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A review of the history, epidemiology and control of Human Coronavirus (HCoV) Infections

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Abstract
Background: Coronaviruses were not regarded as important infectious agents of humans until 2002 when the outbreak of the severe acute respiratory syndrome (SARS) was reported. The purpose of this review is to improve knowledge and understanding of the coronaviruses and their epidemiology, transmission dynamics, and control.
Methodology: This article is a reviewed of 48 original peer reviewed articles sourced from Electronic databases such as PubMed, Google Scholar, Scopus, and African Journal Online, 3 online and printed textbooks, and 19 reports on COVID-19 pandemic by recognized health professional bodies such as the World Health Organization, Centers for Disease Control and Prevention, as well as findings of pharmaceutical companies and test kit manufacturing companies. Keywords used in the search were Coronavirus, Epidemiology, Immune, MERS, SARS, SARS-CoV-2.
Result: Seven human coronaviruses, the human coronavirus (HCoV)-229E, HCoV-OC43, HCoV-HKU1, HCoV-NL63, severe acute respiratory syndrome coronavirus (SARS-CoV), SARS-CoV-2 and Middle East respiratory syndrome coronavirus (MERS-COV) because human diseases characterized by upper and lower respiratory tract symptoms. They are transmitted most through infectious droplet which can be inhaled or picked from hard surfaces with the hand as formites into eyes, nose and mouth. Epidemiologically, coronaviruses can be grouped into two: the endemic (HCoV-229E, HCoV-OC43, HCoV-HKU1, HCoV-NL63) and the pandemic (SARS-CoV, SARS-CoV-2 and MERS-COV) coronaviruses. The pandemic coronaviruses have inflicted devastating public health and economic damage on many countries since its first appearance among humans in 2002.
Conclusion: The endemic coronaviruses have been circulating in the human population for more than 50 years. The coronaviruses with pandemic potential emerged recently, identified between 2002 and 2019. The SARS-CoV pandemic came in 2002 and disappeared shortly after, but the MERS-CoV which emerged in 2012 is still circulating in certain countries. The current pandemic of SARS-CoV-2 which started 2019 in China may disappear in one or two years like SARS-CoV or persist in some countries like the MERS-CoV.

Keywords: *Coronaviridae; middleEast respiratory syndrome; SARS Cov2; OC43 HCOV; Immune; epidemiology.*

Résumé
Contexte : Les coronavirus n'étaient pas considérés comme des agents infectieux importants pour l'homme jusqu'en 2002, lorsque l'épidémie du syndrome respiratoire aigu sévère (SRAS) a été signalée. Le but de cette revue est d'améliorer les connaissances et la compréhension des coronavirus et de leur épidémiologie, leur dynamique de transmission et leur contrôle. *Méthodologie* : cet article est une revue de la littérature de 48 articles originaux évalués par des pairs provenant de bases de données électroniques telles que PubMed, Google Scholar, Scopus et African Journal Online, 3 manuels en ligne et imprimés et 19 rapports sur la pandémie de COVID-19 rédigés par un professionnel de la santé reconnu. des organismes tels que l'Organisation mondiale de la santé, les Centers for Disease Control and Prevention, ainsi que les conclusions des sociétés pharmaceutiques et des fabricants de kits de test. Les mots clés utilisés dans la recherche étaient Coronavirus, Epidemiology, Immune, MERS, SARS, SARS-CoV-2.
Résultat : Sept coronavirus humains, le coronavirus humain (HCoV)-229E, HCoV-OC43, HCoV-HKU1, HCoV-NL63, le coronavirus du syndrome respiratoire aigu sévère (SRAS-CoV), le SARS-CoV-2 et le coronavirus du syndrome respiratoire du Moyen-Orient (MERS-COV) en raison de maladies

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humaines caractérisées par des symptômes des voies respiratoires supérieures et inférieures. Ils sont principalement transmis par des gouttelettes infectieuses qui peuvent être inhalées ou prélevées sur des surfaces dures avec la main sous forme de formites dans les yeux, le nez et la bouche. Épidémiologiquement, les coronavirus peuvent être regroupés en deux : les coronavirus endémiques (HCoV-229E, HCoV-OC43, HCoV-HKU1, HCoV-NL63) et pandémiques (SARS-CoV, SARS-CoV-2 et MERS-COV). La pandémie de coronavirus a infligé des dommages dévastateurs à la santé publique et à l'économie dans de nombreux pays depuis sa première apparition chez l'homme en 2002.

Conclusion : les coronavirus endémiques circulent dans la population humaine depuis plus de 50 ans. Les coronavirus à potentiel pandémique sont apparus récemment, identifiés entre 2002 et 2019. La pandémie de SARS-CoV est arrivée en 2002 et a disparu peu après, mais le MERS-CoV apparu en 2012 circule toujours dans certains pays. La pandémie actuelle de SARS-CoV-2 qui a débuté en 2019 en Chine pourrait disparaître dans un ou deux ans comme le SARS-CoV ou persister dans certains pays comme le MERS-CoV.

Mots-clés *: Coronaviridae, syndrome respiratoire du Moyen-Orient ; SRAS-CoV-2; OC43 HCOV ; Épidémiologie immunitaire CV 5011*

Introduction

Coronaviruses are a group of respiratory tract pathogens that are similar in many respects including mode of transmission and ability to cause upper respiratory tract disease as well as viral pneumonia. They are enveloped RNA viruses possessing widely spaced club or petal-shaped projections arranged in a characteristic crown-like fashion (Figure 1). They have four or five major structural proteins, the membrane protein (M), the spike protein (S), envelop protein (E), and for some coronaviruses, the hemagglutinin-esterase (HE) protein, and a helical nucleocapsid that is formed by the genome and the viral nucleoprotein (N).[1] They belong to the family coronaviridae which is divided into two subfamilies: Orthocoronavirinae and Torovirinae. The Orthocoronavirinae are further divided into four genera: genus *alphacoronavirus,* genus *betacoronavirus, genus deltacoronavirus and genus gammacoronavirus* [2]. The human coronaviruses can be found in two genera: alphacoronavirus and betacoronavirus. (Figure 2)

Coronaviruses have caused mild diseases like colds [3] as well as major epidemics of respiratory disease that affected many countries. In 2002, Severe Acute Respiratory Syndrome (SARS) coronavirus-(CoV) was first reported from China as the causative agent of a respiratory disease affecting about 8000 people in 29 countries with a death toll of about 800 people [4]. Ten years later, an outbreak of another coronavirus disease occurred in Saudi Arabia caused by the Middle East respiratory syndrome (MERS)-CoV which was characterized by high mortality with case fatality rate of 35% [4]. In, 2019, a new coronavirus, SARS-CoV-2 was reported from China causing a pandemic that has so far infected over five million people with more than three hundred thousand deaths in about 180 countries as at October 2020 [4].

Coronaviruses also exist in domestic animals and have been recognized for decades as causative agents of respiratory and gastrointestinal diseases in different animal species.[5] They are responsible for major economic losses in the livestock industry and are an important cause of morbidity and mortality among companion animals such as dogs and cats. The role of Coronaviruses as an important pathogen of livestock was highlighted by the emergence of a new swine acute diarrhea syndrome coronavirus (SADS-CoV). This virus reportedly resulted in the death of over 24, 000 piglets in China in 2017[6].

Besides humans and domestic animals, Coronaviruses have been identified in a wide variety of laboratory or wild animals including rodents, rabbits, bats, deer, antelopes, wild cattle, giraffes, civet cats, and others [7]. Some are aetiological agents of diseases such as mouse hepatitis, while others are habored asymptomatically by these animals, serving as their reservoir hosts or intermediate hosts from which new coronaviruses can emerge and or transmitted to humans [8].

Before the emergence of the SARS-CoV in humans in 2002, coronaviruses were not regarded as major pathogens of humans. The epidemics of SARS-CoV, MERS-CoV and the current pandemic of SARS-CoV-2 has drawn attention to the public health importance of coronaviruses. In this review, we focus on the history, epidemiology, prevention and control of human coronavirus infections, and thus provide information that will foster a better understanding of their public health importance.

Methodology

This article is a reviewed literature of original and review articles, sourced from the internet using search engines including Bing, Google and Yahoo. Electronic database searched included PubMed, Google Scholar, Scopus, and African Journal Online. Information was also sourced from printed textbooks such as Mandell, Douglas, and Bennett's Principles and practice of infectious diseases and Oxford Handbook of Medicine and Microbiology. Reports and findings on this present pandemic by recognized health professional bodies such as the World Health Organization, Centers for Disease Control and Prevention, Nigerian Federal Ministry of Health, United Nations Children Emergency Fund was also reviewed, as well as findings of pharmaceutical companies and test kit manufacturing companies.

Relevant chapters in the text books and findings reported in original articles relating to the subject in this review article were accessed and adequately referenced while the part of the published articles not relevant for this study were left out. Keywords used in the search include Coronaviruses, SARS-CoV, MERS-CoV, SARS-CoV-2 and Epidemiology used singly or in combination. The study period spanned 1st March 2020 to 30th June 2020.

Articles and materials included in the review were written in English-language. Articles that were not written in English language were excluded irrespective of their relevance because of language barrier. Full-text articles on human coronaviruses published in peer-reviewed journals were likewise included while studies which did not contain write-up on human coronaviruses were excluded from the final analysis.

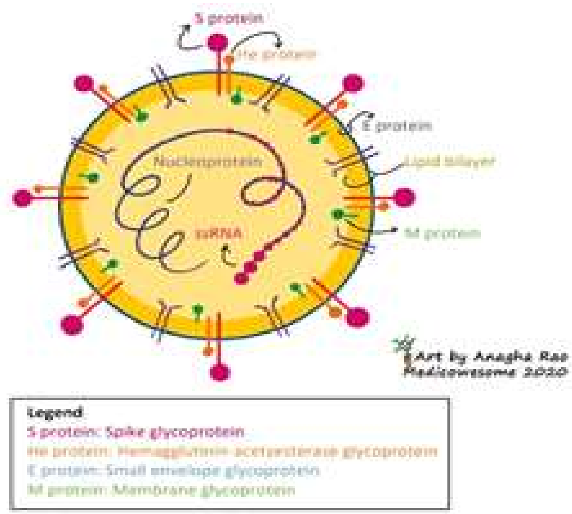

Fig. 1: Diagramatic Representation of Coronavirus Particle
Source: Anagha Rao. SARS CoV2 molecular structure. https://www.bing.com/images

Abstracts were assessed for conformity with the inclusion criteria. Abstracts out of the scope of the study were excluded and the full text of the included articles were downloaded for a detailed review. The systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA-P) guidelines (Fig. 1).

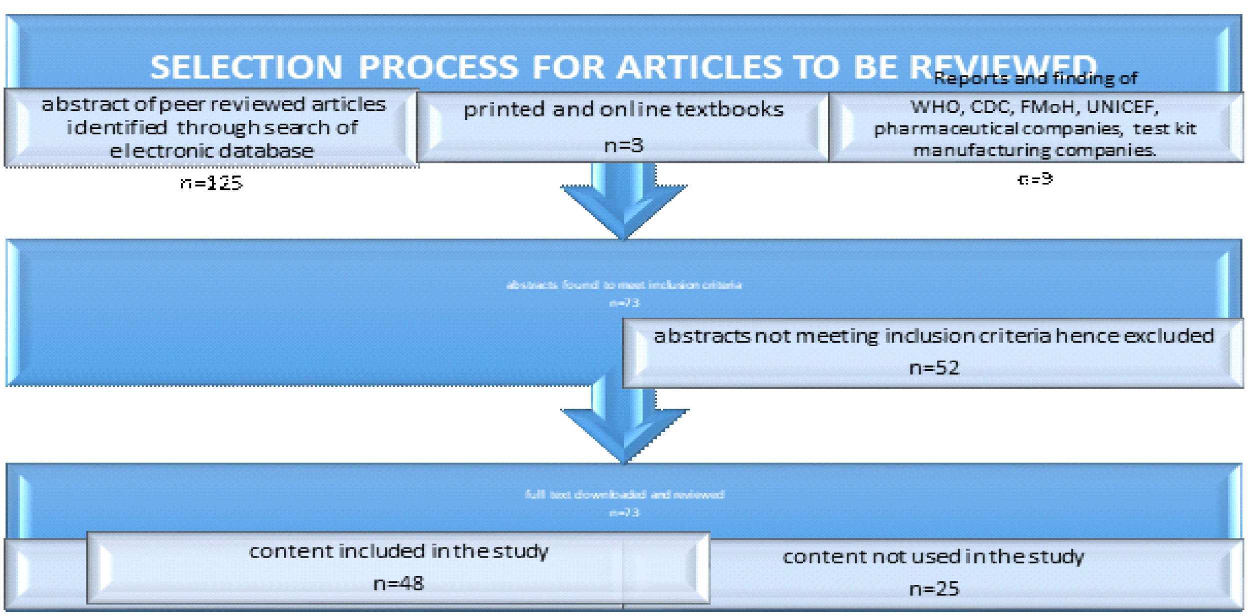

Fig.2: PRISMA flow diagram showing the process of selecting of articles to be reviewed.

Of 125 identified studies, 52 articles were excluded as content were not relevant to the subject being studied. The full-text of the remaining 73 articles were downloaded and reviewed.

Result

History of Human Coronaviruses

Although the first coronavirus, the infectious bronchitis coronavirus of chicken was identified in 1937 [9], the first human coronavirus (HCoV) was not isolated until 1965 when scientists identified a coronavirus designated B814 from the nasal discharge of patients with common cold [10]. Human coronavirus – 229E (HCoV-229E) was isolated from the respiratory tract of a patient with upper respiratory tract infection and was adapted to grow in organ cultures of human embryonic trachea. Further studies revealed that the virus had particles that were morphologically similar to those of infectious bronchitis virus [11]. More strains of the virus were subsequently isolated in organ culture and in 1967 Hamre and Procknow [12]. McIntosh et al isolated another coronavirus, HCoV-OC43 in organ cultures and adapted it to grow in intracerebrally inoculated suckling mice [13]. HCoV-NL63 was isolated from the aspirate from a seven month old boy with pneumonia in the Netherlands in 2004 and also from patients with illnesses characterized by coryza, conjunctivitis, fever and bronchiolitis [14]. HCoV-HKU1 was first isolated from a 71-year old man in Hong Kong who was admitted into hospital with pneumonia and bronchiolitis in 2005 [15].Studies have shown that HCoV-NL63 and HCoV-HKU1 circulate in many countries as imported agents of acute respiratory illnesses of children and adults [16].

Three pathogenic coronaviruses SARS-CoV, MERS-CoV and SARS-CoV-2 causative agents of pandemics of respiratory disease were isolated from Asia between 2002 and 2019. A novel coronavirus isolated from sputum and saliva of patients with atypical pneumonia in China in late 2002 was named SARS COV and caused a disease known as the Severe Acute Respiratory syndrome (SARS) [3,17]. The Middle East Respiratory Syndrome Coronavirus (MERS-CoV) was first identified in the Kingdom of Saudi Arabia in 2012 [4,18]. The virus was isolated from the sputum of a 60-year-old man who presented with community acquired pneumonia and subsequently developed a fatal disease associated with acute renal failure and respiratory failure [18].

COVID-19, a pneumonia-like disease caused by the virus SARS-CoV-2 started in Wuhan City, Hubei Province, China in December, 2019 where a cluster of cases of pneumonia of unknown cause were noted and the World Health Organization (WHO) was duly intimated. By January 2020, the WHO announced the causative agent as a novel coronavirus which has not been previously isolated from any clinical sample before the outbreak. The virus was subsequently referred to as nCov (novel coronavirus) [19]. The Coronavirus Study Group (CSG) of the International Committee on Taxonomy of Viruses designated the aetiological agent 'Severe Acute Respiratory Syndrome Coronavirus 2' (SARS-CoV-2) [19]. By 30th of January, 2020, the WHO declared the disease as a public health emergency of international concern (PHEIC) and formally declared it a pandemic on 11 March 2020 [19]. As of May 2020, about 5.8 million confirmed cases have been diagnosed in 213 countries and territories with about 350,000 deaths.

Epidemiology of Coronaviruses

Epidemiologically, coronaviruses can be grouped into two: the endemic and the pandemic coronaviruses. The endemic coronaviruses include HCoV-229E, HCoV-OC43, HCoV-NL63 and HCoV-HKU1.These viruses circulate in the human population mostly causing mild upper respiratory tract infections in healthy immunocompetent adults. Infections by HCoV-229E, HCoV-OC43 are worldwide in distribution as revealed by serological surveys carried out in different parts of the world [20] [21]. Infections are common in childhood; antibody is prevalent at early age in children and increases with age and by adulthood the prevalence of antibody may be close to 100%.

Endemic coronaviruses share similar seasonal variability with other viral acute respiratory tract infections hence, outbreaks are commoner in the winter season than summer in the temperate countries, occurring in a 2 to 3- year cycle. During these outbreaks, clinical and subclinical infections occur and virus is shed into the environment. The role of endemic coronaviruses in the overall picture of acute respiratory tract illness among adult patients was studied by several investigators including Nicholson *et al* [22] in 1993 who showed that the prevalence of HCoV-43 and HCoV-229E was 16% among adult patients with asthma in England. Another study revealed a marked variation in the annual prevalence of coronavirus infection among individuals with upper respiratory tract infections in the United States, and that the annual variation in the prevalence of HCoV-229E infection could be as wide **as** 1% to 35% [23**]**. Limited data is available on coronavirus activity in Africa, however studies revealed that all endemic coronaviruses are circulating in sub-Saharan Africa and contributing to the aetiology of upper respiratory tract illnesses in the African continent. [24-27].

Three pandemic coronaviruses have emerged in the last 18 years: SARS COV, MERS COV and SARS COV-2, and have all caused human diseases in many geographical regions of the world. Whereas SARS-CoV and MERS-CoV affected 26 and 27 countries, respectively, SARS-CoV-2 was identified in at least 213 countries and territories. All ages are affected, but children and young adults are less susceptible to severe disease. There is a gender difference in susceptibility to infection with higher case fatality of all three virus infections occurring in males than females [27-30]. Advanced age, and comorbidities including cardiovascular diseases such as heart disease, hypertension, diabetes mellitus are risk factors of SARS COV, MERS COV and SARS COV-2 infection.

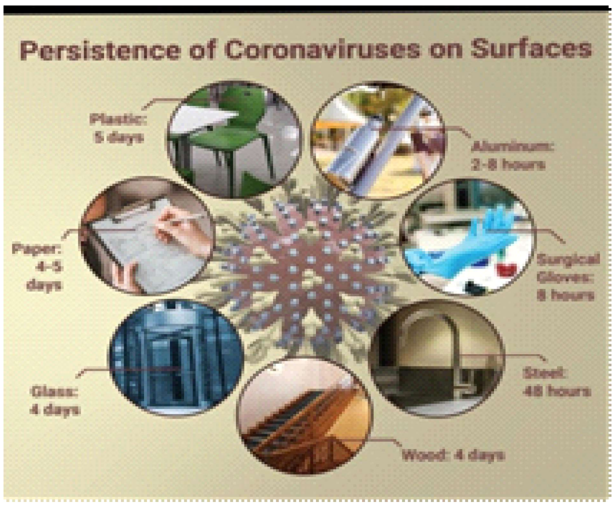

Fig. 3: Persistence of coronavirus on surfaces
Source: *J Hosp Infect* DOI: https://doi.org/10.1016/j/jhin.2020.01.022

Coronaviruses are mainly transmitted from human to human by large respiratory droplets that enter the atmosphere when an infected person coughs, sneezes or talks, or by direct contact with infected individuals, or by indirect contact with infected secretions on surfaces or objects used by medical personnel on infected patients. Infective virus can survive and remain infectious on inanimate objects for periods ranging from hours to several days with longer survival at low temperatures and humidity (Figure 2). MERS-CoV can also be transmitted to humans as a result of contact with dromedary camels and consumption of raw camel's milk [31].

During human-to-human transmission of SARS-CoV, MERS and COVID 19, an individual case often transmits infection to very few others, 2 to 4, however, super-spreading events can occur during which a single patient may infect several to many more people [32]. Airborne transmission may also occur, and has been documented during medical procedures such as noninvasive positive pressure ventilation, intubation, high-frequency oscillatory ventilation, as well as a variety of other procedures on SARS-CoV, MERS and COVID 19 patients [33]. Environmental contamination is commonly detected in the vicinity of patients, which could constitute a source of infection to hospital personnel, thus emphasizing the need for careful surface hygiene management [34]. SARS-CoV patients are infectious when symptoms appear and are most infectious during the second week of illness. MERS-CoV infected patients are most contagious only after lower respiratory disease have developed, whereas, SARS-CoV-2 infected patients are infectious before the onset of clinical symptoms and after [35,36].

The zoonotic origin of human coronaviruses has been reviewed by several authors including Joseph and Fagbami and Cui *et al* [4,37]. All human coronaviruses are believed to have originated from bats or mice, however, human infections were acquired through intermediate hosts that are domestic or wild animals. Although the endemic viruses are well adapted to humans and spreading by person to person transmission in communities, it is believed that HCoV-229E and HCoV-OC43 entered the human population from bats through alpaca and cattle, respectively [38,39].

The SARS epidemic began with the spread of a closely related bat virus first to palm civets or other animals sold in live wild game markets and then transmitted to humans [40]. Primary cases of MERS-CoV were believed to have been acquired from camels through exposure to nasal or other body secretions of the infected animal, via the consumption of raw camel milk, or via environmental contamination [41]. SARS-COV-2 is thought to have originated from the Huanan seafood market in Wuhan from where the virus probably 'jumped' into humans through snakes or mink or pangolins as intermediate host [4,42]

Prevention and control of coronavirus infections

The most important preventive and control measure of viral infections is immunization, but there are no licensed human coronavirus vaccines at present, however, experimental vaccines against SARS-CoV and MERS-CoV infections are available. Strategies used for development of these vaccines include attenuated and inactivated vaccines, recombinant S-protein-based vaccines, viral-vectored vaccines and DNA based vaccines [43-45]. Most of these vaccines generated good immune response, although some induced short- term immunity and/or adverse reactions in animal models [46]. It was shown by Agrawal *et al* [47], and Bolles *et al* [48] that in SARS-CoV infection, subsequent vaccination resulted in failure to control viral replication, enhanced clinical disease and pathology characterized by abnormal Th2 CD4 responses. It was also shown that neutralizing antibody targeting the receptor-binding domain of the spike protein of SARS-CoV and MERS-CoV can produce antibody dependent enhancement (ADE) leading to increased virus entry into Fc receptor-bearing cells in vitro [49] which could lead to enhanced disease.

The phenomenon of ADE was first demonstrated in dengue by Halstead *et al* [50] and was later demonstrated experimentally with African flaviviruses by Fagbami *et al*.[51] It occurs when antibody bound to the virus is internalized by macrophages facilitating enhanced viral replication inside the macrophages. ADE has been shown to play a role in the pathogenesis of dengue haemorrhagic fever shock syndrome and other virus infections [52].

Because of the importance of COVID-19, many institutions are involved in vaccine development against SARS-CoV-2. At present up to 100 SARS-COV-2 vaccine candidates are being developed with a few of them at the phase 1 and phase 2 clinical trials. Strategies used in the development of SARS-CoV and MERS-CoV, and some newer strategies are currently being used to develop SARS-CoV-2 vaccine (Table 1). Although SARS-CoV and SARS-CoV-2 use similar receptors (ACE2) to enter, it is not clear whether immunopathology provoked by some SARS-CoV vaccines will also occur with SARS-CoV-2 vaccines.

Other preventive measures used for the control of pandemic coronavirus diseases, particularly COVID-19 include avoidance of crowded public places, and if individual must appear at such places, a social distance of at least 6 feet must be maintained and a face mask worn to cover the nose .and mouth. The concept of social distancing involves minimizing all non-essential large gatherings irrespective of documented case of COVID-19 in the area. This reduces the likelihood of transference of the virus thereby ensuring that transmission remains clustered in pockets, such that each identified case can be tracked, isolated, its contact or likely source of infection traced, and further spread of infection contained and limited to individuals within these pockets. Hand washing with soap and clean running water is also an effective way of preventing transmission of many infectious diseases. Soap dissolves the lipoproteins of the viral envelope leading to the inactivation of the virus.

Alcohol hand sanitizer should be used when hand washing is not feasible or in addition to hand washing. Alcohol is a potent chemical for inactivating enveloped viruses including coronaviruses, hence, these sanitizers are effective for hand disinfection. Other methods aimed at preventing transmission of pandemic coronaviruses by direct and indirect contact include respiratory hygiene which involves coughing into COVID elbows, covering the mouth with disposable tissue paper during cough or sneeze, cleaning and disinfecting surfaces like bench tops, door handles, faucets, and every other hard surface that is constantly or frequently touched, avoiding touching the eyes, nose, mouth, face with the hand, and staying at home when sick and calling the health authorities to assess the condition.

Conclusions

Although the endemic coronaviruses have been circulating in the human population for more than 50 years, it is the pandemic coronaviruses SARS-CoV, MERS-CoV, and SARS-CoV-2, which were identified between 2002 and 2019, that inflicted devastating public health and economic damage on many countries. The SARS-CoV pandemic came in 2002 and disappeared shortly after, but the MERS-CoV which emerged in 2012 is still circulating in certain countries. The current pandemic of SARS-CoV-2 started several months ago in China, and may behave like SARS-CoV and disappear in one or two years, or persist in certain countries like MERS-CoV.

The outbreaks of SARS-CoV, MERS and SARS-CoV-2 has taught countries and their academic and medical communities lessons on emergency preparedness and routine surveillance which often facilitate early detection and control of disease outbreaks. The outbreak of SARS-CoV-2 has done more damage to the health of the people and their livelihood than any other coronavirus. Controlling the virus requires a robust testing programme and immunization. Lack of rapid tests such as antigen detection by ELISA and immunofluorescence, and assays for antibody detection has considerably limited the number of individuals that can be tested. Immunization is perhaps the most effective method to control SARS-CoV-2, but requires developing safe and effective vaccines against the virus. Experiences gained by scientists in the development of SARS-CoV and MERS-CoV experimental vaccines may well be useful in SARS-CoV-2 vaccine development.

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