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Dr. Devesh Bhomia
Associate Professor, General
Surgery, S. K Government
Medical College, Bajaj Gram,
Sikar, Rajasthan, India

Dr. Neha Bhomia
Research Scientist (Medical),
ICMR Project, Department of
Microbiology, SMS Medical
College, Jaipur, Rajasthan,
India

Potential relevance of covid-19 in systemic health of patients: A study to analyze the association between COVID-19 & other systemic co-morbidities in SARS CoV-2 positive patients

Dr. Devesh Bhomia and Dr. Neha Bhomia

Abstract

Background: Coronavirus disease 2019 (COVID-19), caused due to a novel coronavirus SARS-CoV-2, has swept across the planet and has become a public health emergency of international concern. Among patients with COVID-19, almost all organ systems (cardiovascular, gastrointestinal, renal, hepatic, endocrine and nervous system) have been reported to be involved.

Aim: The main aim of this study was to assess the clinical presentation of COVID-19 along with the risk of other systemic co-morbidities in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive patients.

Methods: A total of 100 patients met the inclusion criteria and gave their signed informed consent. A questionnaire of 20 questions regarding the general and systemic health condition was given to these patients during the convalescence. A descriptive statistic was performed. Data were analyzed to assess the statistical significance.

Results: The results showed the most prevalent clinical symptom was fatigue 74% (male=45%, female=29%) followed by fever 71% (male=48%, female=23%), cough 63% (male=37%, female=26%), dyspnea 45% (male=22%, female=23%) and diarrhea 41% (male=24%, female=17%). The most prevalent comorbidities were hypertension 49% (male=36%, female=13%) followed by diabetes 34% (male=26%, female=8%), respiratory diseases 28% (male=24%, female=4%) and cardiovascular disease 16% (male=11%, female=5%). Further correlation was analyzed between each sign & symptom & systemic co-morbidities with respect to gender. No statistical significance was observed between fever, cough, fatigue, diarrhea with respect to gender. However, statistical significant value was observed in dyspnea with respect to gender. (p value = (0.012). Among co-morbidities, statistical significant value was observed in hypertension (p value=0.03), diabetes (p value=0.045) and respiratory diseases (p value=0.003) with respect to gender. No correlation was seen between cardiovascular disease and gender.

Conclusion: This study depicts the effects of COVID-19 on systemic health of patients thus emphasizing that the disease can be present in various forms and the healthcare workers need to be extra vigilant, approaching all patients with a high index of suspicion. Further studies are necessary to better understand the symptoms of this new virus in order to faster detect its presence in humans.

Keywords: SARS-CoV-2, coronavirus, diabetes, cardiovascular, hypertension

Introduction

COVID-19 has been declared as a pandemic by the World Health Organization (WHO) on March 12, 2020. In December 2019, there was an outbreak of a highly contagious pneumonia in Wuhan city of China, caused due to an enveloped RNA beta coronavirus phylogenetically similar to severe acute respiratory syndrome coronavirus (SARS-CoV), named as SARS-CoV-2 [1]. The pneumonia was designated as coronavirus disease 2019 (COVID-19) [2]. Although the initial transmission was thought to be zoonotic, it is now spreading from person to person through droplets (directly or through contaminated surfaces) and possibly aerosols with a mean incubation period of 5.2 days [3, 4]. Patients commonly present with fever, cough, shortness of breath, myalgia, fatigue, and less commonly with sputum production, hemoptysis, headache, and diarrhea [5-7]. Elderly males with comorbidities (diabetes, hypertension, and coronary artery disease) are more likely to be affected [6] as compared to children, who either are not infected or have only undetectable disease [8].

Corresponding Author:
Dr. Neha Bhomia
Research Scientist (Medical),
ICMR Project, Department of
Microbiology, SMS Medical
College, Jaipur, Rajasthan,
India

Huang *et al.* [6] firstly reported the clinical features of 41 confirmed patients, and indicated 13 (32%) of them had underlying diseases, including cardiovascular disease, diabetes, hypertension, and chronic obstructive pulmonary disease. Subsequently, Wang *et al.* [9] reported findings from 138 cases of COVID-19; the results suggested that 64 (46.4%) of them had comorbidities. This suggested that comorbidities may be risk factors for adverse outcomes. Assessing the prevalence of these chronic diseases is the basis for mitigating complications in patients infected with SARS-CoV-2. COVID-19 interacts with the systemic health of the patient on multiple levels, increasing morbidity with underlying conditions and provoking dysfunction.

Pathogenesis: SARS-CoV-2 infection is caused by binding of the viral surface spike protein to the human angiotensin-converting enzyme 2 (ACE2) receptor after activation of the spike protein by trans membrane protease serine 2 [10]. ACE2 is expressed in the lung (principally type II alveolar cell) [11] and appears to be the predominant portal of entry. ACE2 is

highly expressed in the heart as well, counteracting the effects of angiotensin II in states with excessive activation of the renin-angiotensin system, such as hypertension, congestive heart failure, and atherosclerosis [8]. In addition to the heart and lung, ACE2 is expressed in the intestinal epithelium, vascular endothelium, and kidneys, providing a mechanism for the multi-organ dysfunction that can be seen with SARS-CoV-2 infection [12, 13]. Once the pathogen (SARS-CoV-2) enters the human body, it invades the alveoli and links to the angiotensin-converting enzyme 2 (ACE2) receptor of type 2 pneumocytes through their spike protein [14]. Diverse manifestations of the disease are due to the direct effects of the virus or inflammatory mediators especially IL1, IL6, and TNF-alpha. SARS-CoV-2 induces an alveolar-interstitial inflammation with a high risk of acute pulmonary edema or acute respiratory distress syndrome [15-19]. Its worth to mention that the pathogenesis of COVID-19 also entails a systemic inflammation with several consequences.

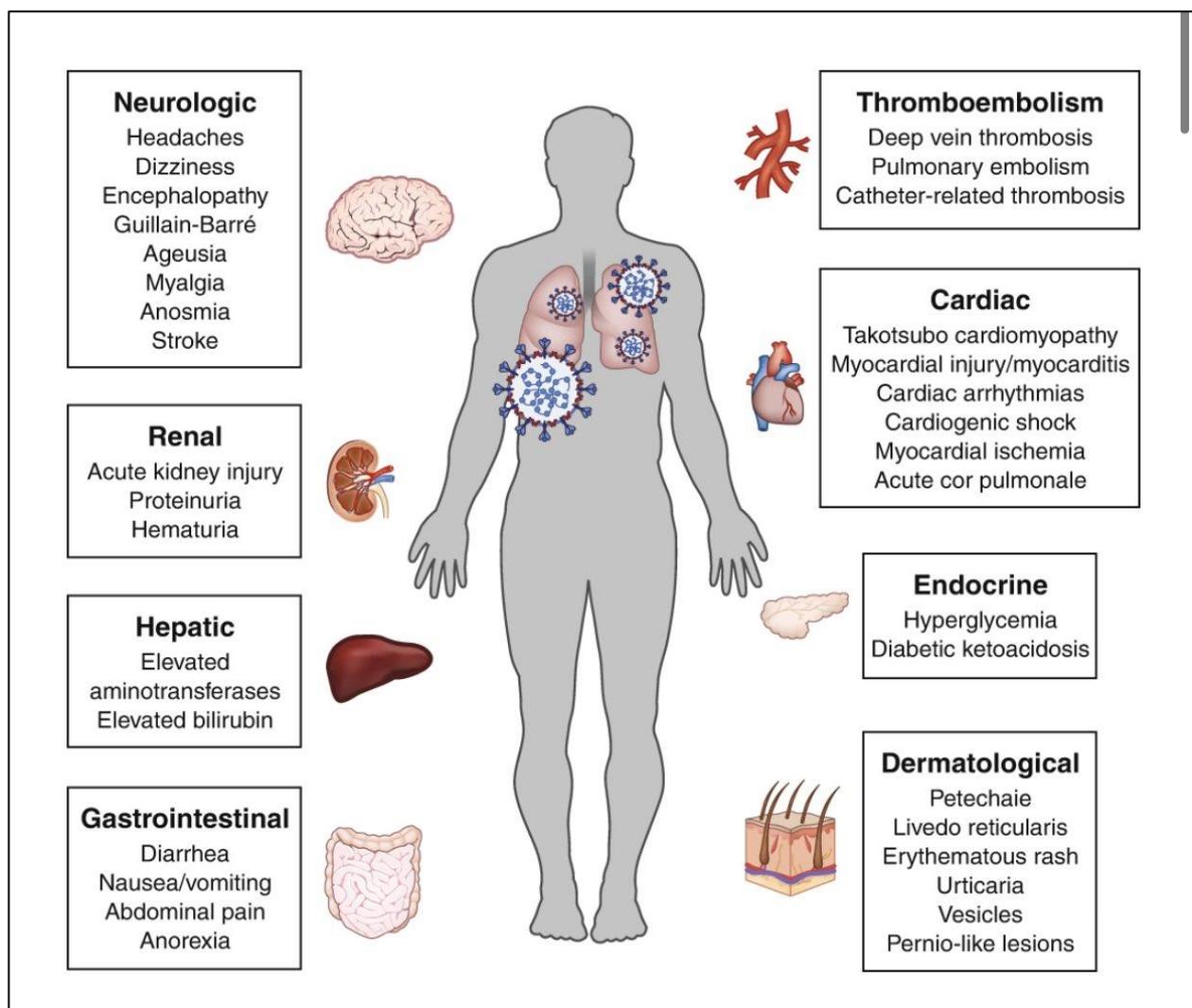


Fig 1: Systemic Manifestations of COVID-19

Study Design: A total number of 100 patients were enrolled in this study. It was conducted in a period of three months (from Feb 2021 to April 2021). The survey was completed by 100 patients who met, during the described period, the inclusion and exclusion criteria. The average age of the participants was 47.38 years. Of these, 63% were males and

37% females. A specific questionnaire of 20 questions was submitted to these patients detected by SARS-CoV-2, hospitalized at SMS Medical Hospital, Jaipur with the aim to collect information related to signs & symptoms and other co-morbidities during the manifestation of COVID-19. The inclusion criteria were patients of both sex and of any

age hospitalized for COVID-19 at the above mentioned hospital able to give their consent to participate in the study. The exclusion criteria were patients of both sex and any age hospitalized for COVID-19 at above mentioned hospital in need of intensive care and/or who were unable to give their consent to participate in the study. All the questionnaires were given to the patients during the doctor routine visits in that department. Then, all the papers were collected in a separate box with all the recommendations to reduce the contagion. Data collection took place in the time period from February to April 2021.

Statistical Analysis: Some of the answers were codified as dichotomous variables, namely as Yes/No responses, or in general as categorical variables. Given the nature of our survey we computed descriptive statistics for most of the questions. For each question, we computed the percentage of the respondents that gave a particular answer with respect to the number of total responses to the question. Further correlation was analyzed between each sign & symptom & systemic co-morbidities with respect to gender using t-Test, to assess the statistical significance. All statistical comparisons were conducted with a significance level of $p < 0.05$. Statistical analyses were performed using the t-Test: two sample assuming equal variances.

Results

The results showed the most prevalent clinical symptom was fatigue 74% (male=45%, female=29%) followed by fever 71% (male=48%, female=23%), cough 63% (male=37%, female=26%), dyspnea 45% (male=22%, female=23%) and diarrhea 41% (male=24%, female=17%). The most prevalent comorbidities were hypertension 49% (male=36%, female=13%) followed by diabetes 34% (male=26%, female=8%), respiratory diseases 28% (male=24%, female=4%) and cardiovascular disease 16% (male=11%, female=5%). Further correlation was analyzed between each sign & symptom & systemic co-morbidities with respect to gender. No statistical significance was observed between fever, cough, fatigue, diarrhea with respect to gender. However, statistical significant value was observed in dyspnea with respect to gender. (p value = (0.012). Among co-morbidities, statistical significant value was observed in hypertension (p value=0.03), diabetes (p value=0.045) and respiratory diseases (p value=0.003) with respect to gender. No correlation was seen between cardiovascular disease and gender.

Discussion

Recent studies illustrates about the systemic manifestations and associated co-morbidities in SARS CoV-2 positive patients. The main aim of this study was to analyze the association between COVID-19 & other systemic co-morbidities in SARS CoV-2 positive patients. The total of 100 patients was included in our study. The average age of the participants was 47.38 years. Of these, 63% were males and 37% females. MERS-CoV and SARS-CoV have also been found that males are more likely to be infected than females^[20, 21]. It is customary to think women are less likely to be affected by many bacteria and viruses than are men, partly because of their more robust innate and adaptive immune responses^[22]. Elderly people and severe patients are more susceptible to SARS-CoV-2, which may be associated with a higher frequency of comorbidities^[13].

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Further correlation was analyzed between each sign & symptom & systemic co-morbidities with respect to gender. No statistical significance was observed between fever, cough, fatigue, diarrhea with respect to gender. However, statistical significant value was observed in dyspnea with respect to gender. (p value = (0.012). Among co-morbidities, statistical significant value was observed in hypertension (p value=0.03), diabetes (p value=0.045) and respiratory diseases (p value=0.003) with respect to gender. No correlation was seen between cardiovascular disease and gender. Overall, the severe patients were older^[9] and had more significant number of comorbid conditions than those who were non-severe. These results may suggest that age and comorbidities are risk factors for critical patients. Diseases such as hypertension, diabetes, respiratory system disease, cardiovascular disease, and their susceptibility conditions may be linked to the pathogenesis of COVID-19. Chronic diseases share several standard features with infectious disorders, such as the pro-inflammatory state, and the attenuation of the innate immune response. For instance, diabetes occurs in part because the accumulation of activated innate immune cells in metabolic tissues leads to the release of inflammatory mediators, especially IL-1 β and TNF α , which promote systemic insulin resistance and β -cell damage^[26]. Additionally, metabolic disorders may lead to low immune function by impairing macrophage and lymphocyte function^[27], which may make individuals more susceptible to disease complications^[20]. Recently, Guo *et al.*^[28] retrospectively analyzed the clinical data of patients with viral pneumonia and found that the absolute count levels of CD3+T cells, CD3+CD8+ T cells and CD3+CD4+ T cells in the deceased group were significantly lower than those in the survival group, suggesting that the levels of various inflammatory factors in the deceased group were higher than those in the survival group. A prospective case control study about seasonal influenza was conducted by Hong *et al.* (2014)^[29] in which results showed that diabetes and chronic cardiovascular disease were significantly related to development of complications, and diabetes was an independent risk factor for severe seasonal influenza (or 3.63, 95% CI: 1.15–11.51, p = 0.02). Furthermore, Alraddadi *et al* conducted a study and analyzed the risk factors for patients with MERS-CoV infection; finding

diabetes, smoking, and heart disease were also significantly associated with MERS-CoV illness^[30].

Although this study reports interesting data of 100 COVID-19 hospitalized patients, it has its own limitations. Firstly, the small sample size, only 100 patients were enrolled because of difficulty in enrolling patients with the above mentioned criteria during that period and the difficulty in having personnel available to administrate the questionnaire. The questionnaires probably should have been done in a more specific way to better understand the pathophysiology to the disease.

Conclusion

COVID-19 is a global pandemic evolving in real time. It is a highly infectious disease with multitude of effects involving almost all systems of body. It can be life-threatening in elderly patients with multiple comorbidities. The COVID-19 pandemic is an example of a multi-systemic infectious disease that needs early collaboration with diverse clinical specialties to curb the burden of the disease.

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