart palpitations, diarrhoea and headache	Lymphopenia (72.3%)	Multiple, bilateral, peripheral ground-glass opacities and consolidations or cord-like shadows (CT imaging)	Internal medicine, ICU	Experimental antibiotics (86.9%), antiviral therapy (76.6%), immunoglobulin G, systemic CTS	16 died (11.7%)
Kim et al. [14]	Fever	Myalgia	Leukopenia, thrombocytopenia and hepatic abnormalities	Multiple ground glass opacities located in both sub pleural spaces	N/A	Support, lopinavir/ ritonavir	Favorable
Lei et al. [5]	Fever (81.8%)	Cough (48%), myalgia or fatigue (32.1%), heart palpitations, diarrhoea and headache	Lymphopenia (72.3%)	Multiple, bilateral, peripheral ground-glass opacities and consolidations or cord-like shadows (CT imaging)	Internal medicine, ICU	Experimental antibiotics (86.9%), antiviral therapy (75.6%), immunoglobulin G, systemic CTS	16 died (11.7%)
Wang et al. [12]	Fever (98.6%)	Cough (48%), myalgia or fatigue (32.1%), heart palpitations, diarrhoea and headache	Lymphopenia (72.3%)	Multiple, bilateral, peripheral ground-glass opacities and consolidations or cord-like shadows (CT imaging)	Internal medicine, ICU	Experimental antibiotics (86.9%), antiviral therapy (75.6%), immunoglobulin G, systemic CTS	16 died (11.7%)
Holshue et al. [4]		Dry cough, nausea and vomiting, abdominal discomfort, diarrhoea, fatigue, rhinorrhoea	Leukopenia, thrombocytopenia, elevated creatine kinase and lactate dehydrogenase, hepatic abnormalities	Lower lobe pneumonia, bilateral basilar streaky opacities	Internal medicine	Support; vancomycin plus cefepime (begin from Day 9); remdesivir	Favorable
Chen et al.	Fever	Cough (80%), breath shortness (30%), headache (7%), confusion (8%)	Lymphopenia (35%), thrombocytopenia (12%), AST increased (35%), ALT increased (28%)	Bilateral consodilations (75%) on CT or CXR	N/A	Experimental antibiotics, support, antiviral and antifungal	11 died (11%)
Rothe et al. [6]	Fever	Productive cough	N/A	N/A	Internal medicine, ICU (100%)	N/A	Favorable
Ren et al. [9]	Fever (100%)	Cough (100%), dyspnoea (100%), myalgia (60%)	Leukopenia (20%), slightly increased ALT (40%)	Bilateral groundglass opacities (100%), consolidations (80%) on CXR	Internal medicine, ICU (100%)	Support, empirical antibiotics	1 died (20%)

Moreover, prolonged prothrombin time was noticed in approximately 59% of adults in the case series of Wang et al. (2019).

Complications and mortality: Out of 41 patient reports by Huang et al. (2020) four (10%) were confined of superinfection and the risk increased with the intensity of the care (ICU care 31% Vs. no ICU care 0%, $P=0.0014$) in the present cohort study. During the acute phase almost all the patients were treated with experimental antibiotic coverage. The complication in the clinical progression of up to 29% of patients (12) [1] with or without specific bacterial superinfection ascended the risk of acute respiratory distress syndrome. In nearly 12% of the patient's increase in troponin I count was reported. Five cases also reported acute cardiac injury in the cohort study presented by Huang et al. (2019).

Klebsiella pneumoniae has been reported by authors (Chen, 2020) 1780 deaths have been reported by the first wave of 2019-CoV, despite the condition of the illness was mild in most of the cases. According to the review of Wang and colleagues (Wang, 2009) underlined diseases, demographic characteristics of deaths have been reported in the Wuhan epidemic. It is also noticed that adults (>70-years-old) have been reported with a shorter period between first symptom and death [11.5 (range 6-19) days Vs. 20 (range 10-41); $P=0.033$] when compared with the younger population [17-18]. Hence the severity in the elderly patients for 2019-nCoV illness [1, 4-15] has increased incessantly. A median period between symptomatic stage to death (median days 14) has been developed by Wang and colleagues [19], 2019-nCoV. It is somehow represented on a similar note to SARS-CoV (median days 17.4) of MERS [12, 17-18] and MERS-CoV (median days 14).

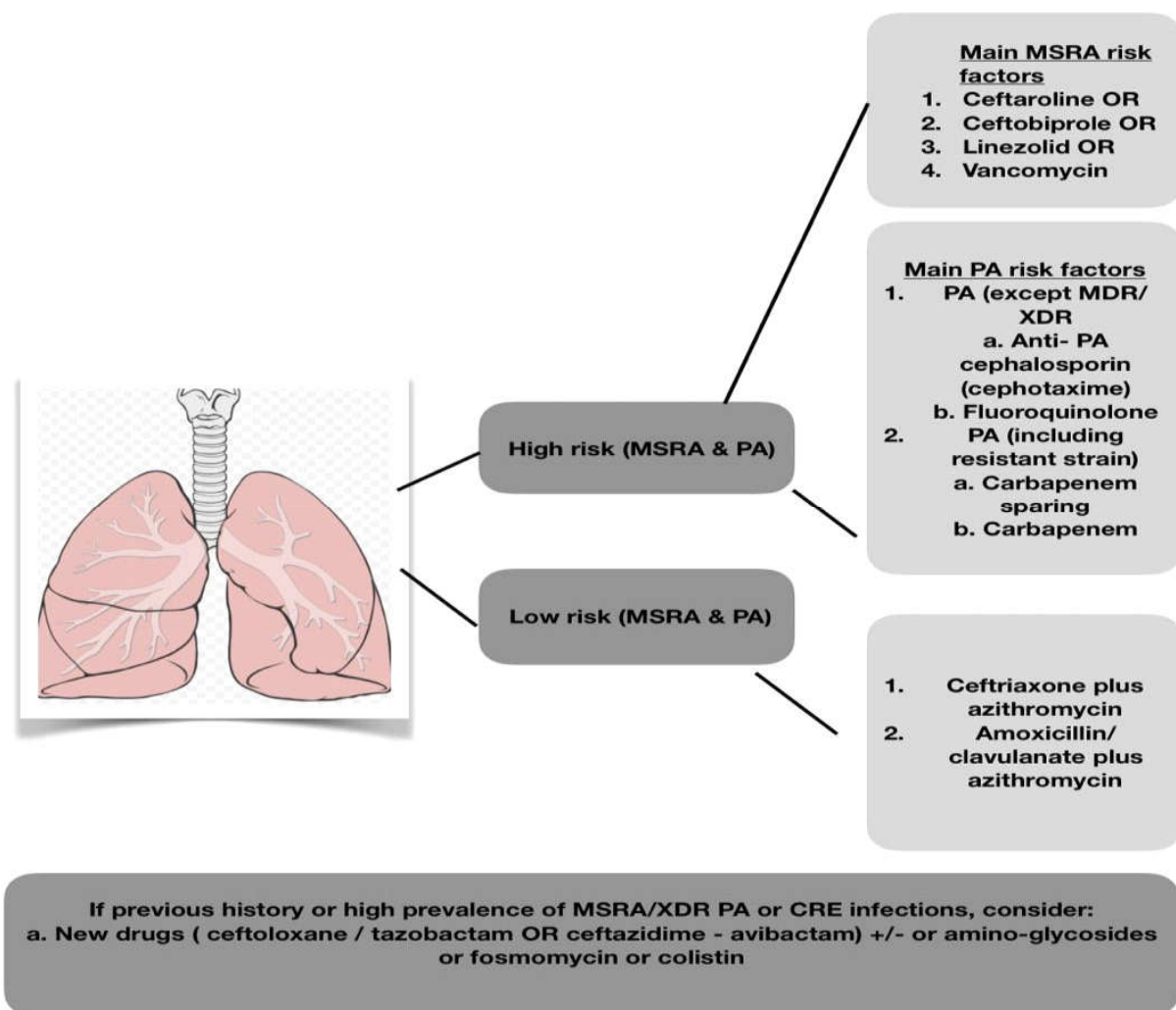


Fig. 1 showing MDR: multidrug-resistant, MRSA: methicillin-resistant *Staphylococcus aureus*, RT-PCR: positive reverse transcription

According to this finding, further consideration of the heart tropism of 2019-nCoV and cardiovascular risk of infected patients during such acute illness is needed. A low rate (4%) of fungal isolates with the clinical need of experimental antifungal treatment, with one case of *Candida glabrata*, three cases of *C. albicans*, and one case of *Aspergillus flavus* isolation (Chen, 2019), has been reported by Chen et al. Moreover, a reduction in the rate of bacterial respiratory isolates, mostly *Acinetobacter baumannii* and

DISCUSSION

The scientific turmoil is trying to keep up with the daily assessment of the real extent of the COVID-19 epidemic. Outside China the true extent of this new disease is still to be known for its features. However, we have our previous lesson from epidemics such as SAR-CoV and MERS-CoV. To define 2019-nCoV has become a rather difficult task due to the scarcity in its noticeable clinical features, it's a

microbiological diagnosis and also because it has occurred during the peak of seasonal influenza. The Covid-19 resembles previous features of Coronavirus infection in its clinical features like respiratory symptoms along with high rate of fever while the unusual phenomenon of this new disease such as symptoms of Rigors and chills was seen in 74% of SARS-CoV and 89% of MERS-CoV respectively. Like many other viral infections, the pattern of presentation of this novel coronavirus is unspecific while most of the comorbidities viz., cardiovascular disease such as hypertension, diabetes, and smoking habit have been reported similar to MERS-CoV. Although we don't have a precise view of but chronic illness has been reported to a much lesser extent. A clinical and radiological pneumonia has been reviewed amongst novel coronavirus patients thus calling for the review of bacterial superinfection like in influenza virus outbreak and prescribing empirical antibiotic coverage accordingly. As of 2003, reports of an increase of methicillin-resistant staphylococcus aureus (MSRA) is seen from pre- SARS to during the SARS period (from 3.53 to 25.3%) requiring an increase in the rate of the need of ICU and MRSA specific ventilator acquired pneumonia. A great deal of superinfection can be reduced by considering anti- MSRA empirical treatment for novel coronavirus infection. MRSA, pseudomonas aeruginosa bacterial superinfection and multidrug-resistant gram negative bacilli colonization are often difficult to treat, thus accessing to its risk according to other systemic ailments like lung abnormalities and cardiovascular comorbidities, severe systemic pneumonia, and drug-related toxicity are crucial points of all suspected cases of the COVID-19. Based on common risk factors of P. aeruginosa and MRSA, a treatment protocol is proposed as shown in Fig 1.

Viral infections such as influenza and other classical risk factors like hematological patients, solid-organ and hematopoietic stem cell transplant recipients, HIV patients are supposed to be at a greater risk of fungal infection but surprisingly it shows low risk of fungal co-infection. Thus only in patients with critically new pulmonary infiltrate and viral pneumonia. This pattern superimposed should be considered for empirical antifungal treatment with diagnosis by invasive technique and use of fungal biomarkers. A wide range of management alternatives are reported in the current situation in which specific antiviral treatment is inconclusive. Antiviral treatment has been described effective amongst 76% of the population of 99 patients by Chen et al. having a median duration of 3 days. On the other hand, remdesivir has shown to have good results in patients treated by Holshue et al.

Conclusion

With the isolation of suspected cases, focus on prompt diagnosis, and infection control procedures, we have to be ready for the further challenges that are going to be thrown by the outbreak also keeping the previous lessons learned from MERS-CoV and SARS-CoV virus in mind. Anticipating the complications and evolutions in the course of 2019-nCoV epidemic is the need of the hour.

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