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# FORWARD

*Dear Colleagues,*

*IJST was a fruitful effort issued by the International Centre for Advancement of Sciences and Technology – ICAST, which tries to take part in both globalization and revolution in information and communication technologies, because S&T development becoming not only the key elements of economic growth and industrial competitiveness, but also essential for improving the social development, the quality of life and global environment. ICAST took then a decision to establish a scientific alliance with TSTC (Tharwa for scientific Training & Consultations) and this alliance comes to support the efforts towards publishing IJST.*

*Today, we announce a new issue of our journal, that is the first issue from the sixteen volume of IJST, March, 2021. It is a special issue concerning COVID-19 pandemic with special research attempts in Jordan.*

*Finally, I hope that all significant figures of sciences whom joined the editorial board, the researchers, and the readers of our journal will keep IJST between their eyes and contribute in continuing its journey, with their remarks, valuable recommendations and their researching outcomes.*

*Thanks a lot for all who support IJST.*

***Editor-in-Chief***
***IJST***
***Abdul Jabbar Al- Shammari***

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# Diagnostic findings of Complete Blood Counts (CBC) for COVID-19 patients in Jordan

**Abdul Jabbar N. Al-Shammari, Saadaldin Al-Shafie and Mohammad Al-Faouri**

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***ABSTRACT***

A Coronavirus disease-19 (*commonly known COVID-19*) is a pandemic disease that affects more than 100 million persons around the world. The number of positive cases reported in Jordan was more than 400 thousands. The Jordanian Ministry of Health followed a treatment protocol requiring transferring critical cases to hospitals to be subjected to intensive care, while other cases less affected by the virus were asked to quarantine at home.
The objective of this study was to investigate the complete blood picture among COVID-19 patients and correlated it to the disease to quantify an admission laboratory and comorbidity features associated with a critical cases. A retrospective cohort study was conducted of twelve individuals admitted to one governmental Hospital in Jordan. Data were collected from November to December 2020. Information was drawn from patients' electronic medical records "Hakeem software" to collect previous CBC results for these patients. All patients were confirmed as positive for COVID-19 based on a history of exposure to the virus, clinical manifestations, lungs computed tomography (CT scan), and Nasopharyngeal swab samples were handled as per standard procedure and analyzed nucleic acid amplification test by reverse transcription-polymerase chain reaction (RT-PCR) according to the protocol of diagnosis and treatment. Overall, data of 12 confirmed cases as COVID-19 were analyzed. The median age of subjects involved in the present study was 50 years. Data from 8 males (66.7%) and 4 females (33.3%) were used for analysis. The CBC findings reveal lower HGB, reduced PCV, and slightly lowers RBC levels in patients with comorbid conditions. Besides, there was a significant difference in RBC, HGB, PCV, MCV. The abnormalities of HGB, PCV, and RBC or anemia were observed in patients with comorbidities. These abnormalities explained the symptoms of fatigue and dyspnea observed in the population of the present study. our observations show a significant difference in leukocytosis, decreased levels of lymphocytes, increase the level of neutrophils. During the incubation period, usually ranging from 1 to 14 days, and during the early phase of the disease, when non-specific symptoms are present, peripheral blood leukocyte.
In summary, the present study has shown the CBCs of 12 COVID-19 cases and the most likely laboratory findings in these patients were abnormalities in CBC. We recommend that the clinicians should consider these parameters when reading the CBC of COVID-19 patients.

Keywords: CBC, COVID-19, pandemic, RBC, HGB, PCV, MCV

## *INTRODUCTION*

Coronavirus disease (*commonly known COVID-19*) is caused by SARS-CoV-2 (Severe acute respiratory syndrome coronavirus-2) which produces ferriable pandemic disease. SARS-CoV-2 is approximately 80% similar to SARS-CoV-1 that invades host human cells by binding to Angiotensin Converting Enzyme -2 (ACE-2) receptors [1, 2]. The disease was firstly reported in Wuhan city, China in December 2019, after a while, it has spread worldwide and infected over 100 million Parsons. The World Health Organization (WHO) had characterized the disease as a pandemic.

COVID-19 is an Airborne disease, where people become infected after exposing to droplets and aerosols expelled from affected individual [1, 2]. It can spread as early as two days before infected persons show symptoms (pre-symptomatic), and from asymptomatic (no symptoms) individuals. People remain infectious for up to ten days in moderate cases, and two weeks in severe cases. The disease is characterized by elevation of body temperature, dry coughing, breathing difficulties, loss of taste and smell, one of serious complications is the viral pneumonia and severe acute respiratory syndrome (SARS). Less common symptoms include fatigue, shortness breath, headache, muscle and joint pain, vomiting, diarrhea and skin rash [3]. The seriousness of the disease is 20%, that's mean one of five persons may need to enter ICU due to difficulty breathing, persistent chest pain, bluish face or lips, coordinating during walking and sudden confusion [3-5]. Laboratory findings, especially complete blood counts (CBCs) play an essential role when dealing with infectious diseases. As the investigation into the novel COVID-19 continues to grow, we aim to report the CBC findings of the COVID -19 in Jordan, hoping that this report will provide useful information to all physicians and support the patient's management. This report aims to investigate the significant changes observed in the CBC of mild and severe COVID-19 patients.

## *MATERIALS AND METHODS*

A retrospective, cohort study was applied on a sample of twelve individuals admitted to one governmental hospital in Jordan. Data were collected from November to December 2020. Information was drawn from patients' electronic medical records "Hakeem software" to collect previous CBC results for those patients. All patients were confirmed as positive for COVID-19 based on a history of exposure to the virus, clinical manifestations and lungs computed tomography (CT scan). Nasopharyngeal swab samples were handled as per standard procedure, then nucleic acid amplification test was done by reverse transcription-polymerase chain reaction (RT-PCR) according to the protocol of diagnosis and treatment. Overall, data of 12 confirmed cases as COVID-19 were analyzed.

All procedures performed in the present study were in accordance with the ethical standards of the national research committee. We compared CBC results before and after confirming diagnoses of the COVID-19. Data from 12 Patients reflecting the value of blood cell count patients with severe/mild COVID-19 are summarized in tables (1 and 2). The laboratory findings included white blood cells (WBCs), red blood cells (RBCs), hemoglobin (HGB), platelets (PLT), neutrophils, lymphocytes, mean corpuscular volume (MCV), and Packed Cell Volume (PCV) and with the 1964 Helsinki Declaration and its later amendment's tests were performed in the medical laboratory located on the same Governmental Hospital accordingly to GLP guide [7].

## *RESULTS AND DISCUSSION*

Data of 12 confirmed cases as COVID-19 were analyzed. The median age of subjects involved in the present study was 50 years. Data from 8 (66.7%) males and 4 (33.3%) females were used for analysis (Table 1).

The CBC findings revealed lower HGB and reduced PCV and slightly decrease in RBC levels in patients with comorbid conditions. In addition, there were significant differences in RBC, HGB, PCV, MCV (Table 2). The abnormalities of HGB, PCV, and RBC or anemia were observed in patients with comorbidities and were explained by the inability of the bone marrow to produce enough RBCs to carry oxygen (Figures 1-3), due to lung damages induced by the COVID-19, which makes gaseous exchange difficult. These abnormalities explained the symptoms of fatigue and dyspnea observed in the population of the present study. On other hand, the presence of comorbid conditions of these patients might interfere with RBC production due to existing inflammation (Figure 3). Our observations reflected significant differences of leukocytosis, decreased levels of lymphocytes and increase level of neutrophils, during the incubation period, usually ranging from 1 to 14 days, and during the early phase of the disease, when non-specific symptoms are present, peripheral blood leukocyte (Table 2, Figures 1-5). Following viremia, SARS-CoV-2 primarily affects the tissues expressing high levels of ACE-2 including the lungs, heart and gastrointestinal tract. Approximately 7 to 14 days from the onset of the initial symptoms, there is a surge in the clinical manifestations of the disease with a pronounced systemic increase of inflammatory mediators and cytokines, which may even be characterized as a "cytokine storm" [8]. At this point, significant lymphopenia becomes evident (Figure 5). Although more in-depth research on the underlying etiology is necessary, several factors may contribute to COVID-19 associated lymphopenia. It has been shown that lymphocytes express the ACE2 receptor on their surface [9], thus SARS-CoV-2 may directly infect those cells and ultimately lead to their lysis. Furthermore, the cytokine storm is characterized by markedly

increased levels of interleukins (mostly IL-6, IL-2, IL-7, granulocyte colony stimulating factor, interferon-γ inducible protein 10) and tumor necrosis factor (TNF)-alpha, which may promote lymphocyte apoptosis.10-12 Substantial cytokine activation may be also associated with atrophy of lymphoid organs, including the spleen, and further impairs lymphocyte turnover [10], Coexisting lactic acid acidosis, which may be more prominent among cancer patients who are at increased risk for complications from COVID-19,14 may also inhibit lymphocyte proliferation [11] .

**Table (1): CBC findings base line results of all recruitment patients Pre- confirmed Diagnostics of COVID -19**

| | | Pt.1 | Pt.2 | Pt.3 | Pt.4 | Pt.5 | Pt.6 | Pt.7 | Pt.8 | Pt.9 | Pt.10 | Pt.11 | Pt.12 | REF. LIMIT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Feature | Age | 58 | 81 | 63 | 54 | 74 | 73 | 79 | 76 | 78 | 51 | 24 | 22 | |
| | sex | MALE | F | M | M | F | F | M | M | M | M | F | F | |
| CBC | HB | 14.3 | 13.3 | 13.4 | 13.1 | 10.8 | 14 | 13.9 | 14.1 | 14.4 | 13.3 | 12.8 | 13.8 | M: 12.6-17.4 g/dl F:11.7-15.5 g/dl |
| | PCV | 41.4 | 43 | 42.4 | 38.3 | 33.0 | 42 | 42.4 | 45.6 | 43.5 | 40.6 | 42.7 | 42 | M:37-51% F:35-45% |
| | RBC | 4.84 | 5.6 | 5.14 | 4.73 | 3.45 | 4.6 | 5.58 | 5.4 | 5.18 | 4.61 | 4.8 | 4.8 | M:3.8-5.8 10'6/ul F:4.3-5.1 10'6/ul |
| | MCV | 85.5 | 76.6 | 82.5 | 81.0 | 95.7 | 90 | 76.0 | 84.4 | 84 | 88.1 | 89 | 85 | M:80-100 fl F:81-100 fl |
| | WBC | 5.45 | 14 | 4.7 | 4.65 | 9 | 9 | 11.5 | 9.17 | 8.8 | 8.7 | 4.5 | 4.2 | M:4.5-11 10'3 /µl F:4.5-11 10'3 /µl |
| | NEU. | 73 | 78.3 | 77.9 | 75.7 | 86.3 | 63 | 90 | 88.3 | 88.1 | 92 | 58 | 59 | M:35-80 % F: 35-80 % |
| | LYM. | 14.9 | 17.9 | 21.8 | 17.4 | 13.1 | 26.6 | 5 | 8.1 | 10.8 | 7.5 | 40.4 | 40.8 | M:18-44% F:18-44% |
| | PLT | 254 | 168 | 109 | 172 | 259 | 153 | 182 | 203 | 177 | 172 | 178 | 172 | M:150-440 10'3 /ul F:150-440 10'3 /ul |

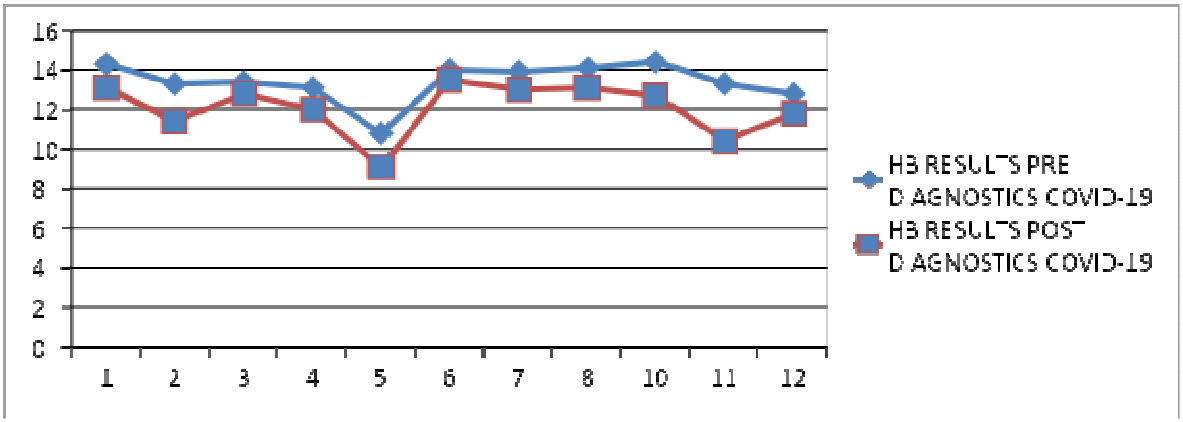


**Figure (1): Hemoglobin values (%) of 12 patients under this study**

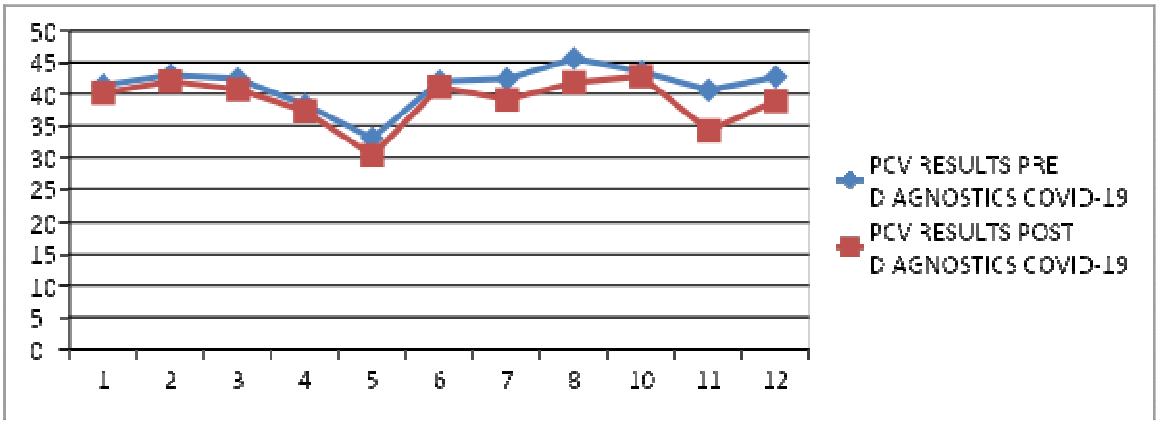


**Figure (2): Packed Cell Volume (PCV) value of 12 COVID-19 patients.**

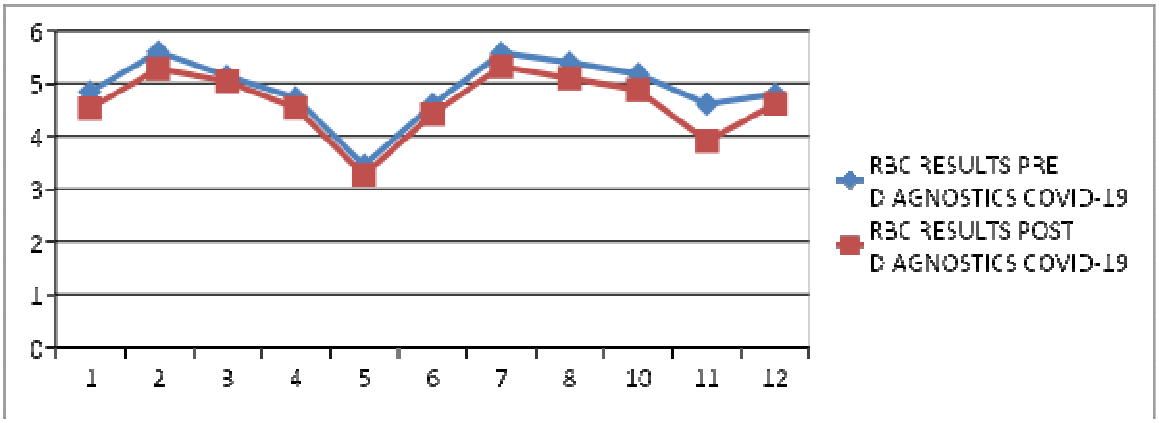


**Figure (3): Red Blood Cell (RBC) count of 12 COVID-19 patients**

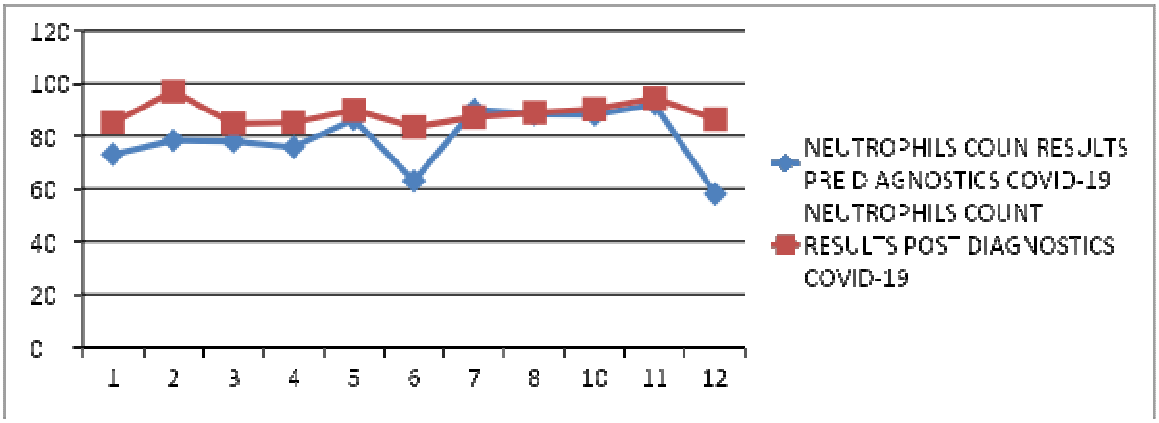


**Figure (4): Neutrophils count for the 12 patients under this study**

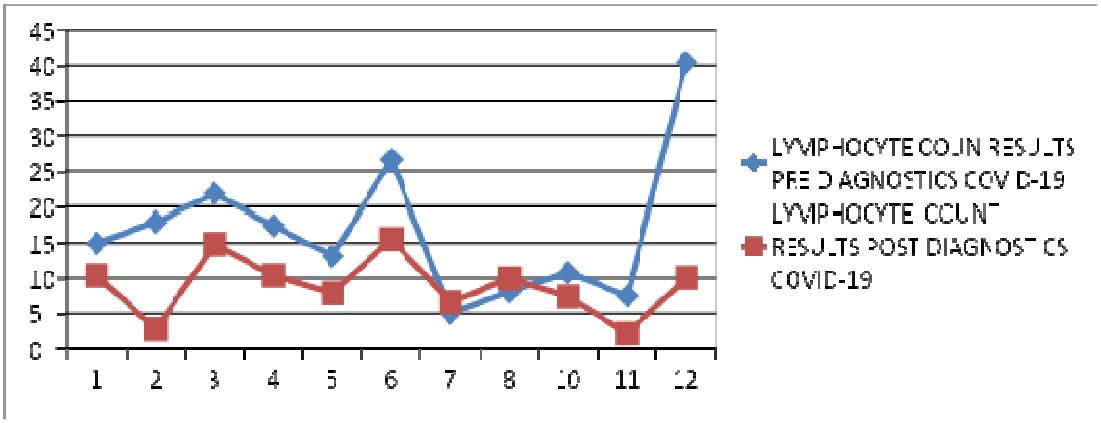


**Figure (5): Lymphocytes counts for the patients in the study**

**Table (2): CBC findings of all recruitment patients confirmed Diagnostics of COVID -19, after 3-5 days confinements in the hospital**

| | | Pt.1 | Pt.2 | Pt.3 | Pt.4 | Pt.5 | Pt.6 | Pt.8 | Pt.9 | Pt.10 | Pt.11 | Pt.12 | REF. LIMIT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Feature | Age | 58 | 81 | 63 | 54 | 74 | 73 | 79 | 76 | 78 | 51 | 24 | |
| | sex | M | F | M | M | F | F | M | M | M | M | F | |
| CBC | HB | 13.1 | 11.4 | 12.8 | 12 | 9.1 | 13.5 | 13 | 13.1 | 12.7 | 10.4 | 11.8 | M: 12.6-17.4 g/dl<br>F:11.7-15.5 g/dl |
| | PCV | 40.2 | 42 | 40.7 | 37.3 | 30.3 | 41.1 | 39.1 | 41.8 | 42.8 | 34.2 | 38.9 | M:37-51%<br>F:35-45% |
| | RBC | 4.53 | 5.28 | 5.11 | 4.53 | 3.18 | 4.69 | 5.74 | 5.4 | 5.13 | 3.91 | 4.79 | M:3.8-5.8 10'6/ul<br>F:4.3-5.1 10'6/ul |
| | MCV | 92.3 | 81.4 | 81.8 | 92.3 | 95.9 | 92.1 | 80.7 | 85.4 | 84 | 87.5 | 96 | M:80-100 fl<br>F:81-100 fl |
| | WBC | 11.7 | 17.5 | 4.6 | 11.7 | 10 | 9.2 | 16.6 | 10.1 | 8.07 | 14.5 | 13.01 | M:4.5-11 10'3 /µl<br>F:4.5-11 10'3 /µl |
| | NEU. | 85.1 | 96.9 | 84.7 | 85.1 | 89.8 | 83.4 | 87.2 | 88.9 | 90.2 | 94.2 | 86.4 | M:35-80 %<br>F: 35-80 % |
| | LYM. | 10.4 | 2.8 | 14.8 | 10.4 | 7.9 | 15.5 | 6.6 | 10.0 | 7.4 | 2.1 | 10.1 | M:18-44%<br>F:18-44% |
| | PLT | 481 | 301 | 142 | 481 | 240 | 214 | 93 | 189 | 189 | 280 | 245 | M:150-440 10'3 /ul<br>F:150-440 10'3 /ul |

Cavezzi *et al.* described the pathophysiology of such a case, he mentioned that SARS-CoV-2 can interact with hemoglobin molecules on the erythrocyte through ACE2, CD147, and CD26 receptors. This viral-hemoglobin interaction will cause the virus to attack the heme on the 1-beta chain of hemoglobin and causing hemolysis [13], then the virus may mimic the action of hepcidin which increases circulating and tissue ferritin (affecting liver, spleen, bone marrow, and muscles mainly), while inducing serum iron deficiency and lack of hemoglobin. The resulting hyper-ferritinemia will give rise to ferroptosis, with high oxidative stress and lipoperoxidation that can precipitate the inflammatory/immune over-response (cytokine storm) and causing a severe outcome of the disease [13,14]. Replenishing the oxygen carrying capacity of blood could be the key to addressing COVID-19 induced hypoxia.

Ejigu *et al.* reported a case study, demonstrating a patient with cardiac arrest and multiple comorbidities including: chronic obstructive pulmonary disease, congestive heart failure, and anemia secondary gastrointestinal bleeding [14]. The patient subsequently tested positive for SARS-CoV-2 and this ultimately progressed to pulmonary disease with bilateral interstitial infiltrates on his chest X-ray. The patient was anemic and treatment with packed red blood cells was undertaken.

Initially, the patient was intubated for ventilation of acute respiratory failure [14].
Table (2) and figure (6) show the results of platelet count in the twelve patients in this study. Abnormal platelet count was reported. Pluta and Trzebiki described thrombocytopenia and said that this pathological condition is quite common in patients in Intensive care unit [15]. The decreasing platelet count usually indicates the dysfunction of organs or systems and leads to a disorder of homeostasis. Studies found that thrombocytopenia in the ICU tended to increase the risk of death [16].

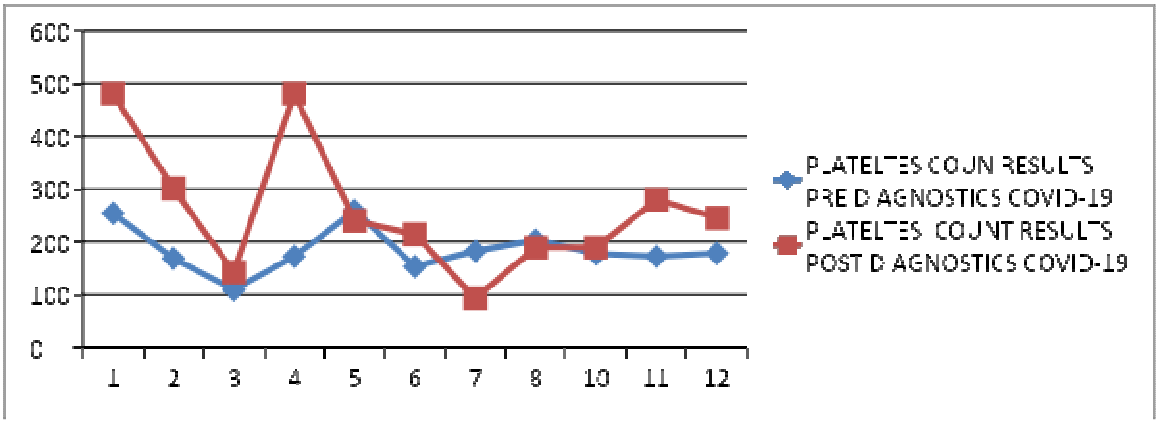


**Figure (6): Platelet counts. Patients 1,4 & 11 have the highest level**

Lagunas-Rangel [17] and Xia *et al.* [18] described the neutrophil-lymphocyte ratio, and they stated that the ratio (NLR) may be useful to serve as indicator of severe COVID-19. Additionally, critically ill COVID-19 patients show higher NLR when compared with non-ICU patients [19] found that approximately 80% of SARS-CoV-2 patients infected with bilateral pulmonary involvement have increased NLR. A Chinese study aimed at assessing the NLR cut-off value for progression of disease reported that NLR>3.3 is independently associated with more severe COVID-19 [18]. A European study conducted in Italy showed that severe patients are also older and had higher NLR compared with non-severe patients, suggesting that NLR may be a useful marker to early screening of COVID-19 patients [19, 20]. Patients with chronic diseases may progress from mild symptoms to severe disease; NLR should be monitored starting from hospitalization, because high NLR concentrations potentiate the symptoms' severity and thus the mortality rate of COVID-19.

## *CONCLUSION*

The present study concludes that the CBC tests must be done for COVID-19 patients. The abnormalities results indicated that the disease is a severe and thus the mortality rate may be increased. Clinicians should consider these parameters when reading the CBC of COVID-19 patients.

### *Limitations of the study:*

It is very difficult to obtain retrospective data for in-patients in the hospitals; on the other hand, the prior documentation of comorbidity is likely being biased. However, such missing data are likely to diminish the predictive power of any given diagnosis. The second limitation is the little number (Only twelve patients involved in this study) was reached under these circumstances.

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# Possible theories of transmissions of COVID19 from China to other countries

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***ABSTRACT***

SARS-CoV-2 is a novel strain of coronavirus that has not been in the past identified in humans. It has been declared a pandemic, which has spread to several countries around the world. COVID-19 and novel coronavirus (SARS-CoV-2) infections, their biological features are considered challenges for the treatment and prevention. The outbreak of SARS-CoV-2 (COVID-19) has been reported as the introduction of the third highly pathogenic coronavirus that crossed the species barrier and spread into the human population. However, the World Health Organization (WHO) website and/or relevant country guidelines are the most recent updates and guidelines can refer to it. in this report We tried to limit the possibilities to transmission of SARS-COV-2 in countries although it originates in one country and these possibilities that we came up with are Travelers and trade which the reasons are divided into the role of illegal trade in wild animals for the SARS-COV2, electromagnetic waves and transportations through cold chain.

***Keywords:*** SARS-CoV-2, COVID-19

## *INTRODUCTION*

The coronavirus disease 2019 (COVID-19) pandemic, caused by a new Coronavirus- Sever acute respiratory syndrome coronavirus 2 (SARS-COV-2) with a different genetic makeup of SARS-COV-1, which occurs in China during 2002-2003, and MERS in Saudi Arabia at 2012 [1,2,3]. COVID19 is a respiratory disease transmitted by droplet and caused a worldwide pandemic. The disease was first emerged in December 2019, when a cluster of patients with pneumonia of unknown cause was recognized in Wuhan, China [4,5]. From 30 December 2019 through 11 October 2020, over 37 million COVID-19 cases and 1 million deaths have been reported globally [6]. The disease spread to the whole China, and its neighbors' countries such as South Korea and Taiwan and over time, the disease struck the European countries- Italy, Spain and Britain into hotbeds, beside Iran in Middle East claiming the lives of thousands [7-10]. The world Health Organization (WHO) report had identified international spreading, human to human spreading and the travel risk. On February 29,2020 trade restrictions to countries with outbreaks or advising against travel were recommended [12-15] (Figure 1).

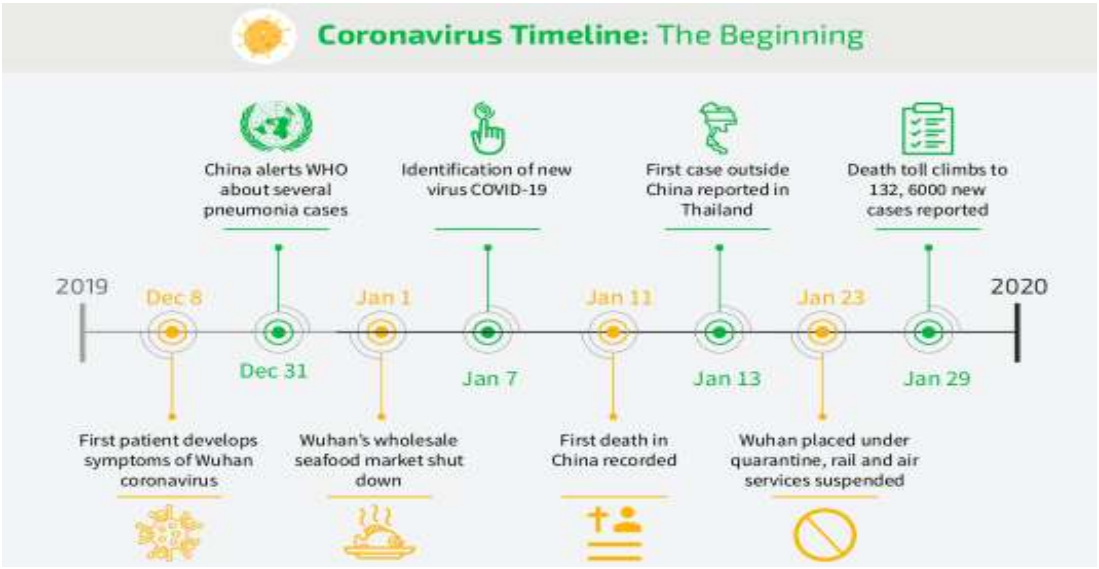


**Figure (1): The Time-line for COVID-19 outbreak (WHO)[15].**

The high infectivity of the disease led many governments to adopt strict regulations and measures with the aim of controlling its spread. The WHO has no direct authority over countries but its objectives are to declare global health threats, organize prevention efforts and provide recommendations so could have done earlier and stronger warning about domestic and international travel risks and the need to restrict or ban travel [16].

On March 2020, the disease had spread to almost the world, and WHO announced that the disease is a pandemic [17]. The novel coronavirus outbreak has affected supply chains around the world as the virus itself has spread from China to many countries across Asia, Europe, the Middle East, Canada and the United States [6,15].

The current article reviewed the possible theories for transmission of SARS-CoV-2 from China to the world countries with special emphasis on new speculations to reaching an explanation of pandemicity of the disease.

## *DATA AND METHODS*

To conduct our possible theories for transmission of Coronavirus Disease -19 (COVID19), we collected epidemiological data from scientific articles published around the World including World Health Organization (WHO), CDC (USA), the Chinese Health Center (NHC) and European CDC.

Tracking the spread of infections depend upon maps published during the outbreak, and estimation the number of cases according to reports of countries and the WHO information website.

## *RESULTS AND DISCUSSION*

**Origin of the disease:**

Figure (2-a) shows the origin of the disease. The story started in China; SARS-CoV-2 was first outbreak at Wuhan, China, when a cluster of pneumonia cases reported had been related to a seafood market in late December 2019. Initially the infection emerged as viral pneumonia from unknown microbial agents [18]. China reported this pneumonia of unidentified cause first to WHO country office on December 31, 2019

[6]. The Chinese Center for Disease Control and Prevention identified the virus as novel coronavirus isolated from the throat swab sample of an infected patient on January 7, 2020 [19]. At that time, the 2019 novel coronavirus has killed 4 and infected more than 200 in China, before the Chinese scientists confirmed that it can be transmitted from person to person [18,19]. However, WHO was confused and unsure of the necessity of declaring a public health emergency.

**Theories of transmissions:**

**1) Mobilization and travelling of people:**

The peak of the epidemic in China was in late January and early February, 2020 and it has reported several thousand new cases of COVID-19 [18,19]. Later on, WHO declared the disease as Public Health Emergency of International and officially named the disease caused by the novel CoV2 as coronavirus disease 2019 (COVID-19) [6]. Up to January 31, 2020, COVID-19 had spread to 19 other countries, infecting 11,791 persons and causing 213 deaths (Figure 2-b) [11]. In early and middle January 2020, the virus spread to other Chinese, helped by the Chinese New Year migration and Wuhan being a transport hub and major rail interchange. Although a COVID-19 had already spread, on 23 January 2020, Wuhan City was locked down – with all travel in and out of Wuhan prohibited – and movement inside the city was restricted [12]. Using 2019 data from the International Air Transport Association (IATA), all cities in China that received at least 100 000-airline passengers from Wuhan during February through April 2019. Word has since developed into a global pandemic and has affected huge numbers of people in Iran, South Korea, and Italy and has pushed a spike in worldwide cases across over 150 countries [13].

Because of the delay in closing travel from China, the virus spread to major countries like South Korea, Italy, Russia, Germany, India, and the U.S. By 20 January 2020, there were reports of confirmed cases from three countries outside China: Thailand, Japan and South Korea [14]. The high infection disease vulnerability index (IDVI) scores indicate these countries have greater capacity to respond to outbreaks [15].

Figure (1) provides a global scenario of the spreading of the disease from China to others countries. The total number of COVID-19 positive cases and total number of deaths until March 25, 2020 were extracted from World Health Organization situation report 2020 (Figures 2 a and b).

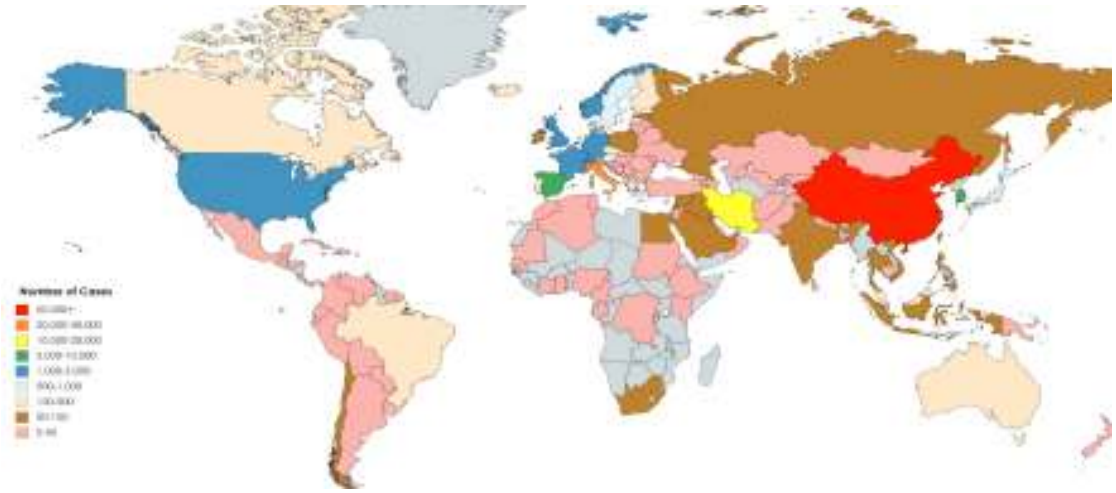

**Figure (2-a): Worldwide distribution of the novel coronavirus disease 2019 (COVID-19) as of March 14, 2020 [16]**


**Figure (2-b): Worldwide distribution of the novel coronavirus disease 2019 (COVID-19) as of March 23, 2020 [16]**

**2) Zoonotic transmissions' theory:**

A study team from South China Agricultural University pointed out that pangolins may be one of the intermediate hosts of SARS-CoV-2, through which the virus may spread to humans. Relevant research teams are being organized by the Chinese government to further support this view [17-19]. Initially, the outbreak seemed to have been caused by zoonotic transmission in the setting of a seafood market in Wuhan [20], where wild animals were sold. It was a possibility that the animals could have served as disease reservoirs, but that was not definite by any credible source. Epidemiological surveys have shown that 27 of 41 people with the earliest onset have visited the market [18,19]. Post hoc investigations also revealed that there was a wildlife trade in this market, and SARS-CoV-2 has been isolated from the market's environment. It was not long before droplet and contact person-to-person transmission became known as the primary mode of transmission [4]. The methods of transmission were led to a rapid increase in the number of cases in China outside Wuhan, with 31.3% of all patients having recently visited the city and 72.3% having recently been in contact with its residents [21-23]. Despite a significant infectivity rate, the case-fatality rate among confirmed cases of COVID-19 is estimated at 3.7%, with the majority of deaths typically occurring among the elderly (age > 80 years), patients having multiple comorbidities, and the immunocompromised population [21]. Human-to-human transmission emerged shortly thereafter, and patients with COVID-19 have become the main source of infection [19]. COVID-19 may be capable of transmission during the incubation Period. [22,23]. These patients are difficult to diagnose and isolate in time, which causes great difficulties in the prevention and control of the disease [24].

In addition, the presence of the virus can be identified in patients during the recovery stage, indicating the possible risk of fecal□oral transmission, especially in fecal specimens requiring longer detoxification times [23].

**3) The possible role of illegal trade of wild animals in transmission of SARS-COV-2:**

The spread of diseases from animals to other animals available via Transportation and storage of animals for wildlife trade at these markets , SARS-CoV-2 the causative virus is a beta coronavirus that originated in bats, much like SARS and MERS diseases, It is currently unknown as to precisely how the virus was transmitted from animals to humans but the threat of bats spreading disease has been a long□held concern for public health officials and biological researchers, An examination into these forms of contagion supports the hypothesis that COVID-19 potentially transmitted from bats to another susceptible animal, such as a pangolin, and then to a human [25].

Pangolins, considered the most-trafficked mammals on Earth [26]. This included illegal trade reported, globally Between August 2000 and July 2019 the equivalent of an estimated ~895,000 pangolins were trafficked, though the actual figure is likely higher (32). The scales are used in the meat is consumed as a luxury dish and traditional medicines. Historically, the skins have also been used in a lucrative leather industry. Most demand for pangolins is coming from Asian countries and in particular from China and Vietnam [27].

Similarly, pangolins are a group of only 8 species, endangered that live in Asia and Sub-Saharan Africa. They are nocturnal and solitary animals in nature, they meet conspecifics only to mate and live-in ground borrows or hollow trees [28], but unlikely in natures to get their chances in contact with bats and become an intermediate host of pathogens. However, pangolins

forced to survive in small cages after captured in wet markets, surrounded by alive and dead bats. Under such conditions, and due to the weak immune system of pangolins, an infection becomes very likely [29]. Malaysian Pangolins have Pangolin-CoV and this virus has 90% homology with the human SARS CoV 2. In addition, the receptor binding motif (RBM) encoded by the segment of SARS CoV 2 genome which is puts forward Pangolins as an alternative host for the current coronavirus [30]. Although, at the genomic level, SARS-CoV-2 was closer to Bat-CoV-RaTG13 genetically than pangolin-CoV-2020, However, does not support that SARS-CoV-2 evolved directly from the pangolin-CoV and only suggest that pangolins could be natural hosts of Beta-coronaviruses with an unknown potential to infect humans [31] Germany emerged as a transit country, especially for pangolins being shipped to Asia from Africa, the majority of shipments involving [32]. But, the pandemic situation in Germanys often compared with that in other European countries favorably, particularly the UK. According to the World Health Organization, by 23 June 2020, the rate of infection reported in Germany was almost half the rate reported in the UK and the reported mortality from COVID-19 was a sixth of that in the UK. However, COVID-19 became a notifiable disease in Germany, earlier than in the UK [33]. As of 2 April, 2020 official statistics showed that 872 deaths from COVID-19 had been recorded in Germany from 73 522 confirmed cases, translating to a fatality rate of 1.2% and less than other Europe country [34]. Thailand is recognized as a transit country for illegal trade in various species of endangered wildlife [35]. In 22 January 2020, the first case of COVID-19 in Thailand was detected. Until mid-March, the number of infected cases had slightly increased at a slow rate in the first period. After mid-March, the number of new cases sharply increased until 26 March at an average rate of 25.1% per day [36]. Animal products "Civet"

During the SARS outbreak in 2002, reports were blame the musk palm civets as source of infections, and in 2004 was confirmed as the direct origin of SARS cases with mild symptom (nnn). Sequence analysis were highly homologous between human SARS-CoV with the SARS-CoV-like virus in masked palm civets nt with identity over 99.6%, indicating the virus has not been circulating in the population of masked palm civets for a very long time, revealed 26 conserved single-nucleotide variations (SNVs) in the viruses from masked palm civets in Alignment of 10 complete viral genome sequences from masked palm civets with those of human SARS-CoVs. Gradually these conserved SNVs were lost from the genomes of viruses of the 2003 SARS epidemic that isolated from the early phase to late phase human patients [19,37,38]. The musk palm civets in china were husbandry in farms for two purpose; food and exports as original ingredients of perfumes, tracked back of the use of perfumes to many cavitations early. Historically, perfumes were composed of natural ingredients exclusively extracted from plants and glands of animals, essential oil mainly (e.g., Musks). As perfumes ingredients, the Civets gland located at the postal end of cats, extract the glands by Chinese in un mercy methods during the living cats without anesthesia [39]. Extraction method of civet glands is oftenly associated with discomfortable and harm to masked civets' cats. The Corona virus in cats will contaminate the products after activated. The glands exported to France, Spain and Italy. Depending on the expression, distillation, material and solvent extraction are techniques mainly used to extract the odorant components from glands. Alcohol percentage used was less than 30% and this percentage not enough to kills the harbor virus in the Civets gland [20,40].

**4) Electromagnetic waves theory:**

Feoli *et al.,* found in Italy that the spreading of the COVID-19 pandemic can be described as a wave packet propagation in a dispersive medium where lockdown effect is simulated by the dispersion relation of the medium [41]. Feoli *et al.* stated that expanding a previous statistical analysis based on the Italian Civil Protection during 100 days as the official data, from March 2nd to June 9th . As uncertain the total number of people infected with the virus, in have considered the sum of hospitalized patients and the deceased and trend of ICU patients. Depending on four free parameters, both the corresponding curves are well approximated by the same function. The model allows to predict the short-term behavior of the pandemic and to estimate the benefits due to lockdown measures [42]. The World Health Organization (WHO) stated that There is no scientific evidence that would explain why exposure to radiofrequencies that have been around for decades would facilitated a biological illness [43].

Viral diseases have emerged and developed for thousands of years and the outbreak of COVID-19 and the installation of 5G in China is obviously coincidental. The most recent of viral diseases are MERS-CoV (Middle East Respiratory Syndrome coronavirus) in 2012 in Saudi Arabia, SARS (Severe Acute Respiratory Syndrome) in 2013 in China, and Ebola (hemorrhagic fever) in West Africa in 2013, which all affected before the arrival of 5G on different populations and developed well. It should also be noted that the spread of this epidemic has nothing to do with existing 5G networks development absolutely and has spread around the world largely via the international transportation development, even in countries where 5G has not been deployed. It is of course understandable that when a new technology is rolled out there are worries in the population, despite the use of waves that are known and whose health effects have been studied. However, this concern is totally unfounded, because all international organizations have confirmed recently that 5G is harmless [43].

**5) Transportation through cold-chain:**

One hypothesis is proposed that the virus may be transported via cold chain transportation and imported by contaminated fish from Europe. Another possible transmission mode may be that asymptomatic symptoms international travelers with false negative of

nucleic acid test spread the virus into China, and the virus by infected humans by infected humans by infected humans by infected humans by infected humans by infected humans was transmitted to the market may provide an ideal environment for amplification of virus by the humid and chilled air and suboptimal hygienic conditions in the market and subsequently the virus was spread by visiting in the markets and people working resulting in the re-emerging outbreak of COVID-19 [44].

Sporadic COVID-19 cases, Dalian and Tianjin of China, that had participated in the transport of the infected batch of imported frozen products have been reported. Meanwhile, environmental swab samples related to imported cold chain food contacted by the cases were tested nucleic acid lively for SARS-CoV-2 [44].

## *CONCLUSION*

The initial epicenter of the disease shifted from Wuhan to Europe to the USA. CoV2 spread is also increasing exponentially. The 2019-novel coronavirus (2019-nCoV, also, SARS-CoV-2 and COVID-19 virus) is the cause of Coronavirus Disease-2019 (COVID-19), a major pandemic that threatens millions of lives and the global economy. All the major airports of world were made fully equipped to scan and isolate passengers arriving from other countries or any other infected region. The delay in announcing the coronavirus and the closer of airports contributed to the spread of Corona between countries and international destinations across East Asia. Several cases have spread internationally via air travel to Japan, South Korea, Taiwan, Thailand and the USA. The disease cross-borders from China to neighbors' countries and to the world's through traveler's mainly and trade between China and others countries includes Goods and animal products. the spread of diseases from animals to other animals available via Transportation and storage of animals for wildlife trade at these markets, but the threat of bats spreading disease has been a long-held concern for public health officials and biological researchers, an examination into these forms of contagion supports the hypothesis that COVID-19 potentially transmitted from bats to another susceptible animal, such as a pangolin, and then to a human. involved in the shipping process, if one infected person can contaminate others who are thousands of miles away regarding to air shipments and at least some transatlantic shipments. During such challenging times such as the COVID-19 pandemic have of special importance No scientific evidence that would link between the global spreading of COVID-19 and electromagnetics' waves (5G's).

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# The Correlation between temperature, relative humidity and spreading of SARS-COV-2 in Jordan

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***ABSTRACT***

As the respiratory viruses are expelling from an infected person to the environment through coughing, sneezing, and talking, the environmental temperatures and relative humidity may increase or decrease the viability of virus survival in the air or on the innate objects that will affect the survival and spreading of the viruses. The Novel Coronaviruses (SARS-CoV-2) are transmitting through air droplets and staying in the air for a while until finding the new host, or maybe dried and destroyed by the effect of climate factors. The current study aimed to investigate the correlation between the climate factors such as the temperature and relative humidity on the spreading of SARS-CoV-2 in Jordan during months after the opening of all sectors in the country. The climate in Jordan is influenced by the location of Jordan between the subtropical aridity of the Arab desert regions, and the subtropical humidity in the Eastern Mediterranean region. To approach the goal of the study, we obtained the daily epidemic situation by case numbers and percentage of positive ratio from the website of the Jordanian Ministry of Health. On the other hand, the meteorological recordings of temperatures and relative humidity were obtained from the Arab center for Meteorology during August- November 2020.
Results showed that there are disciplined data, which indicated there is no influence of climate in spreading of COVID-19 in Jordan, neither the temperatures nor the relative humidity in the epidemiological pictures.

***Keywords:*** SARS-CoV-2, air droplets, humidity, temperature.

## *INTRODUCTION*

The novel Coronavirus (SARS-CoV-2) is the causative agent of pandemic Covid-19. The story of the outbreaks of disease started from Wuhan province in China [1]. Chinese authorities reported a new case of pneumonia caused by a novel virus belonged to Coronaviridae family [2], and then informed the World Health Organization (WHO) on December 31, 2019 [3]. The virus causes respiratory disorders and transmitted by direct contact with an infected person's respiratory droplets (coughing and sneezing), as well as contact with infected surfaces. SARS-CoV-2 can live for hours on surfaces, but a simple disinfectant can eliminate it [4]. The World Health Organization (WHO) declared on March 11$^{th}$,2020 that COVID-19 is global pandemic and needs better understanding. The hypothesis written in virology textbooks and literatures reveals that the temperatures and relative humidity can affect in some manner the viability of viruses [5]. On the other hand, they proposed that high temperature and humidity- together- have a combined effect on inactivation of coronaviruses and moderate conditions can support survival time of virus on surfaces and facilitate the transmission [6-11]. Mecenas *et al,* had reviewed (517) articles concerning the effects of temperature and relative humidity on the survival of SARS-C0V-2, and they concluded that; cold and dry conditions were potentiating factors on the spread of the virus [12]. In addition, they concluded that warm and wet climates seem to reduce the spread of COVID-19 [13-16]. Also they stated that, these variables alone could not explain most of the variability in disease transmission [18-20]. Thus , there are discipline theories about the correlation of climate conditions and the transmission of COVID-19. We found that more studies are needed to conclude such facts.

The current study put in mind that the seasonal behavior of any country may affect the viability of virus, which influences the spread of virus in various climates according to various geographical areas that may affect the transmission of virus. We investigated the correlation between the spread of SARS-CoV-2 virus in Jordan and its relation with the country climate features during the period from August to December 2020.

## *MATERIALS AND METHODS*

**1. Total number of cases:** The total number of daily reported cases in Jordan were taken from the Jordanian Ministry of Health website (www.moh.gov.jo) [6]. The total number of individuals were daily examined and number of positive cases (number of positive COVID-19 cases/total tests were conducted) *100%]. The criteria used by WHO that the country situation is acceptable if the percentage 5% or less.

**2. Meteorology Data.** The daily temperature and relative humidity during August- December 2020 were provided by the Arab Weather Center for Meteorology. The months of lockdown were excluded to prevent the results bias.

**3. Statistical analysis:** Simple T-test was used. Numerical variables were described with means and standard deviations. The mean value of accumulative during weekdays, and the number of positive cases related to RH if the temperature is constant (between 20-25$^0$C).

## *RESULTS*

The current study was limited for months after the lockdown period, started from August to December 2020. In August, the temperatures were around 25-27 $^0$C and the relative humidity was (RH%) between 40-49%. The percentage of positive cases was less than 1% (Tables 1-a and b), it seems logical because the virus is being inactivated under RH% between 40-60%, as reported in the same conditions for SARS [13].

**Table (1-a): The total COVID-19 cases reported during August 2020 correlated with the daily reported temperature and relative humidity.**

| Date | Total cases | Total tests | % +ve test * | Temp. ˚C | Humidity % |
|---|---|---|---|---|---|
| 1/8 | 15 | 5342 | 0.28 | 30 | 27 |
| 2/8 | 5 | 4306 | 0.12 | 27 | 32 |
| 3/8 | 5 | 4332 | 0.12 | 27 | 43 |
| 4/8 | 6 | 4781 | 0.13 | 26 | 53 |
| 5/8 | 7 | 5964 | 0.12 | 27 | 42 |
| 6/8 | 1 | 6125 | 0.02 | 26 | 50 |
| 7/8 | 5 | 5976 | 0.08 | 27 | 41 |
| 8/8 | 9 | 5827 | 0.15 | 28 | 30 |
| 9/8 | 6 | 5925 | 0.10 | 27 | 40 |
| 10/8 | 16 | 6286 | 0.25 | 25 | 56 |
| 11/8 | 15 | 6253 | 0.24 | 23 | 65 |
| 12/8 | 20 | 6641 | 0.30 | 24 | 61 |
| 13/8 | 17 | 6691 | 0.25 | 25 | 60 |
| 14/8 | 9 | 7407 | 0.12 | 26 | 60 |
| 15/8 | 10 | 6600 | 0.15 | 26 | 43 |
| 16/8 | 39 | 6409 | 0.61 | 26 | 42 |
| 17/8 | 20 | 6171 | 0.32 | 26 | 44 |
| 18/8 | 40 | 6989 | 0.57 | 27 | 32 |
| 19/8 | 44 | 7294 | 0.60 | 28 | 29 |
| 20/8 | 16 | 7758 | 0.21 | 28 | 31 |
| 21/8 | 34 | 7367 | 0.46 | 27 | 38 |
| 22/8 | 44 | 8934 | 0.49 | 25 | 39 |
| 23/8 | 33 | 7827 | 0.42 | 24 | 50 |
| 24/8 | 30 | 7468 | 0.40 | 24 | 61 |
| 25/8 | 77 | 10569 | 0.73 | 26 | 48 |
| 26/8 | 40 | 14035 | 0.29 | 26 | 57 |
| 27/8 | 45 | 13950 | 0.32 | 27 | 42 |
| 28/8 | 68 | 9274 | 0.73 | 26 | 37 |
| 29/8 | 24 | 9615 | 0.25 | 25 | 42 |
| 30/8 | 73 | 9110 | 0.80 | 23 | 57 |
| 31/8 | 68 | 9209 | 0.74 | 24 | 57 |

**[(number of positive COVID-19 cases/total tests were conducted) *100%]*

**Table (1-b): Correlation between number of positive cases for COVID-19 and the average of temperatures and relative humidity for August 2020(Weekly records).**

| week | total cases | total tests | % positive test * | Avg. temp. ˚C | Avg. Humidity % |
|---|---|---|---|---|---|
| (1):1-8/8/2020 | 53 | 42653 | 0.12 | 27 | 40 |
| (2): 9-16/8/2020 | 132 | 52212 | 0.25 | 25 | 53 |
| (3): 17-24/8/2020 | 261 | 59808 | 0.44 | 26 | 41 |
| (4): 25-31/8/2020 | 395 | 75762 | 0.52 | 25 | 49 |

Tables (2-a and b) show the number of positive cases and total number of examined individuals during September 2020. In September, 2020 the story was little bit different, the RH % during days 1-16 September were (31-39%) and during the last two were between (42-47%) with temperatures between 27-32 $^{0}$C. Neither the temperature nor the RH had impacts on the results, since the percentage of positive cases increased to 2.52 and above 5% during the 3$^{rd}$ and 4$^{th}$ weeks respectively (Tables 2-a and b).

**Table (1-a): The total COVID-19 cases reported during September, 2020 correlated with the daily reported temperature and relative humidity.**

| Date | Total cases | Total tests | % +ve test * | Temp. ˚C | Humidity % |
|---|---|---|---|---|---|
| 1/9 | 63 | 10861 | 0.58 | 31 | 48 |
| 2/9 | 64 | 10847 | 0.59 | 30 | 32 |
| 3/9 | 72 | 11242 | 0.64 | 33 | 32 |
| 4/9 | 68 | 11875 | 0.57 | 34 | 18 |
| 5/9 | 52 | 9268 | 0.56 | 34 | 20 |
| 6/9 | 58 | 11925 | 0.49 | 31 | 30 |
| 7/9 | 67 | 8967 | 0.75 | 31 | 34 |
| 8/9 | 103 | 12104 | 0.85 | 32 | 39 |
| 9/9 | 78 | 9765 | 0.80 | 30 | 52 |
| 10/9 | 80 | 15784 | 0.51 | 31 | 38 |
| 11/9 | 206 | 18007 | 1.14 | 33 | 39 |
| 12/9 | 117 | 9222 | 1.27 | 31 | 50 |
| 13/9 | 252 | 11322 | 2.23 | 29 | 37 |
| 14/9 | 214 | 10010 | 2.14 | 28 | 30 |
| 15/9 | 149 | 14744 | 1.01 | 28 | 34 |
| 16/9 | 175 | 14762 | 1.19 | 30 | 37 |
| 17/9 | 279 | 14849 | 1.88 | 31 | 41 |
| 18/9 | 213 | 11766 | 1.81 | 30 | 36 |
| 19/9 | 196 | 11484 | 1.71 | 28 | 37 |
| 20/9 | 239 | 13437 | 1.78 | 28 | 28 |
| 21/9 | 266 | 12867 | 2.07 | 26 | 38 |
| 22/9 | 634 | 12260 | 5.17 | 24 | 65 |
| 23/9 | 363 | 16931 | 2.14 | 24 | 66 |
| 24/9 | 549 | 15282 | 3.59 | 24 | 62 |
| 25/9 | 620 | 14064 | 4.41 | 24 | 58 |
| 26/9 | 850 | 13488 | 6.30 | 24 | 54 |
| 27/9 | 431 | 15384 | 2.80 | 27 | 43 |
| 28/9 | 734 | 16453 | 4.46 | 28 | 33 |
| 29/9 | 823 | 16851 | 4.88 | 29 | 28 |
| 30/9 | 1776 | 16621 | 10.69 | 29 | 33 |

**[(number of positive COVID-19 cases/total tests were conducted) *100%]*

**Table (2-b): Correlation between number of positive cases for COVID-19 and the average of temperatures and relative humidity for September 2020(Weekly records).**

| Week | Total cases | Total tests | % positive test | Avg. temp. | Avg. Humidity % |
|---|---|---|---|---|---|
| (1): 1-8/9/2020 | 547 | 87089 | 0.63 | 32 | 31 |
| (2): 9-16/9/2020 | 1271 | 103616 | 1.23 | 30 | 39 |
| (3): 17-24/9/2020 | 2739 | 108876 | 2.52 | 27 | 47 |
| (4): 25-30/9/2020 | 5234 | 92861 | 5.64 | 27 | 42 |

In October 2020, the number of positive cases increased and the percentage of the positive test was above 5% . During the last week, the percentage had raised to 13% (Tables 3- a and b). It is difficult to draw any conclusions because when the RH% at the last week was 20% (this is suitable for the viability of viruses), the percentage of positive cases reached 13% (it seems logical with the hypothesis), but if we look at the third week, we notice that the percentage of positive cases was 10%, but the RH% was 43(suppose the virus is inactivated).

**Table (3-a): The total COVID-19 cases reported during October, 2020 correlated with the daily reported temperature and relative humidity.**

| Date | Total cases | Total tests | % +ve test * | Temp. ˚C | Humidity % |
|---|---|---|---|---|---|
| 1/10 | 1276 | 17800 | 7.17 | 25 | 49 |
| 2/10 | 549 | 12153 | 4.52 | 23 | 59 |
| 3/10 | 1099 | 20240 | 5.43 | 22 | 63 |
| 4/10 | 891 | 20381 | 4.37 | 21 | 66 |
| 5/10 | 1824 | 20034 | 9.10 | 23 | 53 |
| 6/10 | 1537 | 19169 | 8.02 | 25 | 37 |
| 7/10 | 1199 | 20507 | 5.85 | 26 | 26 |
| 8/10 | 1317 | 20339 | 6.48 | 27 | 20 |
| 9/10 | 1246 | 15961 | 7.81 | 20 | 53 |
| 10/10 | 1235 | 12280 | 10.06 | 26 | 23 |
| 11/10 | 928 | 17505 | 5.30 | 23 | 67 |
| 12/10 | 1147 | 21948 | 5.23 | 23 | 55 |
| 13/10 | 2054 | 25736 | 7.98 | 25 | 50 |
| 14/10 | 2423 | 25295 | 9.58 | 21 | 65 |
| 15/10 | 2459 | 27648 | 8.89 | 20 | 68 |
| 16/10 | 1539 | 17645 | 8.72 | 20 | 64 |
| 17/10 | 1505 | 12876 | 11.69 | 22 | 53 |
| 18/10 | 1520 | 20097 | 7.56 | 24 | 43 |
| 19/10 | 1364 | 24575 | 5.55 | 24 | 36 |
| 20/10 | 2035 | 25496 | 7.98 | 23 | 39 |
| 21/10 | 2648 | 24481 | 10.82 | 24 | 29 |
| 22/10 | 2821 | 23115 | 12.20 | 25 | 36 |
| 23/10 | 2489 | 17007 | 14.64 | 23 | 54 |
| 24/10 | 1820 | 11979 | 15.19 | 23 | 56 |
| 25/10 | 2377 | 14861 | 15.99 | 23 | 26 |
| 26/10 | 1968 | 19159 | 10.27 | 25 | 14 |
| 27/10 | 3800 | 29606 | 12.84 | 26 | 13 |
| 28/10 | 3087 | 24497 | 12.60 | 23 | 21 |
| 29/10 | 3443 | 25558 | 13.47 | 21 | 28 |
| 30/10 | 3921 | 28958 | 13.54 | 23 | 19 |
| 31/10 | 3301 | 22513 | 14.66 | 25 | 18 |

**Table (3-b): Correlation between number of positive cases for COVID-19 with temperatures and relative humidity in October, 2020(Weekly records).**

| Week | Cases | total tests | % positive test * | Temp(˚C) | Humidity % |
|---|---|---|---|---|---|
| (1): 1-8/10/2020 | 9692 | 150623 | 6 | 24 | 47 |
| (2): 9-16/10/2020 | 13031 | 164018 | 8 | 22 | 56 |
| (3): 17-24/10/2020 | 16202 | 159626 | 10 | 23 | 43 |
| (4): 25-31/10/2020 | 21897 | 165152 | 13 | 24 | 20 |

In November 2020, Jordan reported the highest number of positive cases and the percentage of positive cases was between 18-24%. The temperature was quite cold between 13-17 $^{o}$ C and the percentage of RH was between 70-76%. It seems acceptable of hypothesis, the prediction temperature and RH are enhancing the viability of viruses, but we can't draw the conclusions without taking the whole pictures for other months described previously (tables 4-a and b).

**Table (4-a): The total COVID-19 cases reported during November, 2020 correlated with the daily reported temperature and relative humidity.**

| Date | Total cases | Total tests | % +ve test * | Temp. ˚C | Humidity % |
|---|---|---|---|---|---|
| 1/11 | 3259 | 19588 | 16.64 | 19 | 68 |
| 2/11 | 5877 | 33846 | 17.36 | 19 | 77 |
| 3/11 | 4833 | 20887 | 23.14 | 17 | 80 |
| 4/11 | 4658 | 20737 | 22.46 | 19 | 65 |
| 5/11 | 4630 | 25258 | 18.33 | 17 | 69 |
| 6/11 | 5384 | 23306 | 23.10 | 15 | 87 |
| 7/11 | 3554 | 13642 | 26.05 | 14 | 87 |
| 8/11 | 4519 | 23056 | 19.60 | 16 | 75 |
| 9/11 | 5665 | 27689 | 20.46 | 17 | 73 |
| 10/11 | 5996 | 27324 | 21.94 | 17 | 60 |
| 11/11 | 5419 | 21342 | 25.39 | 16 | 66 |
| 12/11 | 5685 | 24128 | 23.56 | 17 | 65 |
| 13/11 | 4469 | 16771 | 26.65 | 17 | 70 |
| 14/11 | 4750 | 16502 | 28.78 | 15 | 77 |
| 15/11 | 2373 | 9583 | 24.76 | 16 | 65 |
| 16/11 | 5861 | 26475 | 22.14 | 18 | 53 |
| 17/11 | 6454 | 27441 | 23.52 | 19 | 50 |
| 18/11 | 7933 | 30792 | 25.76 | 16 | 62 |
| 19/11 | 5470 | 24210 | 22.59 | 15 | 57 |
| 20/11 | 4940 | 22819 | 21.65 | 14 | 69 |
| 21/11 | 3826 | 18518 | 20.66 | 13 | 78 |
| 22/11 | 5268 | 23953 | 21.99 | 13 | 78 |
| 23/11 | 4981 | 25349 | 19.65 | 13 | 82 |
| 24/11 | 4586 | 24664 | 18.59 | 13 | 80 |
| 25/11 | 5025 | 27098 | 18.54 | 14 | 53 |
| 26/11 | 5000 | 25964 | 19.26 | 14 | 73 |
| 27/11 | 4580 | 26257 | 17.44 | 11 | 91 |
| 28/11 | 3108 | 17755 | 17.50 | 13 | 77 |
| 29/11 | 3598 | 20767 | 17.33 | 12 | 76 |
| 30/11 | 5123 | 25239 | 20.30 | 13 | 73 |

**Table (4-b): Correlation between number of positive cases for COVID-19 with temperatures and relative humidity in November, 2020(Weekly records).**

| Week | Cases | total tests | % positive test * | Temp(˚C) | Humidity % |
|---|---|---|---|---|---|
| (1); 1-8/11/2020 | 36714 | 180320 | 20.36 | 17 | 76 |
| (2): 9-16/11/2020 | 40218 | 169814 | 23.68 | 17 | 66 |
| (3): 17-24/11/2020 | 43458 | 197746 | 21.98 | 15 | 70 |
| (4): 25-30/11/2020 | 26434 | 143080 | 18.47 | 13 | 74 |

Tables (5-a and b) reveal the correlation between the number of positive cases for COVID-19 and the seasonal behaviors during the period 1- 18 December 2020. Controversies results were reported in this table when the temperature is alike (12-14$^{o}$ C) and the RH % is diversely (first week 78%) and the second week is 58%. According to a hypothesis, the temperature is fixed and the percentage of RH is diverse, but the results as the same.

So, we can conclude that neither temperature nor relative humidity have a role in increasing the spread or transmission of SARS-CoV-2 in Jordan under the conditions applied in the current experiment.

**Table (5-a): Correlation between number of positive cases for COVID-19 with temperatures and relative humidity in December, 2020 (Daily records).**

| Date | Total cases | Total tests | % positive test * | Temp. (˚C) | Humidity % |
|---|---|---|---|---|---|
| 01/12 | 4187 | 26050 | 16.1 | 14 | 64 |
| 02/12 | 3591 | 24615 | 14.6 | 12 | 67 |
| 03/12 | 4029 | 25260 | 15.9 | 13 | 66 |
| 04/12 | 3116 | 21761 | 14.3 | 11 | 85 |
| 05/12 | 3160 | 18624 | 16.97 | 10 | 88 |
| 06/12 | 2576 | 16979 | 15.17 | 11 | 88 |
| 07/12 | 3980 | 25051 | 15.89 | 11 | 83 |
| 08/12 | 3062 | 22308 | 13.73 | 11 | 81 |
| 09/12 | 3088 | 23420 | 13.19 | 12 | 65 |
| 10/12 | 2902 | 22502 | 12.9 | 14 | 76 |
| 11/12 | 2338 | 19225 | 12.16 | 13 | 74 |
| 12/12 | 1816 | 13268 | 13.69 | 14 | 50 |
| 13/12 | 2339 | 18712 | 12.5 | 13 | 47 |
| 14/12 | 2863 | 21717 | 13.18 | 15 | 37 |
| 15/12 | 2547 | 20827 | 12.23 | 18 | 35 |
| 16/12 | 2561 | 22540 | 11.36 | 18 | 38 |
| 17/12 | 2221 | 21176 | 10.49 | 12 | 68 |
| 18/12 | 1708 | 17735 | 9.63 | 11 | 87 |

**Table (5-b): Correlation between number of positive cases for COVID-19 with temperatures and relative humidity in December, 2020(Weekly records).**

| Week | Total cases | Total tests | % positive test * | Temp. (°C) | Humidity % |
|---|---|---|---|---|---|
| (1): 1-8/12/2020 | 27701 | 180648 | 15.33 | 12 | 78 |
| (2): 9-18/12/2020 | 24383 | 201122 | 12.12 | 14 | 58 |

* *Percentage of positive cases = Number of positive cases/total number examined*

Temperature versus percentage of positive COVID-19 cases related to daily tests were conducted in October and November 2020, the temperature is not significantly changed so it is difficult to correlate between the daily temperature and incidence of COVID-19.

The P- values for the Humidity **vs** percentage of positive cases in (October and November/2020) = .82 /.96, no significant correlation between humidity and percentage of positive cases (Table 6)**.**

**Table (6): Statistical P- values for temperatures during October and November 2020**

| Data | p-value | Result |
|---|---|---|
| Humidity **Vs** percentage of positive cases (October 2020) | 0.82 | >.05 not significant |
| Humidity **Vs** percentage of positive cases (November 2020) | 0.96 | >.05 not significant |

***DISCUSSION***

Among the various theories published after the outbreak of COVID-19, the environmental influences on the spread and transmission of the disease those related to climate changes are of primary importance, but are potential indirect and therefore more difficult to draw a conclusion. Arguments which supported the hypothesis came from several research papers:

An early note reported by Du Prel et al. linked between viral seasonality transmission and the climate (temperatures and Relative humidity) over six years study in Germany [5].

According to a Chinese researchers, they concluded that there could be a relationship between the change in temperature, and the large transmission of the COV-2 Coronavirus, and there are better temperatures for the transmission of the virus [9,13,16,18,19]. Also, other countries reported the same conclusions; Bangladesh [11], New York [21], Indonesia [22], Spain [26], Iran [24], and Italy [25]. Price *et al.* demonstrated that unlike the non-enveloped viruses that circulate throughout the year, enveloped viruses, including influenza and respiratory virus (RSV), tend to be more seasonal, with a clear preference for colder temperature [7]. Lower temperatures appear to enhance lipid arrangement in the viral envelope and improve stability of the influenza virus [7]. This enhances the ability of the virus to remain protected outside the body for a longer period of time. Moreover, a systematic review examined the factors affecting influenza survival on various scales and revealed that virus survival is longer at lower temperatures [8]. The temperature has been an environmental driver of the COVID-19 outbreak in China, and temperatures above 8 to 10 degrees Celsius have been associated with a lower rate of daily confirmed cases of COVID-19 [9]. No correlations were also reported by other's [17,20]. Climate changes have been linked to other virial infection such as Ebola virus or bacterial infection (Cholera) or protozoal infections like malaria [5]. It is hard to make link without related to others factors such as host, vectors and pathogens. Previous, non-COVID19 related studies associating infectious diseases to climatic conditions. The role of other potential environmental determinates of COVID-19, including air pollution and other environmental pollutants [12, 17-20].

With the presences of contravention studies about the relation between spreading of COVID-19 and seasonal climate behaviors, bring our attention; especially there is no study in the Jordan and surrounding area dealing with this issue. The current study was designed to examine the hypothesis as the climate in Jordan is influenced by the location of Jordan between the subtropical aridity of the Arab desert regions, and the subtropical humidity in the eastern Mediterranean region. To approach the goal of the study we obtained the daily epidemic situation by case numbers and percentage of positive ratio from the Website of the Jordanian Ministry of Health, on the other hands the meteorological recorded of temperatures and relative humidity were obtained from the Arab

center for meteorology during August to December 2020.

In Jordan the policy of lockdowns for all sectors have been applied during first months of the COVID-19. The total number of cases did not exceed 1218 cases, the number of cases per million of population did not exceed 119 until July 20, 2020 [6]. After August, 2020 reopened many closed sectors and the cases were increased until in November number of cases reached 5 thousand per day.

In August, the temperatures were around 25-27 $^0$C and the relative humidity (RH%) between 40-49%. The percentage of positive cases was less than 1% (Tables 1-a and b), it seems logical because the virus is inactivating under RH% between 40-60%, as reported by Chan et al. [13].

In September, 2020 the story little bit different, the RH % during days 1-16 September (31-39%) and during the last two weeks the RH% was between 42-47% with temperatures between 27-32 $^0$C. Neither the temperature nor the RH effects the results, since the percentage of positive cases increase to 2.52 and above 5% during the 3$^{rd}$ and 4$^{th}$ weeks respectively (Tables 2 -a and b). The SARS-Cov-2 is an enveloped virus, during lower temperatures appears to enhance lipid arrangement in viral envelope and improve stability of the influenza virus [8]. This enhances the ability of virus to remain protected outside body for a long period of time [8]. It is difficult to draw any conclusions during October, 2020 because when the RH% at the last week was 20% (this is suitable for the viability of viruses) the percentage of positive cases reached 13% (it seems logical with the hypothesis), but if we look to the 3rd week, the percentage of positive cases was 10%, but the RH% was 43 (suppose the virus is inactivated).

In November 2020, Jordan reported the highest number of positive cases and the percentage of positive cases was between 18-24%. The temperature is quite cold between 13-17 $^o$ C and the percentage of RH is between 70-76%. It seems acceptable of hypothesis, the prediction temperature and RH are enhancing the viability of viruses, but we can't draw the conclusions without taking the whole pictures for others months described early.

One of the limitations of this study is how to get the data continuously. Table (5-a) reveals the correlation between the number of positive cases for COVID-19 and the seasonal behaviors. Controversies results were reported in this table when the temperature is alike (12-14$^o$ C) and the RH % is diversely (first week 78%) and the second week is 58%. According to a hypothesis, if the temperature is fixed and the percentage of RH is diversely, but the results as the same. So, we can conclude that neither temperature nor relative humidity has a role in increasing the spreading or transferability of SARS-CoV-2 in Jordan under the conditions applied in the current experiments.

If we compare the current study with others reported studies concerns the SARS-CoV-2, temperatures and RH were influenced the spreading of COVID-19 (5-16), while other studies denied the effects [17-20]. This is due to different parameters used in each study, in addition the other factors may not include in such studies.

## *CONCLUSION*

The current study did not correlate the temperatures and relative humidity in Jordan with contributions to spread of COVID-19.

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# Vaccines development against Novel Coronavirus (SARS-CoV-2)

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***ABSTRACT***

In December 2019, the outbreak of pneumonia caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to a serious pandemic in China and other countries worldwide. So far, more than 460,000 confirmed cases were diagnosed in nearly 190 countries, causing globally over 20,000 deaths. Currently, the epidemic is still spreading and there is no effective means to prevent the infection. Vaccines are proved to be the most effective and economical means to prevent and control infectious diseases. Several countries, companies, and institutions announced their programs and progress on vaccine development against the virus. While most of the vaccines are under design and preparation, there are some that have entered efficacy evaluation in animals and initial clinical trials. This review mainly focuses on the progress and prospects on field of vaccine development against SARS-CoV-2.

***Keywords:*** vaccine, SARS-CoV-2, pandemic COVID-19.

## *INTRODUCTION*

Viruses are infectious, obligate intracellular parasites composed of genetic material either DNA or RNA, and surrounded by a protein coat, sometime the protein coats cover by an extra- layer of the outer envelope. Viruses are not grouped within the large domains of life; Eucaryotic and prokaryotic kingdoms. The relationships between viruses and humans go for thousands of years, and the viruses caused several diseases for humans, ranging from mild illness to fatal conditions. RNA viruses have a higher mutation rate than DNA viruses; RNA viruses mutate 1,000 times more than DNA viruses [1].

A new epidemic of Severe Acute Respiratory Syndrome (SARS) Coronavirus has emerged since December 2019, namely SARS-CoV-2 or COVID-19, in Wuhan, the capital of Hubei Province, China. An outbreak of atypical pneumonia named COVID-19 caused by this virus has been reported [2, 3], and the pattern of human-to-human transmissibility of the virus has occurred nationally and internationally [4, 5]. There is no treatment or vaccines are available since the virus emerged for the first time to infect human being s. More than 150 pharmaceutical companies and vaccine producer agents were in the race to approach the goal to immunized the people [6]. The current review tries to focus on the developments of vaccines against SARS-CoV-2 with a complete description of the mechanisms of each vaccine.

### Structures and antigenic determinates of SARS-COV-2

The SARS-COV-2 is a positive single-stranded RNA virus with a small size ranging from 60-90 nm. The RNA takes helical shape and covered with protein to form nucleocapsids. The virus surrounded by envelope derived from host membrane (Figure 1) [7]. Three important surface viral proteins presences on the surface; S protein (spike glycoprotein), which mediates interaction with the receptors on the cell surface ACE2 and composed of two subunits S1 and S2. The S1 subunit, which share 70% sequence identity with bat SARS-like CoVs and Human SARS-CoV, while S2 subunit that shares 99% sequence identity with bat SARS-like CoVs and human SARS-CoV [8]. The M and E glycoproteins are required for viral morphogenesis and maturation of virion. Most of the differences were found in the external subdomain that primary responsible for interaction of ligand and host receptors. The spike glycoprotein was intensively cloned expressed and crystallize to solve the spike glycoprotein structure which is useful in treatment and vaccine productions [9]. The S2 comprises two heptads repeat regions known as HR-N and HR-C, which form the coiled-coil structures surrounded by the protein ectodomain. The S protein has been found to exhibit a furin cleavage site (PRRARS'V) at the interface between S1 and S2 subunits that is processed during the biogenesis [10].

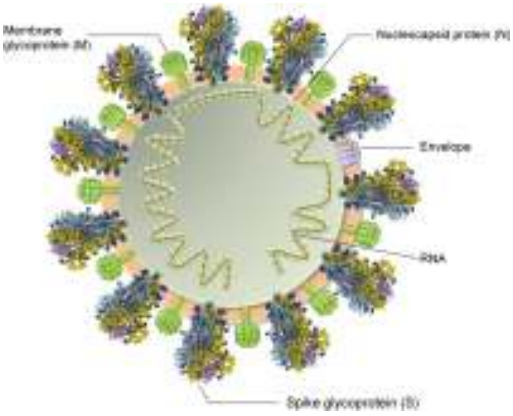


**Figure (1): SARS-CoV-2. Structure. Helical nucleocapsid comprising virial RNA. Surface viral glycoprotein (S), M and E. [7]**

### SARS-CoV-2 mechanisms of infection and immunity

Cell infection by pathogenic agents may trigger host humoral and cellular immunities essential to eliminate the viral infection. However, an uncontrolled or insufficient immune response may lead to immunopathology and cause severe damage to patients, a deeper understanding of the immune response induced by SARS-CoV-2 infection may lead to new immunotherapies while reducing the potential risk of inflammation [5].

The best-known cellular infection mechanism of SARS-CoV-2 is mediated by the cell surface receptor ACE2, similarly to SARS-CoV, several studies have shown that the SARS-CoV-2 was able to infect cells that were genetically modified to express solely the ACE2 receptor, as this ACE2 receptor is predominantly found in the human epithelia of lung and small intestine, the SARS-CoV-2 is more likely to infect the respiratory and gastrointestinal tracts. Moreover, it has been suggested that the brain may also be infected by this virus, as COVID-19 patients present neurological signs, such as the hyposmia at early stages of infection, but also nausea, vomiting, headache and cerebral damage14 at severe situations. SARS-CoV was indeed found in the brain of animals and patients, it has been suggested that SARS-CoV-2 enters into the brain through the cerebral circulation, due to the presence of the ACE2 receptor on the endothelium, or from the cribriform plate close to the olfactory bulb, which can justify at least in part the altered sense of smell. In fact, glial cells and neurons are known to express ACE2, being, therefore, potential targets for SARS-CoV-2 [5].

**Immune response against SARS-Cov-2**

**Humoral immunity:**

IgM and IgG antibodies to SARS-CoV-2 are detectable within 1–2 weeks after the onset of symptoms in most infected individuals [11,12]. Although the connection between neutralizing antibodies and antigen-specific T cells and disease severity and clinical outcomes remains to be understood, high levels of neutralizing antibodies are observed in convalescent individuals, which correlate with T cell responses, particularly those of CD4+ T cells, and seem to offer some benefits in studies of treatment with convalescent plasma. Jeyanathan et al. [13] indicated that the magnitude of neutralizing antibody responses is positively correlated with disease severity. Thus, whereas antibody responses wane within weeks after infection in most people infected with SARS-CoV-2, which is a feature of antibody responses to other 'common cold' coronaviruses, the magnitude of the neutralizing antibody response in asymptomatic individuals isn't only smaller but also decreases faster than in symptomatic individuals.

The major target of neutralizing antibodies to coronaviruses is the S protein, which is consist of S1 and S2 domains, S1 is membrane distal and contains the RBD that binds to the cellular receptor ACE2, S2 is membrane proximal and features a role in membrane fusion. The S proteins of SARS-CoV and SARS-CoV-2 are 88% identical and both bind to ACE2 with high affinity, Certain monoclonal and polyclonal antibodies raised to the protein S of SARS-CoV can cross-neutralize SARS-CoV-2, antibodies that bind to the S1 RBD block its interaction with ACE2, whereas those that bind to other regions of S1 and S2 can inhibit conformational change of the S protein and block membrane fusion, respectively [14].

During natural immune responses to SARS-CoV-2, high titers of antibodies are also generated against nucleoprotein (N) —the foremost abundant viral protein. Although antibodies to N are unlikely to neutralize the virus, they need been reported to supply protection against mouse hepatitis virus, a coronavirus of mice. these antibodies were IgG2a, indicating that they may exert protection through Fc-mediated effector functions instead of direct virus neutralization. Somewhat unusually, several studies have reported that IgA responses to S protein peak before than IgM responses and are more pronounced, which makes IgA a potentially attractive target for antibody-based diagnostic assays. The mechanistic basis of this early induction of S-specific IgA isn't yet clear [15]. Temperton et al. [15] and other scholars [11-14] still believe that the durability of antibody responses to SARS-CoV-2 is yet understood. There are currently no immune correlates of protection for SARS-CoV-2 or other human coronaviruses. Thus, it's unclear what titer of neutralizing antibodies is sufficient to confer protection against infection. Establishing such correlates are going to be essential to guide the event of effective COVID-19 vaccines [16].

However, previous longitudinal studies of patients with SARS-CoV infection reported substantial waning of neutralizing antibody titers between 1 year and couples of years after infection [15]. But during the phases of vaccine development by three companies stated that the immune reaction is going to be initiated after two -three weeks, the booster does will evoke the Ab's for at least one year [15].

**Cell-mediated immunity:**

The successful of any human vaccine depend mainly on the productions of antibodies against the causative agent such as virus or bacteria. Previous studies on viral vaccine such as measles and influenza vaccines, suggested that the requirements of both humoral and cellular immensity, the later enhance the CD4+ T cell helper for optimal production of antibodies and the CD8+ T- cell stimulation in host defense [15].

Furthermore, if neutralizing antibody-mediated protection is incomplete, cytotoxic CD8+ T cells are crucial for viral clearance. Grigoryan& Pulendranwas found that among people who had recovered from COVID-19, 100% had S protein-specific CD4+ T cells and 70% had S protein-specific CD8+ T cells in the circulation, and preclinical studies show a protective role.

Furthermore, if neutralizing antibody-mediated protection is incomplete, cytotoxic CD8+ T cells are crucial for viral clearance. Grigoryan and Pulendranwas among people who found that during the pre-symptomatic period of SARS-CoV-2 infections, the virus may mediate innate immune suppression and induced delayed T-cells activation, particularlyCD8+ T cells, as is the case for SARS and MERS [13]. People who have recovered from COVID-19 seem to have high levels of both neutralizing antibodies and T cells, and, compared with severe cases, milder cases of COVID-19 have greater numbers of memory CD8+ T cells within the tract. Tregoing et al. submitted evidence that suggests that the induction of such lung tissue-resident memory T cells (TRM cells) will depend on the route of vaccination. Respiratory mucosal vaccination induces strong lung TRM cell responses, whereas parenteral vaccination fails to try to so [16]. Experimentally, the airway TRM cells elicited by respiratory mucosal vaccination offered robust protection against SARS-CoV infection, the T helper T cell (TH cell) phenotype of vaccine-induced T cells is additionally relevant to the protection they mediate. Less severe cases of SARS were related to accelerated induction of TH1 cell response, whereas TH2 cell responses are related to enhancement of lung disease following infection in hosts parenterally vaccinated with inactivated SARS-CoV viral vaccines. Thus, COVID-19 vaccine-induced TRM cells should have a TH1 cell-

like phenotype [16]. These lines of evidence, alongside data suggesting that T cell-mediated immunity generally may be a more reliable correlate of vaccine protection than antibody titers in seniors, strongly support the inclusion of T cell responses in COVID-19 vaccine design [16].

## Cross-reactivity among Human Coronaviruses

There are seven groups of Coronaviruses infected human beings, Wang et al. [17] mentioned that the Coronavirus cross-reactive T cells can be specific for both spikes and other's virus protective proteins, the extent of vaccine-boosted cross-reactive T cell responses induced by most protein subunit and recombinant viral-vectored COVID-19 vaccines, which are currently based only on the S protein, are going to be different from those boosted by multivalent COVID-19 vaccines like those supported inactivated SARS-CoV-2 virus. One exception might be the utilization of live attenuated SARS-CoV-2 vaccines because the pre-existing cross-reactive immunity may limit the potency of such vaccines. Finally, it's noteworthy that the many presence of cross-reactive immunity in some individuals involves consideration of stratifying clinical test participants receiving candidate COVID-19 vaccines consistent with their status of pre-existing coronavirus immunity [17].

## Vaccines development against SARS-CoV-2

**Types of vaccine prepared against COVID-19:**
There are more than 150 vaccines trails were developed by many pharmaceutical companies around the worlds. Ten of these vaccines' trails reach's the phase three and some current use as emergencies requesting (Table 1).

**Table (1): Types of vaccines trails against SARS-COV-2**

| Company of manufactured | VACCINE Technology | Country of manufactured | Dosage | Storage |
|---|---|---|---|---|
| BioNTech /Pfizer | mRNA | USA/Germany | 0.3 ml two dose 21 day apart | -70C |
| Moderna / NIAID | mRNA | USA | 0.5 ml two dose 28 day apart | -20C |
| Novavax | Protein subunit | USA | 2 dose- 21 day | +2-8C |
| University ofOxford/AstraZeneca | Viral vector * | UK/ Sweden | 2 dose/ 12 days a part | +2-8 C for 3 months -20 C for 2 years |
| CanSino Biological Inc. / Beijing Institute of Biotech | Viral vector * | China/Pakistan | 2 dose/ 21 days a part | +2-8 C for 3 months -20 C for 2 years |
| Gamaleya Research Institute Sputnik V | Viral vector | Russia | 2 dose/ 28 days a part | +2-8 C for 3 months -20 C for 2 years |
| Johnson & Johnson | Viral vector | USA | 1 dose | +2-8 C for 3 months -20 C for 2 years |
| Covaxin/ Bhart Biotech. | Inactivated virus | China/India | 2 dose -21 day | +2-8 C for 3 months |
| Wuhan Institute of Biological Products / Sinopharm | Inactivated virus | CHINA | 2 dose -21 day | +2-8 C for 3 months |
| Sinovac | Inactivated virus | China | 2 dose -21 day | +2-8 C for 3 months |

### 1. mRNA vaccines:

Two of the 5 candidate vaccines are based on mRNA methodology. Moderna, a Massachusetts-based biotechnology company and Pfizer-BioNTech has developed mRNA-1273, a lipid nanoparticle-encapsulated mRNA vaccine that encodes a full-length, prefusion stabilized spike (S) protein of SARS-CoV-2 [18-20].

Pfizer, in concert with BioNTech, a German company, is also developing an mRNA platform that is similarly focused on lipid nanoparticle-encapsulated mRNA that encodes for SARS-CoV-2 spike (S) protein. Currently, both vaccines were put in practice. The two-dose vaccine showed promise in animal studies and early-stage clinical trials. But the only way to know whether the vaccine works is

to give it to a large number of people and then follow them over weeks or months to see whether they become infected and symptomatic, these results are compared with those for a group of participants who are given a placebo [16,17,21]. But the information released at this early stage does not answer key questions that will determine whether the Pfizer vaccine, and others like it, can prevent the most severe cases or quell the coronavirus pandemic [20].

Messenger RNA (mRNA) vaccines offer a novel methodology in the field of vaccinology (discuss below). Although this strategy has displayed promise in early studies, mRNA vaccines have never been used commercially to prevent infections. The central dogma reveals that the mRNA is the intermediate step between the translation of DNA and production of proteins in the cytoplasm (..). mRNA vaccines function on the premise that mRNA coded for pathogen antigen can be delivered to human cells and, once there, can be used for production of antigen within the cell. This is unique in that it would lead to a specific immunogenic response without the introduction of live, killed, or subunit portions of the pathogen of interest. However, because mRNA is highly susceptible to extracellular ribonucleases and is rapidly degraded, its surrounded by bubbles of lipids delivery system.

**Synthesis and production of Pfizer-BioNTech mRNA vaccines: also known BNT 162b2:**

During the preclinical studies, the mRNA was highly purified after the extractions from the SARS-COV-2, also they constructed BNT 162b2 (SARS-CoV-2 strain) nucleoside- modified RNA expressing the full length prefusion spike glycoprotein (S)used for vaccine [22].

The piece of RNA that translated to give spike protein was cutting and reproduced. Now, after they entered the huge production commercial phase, using huge quantities of DNA that functions as substrate to be able to produce RNA in an in-vitro transcription method. The bacteria used for this purpose was E. coli (The generation time of E. coli 20 minutes) via the fermentation of transformed bacteria that contain the DNA. The DNA were extracted and then linearization via enzymes, the undergoes in-vitro transcription to produce the RNA.

To protecting the newly synthesis RNA, Lipid nanoparticles (LNPs) was used. The end products (the vaccine) contained: mRNA, Lipids ((4-hydroxybutyl)azanediyl)bis(hexan-6,1-diyl)bis(2-hexyldecanoate), 2{(polyethylene glycol)-2000}-N,N-ditetradecylacetamide, 1,2-Distearoyl-sn-glycerol-3-phosphocholine, and cholesterol), Potassium chloride, monobasic Potassium phosphate, Sodium Chloride, dibasic sodium phosphate dihydrate and sucrose (Pfizer-Biotech COVID-19 vaccine data sheet: https://www.pfizer.com/products/product-detail/pfizer-biontech-covid-19-vaccine).

**2. Viral vector vaccines:**

O'Callaghan et al. [21] stated that two additional strategies involve replication-defective recombinant adenoviral vectors. Unlike the rVSV-vectored vaccine, which uses a replication-competent but harmless virus as a vector, these candidates use either a replication-defective simian adenovirus or replication-defective human adenovirus type 26. Both vectors deliver recombinant SARS-CoV-2 spike (S) protein genes to human cells. Similar to the mRNA vaccines, no vaccines to prevent human disease are commercially available using this strategy. Rather, their clinical use has been limited to 1 licensed vaccine against animal rabies. Johnson & Johnson, the maker of the replication defective adenovirus type 26 vector (Ad26.COV2-S), is now declared that the vaccine ready to use with a single dose. BARDA.9 AstraZeneca, the manufacturer of the replication defective simian adenovirus vector (ChAdOx1 nCoV-19), in combination with the Jenner Institute at the University of Oxford, is similarly pursuing a phase 1/2 single-blinded study AstraZeneca [22].

## *DISCUSSION*

After the outbreaks of SARSCoV2 or COVID-19, there are no specific vaccines available, but there are many vaccines are developed, Attempts are being made for the development of safe and effective prophylactic strategies, the earliest possibility is convalescent sera from the persons who recovered from the COVID19 attack, which can be used as an immediate therapy [16]. The point of a vaccine is to harmlessly expose parts of the virus to the immune system, which then recognizes it as an invader and learns the way to fight it, there are some ways to try to this and researchers are using different approaches. Pfizer/BioNtech (and Moderna) have developed what's referred to as an RNA vaccine. This uses an experimental approach, which involves injecting a part of the virus's ordering into the body, so as to coach the immune system, once inside the body, this starts making viral proteins to train the body. This is a completely new technique [16]. RNA, closely associated with DNA, is present altogether living cells. The strand of it called messenger RNA may be a sequence of ordering that tells cells what proteins to create in order that they will function [17].

To produce an RNA vaccine, scientists develop a synthetic version of some of the virus' messenger RNA, when this is injected into the human body, our cells read it as an instruction to start building the proteins, including, in this case, Covid-19's distinctive 'spike' protein, our bodies then mount an immune response by producing antibodies to fight the virus proteins made by our cells. This prepares our immune system to fight the real virus if we encounter it later on [17].

This is different from the way another vaccines work, where a little a part of the virus itself, or the entire virus (weakened or dead), is injected into the body to trigger an immune response. Graphic showing how RNA vaccines work, a synthetic version of part of the virus' genetic code is injected. It tells our cells to start building the virus protein, triggering an immune response [18].

RNA vaccines hold the promise of being faster, cheaper, more adaptable, and easier to mass-produce than other vaccines because they will be generated quickly. RNA vaccines are supported a process of biochemical synthesis that involves fewer components and fewer steps than the more complex traditional methods, like using inactivated live viruses. This means they are quicker to get into clinical trials and quicker to manufacture once the trials are completed – in a matter of weeks and months [19].

They should be cheaper to develop, only a small amount of RNA needs to be delivered into the body's cells, compared to the much larger micrograms of protein that are required for many other vaccines. This means each individual vaccine dose should be cheaper to purchase, although it is dependent on the price set by pharmaceutical companies and the costs of delivery [20, 21].

They could be more adaptable and easier to manufacture at scale. The same RNA vaccine platform could be used to produce vaccines against different diseases – both known and emerging. A manufacturing plant could, in theory, produce multiple vaccines using the platform, whereas other vaccines, like MMR (measles, mumps, and rubella) and Ervebo (one of the Ebola vaccines), each require their own dedicated manufacturing plant [16]. There are not any other licensed RNA vaccines – the Pfizer-BioNTech vaccine is that the first.

However, researchers have been using the technology for a while, and people have been given RNA vaccines in clinical trials for other diseases, like cancer, the major challenge in the past has been deciding the way to deliver the RNA vaccine into the cell so it survives – our bodies naturally want to destroy foreign RNA molecules, this new use of RNA has only been made possible due to the enormous level of research funding and focus during the pandemic, which has allowed breakthroughs in new technologies [22-24].

The Janssen vaccine instead uses a standard cold virus that has been genetically modified to form it harmless and to seem more like coronavirus at a molecular level. This should train the system to acknowledge and fight coronavirus.

Similarly, the Oxford and Russian vaccines take a harmless virus that infects chimpanzees, and genetically modify it to resemble coronavirus, in the hope of getting a response, two of the big China-made vaccines use the original virus but in a disabled form, so it cannot cause an infection, understanding which method produces the best results will be vital [16].

The speed of COVID-19 vaccine development under the influence of pandemic is remarkable as only in six months from the primary release of SARS-CoV-2 sequences the vaccines enter clinical trials, in context, the rapid pace is mainly attributed to the prior knowledge of S protein and its role in humoral immunity and coronavirus pathogenesis the evolution of multiple vaccine platforms and advanced activities within the process of vaccine development. However, the rapid pace should not interfere with the quality of vaccines, and a substandard vaccine must be avoided to be commercialized even under extreme global demand and pressure [16].

## *CONCLUSION*

Two COVID-19 vaccines won't be enough. The world needs a range of vaccines that have different characteristics, suitable for people of all ages and ethnic groups, including people with underlying health conditions, and able to be distributed and used in all settings around the globe.

They must also be available in the billions of doses. No one or two vaccines will be able to achieve this, and so we must continue to develop multiple vaccines using multiple scientific approaches to be able to control the pandemic.

Over the past decade we've seen the health and economic impact of influenza, SARS, Zika, Ebola and now COVID-19. There are certainly more outbreaks to come, but we do not know when and where they will emerge, which makes preparation difficult. If we can hone new methods of developing vaccines, we'll be much better prepared for any future outbreaks and able to save more lives with vaccines, faster.

That is why the urgent funding gaps in the global response to COVID-19 must be addressed. Only through appropriate funding can innovations like RNA vaccines be made possible.

The world and scientists all over the world are now facing a great challenge towards the Corona virus vaccine as soon as possible, and also this vaccine may take many years to ensure its effectiveness and its effect on people and other things. The vaccine has many basics for dealing with it, the way it is taken, stored, and other negative and positive effects.

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