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Current Status of Pandemic COVID-19: A Review

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Authors' contributions

This work was carried out in collaboration among all authors. All the authors have contributed significantly to highlight the present scenario on the COVID-19 pandemic and methods to control the transmission of the virus. The authors have contributed to write the manuscript and thoroughly reviewed. All authors read and approved the final manuscript.

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ABSTRACT

The severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), is spreading worldwide rapidly from its original city of China. Corona virus has the presence of positive sense Ribonucleic acid (RNA) genetic material. The infection causes mild respiratory disease especially in humans across all age groups. The widespread distribution of corona virus in other organisms such as birds, livestock and mammals such as bats, pangolins etc. makes it an important pathogen of concern. It has also been reported the number of people that act as healthy carriers of the virus are approximately 2%, where they do not show any symptoms of the infection but act as a prime source of transmission. Transmission of the virus is usually through large droplets generated during sneezing and coughing and thus can remain viable for several days in favorable atmospheric conditions but can be controlled by the usage of disinfectants. World Health Organization recommends isolation as most efficacious method for the containment of patients that are affected

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by this virus. At present, there are no particular anti-viral medications or vaccines are correctly present to suppress this infection from spreading. However, Polymerase chain reaction (PCR) methods have proved to be effective for assessing viral RNA but may prove to be very time-consuming assay. Thus, as per the present scenario, more research should be carried out to develop a rapid, user-friendly, diagnostic assay which has high specificity and sensitivity at mass level screening thus enabling the further process of drug designing.

Keywords: SARS-CoV-2; transmission; RNA; virus.

1. INTRODUCTION

The coronaviruses (CoV) fit into a large variety of different groups of viruses that infects diverse animal groups and can cause mild to severe respiratory problems in humans. Before 2012, two extreme disease-causing pathogens i.e. Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) has been reported, which were of zoonotic origin and caused major respiratory illness resulting in several deaths [1]. After long time, another family of coronavirus surfaced up at the end of 2019, in the city of Wuhan in China. It was given the name SARS-CoV-2 or coronavirus disease 2019 (COVID-19). This family of coronavirus has been proved to be more dangerous than previous SARS-CoV and MERS-CoV and has been spread over to almost all parts of the world and claimed over lakhs of lives from the time of its appearance [2]. The SARS-CoV-2 is a member of the β genus family of the coronaviruses that consists of at least four similar structural proteins: Spike (S) protein, envelope (E) protein, membrane (M) protein, and nucleocapsid (N) protein [3]. The large family of coronavirusesare mostly composed of single stranded positive sense RNA viruses with the largest known genome size of about 30-32 Kb, belong to nidovirales order, coronaviridae families and coronavirinae subfamilies further subclassified into alpha-, beta-, gamma- and delta- CoVs [4]. While a new set of coronaviruses (delta coronavirus) is suspected to be evolved from the family of birds (bats) inside the group of coronaviridae, order or superfamily of Nidovirales [5]. The virus mainly affects the respiratory system but it also affects the nervous system, gastrointestinal and hepatic system. These viruses are accountable for about 5-10% of respiratory infections in humans. It has also been recorded that about 2% of the population are possible to be carriers of the viruses [6].

The coronaviruses are classified into three genera- Alpha-coronavirus, Beta-coronavirus and Gamma-coronavirus. Beta-coronavirus is further classified into sub-genera: Embecovirus, Hibecovirus, Merbecovirus, Nobecovirus and Sarbecovirus. MERS, SARS and the novel corona virus 2019 are belongs under the Beta-coronovirus classification. The genomic material present in all coronaviruses was positive-sense single strand RNA molecule [1]. Numerous homogenous genome sequences of SARS-CoV-2 has been introduced to the public database and is presently on the process of investigation by numerous groups to comprehend the physiology, behavior and other qualities of the virus which is quite testing because of the availability of very limited data and the varied classification of the coronaviruses which makes the investigation tedious [7].

2. METHODOLOGY

The information was taken from multipule databses like pubmed, google scholar sources,WHO, Centers for Disease Control and Prevention (CDC) resources etc. The keywords used to search were COVID-19 epidemilogy, SARS-CoV-2, vaccine production, treatment for SARS-CoV-2, transmission and so on. The epidemiology data was taken from the time of the pandemic outburst till late of 22nd November 2020 from the WHO and CDC databases.

3. TRANSMISSION

During the past years of the outbreak of the SARS-CoV, there has been a report of significant increase in the spread of human deadly pneumonia to approximately five landmasses in 2003 [8]. Similarly with the outbreak of MERS-CoV in the year 2012, in Arabian Peninsula, there were reports of the spread of the virus over many individuals, thus showing the predominant zoonotic properties of the virus having the capability of transmitting the infection from the animals to humans and from humans to humans [9].

The SARS-CoVs in general can cause various discomforts with symptoms like difficulty in breathing, fever, pneumonia, pleural infection,

multiple organ failure and in certain severe cases infection leads to fatality. Initially the infectibility of these viruses to humans was negligible and were known only to affect the animals in various surroundings across the globe [10]. But due to variegated factors, the novel corona virus was transmitted to profuse species which includes livestock, birds, and mammals such as bats, pangolins etc. thus making it an important pathogen of concern [11]. The commencing cases of transmission were connected through a head-on display of animals that were infected with the virus through the animal- to- human transmission in Wuhan, China. However due to variety of clinical cases and exposure history have further elaborated that human- to- human transmission of the virus is also possible, thus making it the most prominent forms of transmission [12]. The most common source of infection comes about by the proliferation of respiratory droplets through sneezing, coughingor through close contact between individuals [13]. SARS-CoV-2 exhibits in the wide clinical spectrum which may be further divided intomild, moderate, severe, and critical conditions. The most common symptoms include fatigue (69.6%), fever (98.6%), dry cough and diarrhea [14]. Mild illness includes symptoms of upper respiratory tract viral infections with dry cough, nasal congestion, sore throat, mild fever and headache. Most of the COVID-19 cases are mild in nature. Patients with severe conditions include severe pneumonia, septic shock or sepsis and acute respiratory distress syndrome (ARDS). Approximately (5%) of patients can develop critical infection and reported 49% of mortality rate. WHO recommends isolation as most constructive method to contain all the patients that are affected by the virus [12]. At present, no particular anti-viral medications or vaccines are correctly present to suppress the infection from spreading. However, PCR methods have proved to be effective for assessing viral RNA the limitation being a very time-consuming assay [14].

The pandemic ancestry of SARS-CoV originated from predatory wild games with civet cats which would have contracted the infection from rhinolophid bats [15]. These viruses spread through birds and mammals by means of fomites or through aerogenic as well as fecal–oral courses [7]. However, recent whole genome sequence reports suggested that the virus present in bats were found to be 79.5% similar with SARS-CoV thus indicating that viruses could have been transmitted from the bats through an intermediate host which emphasize the fact that bats as the most probable host of SARS-CoV2 in transmission of the disease to humans [16]. The virus is usually transmitted at a much faster rate via air-droplets that occur due to coughing or sneezing of an infected individual. This can occur in two different ways:

- **Direct contact:** In close proximity with CoV patients (within 1 meter of radius with the infected individual), especially without covering their mouth region when coughing or sneezing.
- **Indirect contact:** In the case of a prolonged stay of the droplets on surfaces or garments. So, when comes to direct contact with such tainted surface or fabrics [17].

4. DIAGNOSIS

Generally incubation period is ranges from 1 to 14 days (time between infecting the disease and occurrence of symptoms) for coronaviruses. However, some individuals that are infected do not exhibit any kind of signs or symptoms of the virus thus become asymptomatic which can lead to wide spread of the infection. The virus was found to be highly stable at 4°C with wide range of pH at normal environmental conditions but are sensitive to heat and highly susceptible to the disinfectants [18,19]. However, different diagnostic approaches were incorporated to diagnose the coronavirus infections. The few most prevalent methodologies practiced were based on the clinical diagnosis, nucleic acid-based detection, immunodiagnostics, and serological based microbial examination [20]. Further researches are paving the way for the development of screening and diagnostic aspects.

4.1 Clinical Diagnosis

Physical examination is the first diagnostic criteria followed into consideration during clinical diagnostics were the patients were examined for most common symptoms like the cough, fever, difficulty in breathing, fatigue, runny nose, headache, viral pneumonia and nasal congestion [6]. Under clinical examination following procedures are included:

4.1.1 Physical examination

Patients are physically examined for the increased temperature abnormalities, shortness

of breath, fatigue, running nose, throat infections, vocal tremor etc. The patients with these symptoms are isolated and quarantined. However, patients with mild symptoms are taken more care as they may not show the signs of infection in the initial stages [16].

4.1.2 CT Imaging

The normal CT imaging show respective fringe lung dispersion, pneumonic parenchyma and consolidative aspiratory opacities. Fringe dispersion were commonly found in patients with MERS-CoV and SARS-CoV infections while pneumonic parenchyma and consolidative aspiratory opacities combination, were usually noticed in SARS-CoV-2 contamination [21]. Concurring to those discoveries, CT imaging has an extraordinary clinical analytic incentive for COVID-19, particularly in the high pervasiveness zone of SARS-CoV-2 contamination [20,22].

4.2 Nucleic Acid Based Detection Methods

Off late, real-time polymerase chain reaction (rRT-PCR) has been proved to be very sensitive test to amplify specific oligo sequences from the respiratory (nasal and throat swab samples) and the blood samples [23]. The sensitivity and the specificity of this assay are very high compared to various other diagnostic approaches thus making it the most suitable diagnostic assay till date. But the assay also recorded few disadvantages as it can detect the virus if only present within the suspect's sample and require skilled professionals to perform the assay. Another strategy which can be followed under nucleic acid detection technique, is the high-throughput sequencing, but is limited due to its high cost and maintenance. More studies are still going on under this diagnostic approach [24].

4.3 Immunodiagnostic and Serological Based Detection Assays

The tool of immunodiagnostics and serological based diagnostic approaches fits well where there are negative correlations with respect to the nucleic acid detection diagnostics methods, but the epidemiological link of the infection is effective [25]. The presence of viral proteins (antigens) and the antibody of COVID-19 infection were diagnosed by rapid diagnostic test (RDT) from the respiratory tract of an individual, lateral flow assay and enzyme based immunosorbent assay (ELISA) wherein the samples (serum or blood) are used for the detection of the presence of the viral antigen and immunoglobulins (IgG and IgM) [26]. However many companies and research institutes from different parts of the world have joined hands together to produce effective diagnostic tests which can detect the infection in the symptomatic patients and in the asymptomatic conditions [27] thus making it significant in understanding the study of disease transmission of rising human CoVs, including the conditions of asymptomatic contaminations [28].

4.4 Microbial Detection Assays

Another approach in the identification and diagnosis of the CoV'sis the preliminary examination of the pathogen following the classical Koch's postulates and further analysis using the electron microscopy [29]. In addition to verifying the existence of the virus, routine sampling of specimens from clinical cases can be useful for monitoring mutations in viral genomes that could influence the efficiency in medical countermeasures, including diagnostic testing. Sequencing of the entire genome of viruses may also inform studies of the molecular epidemiology [18].

5. TREATMENT

5.1 Unani Medicines

Doctors and physicians recommended medications that were prepared from plants that are not toxic and does not possess any side effects. Different parts of the plants were used for production of unani medicines which are well known for their antiviral properties. Plants like *Glycirrhizaglabra, Allium cepa, Allium sativum, Davcusmaritimus* etc. are useful for Unani treatment. Researchers observed that these plants have antiviral properties against SARS, HIV (human immunodeficiency virus), Hepatitis A, B & C, H1N1 etc. [30].

5.2 Immunity Booster

It was noticed that most of the youngsters who were victims of COVID-19 was due to poor immunity. Hence, having a strong immune system can help one fight and survive this pandemic. Traditional methods such as drinking hot water mixed with spices likes turmeric, cumin, coriander, and garlic can help one to increase the immune power and fight off the virus

[31]. Intake of citrus fruits such as oranges, lemon and other vitamin fruits can also help boost the immunity.However, along with all these, medical experts also recommend vitamins and zinc supplements such as Vitamin A, C, D, E, and iodine tablets [31].

5.3 Personal Hygiene

Personal hygiene refers to the steps taken by individuals to maintain overall health and well-being of themselves and the society. Following are the steps recommended by the heath committees to avoid the spread of the virus [32].

- ✓ Washing of hands at regular intervals with soap and sanitization with alcohol- based sanitizers is a must.
- ✓ Social distancing should be maintained in malls, temples, shops, groceries, etc.
- ✓ Wearing a mask or covering the nose and mouth properly is a basic need everyone must follow.
- ✓ Shaking of handing, hugging can be avoided.
- ✓ Immediately get in touch with the doctor if there are symptoms of cough, sneezing, fever, sore throat etc., so not self – medicate.

5.4 Awareness

Spreading awareness via social media, news, mail and surveys is very important in spreading the news of the situation across the area. Knowledge regarding the virus, its origin, incubation period, symptoms, classifications, treatment, and source of spread is a very important factor which should be known to every person residing worldwide and every individual must be educated with regard to the virus [33].

5.5 Vaccine Production

Due to the sudden burst of SARS-CoV-2 virusthat has affected the entire world andthere is unimaginable chaos and panic among people. Doctors and scientists have been working expeditiously to comprehend the morphology of the virus and its mode of attack to discover attainable treatments and develop vaccines to completely get rid the pandemic threat [34]. The conventional strategies used to control further spread of the virus include protocols such as identification of cases, isolation and quarantine, social distance and contact tracking. However, these methods would only control the spread of the virus and not eradicate the virus, therefore on developing COVID-19 vaccines can help to end this pandemic. The development of vaccine is based on three factors: speed, manufacture and deployment at scale that will be accessible globally [35]. Due to the availability of advanced technologies such as computational biology, structure-based antigen design, gene synthesis and protein engineering, vaccines can now be manufacture with precision and promptness [36].

To design a vaccine, the individual in charge of the manufacture of the vaccine must be well versed on the structure and mechanism of the virus [37]. Scientists and physicians are able to design the vaccine as a much faster rate since the information about the virus genomic structure and the morphology is freely available in the databases [38]. Along with the morphological, bioinformatic data and the epitope mapping of the virus. During the development of the vaccine for SERS/MERS CoV, the data and information about the techniques used in the manufacture of the vaccine has been updated in the databases. Using this available information, scientists can move further to design a vaccine for SARSCoV-2 [39,40].

The development of vaccine for the SARS-CoV-2 is bit tedious as this is an unknown virus that has made its first appearance in December 2019 in China. Since there is no past record of this virus, there is no vaccine or drugs that can be apt for curing this illness. From the examination of SARS-CoV-2 virus, it was noticed that this virus was closely associated with the SARS and MERS virus. As a result, vaccines and drugs that were used to cure individuals affected with SARS or MERS can also be used to cure SARS-CoV-2. This was the therapeutic strategy that was suggested to put in immediate to control the mortality rate [41]. Table 1 provides information about few of the drugs and mechanism of action of the drugs that were listed by the scientific and health community. Baricitinib has the ability to possess anti-inflammatory properties and also has the capacity to decrease the access of pathogens, hence this drug was recommended to be administered to those affected with COVID-19 [42,43]. Initially chloroquine and hydroxychloroquine were used for COVID-19 patient but there was heterogeneity in study result [44]. Further chloroquine and hydroxychloroquine were not recommended by physicians and doctors because these drugs showed poor efficacy in their mechanism of action and did not exhibit any improvement in the patients affected by COVID-19 [45,46].

Gilead Sciences Inc. developed a drug-remdesivir and performed human trials on Ebola patients, which showed positive results. Same drug used in animal model for MERS and SARS which showed promising result [47]. Due to the appreciating results obtained on the animal trials, the drug is presently under study in China and U.S. Another drug Favipiravir, developed by the Toyama Chemical of Japan, is a nucleoside of purine that results in incorrect synthesis of the RNA [48]. There are several authorized drug has been used for clinical trials in COVID-19 as listed in Table 1.

6. EPIDEMILOGICAL STATISTICS

The international health system and economy are under immense pressure due to the outburst of the novel coronavirus. The information on the outbreak of this virus was taken from World meter, Centers for Disease Control and Prevention (CDC) and World Health Organization databases [51].

On a global scale, the total number of confirmed cases reported was approximately six billion with around one million confirmed deaths [52]. Till 22

Table 1. List of existing drugs having a therapeutic effect on COVID-19

Name of the drug	Mechanism of action	Indication of disease	Target	Reference
Baricitinib	JAK inhibitor that may hinder the process of inflammation.	It is an approved drug for rheumatoid arthritis	JAK kinase	[42]
Favipiravir (favilavir)	RdRp is a purine which behaves as an alternate substrate that results in inaccurate synthesis of the viral RNA.	viral infections	Unknown	[46]
Lopinavir	Inhibition of viral proteases: 3CLpro or PLpro	Used for the treatment of HIV infections.	viral proteases: 3CLpro or PLpro	[48]
Remdesivir	It is an analogue of the nucleotide, which can bar the process of the viral synthesis of the nucleotide thereby stopping the viral replication.	Used for the treatment of the infection caused by the Ebola virus.	Unknown	[48]
Ribavirin		Used for the treatment of hemorrhagic fevers, RSV infection, hepatitis C,	Unknown	[49]
Arbidol	It is an inhibitor that may cause damage to the binding of viral envelope protein to host cells and stop the entry of viral particles to the target cell.	Used for the treatment of influenza.	S protein/ ACE2d	[50]

November 2020, according to WHO, the total confirmed cases and death cases in different countries in which United States of America (USA) on top position followed by India (Table 2) [53]. In this table, the list of countries in world are represented where the more than 1000 death case reported with either community or clusters level of transmission.

7. COVAX FACILITY

In order to control and end the pandemic outbreak, an effective vaccine must be constructed and delivered. The vaccine should be available to all the countries at an affordable price and must be made available to the public for use. The new COVID-19 Vaccine Global Access Facility (COVAX) helps in developing and distributing these vaccines to low- and middle-income countries so that everyone can receive the cure (https://www.who.int/initiatives/act-accelerator/covax). In the COVAX initiative which was undertaken, around d nine Coalition for Epidemic Preparedness Innovations (CEPI) - supported candidate vaccines have signed up, along with further nine candidates under evaluation and procurement research and development (R & D) funding through COVAX, thereby making COVAX the largest and the most diverse COVID-19 portfolio. Non – binding expressions of interest has been submitted by around eight self-financing countries to the Gavi – coordinated COVAX Facility. The COVAX Advance Market Commitment would support the other ninety-two low- and middle-income countries that are joining. The main goal is to bring the pandemic under control and allow access to vaccines to individuals as quickly as possible [54].

Table 2. Total number of confirmed cases and death cases more than 1000 in different countries of the world [53]

Name	To Confirmed Cases	Total Death Case	Mode of Transmission
Global	57274018	1368000	
United States of America	11597979	250607	Community transmission
India	9050597	132726	Clusters of cases
Brazil	5981767	168061	Community transmission
France	2071499	47917	Community transmission
Russian Federation	2064748	35778	Clusters of cases
Spain	1556730	42619	Community transmission
The United Kingdom	1473512	54286	Community transmission
Argentina	1349434	36532	Community transmission
Italy	1345767	48569	Clusters of cases
Colombia	1225490	34761	Community transmission
Mexico	1019543	100104	Community transmission
Peru	943917	35446	Community transmission
Germany	902528	13884	Clusters of cases
Iran (Islamic Republic of)	828377	43896	Community transmission
Poland	819262	12714	Community transmission
South Africa	762763	20759	Community transmission
Ukraine	612665	10813	Community transmission
Belgium	553584	15352	Community transmission
Chile	537585	15003	Community transmission
Iraq	531769	11883	Community transmission
Indonesia	488310	15678	Community transmission
Czechia	487563	7021	Community transmission
Netherlands	472616	8810	Community transmission
Bangladesh	443434	6322	Community transmission
Turkey	435273	12084	Community transmission
Philippines	415067	8025	Community transmission

Name	To Confirmed Cases	Total Death Case	Mode of Transmission
Romania	403123	9756	Community transmission
Pakistan	368665	7561	Clusters of cases
Saudi Arabia	354813	5745	Sporadic cases
Israel	327327	2744	Community transmission
Morocco	316260	5182	Clusters of cases
Canada	315751	11265	Community transmission
Switzerland	289483	3567	Community transmission
Portugal	249498	3762	Clusters of cases
Austria	234670	2097	Community transmission
Nepal	216965	1298	Clusters of cases
Sweden	208295	6406	Community transmission
Ecuador	183840	13095	Community transmission
Jordan	174335	2116	Community transmission
Hungary	170298	3689	Community transmission
Kazakhstan	165712	2365	Clusters of cases
Panama	151089	2922	Community transmission
Bolivia (Plurinational State of)	143756	8889	Community transmission
Dominican Republic	136784	2306	Community transmission
Costa Rica	128231	1599	Community transmission
Japan	127665	1963	Clusters of cases
Armenia	124839	1931	Community transmission
Oman	121360	1365	Community transmission
Belarus	120847	1081	Community transmission
Bulgaria	118418	2778	Clusters of cases
Guatemala	117757	4067	Community transmission
Egypt	112318	6521	Clusters of cases
Serbia	110351	1140	Community transmission
Ethiopia	104879	1620	Community transmission
Honduras	103551	2853	Community transmission
Croatia	96837	1257	Community transmission
Republic of Moldova	95383	2111	Community transmission
China	92588	4749	Clusters of cases
Greece	87812	1419	Community transmission
Azerbaijan	87163	1079	Clusters of cases
Tunisia	86265	2684	Community transmission
Bosnia and Herzegovina	77994	2209	Community transmission
Libya	76808	1068	Community transmission
Myanmar	76414	1695	Clusters of cases
Kenya	75193	1349	Community transmission
Paraguay	74495	1636	Community transmission
Algeria	72755	2239	Community transmission
Ireland	69802	2018	Community transmission
Kyrgyzstan	69149	1227	Clusters of cases
Nigeria	65982	1165	Community transmission
North Macedonia	52449	1462	Community transmission
Afghanistan	44443	1661	Clusters of cases
El Salvador	37250	1064	Community transmission
Sudan	15530	1185	Community transmission

The nine CEPI- supported candidates are as follows- [55]

- ✓ Inovio, United States of America (Phase I/II)
- ✓ Moderna, United States of America (Phase III)
- ✓ CureVac, Germany (Phase I)
- ✓ Institut Pasteur/Merck/Themis, France/ United States of America /Austria (Preclinical)
- ✓ AstraZeneca/University of Oxford, United Kingdom of Great Britain and Northern Ireland (Phase III)
- ✓ University of Hong Kong, China (Preclinical)
- ✓ Novavax, United States of America (Phase I/II)
- ✓ Clover Biopharmaceuticals, China (Phase I)
- ✓ University of Queensland/CSL, Australia (Phase I)

The target of COVAX is to deliver around two billion doses of safe, effective vaccines by the end of 2021, making sure that these vaccines has passed the regulatory approval and WHO prequalification. These vaccines will be supplied to all the participating countries equally according to their population and by prioritizing the healthcare workers and then distributing to the next vulnerable groups like the elderly and those individuals with pre-existing medical conditions. Buffer of doses will also be designed by the COVAX Facility on case of emergency and humanitarian use.

8. CONCLUSION

The SARS-CoV-2 virus has brought a great discomfort to the entire world. The transmission of this virus across the globe in such a brief duration proves that this virus is a major threat and must not be underestimated. The healthcare systems were not prepeared to handle this global pandemic and failed to save the many lives due to the COVID-19. Therefore, worldwide researcher and scientist are working on vaccines development to get rid of the virus pandemic. However, current strategy tosave the human life and to control the virus spread includs social distancing, increased sanitatioqn and upgrading the quarantine routines. This helped in keeping the virus under control and the transmission of the virus would be stopped eventually thereby reducing the number of confirmed cases. Nevertheless, the increase in the number of cases indicated that the virus may possess mutable biological trends thereby delaying the production of the vaccine. The best remeady against virus are possible through the vaccine development therefore, government institute and private companies are working day nightand reached upto different trial phase.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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