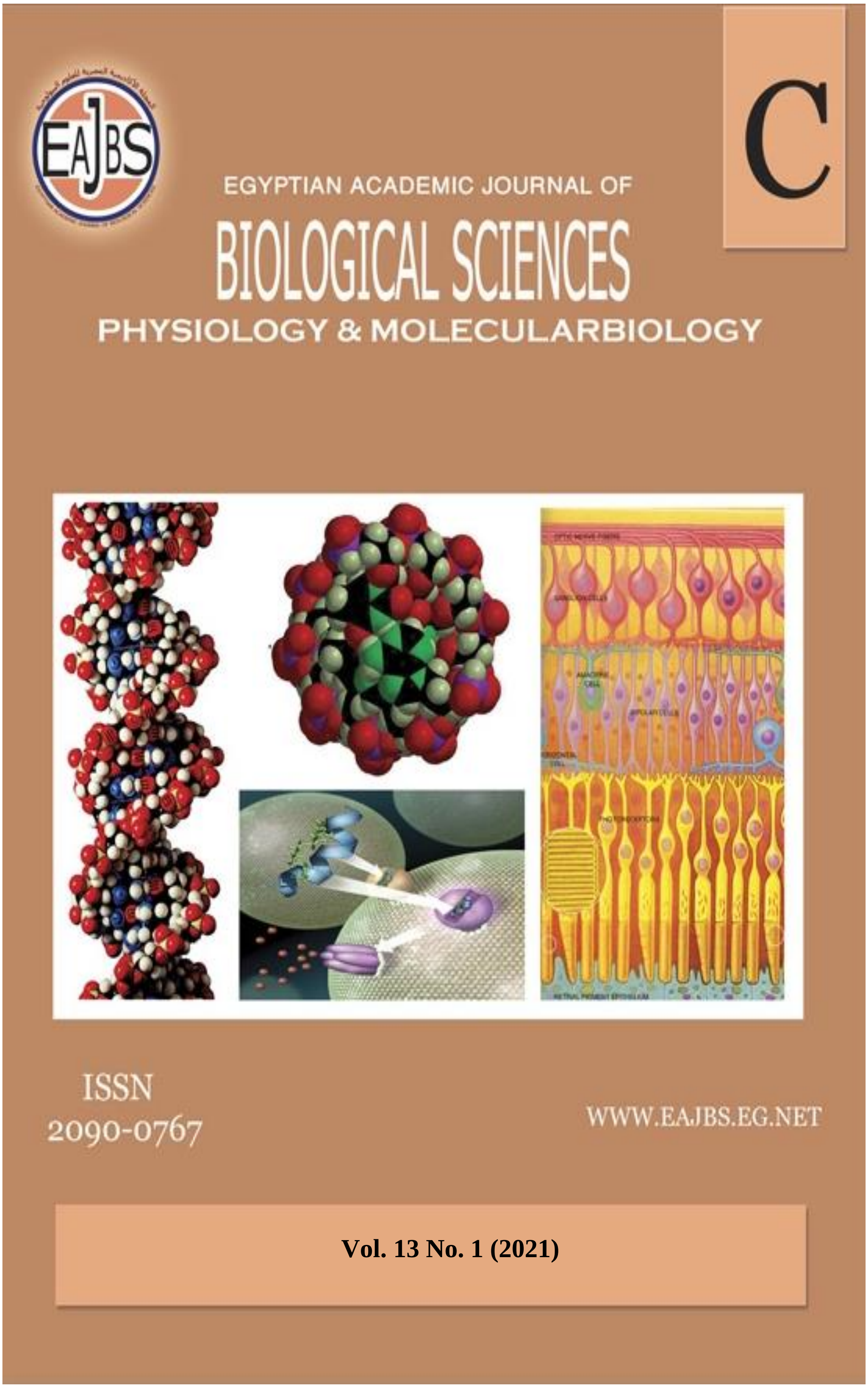

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SARS-CoV-2 & COVID-19. From Virology to Epidemiology: "Epidemiological situation in Algeria and in West Algerian area"

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ABSTRACT

Severe acute respiratory syndrome- coronavirus-2 (SARS-CoV-2) is a new, highly contagious virus causing serious emerging coronavirus disease (Covid-19), it quickly spread globally, causing a pandemic with a large number of deaths and millions of confirmed cases, posing a serious threat to global public health. Algeria was also caught up by the pandemic; the first indigenous outbreak was notified on March 01, 2020, thus announcing the effective start of the epidemic.

Despite the significant progress made by scientists on the basis of various studies and clinical trials, there is currently no specific cure. But the prospect of a preventive or therapeutic vaccine seems increasingly realistic thanks to more intense global cooperation and also by taking advantage of the data collected on SARS and MERS. However, much remains to be learned about immunity against SARS-CoV-2 including the protective immunity induced by vaccines and the maintenance of this immunity.

Therefore, at this time, it is imperative to remain cautious about this virus and to pursue preventative methods to prevent its spread. Algeria very early in adapting with preventive measures which proved to be effective and led to a significant decrease in cases of contamination, especially in western Algeria.

In order to provide a clear overview of the vast literature available, we conducted a review of the literature on the SARS CoV-2 and the disease (Covid-19), while addressing the epidemiological situation in Algeria.

INTRODUCTION

According to the World Health Organization (WHO), viral diseases continue to emerge and represent a serious public health problem. Over the past twenty years, several epidemics have been recorded with the most recent being severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) epidemics which have been considered a major public health problem and can be devastating for the elderly. In December 2019, the first cases of patients who presented with severe unexplained pneumonia (Chaolin et al., 2020) were recorded in Wuhan, Hubei, China (Zunyou, *et al.*, 2020). On December 31, 2019, the epidemic was reported for the first time to the WHO office in China, and investigations led to its connection to the Hunan Wuhan seafood and animal market (Hongzhou *et al.*, 2020). The etiological agent of the epidemic was identified on the 7th January 2020, and in February 2020, the World Health Organization (WHO) gave the name of COVID-19 to designate the disease caused by this virus.

The virus was said to be transmitted to humans probably by the Pangolin in that market in Wuhan in December 2019 (Zunyou, *et al.,* 2020). SARS-CoV-2 behind the 2019 infectious disease (COVID-19) appears to be highly contagious and has spread rapidly globally, becoming a pandemic with a large number of deaths and millions of confirmed cases worldwide leading hence to a serious public health threat.

Algeria, like the rest of the world, was also caught up by the pandemic, the first imported case of Covid-19, an Italian citizen, was reported on February 25, 2020. The first autochthon outbreak was notified on March 01, 2020, in the wilaya of Blida in northern Algeria (43 km southwest of the capital Algiers) when two cases were reported after being in contact with two Algerian people residing in France (ONSA, 2020), thus announcing the effective start of the epidemic. This city was considered as the epicenter of the epidemic in Algeria; by April 21, 2020, Blida was the most affected area in Algeria with a cumulative number of 692 cases (24.6%) out of a total of 2,811. (Hamidouche, 2020). Although its pathobiology is not well understood, since the details of immune responses to this virus have not yet been elucidated, a probable course of events can nonetheless be postulated based on previous studies on SARS-CoV. According to a few authors (Zunyou, *et al.,* 2020), a cell biology perspective is useful in formulating questions about the important characteristics and lessons of the coronavirus epidemic. Currently, there are no clinically approved vaccines or specific therapeutic-drugs available for Covid-19.

In this article, we will discuss the current knowledge about this virus at a structural and epidemiological level knowing that studies on this virus are still ongoing. We will try to provide an overview of the state of play of the epidemiological situation in Algeria and in western Algeria.

Phylogeny and Structure of SARS-CoV-2:

The family of coronaviridae (CoVs) contains four genera (Alpha CoVs, Beta CoVs, Gamma CoVs and Delta CoVs) (Cui. al., 2019), as well as several subgenus. Until 2019, six were known to be responsible for human infections: two alpha coronaviruses (HCoV-NL63, HCoV-229E) and four beta coronaviruses (HCoV-OC43, HCoV-HKUI, SARS-CoV-1, MERS-CoV) (Yin *et al.*, 2018). The new one, SARS-CoV-2, belongs to the Coronaviridae family (Coronavirinae subtype and Beta coronavirus genus) and has been isolated in China from patients suffering from server pneumonia (Ren *et al.,* 2020).

SARS-CoV-2 Genome:

SARS-CoV-2 is a spherical beta-coronavirus, with an enveloped positive RNA genome, the size of its viral genome varies from 27 to 32 kb, under electron microscopy, it appears to carry on its surface structures arranged in a crown (surface protein S). (Na *et al.,* 2020) fig1 (A, B).

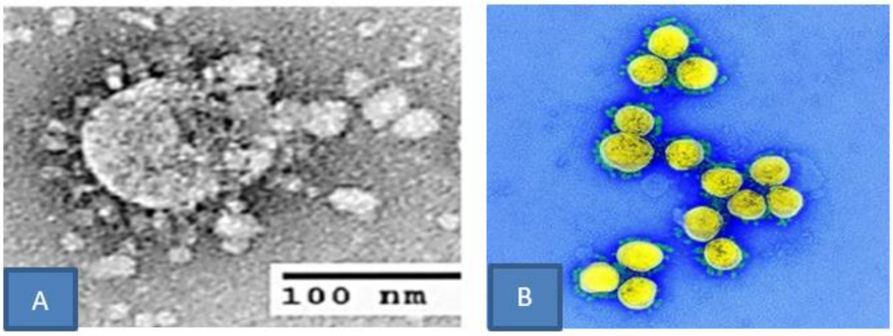

Fig.1. A; Particle transmission electron micrograph: an electronmicroscopic image of a thin section of SARS-CoV-2 within the cytoplasm of an infected cell, showing the spherical particles and cross-sections through the viral nucleo-capsid (Sohrabi *et al.,* 2020).
B. SARS-CoV-2 virus, isolated from a patient. Image captured and enhanced with color at the integrated search center (IRF) of the NIAID in Fort Detrick, Maryland.

The SARS-CoV-2 genome (30 kb) codes for a large non-structural poly-protein (ORF1a and b are translated into two poly-proteins, subsequently cleaved into sixteen non-structural proteins (NSP) essential for viral replication, 4 structural proteins and 5 accessory proteins (ORF3a, ORF6, ORF7, ORF8 and ORF9) (Arunachalam et al, 2020, Chan et al., 2019) (Aiping *et al.,* 2020) and (Jia *et al.,* 2005). The rest of the virus genome codes for four essential structural proteins, including the spike surface glycoprotein (S), the most enigmatic and smallest envelope protein (E) of the major structural proteins, which plays a multifunctional role in the pathogenesis, assembly and release of the virus (Aiping *et al.,* 2020). The membrane protein (M), the most abundant viral protein present in the virion particles, and the core protein (N) which is closely linked to the ribonucleic acid (RNA) genome, are essential for the assembly and infection of SARS-CoV-2 (Fig. 2) (So *et al,* 2020).

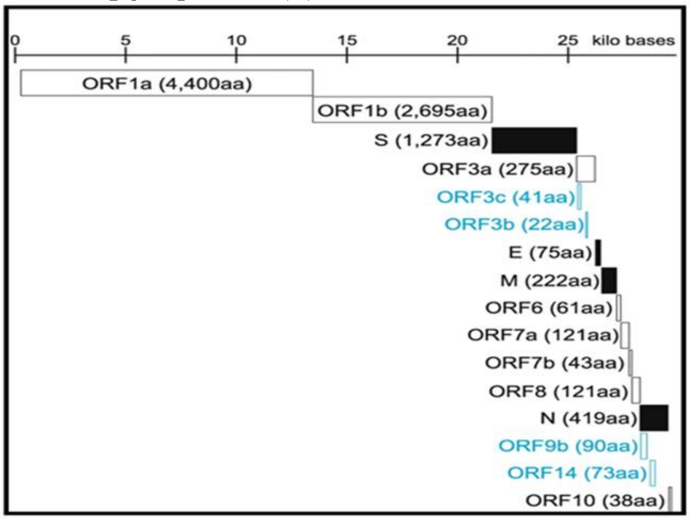

Fig. 2: Genomic structure of SARS-CoV-2.: Schematic genomic structure of SARS-CoV-2 was shown based on the SARS-CoV-2 Wuhan-Hu-1 (NCBI Reference Sequence ID: NC_045512.2). The scale was shown on the top. Each ORF was illustrated based on the NCBI annotation of NC_045512.2, and a rectangle filled with black corresponds to a structural protein. The number in parentheses is the length of amino acid sequence (aa, amino acid). A gene name as well as rectangle colored in light blue was a hypothetical ORF which is not annotated NC_045512.2 currently. ORF3b is based on Konno et al. (Konno *et al.,* 2020) and the others are based on (Davidson et al.,2020 and Jungreis *et al.,* 2020)

Figure 2: Genomic structure of SARS-CoV-2. Schematic genomic structure of SARS-CoV-2 was shown based on the SARS-CoV-2 Wuhan-Hu-1 (NCBI Reference Sequence ID: NC_045512.2). The scale was shown on the top. Each ORF was illustrated based on the NCBI annotation of NC_045512.2, and a rectangle filled with black corresponds to a structural protein. The number in parentheses is the length of the amino acid sequence (aa, amino acid). A gene name, as well as a rectangle colored in light blue, was a hypothetical ORF which is not annotated NC_045512.2 currently. ORF3b is based on (Konno *et al.*, 2020) and the others are based on (Davidson *et al.*, 2020; Jungreis *et al.*, 2020)

Among all structural proteins, the most important potential therapeutic target is the S protein; a leading protein responsible for coronavirus entry into host cells by first binding to a host receptor and then fusing the viral and host membranes. This protein can be cut by host proteases into a subunit S1 (N-terminal) and S2 (C-terminal) region bound to the membrane (Heng *et al.*, 2020) (Fig 3).

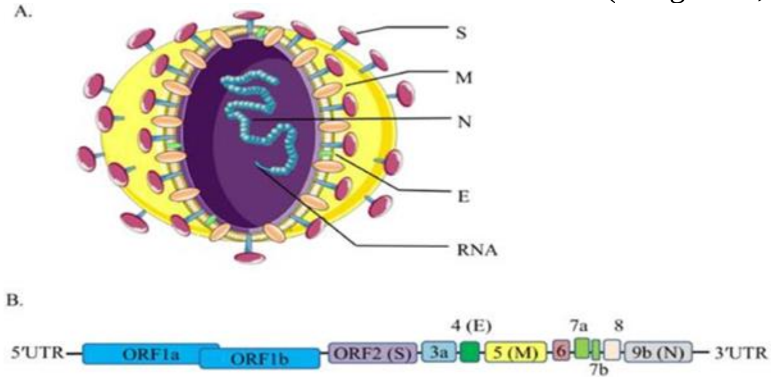

Fig. 3: Structure and genome of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). (A) There are four structural proteins as follows: spike surface glycoprotein (S) (purple); membrane protein (M) (orange); core protein (N) (blue); and the envelope protein (E) (green). Genomic RNA is shown to be enclosed in protein N. (B) The SARS-CoV-2 genome is organized in the order of 5′-replicase (ORF1a / b)-structural protein [spike (S)-envelope (E)–membrane (M)–nucleocapsid (N)]- 3 ′ (Heng *et al.*, 2020).

SARS-CoV-2 Replication Cycle:

As an obligate intracellular microorganism, the coronavirus exploits the machinery of the host cell for its own replication and propagation. Since virus-host interactions are the basis of diseases, knowledge of their interaction is essential.

The life cycle of SARS-CoV-2 begins with the binding of its spike protein to the receptor of the host cell, namely the angiotensin-converting enzyme 2 (ACE2). thus the Coronavirus spike protein is a multifunctional molecular machine that consists of 2 functional subunits: The S1 subunit, where the receptor-binding domain (RBD) is located, it is responsible for binding the surface receptors of the host cells.

The S2 subunit, which mediates entry and subsequent fusion between viral and host cell membranes by forming homotrimers protruding from the surface (Tao *et al.*, 2020, Hoffmann *et al.*, 2020a)

SARS-S engages the angiotensin-converting enzyme 2 (ACE2) as an input receptor and uses the cellular serine protease TMPRSS2 for the priming of the S protein responsible for binding the virus to host cells (Hoffmann *et al.*, 2020). The second step, which is considered to be the most important for viral entry, is the protein cleavage producing the S1 and S2 subunits, mediated by the transmembrane protease receptor serine 2 (TMPRSS2), a member of the Hepsin TMPRSS subfamily (Fig 4).

At this stage, the cleavage of the viral protein by TMPRSS2 becomes crucial because, after the detachment of S1, the remaining S2 viral unit undergoes a conformational rearrangement which results in the fusion between the viral and cell membrane, with a subsequent entry of the virus into the target cell by endocytosis, the release of the viral nucleocapsid into the cytosol of the infected cell, as well as its replication and its infectivity to other cells. Thus the need for TMPSRR2 is confirmed by the evidence that entry of SARS-CoV and SARS-CoV-2 into cells is partially blocked by camostat mesylate, an inhibitor of TMPSRR2 (Hoffmann *et al.*, 2020; Jie *et al.*, 2020)|.

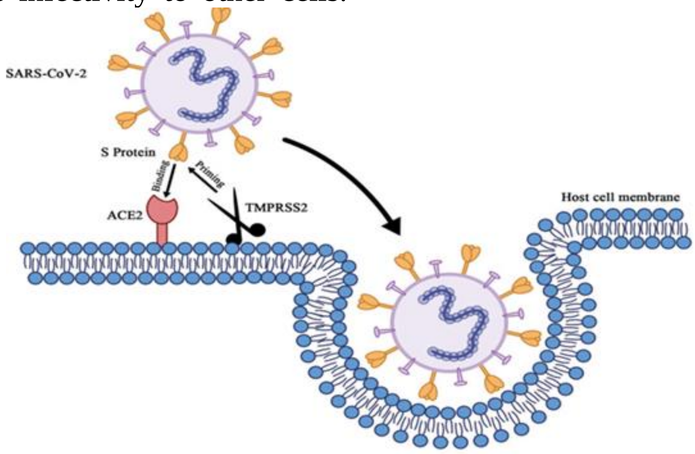

Fig. 4: Schematic of cell entry of SARS-CoV-2. When the trimeric S proteins of SARS-CoV-2 binds to the cellular receptor ACE2, the cellular serine protease TMPRSS2, which is used for S protein priming, entails S protein cleavage at the S1 and the S2 site to facilitates fusion of viral envelop and host cell membranes.

The genomes of all coronaviruses have a similar structure. Following the release of the uncoated viral RNA into the cytoplasm, the virus replication starts with the translation of ORF1a and ORF1b into poly-proteins pp1a and pp1ab via a frameshift mechanism (Weiss *et al.*, 2005). Subsequently, poly-proteins pp1a and pp1ab are processed by internal viral proteases, including the main protease Mpro, a potential drug target whose crystal structure was recently determined for SARS-CoV-2 (Roujian *et al.*, 2020).

Cleavage of the poly-proteins produces 15 mature replicases, which assemble into a replication-transcription complex, engaging them in the synthesis of negative-strand RNA. Complete and multiple sub-genomic negative-strand RNAs are produced. The first serves as a model for new full-length genomic RNAs and the second models the synthesis of sub-genomic mRNAs required to express the structural and accessory protein genes residing in the proximal 3 ′ quarter of the genome (Knoops *et al.*, 2008). Coronavirus RNA replication occurs on a virus-induced reticulo-vesicular network of modified endoplasmic reticulum (ER) membranes (Neuman *et al.*, 2011). Virion assembly rapidly follows with the accumulation of new genomic RNAs and structural components. The N protein form complexes with genomic RNA assembled into helical structures. Then, the trans-membrane M protein, localized on the intracellular membranes of the ER-Golgi intermediate compartment (ERGIC), interacts with other viral structural proteins (S, E and N proteins) to allow virions' budding (Chen *et al.*, 2020) (Huang *et al.*, 2011). After assembly and budding, the virions are transported in vesicles and finally released by exocytosis.

Modes of Virus Transmission:

The Covid-19 is highly contagious even before the appearance of clinical signs, and the speed of the contagion is important since in a few months a pandemic has been declared. The incubation period of SARS-CoV-2 is short and human-to-human transmission occurs within family members.

Chan and colleagues (Chan 2020) reported a case of five patients in a family group, which confirmed person-to-person transmission of Covid-19. Thus, human-to-human transmission of SARS-CoV-2 is proven, with a basic reproduction rate (R0) of between 2 and 4, which means that an infected subject infects on average two to four other people (Chen *et al.,* 2020). Several cases of contamination have been noted in healthcare facilities among healthcare personnel in contact with infected patients. It has been established by several research teams and by the WHO that lasting human-to-human contamination remains the main route of transmission (Phelan *et al.,* 2019; Lescure *et al.,* 2020).

Although it remains unclear whether people without symptoms have viral titers high enough to spread the virus, we must also attach importance to asymptomatic cases, which can play a critical role in the transmission process, also great care should be given to minimize the risks. This new virus is generally transmitted by the respiratory route (projections of droplets of respiratory secretions during coughing and/or sneezing), through close and unprotected contact with an infected person. It is also reported that contact with the hands or during contact with inert surfaces contaminated by the virus can play a role in infection.

The thesis of the transmission of the virus by the air that everyone exhales and inhales, rather than by the only large droplets expelled by sneezing and coughing, has long been neglected by world health authorities until a turnaround operated this summer facing pressure from numerous respiratory virus experts and an accumulation of studies investigating the presence of viral particles of microdroplets suspended in the air emitted by simple speech. Since July (2020), the WHO has considered that the possibility of aerial transmission in public places is possible, especially in overcrowded, closed, and unventilated places. Furthermore, it remains to be determined whether blood transfusion and the transplacental and perinatal pathways can transmit the virus. Until this date, nothing is excluded from the mode of transmission which can bring out other still unknown means.

Diagnosis of SARS-CoV-2 and Immune Response:

In the event of infection, the immune system initially activates the first line of defense, the innate immunity. Adaptive immunity then kicks in. It makes it possible to obtain a specific response against the pathogen present. It relies on the production of antibodies specific for this pathogen, as well as T lymphocytes that are able to recognize and destroy the infected cells. Adaptive immunity generates memory, but each individual responds uniquely to infection, producing various "humoral memory" antibodies. The question arises: what about the Covid-19 infection? This is the biggest unknowns of the Covid-19 crisis and the most important parameter for the rest of this epidemic. When SARS-CoV-2 appeared and began to spread, the severity of the threat was mainly attributed to the novelty of the virus to the human immune system and, therefore, a lack of pre-existing immune memory to quickly clear the virus and limit the progression of the disease.

As soon as the pathogen was identified, the Chinese researchers shared the viral genome in open access. Since then, the diagnosis of SARS-CoV-2 has been carried out either directly by the direct qualitative research of the viral genome by real-time RT-PCR or indirectly, by serological tests carried out on blood samples, in search of antibodies (Abs) directed against the virus.

RNA testing can confirm the diagnosis of SARS-CoV-2 (COVID-19) cases with real-time RT-PCR or next-generation sequencing (Xiao et al 2020; Wenling *et al.,* 2020). Currently, nucleic acid detection techniques, such as RT-PCR, are considered an effective method to confirm the diagnosis in clinical cases of COVID-19. (Gao 2020). This technique is mainly used in Algeria for the diagnosis of patients. It has been shown that viral RNA can be detected from nasal and pharyngeal swab, broncho-alveolar lavage, and blood plasma by RT-PCR targeting the

NP gene of the virus (Chaolin *et al.*, 2020).

The Chinese National Health Commission affirms that laboratory tests for nasopharyngeal and oropharyngeal swab tests have become a standard assessment for diagnosing Covid-19 infection (Chu *et al.*, 2020). Since then, many commercial tests have been developed, they target different genes: RdRp, E, but also the N, S, or ORF1 genes of Sars-CoV-2 allowing earlier identification of infected patients (Ahmed Hussein et al. 2020). Several laboratories around the world have focused on the development and commercialization of their own SARS-CoV-2-specific RT-PCR nucleic acid detection kits (Yu *et al.*, 2020).

Apart from real-time RT PCR, other molecular methods have been developed and evaluated worldwide for the detection of SARS CoV2, including the clustered regularly interspaced short palindromic repeats (CRISPR)-Cas12-based lateral flow test of 40, called SARS-CoV-2 DNA Endonuclease-Targeted CRISPR Trans Reporter (DETECTR) for the detection of SARS-CoV-2 in oropharyngeal and nasopharyngeal swabs after RNA extraction in infected individuals. The assay uses simultaneous reverse transcription in isothermal amplification using the Reverse Transcription Loop-mediated Isothermal Amplification (RT-LAMP) technique, followed by Cas12 detection of the amplified viral sequence. Once cleavage of the reporter molecule confirms detection of the virus, a lateral flow strip is used to confirm the presence or absence of a target virus. This diagnostic method offers a faster and more reliable alternative (95% and 100% for positive and negative predictive agreement, respectively) to the SARS-CoV-2 RT-PCR test performed at the United States Centers for Disease Control and Prevention (Broughton *et al.*, 2020).

Serological Diagnosis:

From a serological point of view, the invasion of the body by the virus leads to the production of large quantities of immunoglobulins (Ig) by the immune system which is released into the blood, among them, IgG and IgM, sometimes even IgA. The presence of these antibodies directed against viral proteins could be used as an indicator of a previous infection regardless of the presence or absence of symptoms; therefore serological tests, such as enzyme-linked immunosorbent assay (ELISA), lateral flow assays (LFA), or chemiluminescence enzyme immunoassays, have been developed to detect the proteins SARS-CoV-2, S or N or IgM / IgG antibodies in serum, plasma and whole blood of infected patients. (Xiang *et al.*, 2020; Amanat *et al.*,2020). Although infection with SARS-CoV-2 induces antibody responses, their levels depend on the severity of the disease and the viral inocula (Huan *et al.*, 2020).

Studies have shown that following contamination with SARS-Cov-2, antibody production begins after the first week of infection and becomes detectable from the second week (Elslande *et al.,* 2020). IgM-type antibodies appear from day 7 (D7) and IgG-type antibodies from D10. The detection of these antibodies, therefore, testifies to exposure to SARS-CoV-2 and could even provide information on the evolution over time of the viral infection, but this does not provide information on the lifespan of these antibodies nor on the fact that they are protective in the long term (neutralizing antibodies).

In Algeria, with the appearance of the first cases, a monitoring and watch committee unit, constituted of the Minister of Health and an expert, was established by the President of the Republic. Government guidelines were quickly taken to identify contagion. Moreover, in order to rapidly test large numbers of patients with the best reliability, molecular and serological tests were undertaken, RT-PCR was the validated test for early diagnosis in Algerian patients suspected of infection with SARS-CoV-2 since this test showed good sensitivity and specificity. At the start of the pandemic, RT-PCR tests were carried out on nasopharyngeal samples for most of our Algerian patients, at the level of the Pasteur Institute in Algiers (Algerian capital). Subsequently, the director-general of the Pasteur Institute in Algeria authorized the opening of new IPA services in several wilayas in order to expand the diagnostic network and contribute to the early detection of cases infected with Covid-19. Since the beginning of April, several universities and hospital laboratories have launched tests for SARS-Cov2, and even at the level of private laboratories (Bull Epi n°2, 2020). However, the logistical needs for the supply of reagents (and the associated cost) for RT-PCR-based tests have been extremely problematic. Indeed the high cost of this test in private laboratories remains beyond the means of most Algerian citizens. This situation has pushed the authorities to opt for other alternatives. On May 11, 2020, the Algerian government officially announces that the rapid serological test conditioned by the company Vital Care will be applied as a complement in the diagnosis of Covid-19 after a series of examinations (Kourta 2020).

Another examination is also used in the diagnosis of covid-19, the chest scanner also makes it possible to make the diagnosis by looking for the main signs suggestive of pneumonic COVID-19. In Algeria, from April 6 (2020), chest scanners were endorsed as an alternative to COVID-19 screening to assess its extent, look for complications, and exclude other differential diagnoses. (Bull Epi n°2, 2020).

Prevention and Therapies:

Covid-19 (Unify Covid-19 or COVID-19) is an emerging disease; the clinical picture is variable, ranging from a simple flu-like syndrome to life-threatening hypoxemic pneumonia. Not only has this disease had a strong impact on the health and quality of life of populations but also on the world economy, requiring an urgent need to find curative therapeutic agents. Considerable progress has been made in the biology, epidemiology, pathophysiology, diagnosis and clinical manifestations of the virus, pushing all researchers around the world to seek effective therapeutic approaches against the disease. According to the WHO, there is no specific drug or vaccine against SARS-CoV-2, however, several approved drugs, including small molecule compounds and monoclonal antibodies (mAbs) have been in clinical trials.

MAbs can be chosen to target specific epitopes of SARS-CoV-2 surface proteins and can inhibit entry of the virus into host cells (including receptor binding, membrane fusion, and cell-binding sites sialic acid), and reduce the replication and progression of the infection. (Balamurugan *et al.*, 2020).

Other alternatives, such as plasma/serum convalescent treatment, allogeneic cell therapy, and traditional Chinese medicine (TCM) are also being investigated for Covid-19 treatment.

Given the challenges facing global health systems and the far-reaching consequences for the global economy, there is an urgent need to develop and globally deploy effective and safe vaccines that trigger the production of antibodies neutralizing proteinic key targets; therefore, protective immune responses, in vaccinated subjects, to lessen morbidity and mortality caused by SARS-CoV-2 infection. Since the start of the SARS-CoV-2 pandemic, scientists around the world have joined forces, collaborating and sharing data to accelerate the development of an effective vaccine. The striking effect of this pandemic is the speed with which research into vaccine development continues. In just a few months there have been 133 vaccines in development including 10 in human trials, according to data released by the WHO (Mullard, 2020).

Numerous candidate vaccines are under development and testing, including nucleic acid vaccines, inactivated viral vaccines, live attenuated vaccines, protein or peptide vaccines, and viral vector vaccines (Bakhiet *et al.*, 2020). (Fig. 5).

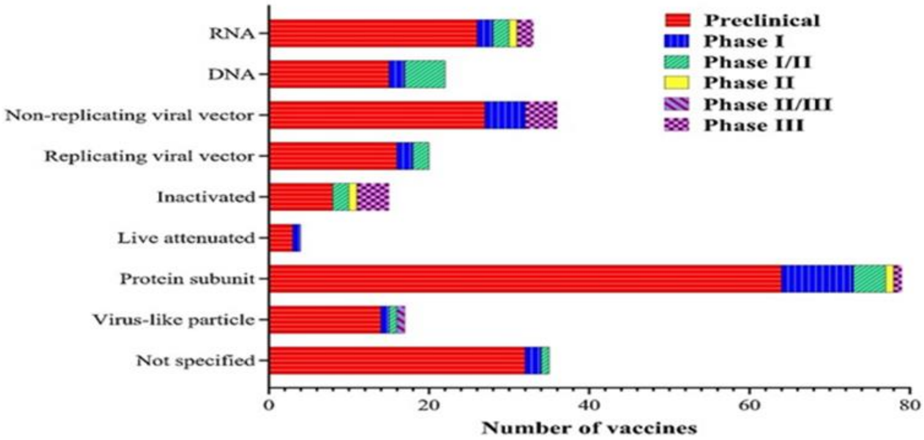

Fig. 5: Number and types of vaccines currently in the preclinical phase and the different clinical trial phases. Data were adapted from the COVID-19 vaccine tracker (Parker *et al.*, 2020).).

As of August 2020, several Phase III vaccine clinical trials, each involving tens of thousands of participants, had started in various locations around the world. The intermediate results of these trials have already provided a first indication of the efficacy and safety of COVID-19 vaccines, some have already passed phase III, among them:

-Moderna and the National Institutes of Health have jointly developed a vaccine based on mRNA (mRNA-1273) consisting of an mRNA sequence encoding optimized for spike glycoprotein encapsulated in lipid nanoparticles (Corbett *et al.*, 2020). This vaccine is considered to be the main anti-SARS CoV-2 mRNA vaccine candidate. The mRNA-1273 vaccine will be easier to store and distribute through the world, it does not require optimal freezing and can be stored in the refrigerator for 30 days or frozen (-15 to -25 ° C) for long time preservation. Moderna plans to manufacture between 500 million and 1 billion doses in 2021 and coordinating distribution with the Centers for Disease Control and Prevention (CDC), USA.

-AstraZeneca, Oxford University (Oxford, UK) and AstraZeneca have developed an experimental vaccine in chimpanzee adenovirus vector (ChAdOx1 / AZD1222) encoding the advanced SARS-CoV-2 glycoprotein (Neeltje van *et al.*, 2020). This vaccine will only require refrigeration for storage, which will facilitate its distribution around the world.

-Pfizer and BioNtech have also developed a series of COVID-19 vaccines based on mRNA-. BNT162b2 which encodes the RBD domain of SARS-CoV-2. This vaccine candidate incorporates modified mRNA and also includes a T4 fibritin-derived trimerization domain to enhance immune response (Mulligan *et al.*, 2020). Pfizer with its partner BioNTech estimates that BNT162b2 vaccine is effective at 95% approximately in preventing disease. This vaccine requires storage at -80 ° C, therefore, logistical problems can be detected.

Several other vaccines are at the end of phase III; however, even if the shadow of an effective vaccine is emerging, many obstacles remain including the logistical difficulties associated with mass production and the delivery of millions or billions of doses to the world population, it is essential to carry out large-scale clinical trials to evaluate the efficacy and safety of vaccines before approving widespread use.

Despite all these advances facing an unknown and worrying disease that has caused high levels of mortality, preventive measures remain for the moment, the main and single way to fight against the spread of this pandemic. Indeed, since WHO declared on January 30, 2020, the coronavirus epidemic as a public health emergency of international concern and elevated it to pandemic status on March 12, 2020 (WHO, 2020), all governments including Algeria have put alert plans and various strategies against this disease to stop its spread. The measures recommended by WHO to control the spread of the virus, such as self-isolation, social distancing, hand washing, the closure of schools and universities, and wearing a mask, is the best strategy prevention to pandemic control, to reduce the total number of deaths and prevent the population from contracting the disease.

Like all countries of the world, Algeria begins early confinement and this was from the first reported cases in Blida. Hard decisions have been taken to avoid an exponential spread of the virus. Algeria has gone from partial confinement to total confinement in certain wilayas. The confinement was tightened as the disease progressed (Pandémie Covid-19. Algérie 2020). The actions used to prevent infection and the spread of the virus were confinement, barrier measures social distancing, quarantine, the locking (closed airspace and maritime links and borders). From March 15, 2020 (Ins. Nat. Santé Pub, 2020), the monitoring unit has ordered to close all schools from primary to university, mosques and places of worship were also closed, the transport in all its forms, and the closure of nonessential businesses.

All these measures helped to stabilize the epidemiological situation related to Covid-19. To assess the effectiveness of the preventive strategy in Algeria face Covid-19, Hamidouche Mohamed, an epidemiologist at the Pasteur Institute of Algeria and at the School of Public Health and Epidemiology of Pasteur in Paris CNAM and his team, carried out a study throughout three areas in Algeria to estimate the number of cases of COVID-19 avoided by the health measures (Hamidouche 2020a). According to these studies, the prevention strategy in Algeria was effective, the author of this study confirm that the total confinement measure of Blida was more than effective in terms of reducing the number of basic reproductions R0, compared to other regions where there was partial confinement, he specifies that “the reproduction rate has gone from 1.69 to 1.14. At the final of the study, the epidemiologist Hamidouche Mohamed said: "Our results show that the preventive measures that have been implemented, either total or partial confinement were generally effective (Hamidouche 2020a).

The current context of this epidemic requires us to adopt a gradual return to normal life with recommended measures such as strengthening protection measures such as the compulsory wearing the mask and hand hygiene, prohibit gatherings in places public, banning weddings and parties, but the return to education with restrictions was adopted.

Epidemiological Situation of Covid-19 in Algeria and the Western:

As of October 6, 2020, 35, 527,480 confirmed cases of Covid-19 recorded worldwide have been notified to WHO, with 1, 044,882 deaths (https://coronavirus. jhu. edu/map.html.2020).

The United States of America comes first with over 7, 459,102 new cases, followed by India (6, 685,082 new cases) and Brazil (4, 927,235 new cases) (https://coronavirus. jhu.edu/map.html.2020). On the same date, Morocco recorded a rate of 254,155 confirmed cases of covid-19 with a confirmed rate of 5,990 deaths. In Algeria, the rate of confirmed cases on the same date was 52,270 cases and 1,768 deaths. In western Algeria, the cumulative confirmed case rate was 9,226 and 171 cumulative deaths (Bull. Épi n° 131/octobre 2020). Almost two months later, the WHO reports that figures as of November 25, 2020 globally show 57.8 million confirmed cases of Covid-19 with a rate of 1.3 million deaths reported worldwide since the start of the pandemic (WHO, 2020). On that date, the United States of America came in the first position with more than 1.1 million new cases, followed by India which posted a rate of 280,000 cases, then Italy which in turn posted a figure quite high for the end of November with a rate of 230,000 new cases, for France a rate of 170,000 new cases was reported in the last week of November. As for the Maghreb, it is also showing an upsurge in figures. These figures tell us about a significant increase in cases of Covid-19 infection for all countries of the world compared to the beginning of October. (WHO, 2020).

For the month of October, the central health region recorded the highest incidence rate (132.64 per 100,000 inhabitants), followed by the East, South and West health regions with incidence rates of 119.64, 119.53 and 105.17 per 100,000 inhabitants respectively (WHO, 2020). The wilayas of Oran, Tindouf and Annaba had recorded cumulative incidence rates of over 200 cases per 100,000 inhabitants; (Fig 6). (INSP, 2020). In terms of mortality, 1,741 cumulative deaths were recorded, a case fatality rate of 3.37% (INSP, 2020/ 1 octobre).

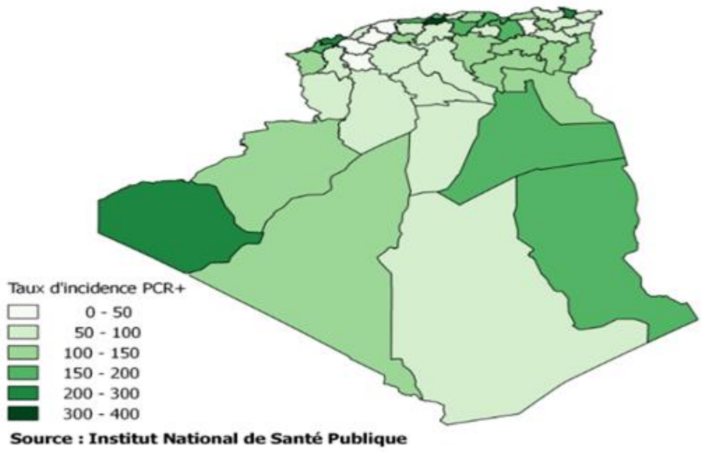

Fig. 6: Distribution of incidence rates by wilaya on October 1, 2020.

Moreover, the analysis of the evolution of the epidemic incidence curve in Algeria shows that the peak was reached on July 24, 2020, (Institut national de santé publique), with the registration of 675 new confirmed cases. Since then, the downward trend is the rule (WHO organization deasCOVID-19). As of October 1, 2020, the number of new incident cases was 160 with the registration of 5 deaths across the national territory (INSP/ 24/07/2020). Fig 7.

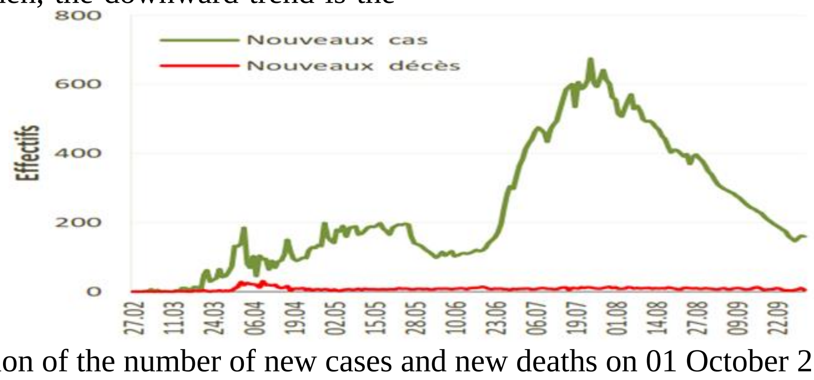

Fig. 7: Evolution of the number of new cases and new deaths on 01 October 2020

Regarding the characteristics of the population, a study carried out at the level of the Nedjma hospital in Oran (annex hospital), which concerned a total of 535 hospitalized patients, from June 12 to September 30, 2020, a slight male predominance was recorded with a frequency of 53.3%. The average age was 51.5 ± 20.7 years. The modal class corresponded to patients aged 60 to 69 years with a frequency of 19.6% of all recorded cases (Fig. 8) (SEMP hôpital Nedjma).

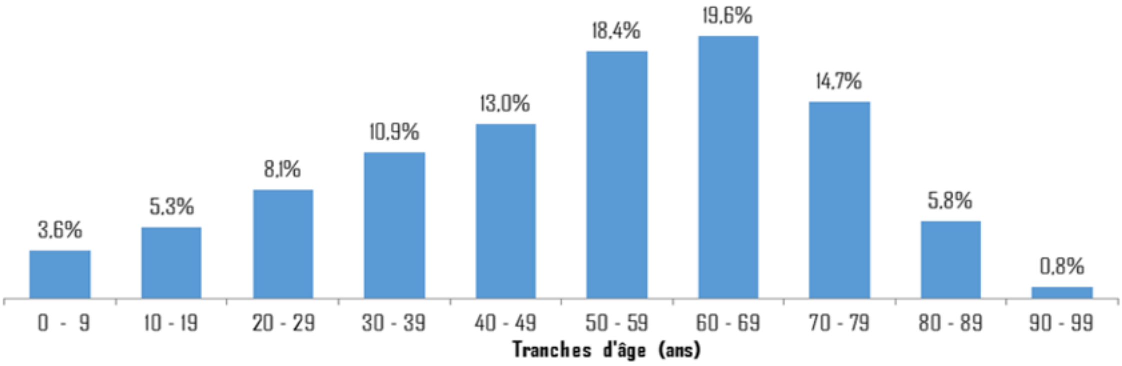

Fig. 8: Distribution of the study population by age group.

Graph number 9, shows the epidemiological situation with regard to COVID-19 in the capital Algiers and in western Algeria as of October 18, 2020, according to epidemiological bulletin N ° 137 of October 19, 2020, the distribution of confirmed cases and deaths by wilaya, shows that the capital Algiers recorded a rate of 6,287 cumulative cases, the city of Oran (capital of western Algeria), to record a rate of 4,145 cumulative cases of covid-19, with 10 new cases, i.e. an incidence rate of 224.13 and 45 cumulative deaths, resulting in a death rate of 2.43 and a case fatality rate of 1.08. We compared these rates over a period from 01 October to 01 December, showing a marked increase in the cities closest to Oran. (Bull épi n° 137, oct 2020).

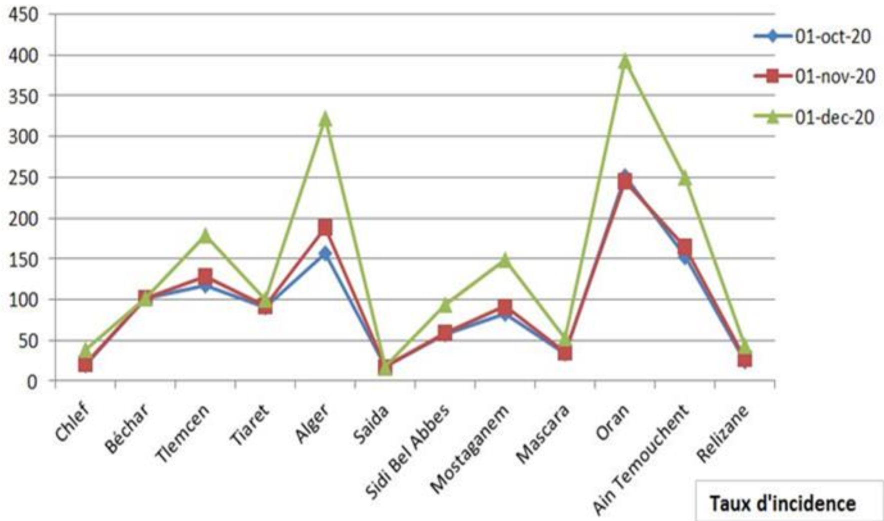

Fig 9: Breakdown of incidence rates by wilaya from October 01 to December 01, 2020.

Still and in the same context, a rate of 83,199 cumulative cases of Covid-19 was recorded until November 30, 2020 in Algeria, which corresponds to an incidence rate of 121, 34 cases per 100,000 inhabitants, with a cumulative death rate of 2431. (INSP, Bul épi n°153, 2020). Algiers the capital recorded the highest number of new confirmed cases during the month of November with a rate of 4,818 cases, and Blida (1,870 cases), the cumulative confirmed cases in western Algeria were 14,767 and a cumulative death rate of 229. On the same date, the city of Oran (capital of the west) recorded 2,634 new cases. We, therefore, conclude that the city of Algiers reports an increase compared to Oran which records a slight decrease (fig10).

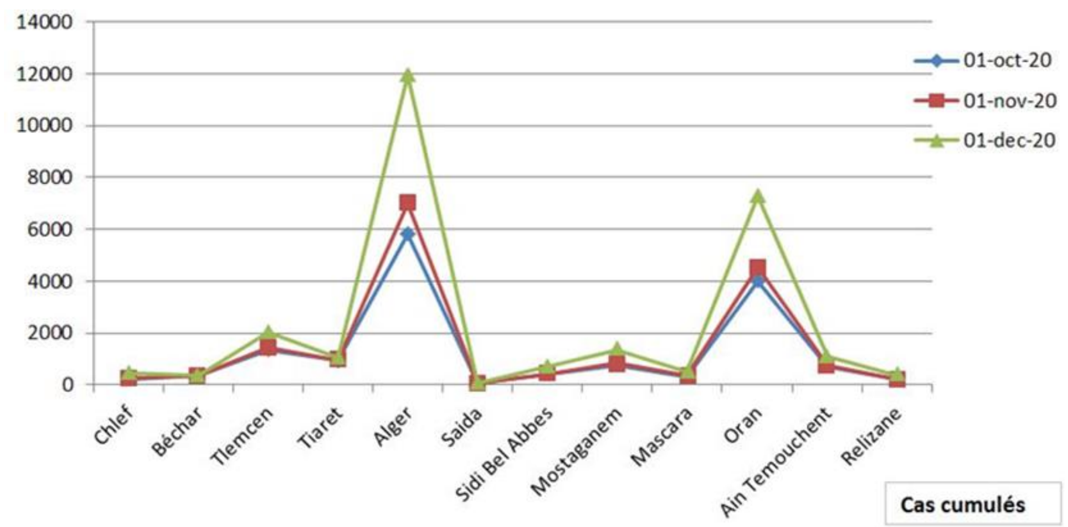

Fig. 10: Cumulative cases in Algiers and the western regions.

For the cumulative deaths recorded on November 29, 2020, Algiers displays the rate of 366 cumulative deaths with a mortality rate of 9.90, for Oran a rate of 59 cumulative deaths was observed on the same date. We note that the cumulative death rate figures, recorded between October 1st to December 1st in the western region, show relatively low rates (fig11). (INSP. Bul épi n° 154. 2020).

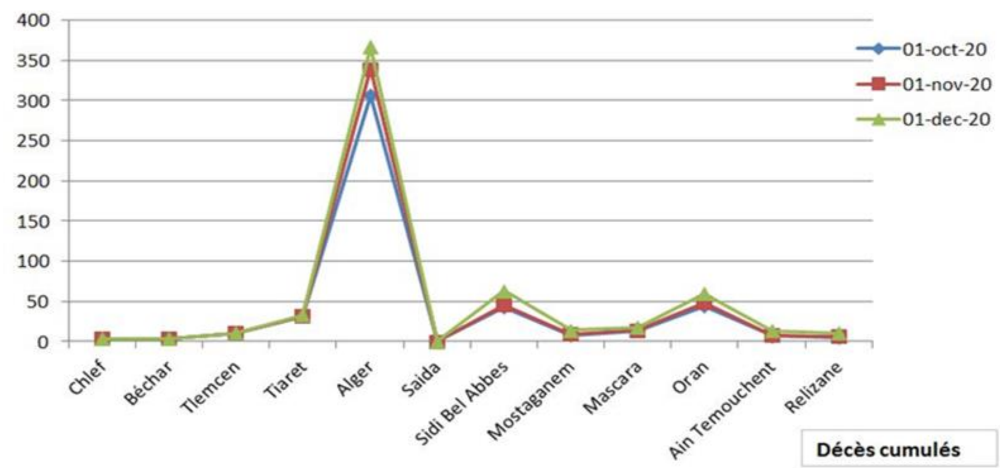

Fig.11: Breakdown of cumulative deaths by wilaya from October 01 to December 01, 2020

Regarding the mortality rate recorded between the dates of October 1 to December 1. (INSP. Bul épi n° 154. 2020), the values observed show that Algiers the capital remains in the lead with rising rates, however, a significant drop in the mortality rate is observed in Oran neighboring towns (Fig 12).

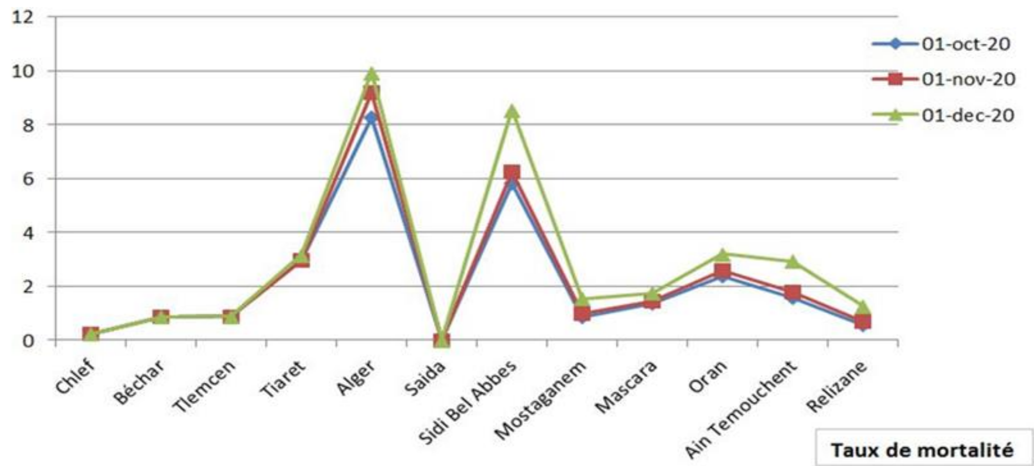

Fig.12: Distribution of death rates in Algiers and western Algeria from October 01 to December 01, 2020

Conclusion:

SARS-CoV-2 is a new and highly contagious virus causing a serious emerging disease that can, in some cases, cause life-threatening hypoxemic pneumonia; authors have even reported serious neurological damage in patients with COVID-19, ranging from disturbances of consciousness, visual impairment and seizures (Kiandokht *et al.*, 2020). COVID-19 represents a major global health challenge for the years to come. SARS-CoV-2 infection likely presents in various phenotypes reflected by differential immunopathogenesis (COVID-19 represents a major global health challenge for the upcoming months and years). SARS-CoV-2 infection likely presents in various phenotypes reflected by differential immunopathogenesis. This disease has had a strong impact on the health and quality of life of populations but above all on the world economy, causing a situation of poverty and deep depression among precarious, fragile and low-income people. Hence the urgency to find preventive and curative therapeutic agents. Despite the significant progress made by scientists on the basis of various studies and clinical trials, there is currently no definitive cure.

However, the prospect of a preventive or therapeutic vaccine seems realistic thanks to more intense global cooperation and also by leveraging the data collected on SARS and MERS; accurate and up-to-date data on the status and timing production and release of vaccines must be accessible to everyone. In the meantime, the collaboration of countries around the world is clearly needed to achieve the desired therapeutic results. Also, much remains to be learned about immunity against SARS-CoV-2 including vaccine-induced protective immunity and the maintenance of this immunity. Therefore, it is wise to continue with preventive methods and barrier gestures to prevent contagion and the spread of the virus. Algeria like the rest of the world has been strongly impacted by covid-19, but the prevention strategies taken very early by the government authorities have allowed a significant decrease in cases of contamination.

The progression of this virus and our understanding of its pathogenesis and epidemiology may already be partly outdated on the day of publication of this article.

Lastly, this virus is very aggressive, even our President of the Republic was affected by this disease, but he escaped unscathed.

The Covid-19 has swept away several of our friends and colleagues, the dean of our faculty has also been swept away by the covid-19, we pay tribute to all the people who died from this virus.

Perspectives:

As soon as the borders open, we plan to do research with the collaboration of a French team (INSERM U976), by exchanging blood and tissue samples taken from patients who have tested positive for Covid-19 and who have recovered.

This team suggests that infection with SARS-CoV-2 induces apoptosis in alveolar cells in late phases of proliferation (Jasper Fuk-Woo *et al.,* 2020). This apoptosis could be induced by serum cytokines found in large amounts in the serum of Covid-19 patients. The study of protein-protein interactions in the control of apoptosis will be the theme of this collaboration.

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