



Systematic Review of Radiology Signs and Drug Delivery in Patients Affected by Covid-19

Zahra Ranjbar¹, Alireza Bahmani², Khatoon Zendehebodi³,
MehrAra Akanchi⁴, Sara Parviz^{5*}

Abstract

This study has focused on the systematic investigation of radiological signs and drug delivery in patients affected by Covid-19. Researchers believe that the pneumonia caused by the infection of Covid-19 (NCIP) started from the seafood market in Wuhan, by the time this article was published, the coronavirus had spread in 28 countries. Evidence shows that the transmission of the corona virus can occur during the epidemic period. The incubation period of the disease is the period of time when a person is unaware of his disease, but is a carrier of the disease. The incubation period of the new corona virus, Covid-19, is estimated to be about 5.2 days. This has caused the rapid spread of the coronavirus disease. Also, after recovering from this disease for some time, there is a possibility of transmission of the disease through the saliva of a patient with NCIP. Since February 5, 2020, more than 25,000 cases of corona virus have been reported and the number of dead patients is increasing. Medical imaging plays an important role in assessing the severity of the Covid-19 infection. Radiologists should be well aware of the imaging findings of this novel coronavirus. Evidence also suggests that chest CT and ultrasound are better at differentiating COVID-19 infection from other respiratory problems. Its usefulness may therefore be limited to ruling out COVID-19 infection rather than distinguishing it from other causes of lung infection. In addition, chest CT imaging had poor sensitivity and high specificity for detecting asymptomatic individuals.

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Introduction

Corona is a family of viruses that includes several members. The Corona family is not a new family and members of this family have caused various respiratory diseases in the past. including the common cold, severe acute respiratory disease, and Middle East respiratory disease, which are caused by the common cold virus, the Sars virus, and the MERS virus, respectively [1-3]. The current outbreak of the coronavirus is a new member of this family that has not been seen in humans before [4]. This new corona virus is called 2019 or nCOV-2019 and it causes the disease of Covid-19. This virus was

found in humans for the first time at the end of 2019 in one of the cities of China, and because it was a new virus related to 2019, it was called the 2019 corona virus. Apparently, this virus was transferred from bats to another animal called the scaly anteater and through that to humans [5]. Although accurate and complete information is not available due to the newness of this virus, but until now this disease has shown itself in the form of respiratory symptoms. The three main symptoms are: dry cough, fever and shortness of breath. In 80% of cases, the symptoms are mild, and the fever can be very mild or severe.

Corresponding author: Sara Parviz

Address: ¹Bachelor of Science in Anesthesia, Master student in Anesthesia Education at Ahvaz Jundishapur University of Medical Sciences, Iran, ²Department of Emergency Medicine, Ali Ibn Abitaleb Hospital, Zahedan university of medical Sciences, Zahedan, Iran, ³Graduated from Bushehr University of Medical Sciences, Head of Internal ICU, Salman Farsi Hospital, Bushehr, Iran, ⁴Pharm D, Pharmacist, Islamic Azad University of Medical Sciences, Tehran Branch, Tehran, Iran, ⁵Advanced Diagnostic and Interventional Radiology Research Center, Department of Radiology, Medical Imaging Center, Tehran University of Medical Sciences, Tehran, Iran

E-mail: ¹zahraranjbar04@gmail.com, ²drbahmani@yahoo.com, ³kh.zd400@gmail.com, ⁴www.mehrra94@gmail.com, ⁵srparviz@gmail.com



In 20% of cases, severe symptoms manifest as severe shortness of breath or severe acute respiratory disease, which can lead to death in some cases [6]. The disease of Covid-19 rarely shows itself in the form of runny nose, sneezing or sore throat. Who gets a more severe form of the disease depends on several factors, the most important of which is the individual's immune system? People who have an underlying disease, such as heart disease, lung disease, blood pressure, or diabetes, are more susceptible to the severe form of Covid-19 disease [7].

Radiology and Corona

People suspected of having COVID-19 need to know quickly if they have been infected so they can receive appropriate treatment, isolate themselves, and notify people they have been in close contact with (Figure 1). Currently, the official diagnosis of COVID-19 requires laboratory testing (RT-PCR) of nasal and throat samples. Performing RT-PCR depends on specialized equipment and it takes at least 24 hours to prepare the result. This test is not very accurate and to confirm the diagnosis, there may be a need to perform a second RT-PCR or another test [8].



Figure 1. Lung scan

Doctors may use chest imaging to diagnose people with symptoms of COVID-19 while they are waiting for RT-PCR results to be ready or when RT-PCR results are negative and the person is showing symptoms of COVID-19. do X-rays or scans produce images of the organs and structures in the chest. X-rays (radiographs) use radiation to produce a 2D image [9]. These images are usually taken in hospitals using fixed equipment and by a radiographer, they can also be done with portable devices. Computed tomography scans use a computer to combine 2D X-ray images and convert them into a 3D image. They require specialized equipment and are performed by radiography

experts in the hospital [10]. Ultrasound scans use high-frequency sound waves to create images. They can be performed in a hospital or other health care facility such as a doctor's clinic (Figure 2).

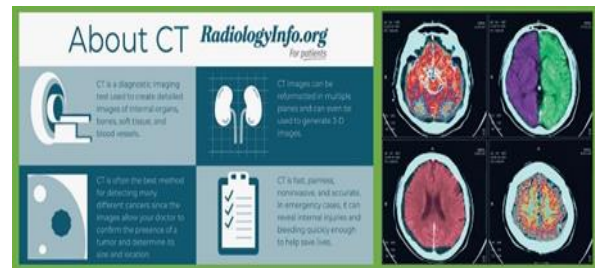


Figure 2 -Computed Tomography (CT or CAT scan) Procedures

Statistical Society

The current study is a systematic review that was used to find relevant articles from SID, PubMed, Web Science, EMBASE, Scopus, Science direct and Google Scholar databases, JAMA Internet database and WHO and CDC website. For the purpose of searching [11], only English articles with the keywords Covid19, treatment, Remdesivir [12], Hydroxychloroquine, ritonavir, lopinavir, Tocilizumab and all possible combinations of these words were used during the years 2019 and 2020. Among the 250 articles obtained, 20 articles had initial conditions, and finally 8 clinical trial articles related to the treatment of Covid-19 were reviewed. We also found 94 studies with 37,631 participants to assess the diagnostic accuracy of chest imaging in investigating people with suspected COVID-19 [13]. Eighty studies each evaluated one imaging method and seven studies each evaluated two imaging methods. All 94 studies used RT-PCR alone or in combination with other criteria as the reference standard for the diagnosis of COVID-19 [14].

Search strategy and selection of articles

Scopus, Google scholar, PubMed databases were searched by searching with keywords such as COVID-19 and Coronavirus 2019 and COVID-19 and drugs to obtain articles related to the selected keywords. Case report articles, editorials and articles that were not published or only an introduction of them were available, as well as summaries of congresses and meetings that were in languages other than English, were ignored [15-17]. Only original research articles that used standard methods to evaluate the effectiveness of different drugs in the treatment of COVID-19 were studied (Figure 3).



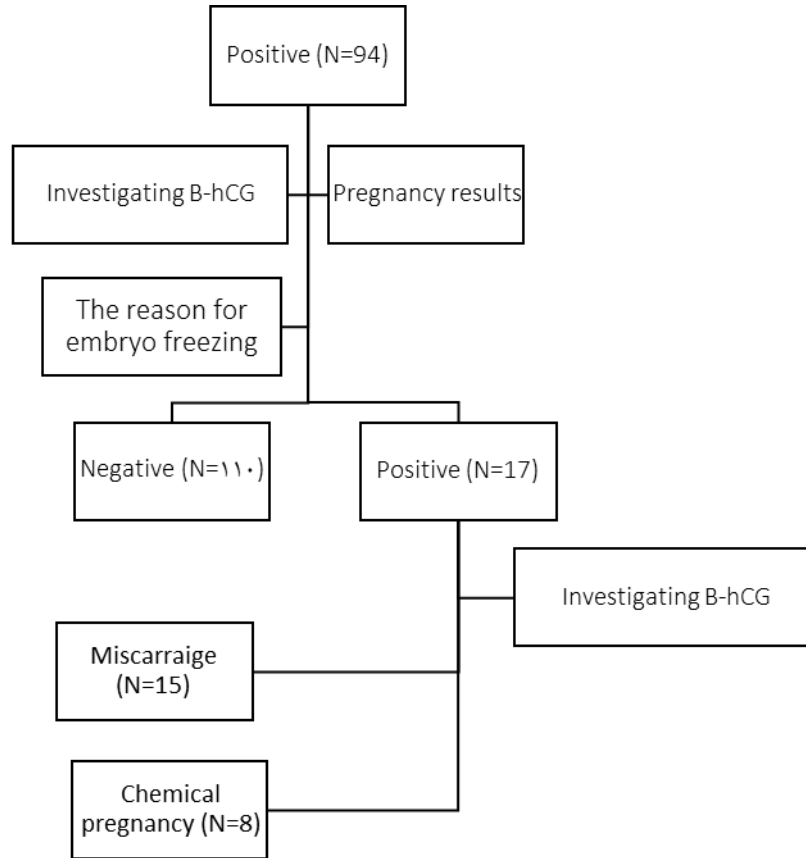


Figure 3. Flow chart of included subjects

Discussion and review

The pooled results showed that chest CT (69 studies) correctly diagnosed it in 87% of people with COVID-19. However, it falsely identified COVID-19 in 21% of people who did not have COVID-19 [18-20].

1- Chest X-ray of suspected persons: pooled results showed that chest X-ray (7 studies) correctly diagnosed this infection in 73% of people with COVID-19. However, it falsely identified COVID-19 in 27% of people who did not have COVID-19 (Figure 4).

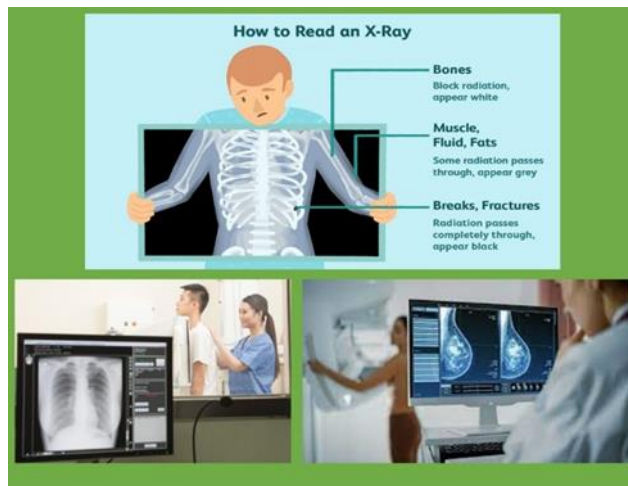


Figure 4. Rays: Uses, Procedure, Results



2- Lung ultrasound of suspected people: the consolidated results showed that lung ultrasound (15 studies) was able to correctly diagnose COVID-19 in 87% of people with this infection. However, it falsely identified COVID-19 in 24% of people who did not have COVID-19 [21].

3- Screening of asymptomatic subjects: We included 10 studies with 3548 asymptomatic participants, of whom 364 (10%) had a final diagnosis of COVID-19. Pooled results from seven studies showed that CT correctly diagnosed it in 56% of people with COVID-19 and misdiagnosed it in 8% of people without COVID-19 (Figures 5 and 6). The use of different drugs in the treatment of COVID-19 has reported different results [22]. For example, in a study conducted on a 50-year-old man admitted on January 21, 2020, the results indicated that the drugs used to reduce the symptoms of this patient were ineffective. The patient came to the clinic with symptoms of fever, chills, cough, fatigue and shortness of breath and was immediately admitted to the influenza ward and received oxygen [23]. The drugs prescribed for this patient included interferon alfa-2b and lopinavir plus ritonavir as an antiviral and moxifloxacin to prevent secondary infection. Due to shortness of breath and hypoxemia, methylprednisolone has been used to reduce lung inflammation. After receiving the medicine, his body temperature dropped from 39 to 36.4 degrees Celsius. However, there was no improvement in other symptoms such as cough, shortness of breath and fatigue in the patient [24]. On day 12 of illness, chest X-ray radiography showed progression in the liver and spread to both lungs. On the 13th day of the disease, the lack of improvement in the patient's symptoms and the continuation of oxygen saturation above 95% were reported. In the afternoon of the 14th day of the disease, hypoxemia and shortness of breath worsened and despite receiving HFNC oxygen therapy (concentration

100%, flow rate 40 liters per minute), the amount of oxygen saturation decreased to 60%, the patient had a sudden cardiac arrest and although aggressive ventilation, chest compression and adrenaline injection were given to him immediately, unfortunately the rescue was not successful and he died [25-27]. In another study in which lopinavir/ritonavir was used, the efficacy of these two drugs was reported. This study was conducted by prescribing this drug to a 54-year-old Korean man living in Wuhan, China. On January 20, 2020, this person entered Korea and the first symptoms of chills and muscle pain appeared on January 22. After contacting a public health center on January 25, he was admitted to the negative pressure room at Gyeonggi Hospital and tested positive for COVID-19 on January 26. Lopinavir 200 mg and ritonavir 50 mg orally were prescribed to the patient. Significantly, from the day after taking lopinavir and ritonavir, the beta load of coronavirus decreased and after that no detectable titer of coronavirus was observed. It is possible that the reduction in SARS-CoV-2 load was due to the administration of lopinavir and ritonavir or both. Therefore, more data should be collected to find out the direct effect of lepinavir and ritonavir on the treatment of COVID-19. By comparing these two studies, it can be concluded that checking the effectiveness of these two drugs needs more evidence and studies, and factors such as the time of drug administration can be effective in the results of these drugs. In addition to these two review articles, another article was published in April 2020 that examined 199 patients with COVID-19, which showed the effect of prescribing lepinavir and ritonavir on the improvement of the disease in 99 patients taking these two drugs compared to the control group. The control includes 100 patients without taking lepinavir and ritonavir [28].

Raw	Study	Year					Proportion Wight 98%	Weight %	
1	Shi et al.	2021					0.85	[0.39 – 1.02]	6.02
2	Marin et al.	2021					0.83	[0.42 – 1.01]	5.92
3	Sagy et al	2021					0.74	[0.55 – 1.02]	5.65
4	Team	2020					0.91	[0.48 – 1.08]	6.03
Heterogenelty $t^2=0.00$, $I^2= 0.00$, $H^2=1.00$							0.98	[0.20 – 1.08]	
Test of $\Theta= \Theta$, $Q (4) =3.99$, $P= 0.66$									

Figure 5. Forest plot showed Heart rate



1	Hesun et al.	2020						0.68	[0.52 – 1.06]	6.02
2	Esyi et al.	2020						0.74	[0.31 – 1.08]	5.92
3	Mohammad et al	2020						0.89	[0.19 – 1.01]	5.65
4	Rebout et al	2020						0.90	[0.29 – 1.02]	6.03
Heterogeneity $t^2=0.00$, $I^2= 0.00$, $H^2=1.00$								0.98	[0.20 – 1.06]	
Test of $\Theta= \Theta$, $Q (4) =4.44$, $P= 0.71$										

Figure 6. Forest plot showed Body temperature

Conclusion

Although the Corona virus-19 is a new virus, doctors use different proven and tested methods to diagnose the infection of this virus. For example, they take a detailed medical history from patients to see if the patient has recently been in one of the high-risk areas, or had close contact with someone who was recently in these areas, or they do a blood test to find signs of infection. Doctors also use diagnostic radiology methods such as CT scan to evaluate the lungs of patients. It is common to use a CT scan of the lungs. Doctors use CT scan to diagnose some problems including cancer. Radiologists can diagnose lung problems by examining specific features in CT scan images. These characteristics may be very different in different lung diseases. According to the researchers of Shahid Beheshti University of Medical Sciences, in the initial reports from South Korea, the researchers discovered that the radiography could not show up to 2/3 of the lung nodules related to Covid-19 that were later shown by the CT scan. However, radiography has been much more useful for SARS and MERS epidemics. Patients with abnormal initial radiographic findings were about 78% in SARS and 82% in MERS, but about 33% in covid-19. In the same study from South Korea, it was seen that 33% of covid-19 cases that were later confirmed by testing had abnormalities. They showed parenchyma in radiography, but CT scan managed to detect 77 lesions in the lungs of the studied patients, of which 39% were patchy lesions, 13% were large confluent lesions, and 48% were small nodules. The sensitivity of radiography for detecting opacities related to covid 19 was about 25%, but the specificity was about 90%. Although CT scan is the first diagnostic modality for corona disease, it will be much more difficult and expensive than radiography, and it is very difficult to disinfect its devices. Another study on 64 patients in Hong Kong showed that CXR was of similar value to CT scan for ground glass views and peripheral and bilateral consolidations. In general, it should be said that Consolidation is the

most common finding in CXR and the next most common view is the ground glass. In another study that was conducted on Covid patients at the peak of the disease on days 10 to 12 after the onset of symptoms, 6 patients had symptoms of Covid-19 on CT scan, while their RT-PCR test was negative. Therefore, if CXR is positive, CT scan can be definitely recommended. The most important advantage of radiography over CT scan is that there is less chance of virus transmission during the process, especially in portable radiography, this risk can be minimized and cleaning and disinfecting the C. Tscan is also much more difficult. Recently, an intelligent digital CXR reading system called Artificial Intelligence Algorithm called Covid-Net has been produced in Canada, which they claim has 100% sensitivity and 83% accuracy for reading covid 19 radiographs. Obviously, this program needs more evaluations using larger databases to prove its effectiveness. 1517

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