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COVID-19 Pandemic an Update for Celiac Community

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Abstract Nobody believed in a new pandemic this year. COVID19 pandemic is a public health issue. The evolution of the COVID19 pandemic is important to be known by everyone in the medical world. Our goals in this narrative review were to analyze novel coronavirus from all points of view: epidemiology, clinical, and the relationship with Influenza Virus.

Keywords: *epidemiology, novel virus, asymptomatic carriers, clinical manifestations, imaging characteristics, laboratory tests*

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1. Introduction

Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), Human coronavirus 229E (HCoV-229E) and Human coronavirus OC43 (HCoV-OC43) were the only coronaviruses known to infect humans [1]. Recombination between defective-interfering RNA and helper virus RNA can be involved in the natural evolution of defective-interfering RNAs [2]. The beginning of 2020 has seen the Global Emergency of Wuhan Coronavirus Disease (COVID-19) caused by a novel coronavirus, named Wuhan Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is a beta coronavirus that affects the lower respiratory tract and manifests as pneumonia in humans [3] and belongs to a clade within the subgenus Sarbecovirus, Orthocoronavirinae subfamily [4]. Other researchers suggested that the new coronavirus should be named as the "2019 acute respiratory syndrome coronavirus" (TARS-CoV), and the disease caused by TARS-CoV should be called 2019 acute respiratory syndrome (TARS) [5].

Genetic analyses of eighty-six complete or near-complete genomes of SARS-CoV-2 revealed many mutations and deletions on coding and non-coding regions [6]. Other phylogenetic analyses of whole-genome sequences showed that it clustered with other SARS-CoV-2 reported to Wuhan [7]. Genome Detective, a web-based software application, was developed for rapid identification and characterization of SARS-CoV-2 genomes [8]. As COVID-19 has affected almost every country in Europe, our goals were to analyze the epidemiology of COVID-19, the latest news from clinical studies about COVID-19 and the relationship with Influenza Virus.

2. How the COVID-19 Pandemic Started?

The latest epidemics of the XXI century were HIV and avian influenza [9]. The Chinese researchers said that the COVID-19 epidemic was growing in December 2019, specifically in China [10], where expected COVID-19 risk was >50% in 130 (95% CI 89-190) cities and >99% in the four metropolitan areas [11]. COVID-19 was in regular evolution [12]

- *From December 2019 until January 2020* - 425 confirmed cases in Wuhan [13];
- On *28 January 2020* - 4500 laboratory-confirmed cases, with > 100 known deaths [14];
- On *7 February 2020* - 31516 infected persons and 638 deaths across 25 countries [15];
- On *9 February 2020* - 37287 cases have been confirmed infection of SARS-CoV-2 in China. 302 cases have also been reported from other 24 countries [16];

- On *10 February 2020* - 40554 cases have been confirmed globally with SARS-CoV-2 [17];
- On *11 February 2020* - 44672 confirmed cases were reported. Among confirmed cases, most were aged 30-79 years (86.6%), diagnosed in Hubei (74.7%), and considered mild (80.9%) [18]. The infection was spreading at an exponential rate, with a doubling period of 1.8 days [19];
- On *14 February 2020* - 49970 confirmed cases were reported nationwide, of which 37884 were in Hubei Province [20];
- On *24 February 2020* - between 37415 and 38028 cases in Hubei and 11588-13499 cases in other provinces were predicated on models. These data suggested that the epidemic growth has slowed, and the containment strategies implemented in China were successfully [21]. Aggressive isolation measures were proposed in China and a progressive reduction of cases was found in the last few days [22]. But the researchers said that with many people returning from an extended holiday, China needs to prepare for the possible rebound of the epidemic [18]. Other reason for a possible rebound of the epidemic would be the fact that a new way of evolution besides mutation in SARS-CoV-2 was reported [23].

Some researchers said that the case-fatality rate (about 2.67%) of COVID-19 among the confirmed cases was lower compared with Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) [24]. The mortality of SARS-CoV-2 in China was 2.3%, compared with 9.6% of SARS and 34.4% of MERS reported by the World Health Organization [25]. Other researchers said that the risk of death among young adults was higher than that of seasonal influenza [26].

The potential intermediate hosts transmitting SARS-CoV-2 to humans were pangolins, snacks, and the turtles (Chrysemys picta bellii, Chelonia mydas, and Pelodiscus sinensis) [27]. But the researchers did not identify the SARS-CoV-2 in animals sold at the market to support the hypothesis of zoonotic origins of SARS-CoV-2 from the Huanan seafood market in Wuhan, Hubei province, China [28]. However, a pangolin coronavirus GX_P2V as a workable model for COVID-19 research was developed [29]. The molecular analysis suggested other intermediate hosts of SARS-CoV-2, namely bats [30]. These bats were used in Traditional Chinese Medicine [31]. The evidence that showed that the COVID-19 could be transmitted from person to person was that more than 1700 bedside clinicians have been infected [32]. COVID-19 was reported to spread via droplets, contact, and natural aerosols from human-to-human [33]. The infection from contact with potentially asymptomatic traveler was reported [34]. Other confirmed asymptomatic carrier of COVID-19 was reported [35]. The infection during the incubation period was also reported [36], but other researchers said that COVID-19 does not have infectivity during the incubation period [37]. The median incubation period was 5.2 days [38], similar to SARS [39]. It was believed that SARS-CoV-2 was transmitted through the respiratory tract and then induced pneumonia. The researchers found the presence of SARS-CoV-2 in anal swabs and blood. More anal swabs positives than oral swabs positives in a later stage of COVID-19 suggested transmitted through oral-fecal routes [40]. The probability of sustained human-to-human transmission was 0.41 (credible interval [0.27, 0.55]) but the probability of sustained human-to-human transmission after hospitalization was only 0.012 (credible interval [0, 0.099]) [41]. The uncertainty prevails over the transmission routes of SARS-CoV-2 [42].

European researchers investigated how the risk was increasing in time in Europe as the number of patients with COVID-19 in China was growing [43]. The first case of COVID-19 infection in children was reported in Shanghai [44]. COVID-19 infections in children from Shaanxi, Gansu, Ningxia, Hebei, Henan, and Shandong were caused by close family contact [45]. The cases from Henan Province were mostly imported cases [46]. Countries with a higher risk of COVID-19 transmissions are France [47], Italy [48], UK [49], Germany, and Russia. One case was reported in these countries [50]. Fourteen cases have been reported in the United States [51]. The first case of SARS-CoV-2 infection has also been reported in Canada [52], Thailand [53], and Nepal [54]. The median with 95% CI of the reproductive number of COVID-19 was about 2.28 (2.06-2.52) on the Diamond Princess Cruise ship [55]. But 226 exported cases (95% confidence interval: 86,449) were prevented because of the drastic reduction in travel volume of mainland China in January and February 2020 [56].

The researchers said that thermal passenger screening on airports was improbable to detect all SARS-CoV-2 infected travelers [57]. Quarantine for COVID-19 increased the possibility of psychological and mental problems. The researchers proposed a structured letter therapy, a psychological intervention approach [58] and, the medical workers need to pay attention to the mental health status of the population [59]. The Italians solution was recommended quarantine open windows and songs at the windows over the empty streets [60]. The diseases prevention were needed to reposition [61]. The laws related to public health, the reform current emergency response system, clarify the dominance and function of disease control and prevention systems in China were suggested update [62]. Despite the high infectivity and the case-fatality rate remains low was recommended [63]. Constant and rigorous self-isolation was recommended [64]. The researchers recommended that the length of quarantine should be at least 14 days, found on the 95th percentile estimate of the incubation period [65], to avoid the risk of virus spread. There was no observable difference between the incubation time for SARS-CoV-2, SARS-CoV, MERS-CoV [66].

3. COVID-19 Clinical Studies Analysis

Chinese researchers from Hubei province proposed for investigations the following factors: the prevention, the diagnosis, the treatment, and the accessibility of medical resources [67]. COVID-19 can be confirmed based on the patient's history, clinical manifestations, imaging characteristics, and laboratory tests [68].

The researchers speculated that SARS-CoV-2 might be detected in the tears and conjunctival secretions in COVID-19 patients with conjunctivitis [69]. So it was necessary to recognize possible early ocular manifestations

[70]. Eye protection against the COVID-19 pneumonia epidemic was suggested by ophthalmic experts [71]. Among patients with pneumonia caused by SARS-CoV-2 fever was the most common symptom, followed by cough [72]. Other patients have muscle soreness, fatigue, well as acute respiratory distress syndrome [73]. Patients with COVID-19 pneumonia usually had a history of travelling in the epidemic area, have been unprotected to patients who had a fever or respiratory symptoms and had associate diseases [74]. The symptoms of patients from different China regions were various; in Zhejiang province, the symptoms were relatively mild compared to Wuhan province [75]. The COVID-19 symptoms in children are usually mild [76].

The majority of patients with COVID-19 pneumonia had normal chest radiographs [77]. But imaging changes in COVID-19 pneumonia are rapid [78]. Chest computed tomography (CT) has a high sensitivity for the diagnosis of COVID-19 and, was considered as a primary tool for the current COVID-19 detection in epidemic areas [79]. CT showed rapidly progressing peripheral consolidations and ground-glass opacities (GGO) in both lungs [80]. So characteristic CT imaging patterns were peripherally distributed multifocal GGO with patchy consolidations and posterior part or lower lobe involvement predilection [81]. The role of radiologists was not only early detection of lung abnormality but also in the suggestion of disease severity. Increasing numbers, extent, and density of GGO on CT indicated disease progression [82]. Chest CT showed the highest severity at ten days after the first onset of symptoms [83]. Children with SARS-CoV-2 infection presented small nodular GGO on chest CT images [84]. A recent article concludes that this new disease must be recognition amongst radiologists [85].

Most patients were diagnosed in the advanced stage with poor prognosis [86]. The following factors led to the progression of COVID-19 pneumonia: age, history of smoking, maximum body temperature on admission, respiratory failure, albumin, C-reactive protein [87]. Severe patients also had white blood cell count, lymphocyte count, and D-dimer level changed [88]. Abnormal coagulation results were associated with poor prognosis in patients with COVID-19 pneumonia [89].

It was developed a rapid and simple point-of-care lateral flow immunoassay which can detect IgM and IgG antibodies simultaneously against SARS-CoV-2 in human blood within 15 minutes which can identify patients at different infection stages. The test sensitivity was 88.66%, and the test specificity was 90.63% [90]. Reverse transcription-polymerase chain reaction (RT-PCR) assay was initially negative for atypical COVID-19 pneumonia [91]. A case of COVID-19 infected pneumonia with twice negative SARS-CoV-2 nucleic acid testing within 8 days was reported [92]. Detectable SARS-CoV-2 viral RNA in blood was a reliable indicator for further clinical severity. The positivity of SARS-CoV-2 viral RNA indicated the presence of virus RNA in extra-pulmonary sites [93]. But RNA positive cases and negative RNA cases shared similar clinical symptoms in 54 patients who were newly diagnosed COVID-19 patients in Wuhan Fourth Hospital [94]. It was needed to find a way to decrease the "false-negative results" of SARS-CoV-2 nucleic acid detection [95]. The positivity of specific IgM antibody, the negativity of viral RNA from pharyngeal swabs but with GGO on chest CT images were significant for early detection and early isolation of SARS-CoV-2 [96]. SARS-CoV-2 viral RNA was detected in feces during convalescence [97]. An asymptomatic child who was positive for a COVID-19 by RT-PCR in a stool specimen after the last virus exposure was reported [98].

A case of a 30-week pregnant woman with COVID-19 delivering a healthy baby with negative RT-PCR tests for COVID-19 was also reported [99]. The laboratory characteristics of COVID-19 pneumonia in pregnant women were lymphopenia ($<1•0 \times 10^9$ cells per L) and increased aminotransferase concentrations [100]. But recently was published a case of a well infant with COVID-19 with high viral load. The cause of COVID-19 infection was human-to-human transmission [101]. The Chinese Neonatal COVID-19 expert working Group established new measures on the prevention and control of neonatal COVID-19 infection [102].

Diarrhea was suggested to be a missing link in the treatment of SARS-CoV-2 [103]. The researchers speculated that COVID-19 might have some relationship with the gut microbiota through the angiotensin-converting enzyme 2 receptor (ACE2) [104]. ACE2 fused to an immunoglobulin Fc domain, providing a neutralizing antibody with maximal breath to avoid any viral escape [105]. But the up-regulation of ACE2 expression in liver tissue may also be the possible mechanism of liver tissue injury caused by SARS-CoV-2 infection [106]. Liver injury was occurred in 22 cases (55%) during the disease [107].

Chloroquine phosphate (chloroquine) had a lot of antiviral effects, including anti-coronavirus. It recommended chloroquine phosphate tablet, 500 mg twice per day for ten days for patients diagnosed as mild, moderate, and severe cases of COVID-19 pneumonia and without contraindications to chloroquine [108]. The most other promising compound were the following: 1.remdesivir (GS-5734), a nucleotide analogue prodrug currently in clinical trials for treating Ebola virus infection; 2.a combination of the human immunodeficiency virus type 1 (HIV-1) protease inhibitors, lopinavir/ritonavir, and interferon-beta (LPV/RTV-INFb) [109].

The need for rapid vaccine development and the potential of a plant system for biopharmaceutical development was discussed [110]. The fast genomic sequencing and open access data were available [111]. Development of epitope-based peptide vaccine against SARS-CoV-2 such as 13 Major Histocompatibility Complex-(MHC) I and 3 MHC-II epitopes that have antigenic properties were also available [112]. These can help to give us more knowledge on the host immune response as well as the plan for therapeutic vaccines shortly. Other researchers observed a set of B cell and T cell epitopes derived from the spike (S) were identified and nucleocapsid (N) proteins and no mutation among the 120 available SARS-CoV-2 sequences. Immune targeting of these epitopes was preliminary identification as a potential vaccine targets for the COVID-19 [113].

4. Influenza and COVID-19

Influenza disease occurred in the 2019 winter in temperate regions, newly emerging SARS-CoV-2 also occurred during the 2019 winter months [114]. Concerning influenza, the plan for preventing COVID-19 pandemic included the following phases: detection, assessment, treatment, escalation, and recovery [115].

Bénézit et al concluded that non-influenza respiratory viruses were common in adults admitted with influenza-like illness (ILI) during three influenza seasons (2012-2015) [116]. Nazareth et al revealed the presence of common respiratory viruses in the lower respiratory tract without causing symptomatic infection [117]. But these studies were published only on February 13, 2020. So, the COVID-19 pandemic could not be predicted in any study and had a case fatality rate of 2.3% compared with the 2009 influenza pandemic with an estimated <1% [118,119,120]. The COVID-19 infection fatality risk-the actual risk of death among all infected individuals-was 0.3% to 0.6% in Japan comparable to the Asian influenza pandemic of 1957-1958 [121]. The influenza infection transmission was more generalized compared to that of COVID-19 said Nature Journal [122]. Another study concluded that transmission characteristics of COVID-19 seem to be of similar size to pandemic influenza indicating a risk of global spread [123]. The huge difference between the COVID-19 and influenza was the fact that in the influenza A (H1N1) pandemic 2009, death was not as frequent in the medical and nursing staff as inpatients [124].

Coronaviruses, like influenza viruses, circulated in nature in various animal species [125]. The original host of this virus was bats and an intermediate host facilitating the emergence of the virus in humans was an animal sold at the seafood market in Wuhan [126]. Other suggested natural reservoirs of coronavirus in Northern Italy were hedgehogs (*Erinaceus europaeus*) [127].

COVID-19 infections showed similar symptoms in the middle of the current influenza season [128]. Ding et al reported 5 patients diagnosed with COVID-19 and influenza virus infection. Common symptoms were fever, cough, and shortness of breath [129]. Since the symptoms are similar to other respiratory infections, differential diagnosis in travelers arriving from countries with wide-spread COVID-19 must include other more common infections such as influenza and other respiratory tract diseases [130]. Wu et al reported a patient with pneumonia with SARS-CoV-2 and H1N1 virus. The researcher said that influenza respiratory symptoms could further complicate the recognition of the SARS-CoV-2 [131]. Therefore primary care patients with ILI were followed to identify COVID-19 patients [132] and influenza-associated pneumonia was a risk factor for the seriousness of COVID-19 disease [133]. The decrease of the interference of the influenza epidemic in the COVID-19 pandemic was suggested [134]. But unlike common viral agents (such as Adenovirus, Rhinovirus, Norovirus, Influenza, Respiratory Syncytial Virus), COVID-19 has not shown to cause more severe disease in immunosuppressed patients [135].

An immediate concern was in the United States, wherein February 21, 2020, 342 women of childbearing age (15–44 years) had been hospitalized in with influenza during the current flu season [136]. On February 26, 2020, Livingston et al concluded that in the United States people should focus their attention on influenza, not on COVID-19 and take preventive measures [137]. In the United States today there are over 46,000 people infected with COVID-19. Researchers from Influenza Division, National Center for Immunization and Respiratory Diseases from the United States evaluated the first case of COVID-19 [138] and the first known person-to-person transmission of SARS-CoV-2 in the United States [139].

Ye et al analyzed the sampling methods from the upper respiratory tract related to infectious diseases such as SARS, MERS, and H1N1 for diagnosing patients with COVID-19 [140]. Currently available and novel emerging diagnostic methods for the common respiratory viruses were not yet well implemented [141]. But diagnostic systems for COVID-19 were developed with urgency [142]. An et al described a patient, with “fever for one week, diarrhea, anorexia, and asthenia.” The H1N1 virus serology was negative and the COVID-19 nucleic acid test was negative. Her body temperature rose to 39.2°C after a business trip. The chest CT showed bilateral multifocal ground-glass opacities. The COVID-19 pneumonia nucleic acid test was positive. The researchers recommended the chest CT for the patients` evaluation with suspected COVID-19 pneumonia [143].

McCarty proposed nutraceuticals for the potential for boosting the type 1 interferon response to influenza and coronavirus [144]. α-glucan-based standardized mushroom extract (AHCC) provided a regulated and protective immune response in humans affected by the West Nile virus, influenza virus, avian influenza virus, hepatitis C virus, papillomavirus, herpes virus, hepatitis B virus and HIV by promoting. So Di Pierro et al. recommended AHCC as a possible therapeutic role in COVID-19 treatment [145]. Because new influenza virus strains emerge every year and requiring new immunizations, Gurwitz said that vaccines based on viral-encoded peptides may not be effective against future coronavirus epidemics and suggested the angiotensin receptor blockers as tentative for SARS-CoV-2 therapeutics [146]. Other researchers recommended the influenza vaccine for uninfected people and health care workers [147].

The 1918 influenza pandemic from London, the United Kingdom with incorporated zoonotic introductions and emigration was a model for future trends and the reporting ratio of the COVID-19 outbreak [148]. The principles described for influenza pandemic preparations for hospitals and intensive care units were used for the COVID-19 pandemic [149,150]. So preparing for a potentially infectious disease pandemic from influenza or COVID-19 was essential for critical healthcare and infrastructure services [151]. The first SARS-CoV epidemic of 2002/2003 and seasonal influenza provided predictive risk mapping using population travel data, and mapping super-spreader trajectories [152]. The existing sentinel primary care-based surveillance systems for influenza were essential to detect community transmission of SARS-CoV-2 [153]. Al-Qaness et al used two different datasets of weekly influenza confirmed cases in the USA and China for a new model for the optimization method for forecasting confirmed cases of COVID-19 [154]. The

Global Initiative on Sharing All Influenza Data (GISAID) public platform disseminated several full genomic sequences of COVID-19 [155]. Lai et al analyzed 52 SARS-CoV-2 genomes available on 4 February 2020 at GISAID. The estimated reproduction number (R-value) was 2.6 (range, 2.1-5.1) compared to 2.4 in December 2019 [156]. Matsuyama et al revealed through GISAID that SARS-CoV-2 infection could be isolated using a TMPRSS2-expressing VeroE6 cell [157]. Stoffel et al proposed One Health a collaborative, multisectoral, and transdisciplinary approach. One Health has the potential to not only save human and animal lives but also to safeguard the global economy [158].

5. Conclusions

COVID-19 is the last pandemic of our time. The onset of the Wuhan epidemic was unclear. The transmission of the disease was from patient to patient. The pandemic was spread so quickly because was transmitted due to asymptomatic carriers. Clinical manifestations among patients with pneumonia caused by SARS-CoV-2 were fever followed by a cough. Imaging characteristics were progressing peripheral consolidations and ground-glass opacities. Serological IgM and IgG antibodies and viral RNA were helpful in the diagnosis. Treatment is not standardized. We recommended persistent and strict self-isolation. Influenza sentinels helped but it is time for other completely different epidemiological strategies and health systems for actual and next COVID pandemic.

Author's Statements

All authors of this paper have read and approved the final version submitted.

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