Possible Factors Leading to the Severe Covid-19 Symptoms and Treatment

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Abstract: Since the outbreak of COVID-19 in 2019, it has spread worldwide through person-to-person transmission, resulting in economic decline and killing millions [1]. The COVID-19 virus is a type of coronavirus, similar to SARS in 2003 and MERS in 2012, and symptoms of it range from mild ones, like fever and cough, to serious respiratory diseases, such as pneumonia. By 2022, 600 million cases had been diagnosed with 6.48 million deaths worldwide. This essay illustrates the factors that cause serious cases, including life habits, gender, age, underlying diseases, race and viral strains and the treatments for them are embodied in the second half, in order to improve the understanding of this virus. Meanwhile, the purpose is also to instruct people to prevent infection.

1. Introduction

COVID-19 is the named SARS-CoV-2 virus that was first detected in Wuhan, China in December 2019. With 600 million cases totally and 6.48 millions of mortality, the medical community has conducted extensive investigations into the causes of serious cases in every patient since the outbreak in order to find out why some patients have serious symptoms, but not others, while attempting to devise specific treatments to treat them. The clinical data shows that patients who develop serious Covid-19 possibly had at least one underlying diseases, such as obesity, asthma and diabetes[2]. Taking obesity as an example, overweight people are at greater risk of developing a serious condition if they are infected with COVID-19 because of the growing risk of ARDS (ARDS) [3].

But what lead to severe cases are not only these diseases that have already existed in patients' body, but also unhealthy lifestyles, such as alcohol abusing, smoking and staying up late. A study conducted in Malaysia of 5889 patients demonstrated a link between cigarette smoking and severe COVID [3][15]. On the other hand, those who continue to adhere to a healthy diet and exercise often reduce their risk of becoming a serious illness.

2. Clinical Symptoms of Severe and Mild Patients

Since the outbreak of COVID-19, whether this virus will primarily cause severe symptoms or moderate ones has been concerned a lot. As result of the invention of vaccine and immunization of many more individuals, people may experience moderate and light symptoms as opposed to severe ones[3]. However, there are still serious cases with a greater death rate than in moderate cases, with severe ARDS, septic shock, or metabolic acidosis, which is highly hazardous[4].

But how can we actually distinguish the difference between severe cases and those mild cases? It is based on the clinical symptoms.

The clinical symptoms of COVID-19 mostly occur in the respiratory part of human body. Fever, respiratory symptoms (including cough, dyspnea, expectoration, hemoptysis, chest tightness, and pharyngalgia), digestive symptoms (including abdominal pain, diarrhea, and nausea or vomiting), and neurological symptoms were the four categories that are divided all initial symptoms into for research purposes (including anorexia, fatigue, myalgia, and headache)[4]. By looking for articles on the clinical features of COVID-19 in China in PubMed, Embase, Web of Science, and CNKI (Chinese Database), researchers were able to clearly describe the contrast between these two groups of patients and provide a solution to this topic[2].

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In the end, they concluded that of the 142 documents originally submitted for the trial, 20 were chosen after screening with 3 326 COVID-19 confirmed cases. In accordance with the "Novel Coronavirus Infection-Induced Pneumonia Diagnosis and Treatment Protocol" edition 4, they categorized all the cases into a severe part and a moderate part. They looked at the initial signs of pharyngitis, such as fever, coughing, stomach discomfort, anorexia, tightness in the chest, diarrhea, dyspnea, expectoration, exhaustion, headache, hemoptysis, and myalgia.[2][3]. In addition, they found the specific difference clinically with severe cases and those of normal patients which contained the symptoms of cough (odds ratio [OR] = 1.4, 95% confidence interval [CI]: 1.2–1.7; p < 0.001), fever (OR = 1.5, 95% CI: 1.2–1.9; p < 0.001), dyspnea (OR = 6.2, 95%

CI: 3.6-10.6; p < 0.001), diarrhea-(OR = 2.6, 95% CI: 1.3-4.9; p < 0.001), fatigue (OR = 2.1, 95% CI: 1.3-3.3; p < 0.01), expectoration (OR = 1.7, 95% CI: 1.2-2.6; p < 0.01), myalgia (OR = 1.6, 95% CI: 0.8-3.1; p < 0.001), hemoptysis (OR = 4.0, 95% CI: 3.1-11.3; P < 0.001), Abdominal Pain (or = 7.5, 95% CI: 2.4-23.4; p < 0.001), and anorexia (OR = 2.8, 95% CI: 1.5-5.1; p < 0.001) had a different distribution in two groups and were statistically significant (p < 0.05)[3].

3. Factors That Lead to Severe Cases

Among the factors contributing to serious illness, I classify the factors into five categories: age, sex, underlying illness, race, virus species, and lifestyle. [3]. For the age, gender and underlying diseases, these three factors are investigated by a group of researchers in Saudi. [16] The following data indicate that the various variables are tested according to a different percentage of the total number of patients who have been tested as show in table 1.

Variables	Total (n = 598)	Moderate $(n = 298)$	Severe (n = 300)	P-Value	
Age (years), mean \pm SD	57 (46–65)	56 (44–64)	58 (48–66)	0.015	
Male sex, n (%)	352 (59)	169 (57)	183 (61)	0.163	
O2 saturation at admission, mean	93 (5)	96 (94–98)	92 (89–95)	< 0.001	
(SD)					
Pre-Existing Conditions, n (%)					
Diabetes	272 (46)	119 (40)	153 (51)	0.004	
Hypertension	244 (41)	108 (36)	136 (45)	0.016	
Obesity (BMI greater than 30)	259 (43)	111 (37)	148 (49)	0.002	
Chronic pulmonary disease	63 (11)	26 (9)	37 (12)	0.096	
Liver disease	3 (0.5)	1 (0.3)	2 (0.7)	0.503	
Renal disease	38 (6)	17 (6)	21 (7)	0.315	

Table 1 Characteristics and Clinical Course of the Patients with Confirmed Sars-Cov-2. [16]

In this figure, N% means the percentage of people with the different traits showed in the variable columns. With the data in this table, we can clearly conclude that for the age section, elderly between 48-66 have the higher risk to become severe cases[16]. Compared to young patients, middle-aged and older people are far more likely to experience symptoms, require hospitalization, and pass away.

Incidentally, based on a recent review of Chinese data, patients aged 80 or over are at greater risk of dying from COVID-19 by over 13%, compared with approximately 0.15% for 30-year-olds and nearly nil for those younger than 20.In terms of gender, men are more likely to suffer from COVID and exhibit more serious signs than females [6]. What's more, the third focused factor, which is underlying diseases, has been clearly listed in this diagram. [16][4]

Men are far more likely to die from COVID-19 than women are, despite the fact that men and women appear to contract it at about the same rates. For instance, men contribute for over 70% of COVID-19 fatalities in Italy and Ireland[4][6].

There are several theories to explain this variation. The first is that immune reactions differ according to sex; for example, flu studies suggest that elderly men often perform worse than elderly women. Additionally, men are more likely to drink alcohol, which lowers immunity and makes them more susceptible to pneumonia.

Underlying illness, which means that the patient was previously infected with COVID. There are

a number of possible conditions that may worsen COVID-19 symptoms, including severe obesity, asthma, diabetes and hypertension. For instance, the proportion of people with diabetes is relatively high (51% in the table)[16]. For the respiratory underlying diseases, the research shows that reduced lung function and a higher risk of lung inflammation are symptoms of asthma and chronic obstructive pulmonary disease, and patients with these conditions frequently use corticosteroid mmune-suppressing medications, which lower immunity to respiratory infections [3]. Similarly, diabetes and high blood pressure are just as common in these respiratory disorders and have an impact on therapy and lead to severe immune reactions, so that people with underlying conditions need to take extra care to prevent the occurrence of serious illnesses [3].

The race is the fifth. Researchers from this particular group found a surprising finding: there is increasing evidence that African Americans are more likely to suffer from serious COVID-19 than whites. Today, it's responsible for more than 70% of Louisiana's COVID-19 deaths, but it's only one-third of the population. Similar inconsistencies can be seen in a number of other countries[3][4]. It is simply too early to identify what causes this apparent susceptibility, but plausible factors include the exceptionally high frequency of illnesses among African Americans, such as hypertension, renal disease, obesity, and diabetes, that have already been associated with severe COVID-19. Socioeconomic elements may also be important, such as poverty, access to healthcare, and health insurance[3][4].

In fig.1 The last factor is called viral strain. As we all know, the evolution of COVID-19 is quick, which is one of the characteristics of this coronavirus, and different strains of them have traits with unpredictable functions[10]. A team of researchers uses a non-integer order derivative in order to present information about the model solutions, uniqueness, and existence using a fixed point theory[11]. And two figures below compare the number of susceptible individuals and exposed cases in five different strains.

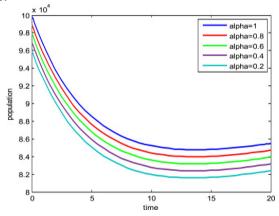


Fig.1 Dynamics of Susceptible Individuals for Various Values[11]

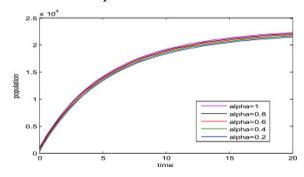


Fig.2 Dynamics of Exposed Individuals for Various Values[11]

As show in fig.2, These Figures make it abundantly evident that when is reduced from 1 to 0.2, the population of susceptible individuals, exposed persons, new variants of COVID-19, old variants of COVID-19, hospitalized individuals, and recovered individuals experience a diminishing effect.

4. New Ways of Treatment for Covid-19 Severe Cases

With the development of time, the treatment for the severe patients has also been more innovative.

In this part of the paper, two known new treatments are included.

The first treatment is called monoclonal antibody drugs [13]. The monoclonal antibody drugs can be classified to two types: S-protein based one and the N-protein based one.

Let's start with drugs based on S-protein, this protein is actually the most important surface protein of the virus, which is also a key target for neutralizing antibodies (NABS). The RBD receptor and ACE2 interact to help the S protein finish the invasion process. SARS-CoV-2 invasion may be successfully stopped if the process of the S protein's interaction to the ACE2 receptor could be efficiently disrupted. Therefore, the majority of neutralizing antibodies target the receptor-binding epitope of RBD and have a neutralizing effect by inhibiting the RBD receptor through competition[13].

For the second drug which is based on N-protein, we should firstly understand the function of it.

The N protein has a high degree of sequence conservation and RNA chaperone activity, which makes it an antagonist of <u>interferon</u> and an inhibitor of virally-encoded RNA interference[14]. The N protein is the main structure of the virus, which is a basic protein composed of 419 amino acids and has a short lysine-rich protein. It is highly immunogenic and has fewer mutations over time than the spike and envelope proteins, which makes it a good target for detection. Additionally, N proteins are involved in the transcription and replication of viral mRNAs, tissue <u>cytoskeleton</u> and immune regulation and regulation of cellular metabolism and cell cycle.

As a result, the N protein can be utilized as a marker protein for virus identification, in the creation of vaccines, and in serological detection. The following describes the steps involved in creating monoclonal antibodies [13][14].

In order to evaluate the efficacy of monoclonal antibodies, a team of researchers is conducting research on the impact of medicines in serious COVID-19 Delta Variant[17]. They carried out an experiment in which 5,356 patients from various regions of the USA were injected with monoclonal antibodies to measure the severity of the results. The concrete figures are summarized in the graph below fig.3.

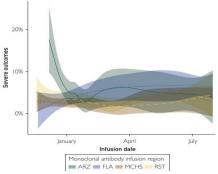


Fig.3 Severe Outcomes from Covid-19 after Mab Infusion[17].

According to the data above, we can conclude that the monoclonal medicines do have effect on the severe outcome. The general trend for serious results from the January-July period is declining, demonstrating that monoclonal antibodies can indeed reduce severe outcomes in the long-term.

For the second treatment, a team in China has launched a specific investigation that can use Chinese traditional medicines(TCM) to cure those severe elderly cases.

According to theory of TCM, healthy qi declines with age, which causes a stealthy emergence of disease signs and symptoms[12]

The research team also list a basic formula for severe cases, let us watch the figure 4 in the following.

Chinese Pinyin name	Latin name	Dose
Zhi mahuang	Herba Ephedrae Praeparata	10 g
Kuxingren	Semen Armeniacae Amarum	10 g
Sheng Shigao	Gypsum Fibrosum(decoct first)	30–90 g
Jinyinhua	Flos Lonicerae Japonicae	20 g
Zhimu	Rhizoma Anemarrhenae	10 g
Zhebeimu	Bulbus Fritillariae Thunbergii	15 g
Quan Gualou	Fructus Trichosanthis	30 g
Tinglizi	Semen Lepidii	15 g
Chishao	Radix Paeoniae Rubra	15 g
Xuanshen	Radix Scrophulariae	20 g
Sheng Dihuang	Radix Rehmanniae	30 g
Sheng Dahuang	Radix et Rhizoma Rhei (decoct last)	6–9 g

Fig.4 The Basic Formula for Severe and Critical Cases[12].

The figure listed above mainly includes one of the reagent combinations of effective TCM treatment for severe cases. The strategy for this combination is to clear the lung, guaranteeing lung functions, toremove toxins[12].

Early detection, diagnosis and treatment of the disease are of paramount importance to the prevention of the latter. Initial intensive care is essential to prevent mild or moderate cases from progressing to severe or critical conditions in patients who present with fatigue, drowsiness, loss of appetite or decreased food intake, constipation, decline in oxygen level, dynamic reduction in serum absolute lymphocyte count, dynamic elevation of inflammatory cytokines and blood coagulation indicators such as D-dimer, and noticeable progression of lung infiltration by chest imaging[12][13].

5. Conclusion

Harming humans health, the number of COVID-19 severe cases must be effectively reduced soon. In this paper, we summarize the influential factors and the related treatment methods of the patients, including the monoclonal antibody and TCM. Knowledge of this helps to better understand the characteristics of COVID and to avoid severe signs of infection. For the factors like gender and age, the organizing of treatment should depend on the conditions of patients, and what we can do is to keep exploring the methods of effective vaccine and medicines, such as the S-protein based drugs, N-protein based drugs, and TCM therapy. However, as far as lifestyle is concerned, it is possible to prevent COVID from becoming infected by avoiding bad habits such as smoking and drinking. In general, to combat COVID-19, it is imperative to prevent serious cases, and to do so, not only do we need to invent medicine, but we also need to act on our own in order to maintain our health.

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