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Sarscov 2 symptoms in Italy, France, Asia and USA

Abstract: On 31 December 2019, China observed a cluster of pneumonia of unknown aetiology in the city of Wuhan, later related to a novel Coronavirus. On 11 march, WHO declared pandemic due to Sars-cov 2 spreading all over the world. This literature review carries out a comparative analysis of the symptoms and manifestations of Sars-Cov 2 in different geographical areas of the globe, highlighting clinical differences.

Keywords: Covid 19; Sars-Cov 2 symptoms; clinical events; etiologies.

1. Introduction

The current outbreak of the novel coronavirus SARSCoV-2 is spreading to many countries[1]. On 31 December 2019, China observed a cluster of pneumonia of unknown aetiology in the city of Wuhan, in Hubei province, among people who had been in Wuhan's South China Seafood City market[2]. On 9 January 2020, the China CDC discovered that its causative agent belonged to coronaviridae family[3]. On 11 February, it was officially named COVID-19 by the

[1] Thirumalaisamy P. Velavan et al., The COVID-19 epidemic, Tropical Medicine and International Health, ss. 278–280.

[2] https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-international-outbreak

[3] https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-international-outbreak

World Health Organization (WHO) [2] and then Sars-cov 2 (*Severe Acute Respiratory Syndrome coronavirus* 2). On 11 march, WHO declared pandemic due to Sars-cov 2 spreading all over the world. Coronavirus are the largest enveloped RNA viruses due to the size of their genoma (28 to 32 kb)[4]. They can affect a variety of systems (hepatic, respiratory, gastrointestinal, and neurological) creating both acute and chronic diseases[5]. People are usually infected by 4 coronavirus: NL63, HKU1, 229E and OC43[6]. These viruses usually create an upper respiratory tract infection with the common cold symptoms[7]. However, coronaviruses, which have a zoonotic origin, such as SARS-CoV, MERS-CoV, and the novel Sars-cov 2, can create more severe illness[8]. SARS-CoV-2 genome is 96% identical at the whole-genome level to a bat coronavirus[9]. The main structural genes are the nucleocapsid protein (N), a small membrane protein (SM), the membrane glycoprotein (M) and the spike protein (S)[10]. This protein (S glycoprotein) is the viral

[4] Parham Habibzadeh1, Emily K Stoneman2, The Novel Coronavirus: A Bird's Eye View; Berend Jan Bosch et al., The Coronavirus Spike Protein Is a Class I Virus Fusion Protein: Structural and Functional Characterization of the Fusion Core Complex.

[5] Thirumalaisamy P. Velavan et al., The COVID-19 epidemic, Tropical Medicine and International Health, ss. 278–280.

[6] Thirumalaisamy P. Velavan et al., The COVID-19 epidemic, Tropical Medicine and International Health, ss. 278–280;_Berend Jan Bosch et al., The Coronavirus Spike Protein Is a Class I Virus Fusion Protein: Structural and Functional Characterization of the Fusion Core Complex, ss.8801–8811; Ding X. Liu et al., Human Coronavirus-229E, -OC43, -NL63, and -HKU1.

[7] Parham Habibzadeh1, Emily K Stoneman2, The Novel Coronavirus: A Bird's Eye View, ss.11:65-71.

[8] Parham Habibzadeh1, Emily K Stoneman2, The Novel Coronavirus: A Bird's Eye View, Int J Occup Environ Med 2020, ss. 11:65-71.

[9] Zhou P, Yang XL, Wang XG et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin.

[10] Thirumalaisamy P. Velavan et al., The COVID-19 epidemic, ss. 278–280.

membrane protein responsible for cell entry in the host[11]. In the specific case of the Sars-cov 2 this protein binds the angiotensin converting enzyme 2 (ACE-2) receptor on the type 2 pneumocytes and ciliated bronchial epithelial cells[12]. The mean incubation period lasts five days, while the median incubation period lasts 3 days (range: 0–24 days)[13].

2. Materials and methods

The aim of this literature review is to evaluate symptoms of Sars-cov 2 in different countries. In order to rich this purpose, data have been collected from scientific literature trough Pubmed database and trough the web site of the main Health Authorities. Key words: 2019-nCoV; SARS-CoV-2; COVID-19; China Epidemic; Children:COVID-19, SARS-CoV-2; Gastrointestinal Manifestations of SARS-CoV-2 Infection; COVID-19 skin manifestation; viral exanthema; Covid 19 Vietnam; Cytokine storm, Immunopathology; Anosmia · Smell · Hyposmia · Dysgeusia · Taste · Loss ·Gustatory · Olfactory · Olfaction · Infection · ENT; Sars-cov 2 USA; Sars-cov 2 Italy; Sars-cov 2 Asia; COVID-19, Epidemiology, Causes, Prevention and control; covid 19 dimond princess; covid 19

[11] Thirumalaisamy P. Velavan et al., The COVID-19 epidemic, ss. 278–280; Parham Habibzadeh1, Emily K Stoneman2, The Novel Coronavirus: A Bird's Eye View, ss. 11:65-71; Berend Jan Bosch et al., The Coronavirus Spike Protein Is a Class I Virus Fusion Protein: Structural and Functional Characterization of the Fusion Core Complex, ss. 8801–8811.

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[13] Thirumalaisamy P. Velavan et al., The COVID-19 epidemic, ss. 278–280; Guan W, Ni Z, Yu H, et al. Clinical characteristics of 2019 novel coronavirus infection in China.

France point epidemiologique; covid 19 Italy; Covid 19 WHO; Coronavirus; Novel coronavirus; 2019-nCoV; SARS coronavirus Outbreak; China; Wuhan; Emerging viruses; Asymptomatic and Presymptomatic SARS-CoV-2 Infections; Sarsc-cov 2 Washington; epidemiologic study; sars-cov 2 South Korea; Sars-cov 2 PAHO; Sars-cov 2 ALI, ARDS; pathogenesis SARS-CoV-2.

3. **Results**

In Italy fever, dyspnea and cough are the most commonly observed symptoms, while diarrhea and hemoptysis are less commonly ones observed. Overall, 5.8% of patients don't have any symptoms at hospital admission. In the 92,5% of cases of hospitalization the beginning diagnosis are pneumonia and respiratory failure. 7,5% diagnosis at the hospitalization time seem not to be related to covid 19. In some cases the hospitalization is apparently related to neoplastic diseases or it is apparently related to cardiovascolar deseases (such as myocardial infarction and heart failure), while in other cases the hospitalization is apparently related to gastrointestinal diseases (such as cholecystis and cirrhosis). Acute Respiratory Distress syndrome have been observed in the majority of patients (97.0% of cases), followed by acute renal failure (22.6%). Many of them have other comorbidities. Superinfection have been observed in 12.4% and acute cardiac injury in 10.8% of cases. 1.9% of cases have critical conditions, 8.1% have no specific symptoms, 13.2% are paucisymptomatic, 19.9% are symptomatic, 15.4% have severe symptoms, 41.9% have mild symptoms[14]. 20% of patients in northern Italian hospitals have the

[14] A.A.V.V., Istituto Superiore di Sanità, Characteristics of SARS-CoV-2 patients dying in Italy Report based on available data on May 7th , 2020; A.A.V.V., Istituto Sueriore di Sanità, Integrated surveillance of COVID-19 in Italy.

following skin manifestations such as urticaria, acral ischemia, livedo reticularis, petechial, morbilliform rashes, vescicular rashes, varicella-like exanthem[15].

Fever	Cough	dyspnea	diarrhea	hemoptysis
76%	38%	73%	6%	1%

Both Italian and French patients have olfactory dysfunction (such as anosmia, hyposmia, phantosmia, parosmia, Nasal obstruction, Rhinorrhea, Postnasal drip, Sore throat, Face pain/ heaviness, Ear pain, Dysphagia) and gustatory disorders (such as impairment of the following four taste modalities: salty, sweet, bitter, and sour)[16]. In France most commons symptoms are fever and cough, while additional symptoms are myalgia, headache, asthenia, loss of appetite, diarrhea, abdominal pain, arthralgia, nausea, sore throat, rhinorrhea, shortness of breath[17]. Some patients are asymptomatic and other have only fever. The great part of them had a benign evolution, but some of them developed pneumonia[18]. The great part of patients which developed a severe disease had at least one comorbidity such as cardiovascular, pulmonary, hepatic, kidney diseases, obesity, diabetes. Mild

[15] Angelo Valerio Marzano et al., Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients.

[16] Jerome R. Lechien et al., Olfactory and gustatory dysfunctions as a clinical presentation of mild−to−moderate forms of the coronavirus disease (COVID−19): a multicenter European study, European Archives of Oto-Rhino-Laryngology.

[17] Jerome R. Lechien et al., Olfactory and gustatory dysfunctions as a clinical presentation of mild−to−moderate forms of the coronavirus disease (COVID−19):a multicenter European study; Gianfranco Spiteri et al., First cases of coronavirus disease 2019 (COVID-19) in the WHO European Region.

[18] Gianfranco Spiteri et al., First cases of coronavirus disease 2019 (COVID-19) in the WHO European Region.

respiratory or gastrointestinal symptoms are predominant among children[19]. Health authorities and media have reported one fatal case in France (16 years of age)[20].

Fever	common
Cough	common
headache	additional
Myalgia arthralgia	additional
Nausea, vomiting and diarrhea	additional
loss of appetite	additional
asthenia	additional
abdominal pain	additional

According to studies in China, fever is the most common symptom (92.8%), followed by cough (69.8%), dyspnea (34.5%), myalgia (27.7%), headache (7.2%) and diarrhea (6.1%)[21], upper airway congestion(61.5%). Rhinorrhea has been noted in only 4.0% [14], a sore throat in 5.1%[22] and pharyngalgia in 17.4%[23] of patients with relevant clinical information. Most patients have a normal white blood cell count, but 56.8% of patients developed leukopenia. A recent study in Beijing reported

[19] A.A.V.V., ECDC, Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK.

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[22] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, ss. 395:507–13.

[23] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China.

that 2 of the 13 patients with SARS-CoV-2 pneumonia were children aged between 2–15 years[24]. Among adult patients, cardiovascular disease and hypertension are the most common comorbidities, followed by diabetes mellitus[25]. Radiological findings of SARS-CoV-2 pneumonia are variable. More than 75% of patients present with bilateral lung involvement[26], and multilobe involvement was also common (71%)[27]. Ground-glass opacity (GGO) is the most common finding from chest computed tomography (CT)[28]. Patients with more severe infection had neurologic manifestations, such as acute cerebrovascular diseases, impaired consciousness, and skeletal muscle injury[29]. Acroischemia, characterized by cyanosis, skin bulla and dry gangrene has been reported in China[30].

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[24] Chang D, Lin M, Wei L, Xie L, Zhu G, Dela Cruz CS, et al. Epidemiologic and clinical characteristics of novel coronavirus infections involving 13 patients outside Wuhan, China.

[25] A.A.V.V., Istituto Superiore di Sanità, Characteristics of SARS-CoV-2 patients dying in Italy Report based on available data on May 7th , 2020.

[26] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, ss. 395:507–13.

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[28] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China; A.A.V.V., Istituto Superiore di Sanità, Characteristics of SARS-CoV-2 patients dying in Italy Report based on available data on May 7th , 2020; Jerome R. Lechien et al., Olfactory and gustatory dysfunctions as a clinical presentation of mild−to−moderate forms of the coronavirus disease (COVID−19):a multicenter European study.

[29] Mao L et al., Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China.

[30] A.A.V.V., Santé publique France, Point épidémiologique COVID-19.

Fever	92.8%
Cough	69.8%
Dyspnea	34.5%
Myalgia	27.7%
headache	7.2%
diarrhea	6.1%
upper airway congestion	61.5%
Rhinorrhea	4.0%
sore throat	5.1%
Pharyngalgia	17.4%
Leukopenia	56.8%

In Japan, the main symptoms identified were fever (72%), cough (62%), pneumonia (65%), sore throat (34 %), general malaise (33%), headache (27%), nasal congestion (27%), diarrhea (17%), nausea and vomiting (8%), acute respiratory distress syndrome (ARDS) (7%), joint or muscle pain (7%)[31]. Respiratory tract symptoms occurred also between passengers and crew of Daimond Princess cruise ship in Yokohama[32].

[31] A.A.V.V., Descriptive epidemiology of 112 confirmed cases of novel coronavirus infectious disease (COVID-19) as reported by the national epidemiological surveillance of infectious diseases (NESID) system and active epidemiological investigation.

[32] Eilif Dahl, Coronavirus (Covid-19) outbreak on the cruise ship Diamond Princess, ss. 5–8 10.

Fever	72%
Cough	62%
Pneumonia	65%
sore throat	34 %
general malaise	33%
nasal congestion	27%
Headache	27%
Diarrhea	17%
nausea and vomiting	8%
joint or muscle pain	7%
ARDS	7%

In Vietnam have been noted symptoms such as dyspnea with hypoxemia, vomiting and loose stools, fever, increased level of C-reactive protein[33].

A study in South Korea, described that the initial symptoms were fever or feeling hot (32.1%), sore throat (32.1%), cough or sputum production (17.9%), chills (17.9%), and muscle ache (14.3%)[34]. However, 10.7 % patients were asymptomatic. In some patients, pneumonia was confirmed using imaging once hospitalized[35].

[33] Lan T. Phan et al., Importation and Human-to-Human Transmission of a Novel Coronavirus in Vietnam.

[34] Insik Kong et al., Early Epidemiological and Clinical Characteristics of 28 Cases of Coronavirus Disease in South Korea, Osong Public Health Res Perspect, ss. 8-14.

[35] Insik Kong et al., Early Epidemiological and Clinical Characteristics of 28 Cases of Coronavirus Disease in South Korea, ss. 8-14.

fever or feeling hot	32.1%
cough or sputum production	17.9%
Chills	17.9%
muscle ache	14.3%
sore throat	32.1%
asymptomatic	10.7 %

In the United Arab Emirates the most common symptoms of COVID-19 are Fever, Tiredness, Dry cough, but Some patients may have aches and pains, nasal congestion, runny nose, sore throat or diarrhea. These symptoms are usually mild and begin gradually[36].

Fever	common
Tiredness	common
dry cough	common
aches and pains	additional
nasal congestion	additional
sore throat	additional
diarrhea	additional
runny nose	additional

In the USA most common typical symptoms are Cough, Shortness of breath or difficulty breathing and Fever[37]. Atypical

[36] Novel Coronavirus (COVID-19), united arab emirates ministry of health and prevention.

[37] A.A.V.V., Characteristics of Health Care Personnel with COVID-19 —United States; Anne Kimball et al., Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility —King County, Washington.

symptoms are malaise, nausea, sore throat, confusion, dizziness, diarrhea, rhinorrhea/congestion, myalgia, headache, chills[38].

Fever	Very common
Cough	Very common
Shortness of breath	Very common
myalgia	Very common
headache	Very common
nausea and vomiting	Common
diarrhea	Common
anosmia	Rare

According to a study in New York City, the most common comorbidities are hypertension (56.6%), obesity (41.7%), diabetes (33.8%)[39], while a study in Washington noted also Chronic lung disease, Cardiovascular disease, Cerebrovascular accident, Renal disease, Cognitive Impairment and Obesity[40]. In children symptoms are similar to the adult ones[41], but Kawasaki disease has been noted in this population as peculiar manifestation[42]. More recent reports also describe gastrointestinal symptoms and asymptomatic infections, especially among young children[43].

[38] Anne Kimball et al., Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility —King County, Washington.

[39] Richardson S. et al., Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area.

[40] Anne Kimball et al., Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility —King County, Washington.

[41] A.A. V.V., Coronavirus Disease 2019 in Children — United States.

[42] Jones VG, Mills M, Suarez D, et al. COVID-19 and Kawasaki Disease: Novel Virus and Novel Case, ss. 537-540.

[43] Thirumalaisamy P. Velavan et al., The COVID-19 epidemic, ss. 278–280.

Fever	Very common
Cough	Very common
shortness of breath	Very common
sore throat	Common
Myalgia	Common
Headache	Common
nausea and vomiting	Less Common
Diarrhea	Less Common

4. Conclusion

a variety of symptoms is typical of Sars-cov2 infection. In particular cough, fever, dyspnea, headache are the most common all over the world in all ages. The initial symptoms of Sars-cov 2 disease are known to be respiratory symptoms such as coughing, in association with fevers; while, additional manifestation can be malaise, nausea and vomiting, sore throat, diarrhea, rhinorrhea/ congestion, myalgia, headache even if the disease epidemiology and phatophysiology remain largely unknown. Kawasaki disease is common in children. Skin manifestations have been observed in some patients. However, the knowledge about this virus is now limited. So considering the importance of this current sanitary issue, further new studies are needed in order to investigate better its clinical features.

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