

Origin and Evaluation of Pathogenic Coronavirus: A Literature Review

Navneet Kaur¹, Aseem Sethi², HC Patil³, Sarbjeet Singh¹, Hashmeet Kaur¹,
Ujjawal Kumar Mishra¹

¹Research Scholar, Department of Pharmacy Practice, Adesh Institute of Pharmacy and Biomedical Sciences, VPO Bhuchoo Kalan, Bathinda, 151001, Punjab, India.

²Research Scholar, Department of Pharmacy Practice, ISF College of Pharmacy, Moga-Ferozepur G.T. Road Moga, 142001, Punjab, India.

³Principal and Professor, Department of Pharmaceutics, Adesh Institute of Pharmacy and Biomedical Sciences, VPO Bhuchoo Kalan, Bathinda, 151001, Punjab, India.

Corresponding Author: Aseem Sethi

ABSTRACT

Coronaviruses are single-stranded RNA viruses with spike projections that give them a crown-like appearance and hence called coronaviruses. There have been two earlier outbreaks of coronaviruses but were not considered as lethal as the new coronavirus that has spread all over the world with a death toll of over 350,000. Two such closely related coronaviruses are Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome coronavirus (MERS-CoV) that occurred at two different times respectively. Coronaviruses come under the Family Coronaviridae and the subfamily named Coronavirinae. There are basically four genera, Alphacoronaviruses and Betacoronaviruses that infect only mammals, while, Gammacoronaviruses and Deltacoronaviruses infect birds. Bats are likely the foremost natural reservoirs of alphacoronaviruses and beta coronaviruses. Quite a few coronaviruses phylogenetically linked with SARS-CoV were identified in bats from entirely different provinces in China and also from European, African, and Southeast Asian countries. The genesis of coronavirus is yet under controversy and needs more attention in identifying the exact onset of its origin and the strains it brings with it.

Keywords: Coronavirus, Severe Acute Respiratory Syndrome, Middle East Respiratory Syndrome, Origin

INTRODUCTION

Coronaviruses are single-stranded, enveloped RNA viruses having surface with spike-like projections that display a crown like structure under the electron microscope.^[1] Coronaviruses cause metastasis and respiratory infections in animals and humans. They weren't believed to be extremely infective to humans until the outbreak of severe acute respiratory syndrome (SARS) between 2002 and 2003 in Guangdong province, China. Prior to the outbreak, coronaviruses largely caused delicate infections in immunocompetent individuals.^[2-5] 10 years

after SARS, another extremely infective coronavirus emerged in the Middle Eastern countries and was named as Middle East Respiratory Syndrome Coronavirus (MERS-CoV).^[6] SARS coronavirus (SARS-CoV) uses angiotensin-converting enzyme 2 (ACE2) receptor and primarily infects ciliated cartilaginous tube epithelial cells and type II pneumocytes.^[7,8] Whereas, MERS-CoV uses dipeptidyl peptidase 4 (DPP4; additionally referred to as CD26) receptor and infects nonciliated bronchial epithelial cells and type II pneumocytes.^[9-11] SARS-CoV and MERS-CoV were transmitted directly to humans from market

civets and dromedary camels, respectively.^[12-14] Each virus was thought to possess originated in bats.^[15-21] In depth studies of those 2 necessary coronaviruses haven't solely light-emitting diode to a much better understanding of coronavirus biology however have additionally been driving coronavirus discovery in haywire globally.^[21-31] During this review, we had a tendency to specialize in the origin and evolution of SARS-CoV and MERS-CoV. Specifically, we had a tendency to emphasize the ecological distribution, genetic diversity, interspecies transmission and potential for pathologic process of SARS-related coronaviruses (SARSr-CoVs) and MERS-related coronaviruses (MERSrCoVs) found in bats, as this data will help prepare countermeasures against future spillover and pathogenic infections in humans with novel coronaviruses.

METHODS

Our initial step to construct a review article was to employ a literature review search. For extracting the valuable published reports, database, like PubMed, Pubmed Central, Elsevier and were used as the main source. Keywords such as coronavirus, severe acute respiratory syndrome, middle east respiratory syndrome, and origin were used. In order to provide quality to the review, extracted articles were independently screened and those satisfying the inclusion criteria were included in the present review.

DISCUSSION

Comparative Examination of Occurrence and Dissemination of Coronaviruses

In the year 2003, the Chinese people were infected with an epidemic wreaking Severe Acute Respiratory Syndrome (SARS) in Guangdong province. The virus was inveterate as a member of the beta coronavirus subgroup and was named SARS-CoV.^[32,33] The infected patients presented respiratory sickness symptoms with a distinguished alveolar injury that resulted in Acute Respiratory Distress

Syndrome (ARDS). SARS primarily occurred in China and quickly spread all around the world with over 8000 infected individuals and 776 deceases. A decade later in 2012, some of Saudi Arabian residents were identified to be diseased with another coronavirus. The identified virus was confirmed as a member of coronaviruses and termed as Middle East Respiratory Syndrome Coronavirus (MERS-CoV). The World Health Organization (WHO) stated that the MERS-coronavirus infected over 2428 persons and resulted in 838 deaths.^[34] The infection of MERS-CoV starts from a subtle upper metastasis injury while progression leads to severe respiratory illness. Almost like SARS-coronavirus, patients diagnosed with MERS-coronavirus suffer pneumonia, trailed by adult respiratory distress syndrome and renal disease.^[35]

Coronaviruses are composed of subfamily Orthocoronavirinae, in the family Coronaviridae, order Nidovirales, and realm Riboviria.^[36,37] They are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry. The genome size of coronaviruses ranges from approximately between 26 to 32 kilobases, one of the vast among RNA viruses.^[38] They have characteristic club-shaped spikes that project from their surface, which in electron micrographs create an image reminiscent of the solar corona from which their name derived.^[39]

Middle East Respiratory Syndrome

MERS, additionally known as a camel influenzaan infectious respiratory tract infection initiated by the MERS-CoV.^[40,41] Symptoms could vary from none, to mild, to severe. Typical symptoms embody fever, cough, diarrhea, and shortness of breath.^[42] The unwellness is usually a lot severe in those with alternative health issues. MERS-CoV is a coronavirus that is believed to be originally originated from bats. Humans are unremarkably infected from camels, either throughout

direct contact or indirect contact.^[43] The spread between humans usually needs direct contact with an infected person. Its spread is unusual outside of hospitals. Thus, its risk to the world population is presently deemed to be fairly low. Diagnosing procedure is generally taken up by rRT-PCR testing of blood and respiratory samples.^[44]

As of 2020, there's no particular vaccine or treatment for the disease; but, diversities are being developed. The WHO suggests that those who come in contact with camels, wash their hands and not to touch sick camels. They also recommend that camel-based food products be suitably barbecued. Treatments that facilitate with the symptoms and support body functioning is also used. The first known case occurred in 2012 in Saudi Arabia and most cases have occurred within the Arabian Peninsula.^[45] About 500 cases have been reported as of January 2020 and about 35 patients diagnosed with the illness died from it. Larger outbreaks have occurred in South Korea in 2015 and in Saudi Arabia in 2018.^[46]

Signs and Symptoms

Early reports compared the viruses to severe acute respiratory syndrome (SARS) and it has been first recognized in Saudi Arabia as SARS-like virus. The first person, in June 2012, had a fever, cough, expectoration, and shortness of breath.^[47,48] One review study from Saudi Arabia gave the foremost common presenting symptoms as fever in ninety eight, cough in eighty three, shortness of breath in seventy two and myalgia in thirty two people. There have been additionally frequent symptoms of movableness of the bowels in twenty sixth, vomit in twenty one, abdominal pain in seventeen November of people. Seventy two of people needed mechanical ventilation. There were additionally three males for each feminine.^[49] MERS can vary from asymptomatic sickness to severe disease leading to acute respiratory distress syndrome (ARDS).^[49,50] Renal disorder, disseminated intravascular curdling (DIC),

and carditis have additionally been recorded.^[51]

MERS Coronaviruses Under Electron Microscope

Middle East Respiratory Syndrome is caused by the MERS coronavirus (MERS-CoV), a species with single-stranded RNA belonging to the genus betacoronavirus that is distinct from severe acute respiratory syndrome coronavirus and also the common-cold coronavirus.^[52] Its genomes are phylogenetically classified into 2 clades, Clades A and B. Early cases of MERS were of biological group A clusters (EMC/2012 and Jordan-N3/2012) whereas new cases are genetically different (Clade B).^[53] The virus grows readily on Vero cells and LLC-MK2 cells.^[54]

Transmission Camels

A study conducted between 2010 and 2013, within which the occurrence of MERS was evaluated in 310 Arabian camels, discovered high titters of neutralizing antibodies to MERS-CoV within the blood serum of those animals.^[55] An extra study sequenced MERS-CoV from nasal swabs of dromedary camels in Saudi Arabia found that they would sequence just like previously sequenced human isolates. Some individual camels were also found to have more than one genomic variant in their cavity.^[56] WHO also presented a report of a Saudi Arabian man became sick seven days after applying topical medication to the noses of many sick camels and later he and one in all the camels were found to own identical strains of MERS-CoV.^[57,58] It is still unclear how the virus is transmitted from camels to humans. WHO advises avoiding contact with camels and to eat solely cooked camel meat, pasteurized camel milk, and to avoid drinking camel urine.^[59] The Saudi Ministry of Agriculture has suggested individuals to avoid contact with camels or wear respiratory masks when around them.^[60] In response, some individuals have refused to be attentive to

the government's recommendation and kiss their camels in defiance of their government's advice.^[61]

Between People

There has been proof of restricted, however not sustained spread of MERS-CoV from person to person, each in households as well as in health care settings like hospitals.^[50,62] Most transmission has occurred in the circumstances of close contact with severely sick persons in health care or household settings and there's no proof of transmission from asymptomatic cases.^[63] Cluster sizes have ranged from one to twenty six individuals, with an average median of 2.7.^[64]

Severe Acute Respiratory Syndrome-related Coronavirus

The SARS-related coronavirus was amongst one in every of many viruses known by the WHO in 2016 as a likely reason for a future epidemic in a new plan developed after the Ebola hemorrhagic fever epidemic for urgent research and development before and through an epidemic towards diagnostic tests, vaccines and medicines. The prediction came to the reality with the 2019–20 coronavirus pandemic.^[65,66]

SARS-related coronavirus could be a member of the genus Betacoronavirus and taxonomic group Sarbecovirus.^[67] Sarbecoviruses, in contrast to embecoviruses or alphacoronaviruses, solely have one papain-like protease (PLpro) rather than 2 within the open reading frame (ORF1).^[68] SARS-CoV was determined to be an early split-off from the beta coronaviruses based on a set of collection of preserved domains that it shares with the group.^[69,70]

Bats serve as the most host reservoir for the SARS-related coronavirus. The virus has coevolved within the bat host reservoir over an extended amount of time.^[71] Recently, they had strains of SARS-related coronavirus evolved and created the cross-species jump from bats to humans, as within the case of the strains SARS-CoV and

SARS-CoV-2.^[72,73] Each of those strains descended from one ancestor, however, they created the cross-species jump into humans individually. SARS-CoV-2 isn't an immediate descendant of SARS-CoV.^[74]

Coronavirus Diversity

Coronaviruses are members of the genus Coronavirinae subfamily Coronaviridae and the order of the Nidovirales- International Committee on Taxonomy of Viruses (ICTV). This subfamily contains four genera: Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus - on the basis of their phylogenetic relationships and genomic structures.^[75] Alphacoronaviruses and betacoronaviruses infect only mammals, while gammacoronaviruses and deltacoronaviruses infect birds. However, most of them can infect mammals.^[24] Alphacoronavirus and betacoronavirus sometimes cause respiratory disease in humans and gastroenteritis in animals. These two health-focused viruses, SARS-CoV and MERS-CoV cause severe respiratory disease in humans, while the other human coronaviruses (HCoV-NL63, HCoV-229E, HCoV-OC43 and HKU1) cause only advanced respiratory infections. at vaccination centers. , although most of them can cause severe infections in children, young children and the elderly.^[76,77] Alphacoronaviruses and betacoronaviruses can be a major disease burden in livestock; these viruses include porcine transmissible gastroenteritis virus, porcine enteric diabetes virus (PEDV), and artiodactyl seaweed Swine Acute Diabetes Syndrome Coronavirus (SADS-CoV).^[78-80] Animal origin: SARS-CoV, MERS-CoV, HCoV-NL63, and HCoV-229E are thought to have originated from bats; HCoV-OC43 and HKU1 may have originated from mice. Farm animals can play the necessary roles as central managers that allow the transmission of virus from natural hosts to humans. In addition, farm animals themselves may have bat-bore or

coronavirus-related illnesses: a genetic sequence similar to the Porcine influenza virus (PEDV) was found in bats and SARS-CoV is a newfound shelter from bats to pigs. At present, 7 of the 11 species of alphacoronavirus given to IphV and 4 of the 9 types of betacoronavirus were known only to bats. Thus, bats are probably the last major natural reservoirs of alphacoronavirus and betacoronaviruses.^[81-84]

Coronaviruses form enveloped and spherical particles of 100–160 nm in diameter. They contain a positive-sense, single-stranded RNA (ssRNA) genome. The 5'-terminal two-thirds of the genome encodes a polyprotein, pp1ab, that is additionally cleaved into 16 non-structural proteins that are concerned in genome transcription and replication. The 3' terminus encodes structural proteins, as well as envelope glycoproteins spike (S), envelope (E), membrane (M) and nucleocapsid (N). Additionally to the genes encoding structural proteins, there are accessory genes that are species-specific and dispensable for virus replication. Here, we tend to compare prototypical and representative strains of four coronavirus genera: Feline infectious peritonitis virus (FIPV), Rhinolophus bat coronavirus HKU2, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) strains GD02 and SZ3 from humans infected throughout the early phase of the severe acute respiratory syndrome epidemic and from civets, respectively. Severe acute respiratory syndrome coronavirus strain hTor02 from humans infected throughout the center and late phases of the SARS epidemic.

Animal Origin and Evolution of SARS-CoV

At the onset of severe acute respiratory disease, most first-line patients had already been described by animals before the development of certain symptoms. The most serious respiratory illness was known by SARS-CoV and later it was discovered that anti-SARS-CoV antibodies in masked civets (*Paguma*

larvata) and animal controllers in the market place.^[85-91] However, over time, a comprehensive study of domesticated and domesticated animals revealed that the SARS-CoV strains found in Christmas curtains are transmitted to them by various animals. In 2005, 2 groups independently reported the development of novel coronaviruses associated with SARS-CoV-named SARS-CoV-infected or SARS-CoV-infected coronaviruses in the horse genus *Rhinolophus*.^[92] These findings suggested that bats acting as natural hosts for SARS-CoV and civets were the sole controllers. Subsequently, several coronaviruses were found phylogenetically associated with SARS-CoV in members from completely different provinces in China and in addition from countries in Europe, Africa and Southeast Asia.^[93-104] According to the ICTV system, only fractions are found in the *Rhinolophus* animal in the European Countries, Southeast Asian countries and in China with various SARS-CoV. Those from *hipposideros* bats in Africa are closely associated with SARS-CoV and should be listed as a new type of coronavirus.^[105] This information suggests that SARS-CoVs are geographically distributed and may have been carrying bats for a very long time. A 5-year study revealed the presence of very different SARS-CoVs than most people in a single cave in Yunnan province, China.^[106,107] This area may be of varying temperature range, and SARS-CoVs in this region contain all the genetic diversity found in other regions of China. In addition, the viral strains present in this one site contain all the genes required to create SARS-CoV. Since no specific SARS-CoV progenitor is found in human tissues even though 15 years of observation and as ribonucleic acid recombination is frequently encountered between coronaviruses 56, it is highly likely that SARS-CoV has recently emerged with a rearrangement of the SARS bat -CoVs in this or in different caves but will still be identified. This hypothesis is consistent with previous data showing that the direct origin of SARS-CoV originated

before 2002.^[108] Reevaluation Furthermore, WIV16, a close relative to SARS-CoV found in bats, may have been re-invented for two types of SARS-CoV. Recombinant sites are located within the S-type, including the protein (S) containing the receptor-binding domain (RBD), and the surface of orf8, which encodes a receptor protein.^[108,103] Bat variants, are expected to emerge novels in the future.^[110,111] We tend to assume that the precise originator of SARS-CoV was created by replication within bats and then transferred to growing fields or to other mammals that pass on the virus to the chemical through oral transmission. When the infected civets were sent to the Guangdong market, the virus spread to the market and began to be transformed before it was spilled to humans.

CONCLUSION

Data gathered on genomic evolution, receptor linkage and pathogenesis revealed that SARS-CoV most likely originated in bats through chronological recombination of bat SARSr-CoVs. Recombination likely arose in bats afore SARS-CoV was presented into Guangdong province via infected civets or other diseased mammals from Yunnan. The presented SARS-CoV underwent swift mutations in *S* and *orf8* and effectively spread in market civets. After numerous autonomous spillovers to people, certain strains underwent extra alterations in *S* and turned into epidemic at the time of SARS outbreak in 2002–2003. Nevertheless, a new serological examination discovered the occurrence of antibodies in contrast to the SARSr-CoV nucleocapsid in people residing around a bat cave but who had not presented solid signs of illness, signifying that the virus can infect people through recurrent interaction.

It is broadly recognized that several viruses have occurred in their natural reservoirs for a very lengthy period. The persistent spillover of viruses from regular hosts to people and other wildlife is mostly due to social actions, including current farmed practices and urbanization. Hence,

the utmost effective method to avoid viral zoonosis is to keep the hurdles between natural reservoirs and human civilization, in observance of the ‘one health’ theory.

REFERENCES

1. Masters PS, Perlman S. Coronaviridae in Fields Virology, 6th ed, Knipe DM, Howley PM. Lippincott Williams & Wilkins. 2013; 2: 825–858.
2. Zhong NS, Zheng BJ, Li YM, et al. Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong, People’s Republic of China. Lancet. 2003; 362: 1353–1358.
3. Drosten C, Günther S, Preiser W, et al. Identification of a Novel Coronavirus in Patients with Severe Acute Respiratory Syndrome. N. Engl. J. Med. 2003; 348: 1967–1976.
4. Fouchier RA, Kuiken T, Schutten M, et al. Aetiology: Koch’s Postulates Fulfilled for SARS Virus. Nature. 2003: 423, 240.
5. Ksiazek TG, Erdman D, Goldsmith CS et al. A novel coronavirus associated with severe acute respiratory syndrome. N. Engl. J. Med. 2003; 348:1953–1966.
6. Zaki AM, van Boheemen S, Bestebroer TM, et al. Isolation of a Novel Coronavirus from a Man with Pneumonia in Saudi Arabia. N. Engl. J. Med. 2012; 367: 1814–1820.
7. Li WH, Moore MJ, Vasilieva N, et al. Angiotensin-converting Enzyme 2 is a Functional Receptor for the SARS Coronavirus. Nature. 2003;426: 450–454.
8. Qian Z, Travanty EA, Oko L, et al. Innate Immune Response of Human Alveolar type II Cells Infected with Severe Acute Respiratory Syndrome-coronavirus. Am. J. Respir. Cell. Mol. Biol. 2013;48: 742–748.
9. Lu G, Hu Y, Wang Q, et al. Molecular Basis of Binding between Novel Human Coronavirus MERS-CoV and its Receptor CD26. Nature.2013; 500: 227–231.
10. Raj VS, Mou H, Smits SL, et al. Dipeptidyl Peptidase 4 is a Functional Receptor for the Emerging Human Coronavirus-EMC. Nature. 2013; 495: 251–254.
11. Scobey T, Yount BL, Sims AC, et al. Reverse Genetics with a Full-length Infectious cDNA of the Middle East Respiratory Syndrome Coronavirus. Proc. Natl Acad. Sci. 2013; 110: 16157–16162.

12. Guan Y, Zheng BJ, He YQ, et al. Isolation and Characterization of Viruses Related to the SARS Coronavirus from Animals in Southern China. *Science*. 2003; 302: 276–278.
13. Alagaili AN, et al. Middle East Respiratory Syndrome Coronavirus Infection in Dromedary Camels in Saudi Arabia. *M Bio*. 2014; 5: e00884–14.
14. Hemida, MG, Briese T, Mishra N, et al. Middle East Respiratory Syndrome (MERS) Coronavirus Seroprevalence in Domestic Livestock in Saudi Arabia, 2010 to 2013. *Euro. Surveill*. 2013; 18: 21–27.
15. Lau, SK, Woo PC, Li KS, et al. Severe Acute Respiratory Syndrome Coronavirus-like Virus in Chinese Horseshoe Bats. *Proc. Natl Acad. Sci*. 2005; 102: 14040–14045.
16. Kan B, Wang M, Jing H, et al. Molecular Evolution Analysis and Geographic Investigation of Severe Acute Respiratory Syndrome Coronavirus-like Virus in Palm Civets at an Animal Market and on Farms. *J. Virol*. 2005; 79: 11892–11900.
17. Ithete NL, Wang M, Jing H, et al. Close Relative of Human Middle East Respiratory Syndrome Coronavirus in Bat, South Africa *Emerg Infect Dis*. 2013; 19: 1697–1699.
18. Ge XY, Li JL, Yang XL, et al. Isolation and Characterization of a Bat SARS-like Coronavirus that Uses the ACE2 Receptor. *Nature*. 2013; 503: 535–538.
19. Yang XL, Hu B, Wang B, et al. Isolation and Characterization of a Novel Bat Coronavirus Closely Related to the Direct Progenitor of Severe Acute Respiratory Syndrome Coronavirus. *J. Virol*. 2016; 90: 3253–3256.
20. Hu Bet, Zeng LP, Yang XL, et al. Discovery of a Rich Gene Pool of bat SARS-related Coronaviruses Provides New Insights into the Origin of SARS Coronavirus. *PLOS Pathog*. 2017; 13: e1006698.
21. Lau SK, Li KS, Tsang AK, et al. Genetic characterization of Betacoronavirus lineage C viruses in bats reveals marked sequence divergence in the spike protein of pipistrellus bat coronavirus HKU5 in Japanese pipistrelle: implications for the origin of the novel Middle East respiratory syndrome coronavirus. *J. Virol*. 2013; 87: 8638–8650.
22. Woo PC, Lau SK, Huang Y, et al. Coronavirus diversity, phylogeny and interspecies jumping. *Exp. Biol. Med*. 2009; 234, 1117–1127.
23. Perlman S, Netland J. Coronaviruses post-SARS: update on replication and pathogenesis. *Nat. Rev. Microbiol*. 2009; 7:439–450.
24. Woo PC, Lau SK, Lam CS, et al. Discovery of seven novel mammalian and avian coronaviruses in the genus deltacoronavirus supports bat coronaviruses as the gene source of alphacoronavirus and betacoronavirus and avian coronaviruses as the gene source of gammacoronavirus and deltacoronavirus. *J. Virol*. 2012; 86: 3995–4008.
25. Graham RL, Donaldson EF, Baric RS. A decade after SARS: strategies for controlling emerging coronaviruses. *Nat Rev Microbiol*. 2013; 11: 836–848.
26. Hu B, Ge X, Wang LF, et al. Bat origin of human coronaviruses. *Virol. J*. 2015; 12: 221.
27. de Wit E, van Doremalen N, Falzarano D, et al. SARS and MERS: recent insights into emerging coronaviruses. *Nat Rev Microbiol*. 2016; 14: 523–534.
28. Su S, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. *Trends Microbiol*. 2016; 24: 490–502.
29. Forni D, Cagliani R, Clerici M, et al. Molecular evolution of human coronavirus genomes. *Trends Microbiol*. 2017; 25: 35–48.
30. Anthony SJ, Johnson CK, Greig DJ, et al. Global patterns in coronavirus diversity. *Virus Evol*. 2017; 3: vex012.
31. Wang L, Su S, Bi Y, et al. Bat-origin coronaviruses expand their host range to pigs. *Trends Microbiol*. 2018; 26: 466–470.
32. Peiris Y, Guan K. Severe acute respiratory syndrome. *Nat Med*; 2004; 10(12) S88-S97.
33. Pyrc K, Berkhout B, Van Der Hoek, L. Identification of new human coronaviruses. *Expert Review of Anti-infective Therapy*. 2007; 5(2): 245-253.
34. Rahman A, Sarkar A. Risk factors for fatal middle east respiratory syndrome coronavirus infections in Saudi Arabia: analysis of the WHO Line List, 2013–2018. *Am J Public Health*. 2019; 109(9): 1288-1293.
35. Memish ZA, Zumla AI, Al-Hakeem RF, et al. Stephens Family cluster of Middle East respiratory syndrome coronavirus

- infections. *N Engl J Med.* 2013; 368(26): 2487-2494.
36. de Groot RJ, Baker SC, Baric R, et al. "Family Coronaviridae". In King AM, Lefkowitz E, Adams MJ, Carstens EB, International Committee on Taxonomy of Viruses, International Union of Microbiological Societies. Virology Division (eds.). Ninth Report of the International Committee on Taxonomy of Viruses. Oxford: Elsevier. 2011; 806–28.
 37. International Committee on Taxonomy of Viruses. "ICTV Master Species List 2009—v10" (xls). 2010
 38. Woo PC, Huang Y, Lau SK, Yuen KY (August 2010). "Coronavirus genomics and bioinformatics analysis". *Viruses.* 2 (8): 1804–20. doi:10.3390/v2081803. PMC 3185738. PMID 21994708. Coronaviruses possess the largest genomes [26.4 kb (ThCoV HKU12) to 31.7 kb (SW1)] among all known RNA viruses (Figure 1) [2,13,16]
 39. Almeida JD, Berry DM, Cunningham CH, et al. "Virology: Coronaviruses". *Nature.* 220(5168): 650.
 40. Parry RL. "Travel alert after eighth camel flu death". *The Times.* 2015.
 41. Middle East respiratory syndrome coronavirus (MERS-CoV). www.who.int. Retrieved, 2020.
 42. MERS Clinical Features. Centers for Disease Control and Prevention. Retrieved 2020.
 43. MERS outbreaks. www.emro.who.int. Retrieved 2020.
 44. MERS-CoV. Interim Guidelines for Clinical Specimens from PUI | CDC. www.cdc.gov. Retrieved 2020.
 45. Zumla A, Hui DS, Perlman S . Middle East respiratory syndrome. *Lancet.* 2015; 386(9997): 995–1007.
 46. Infectious disease outbreaks reported in the Eastern Mediterranean Region in 2018. Epidemic and pandemic diseases. www.emro.who.int. Retrieved 2020.
 47. Zaki AM, van Boheemen S, Bestebroer TM, et al. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N Engl J Med.* 2015; 36(19): 1814–20.
 48. Doucleef, Michaeleen. Scientists Go Deep On Genes Of SARS-Like Virus. NPR Associated Press. Retrieved 2012.
 49. Assiri A, Al-Tawfiq JA, Al-Rabeeh AA, et al. "Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. *Lancet. Infectious Diseases.* 2013; 13(9): 752–61.
 50. Assiri A, McGeer A, Perl TM, et al. Hospital outbreak of Middle East respiratory syndrome coronavirus. *N Engl J Med.* 2013; 369(5): 407–16.
 51. Interim Guidance - Clinical management of severe acute respiratory infections when novel coronavirus is suspected: What to do and what not to do. WHO. Retrieved 2014.
 52. Saey, Tina H. Story one: Scientists race to understand deadly new virus: SARS-like infection causes severe illness, but may not spread quickly among people. *Science News.* 2013; 183(6): 5–6.
 53. Chu Daniel KW, Poon Leo LM, Gomaa Mokhtar M, et al. MERS Coronaviruses in Dromedary Camels, Egypt. *Emerging Infectious Diseases.* 2014; 20(6): 1049–1053.
 54. See Also. ProMED-mail. 20 September 2012. Retrieved 31 May 2013.
 55. Hemida MG, Perera RA, Wang P, et al. Middle East Respiratory Syndrome (MERS) coronavirus seroprevalence in domestic livestock in Saudi Arabia, 2010 to 2013. *Euro Surveillance.* 2013; 18(50): 20659.
 56. Briese T, Mishra N, Jain K, et al. Middle East respiratory syndrome coronavirus quasispecies that include homologues of human isolates revealed through whole-genome analysis and virus cultured from dromedary camels in Saudi Arabia. *M Bio.* 2014; 5(3): e01146-14.
 57. Gallagher J. Camel infection led to Mers death. *BBC News.* Retrieved 2014.
 58. Azhar EI, El-Kafrawy SA, Farraj SA, et al. Evidence for camel-to-human transmission of MERS coronavirus. *N Engl J Med.* 2014; 370(26): 2499–505.
 59. Middle East respiratory syndrome coronavirus (MERS-CoV). www.who.int. Retrieved 2020.
 60. Mers virus: Saudis warned to wear masks near camels. *BBC News.* Retrieved 2014.
 61. Saudi Arabia: Farmers flout Mers warning by kissing camels. *BBC News.* Retrieved 2014.
 62. The Who Mers-Cov Research Group. State of Knowledge and Data Gaps of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in Humans. *PLOS Currents.* 2013;5

63. Rapid advice note on home care for patients with Middle East respiratory syndrome coronavirus (MERS-CoV) infecti on presenting with mild symptoms and management of contacts. WHO. Retrieved 2014.
64. Cauchemez S, Fraser C, Van Kerkhove MD, et al. Middle East respiratory syndrome coronavirus: quantification of the extent of the epidemic, surveillance biases, and transmissibility. *Lancet. Infectious Diseases*. 2014; 14(1): 50–56.
65. Kieny M. After Ebola, a Blueprint Emerges to Jump-Start R&D. *Sci Am B Net*. Retrieved 2016.
66. LIST OF PATHOGENS. World Health Organization. Archived from the original on 20 December 2016. Retrieved 2016.
67. Wong AC, Li X, Lau SK, et al. Global Epidemiology of Bat Coronaviruses. *Viruses*. 2019; 11(2): 174.
68. Woo PC, Huang Y, Lau SK, et al. Coronavirus genomics and bioinformatics analysis. *Viruses*. 2018; 2(8): 1804–20.
69. Woo PC, Huang Y, Lau SK, et al. Coronavirus genomics and bioinformatics analysis. *Viruses*. 2010; 2 (6): 2004–18.
70. Coronaviridae - Figures - Positive Sense RNA Viruses - Positive Sense RNA Viruses. International Committee on Taxonomy of Viruses (ICTV). Retrieved 2020.
71. Gouilh MA, Puechmaille SJ, Gonzalez JP. SARS-Coronavirus ancestor's foot-prints in South-East Asian bat colonies and the refuge theory. *Infection, Genetics and Evolution*. 2011; 11(7): 1690–702.
72. Cui J, Han N, Streicker D, et al. Evolutionary relationships between bat coronaviruses and their hosts. *Emerging Infectious Diseases*. 2013; 13(10): 73.
73. Ge XY, Li JL, Yang XL, et al. Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature*. 2013; 503(7477): 535–8.
74. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2". *Nature Microbio*. 2020; 5(4): 536–544.
75. Masters PS, Perlman, S. Coronaviridae in *Fields Virology*. 2nd (eds Knipe DM, Howley PM) Lippincott Williams & Wilkins. 2013; 825–858.
76. Su S, Lau SK, Lam CS, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. *Trends Microbiol*. 2016; 24: 490–502.
77. Forni D, Cagliani R, Clerici M, et al. Molecular evolution of human coronavirus genomes. *Trends Microbiol*. 2017; 25: 35–48.
78. Brian DA, Baric RS. Coronavirus genome structure and replication. *Curr Top Microbiol. Immunol*. 2005; 287:1–30.
79. Lin CM, Saif LJ, Marthaler D, et al. Evolution, antigenicity and pathogenicity of global porcine epidemic diarrhea virus strains. *Virus Res*. 2016; 226: 20–39.
80. Zhou P, Fan H, Lan T, et al. Fatal swine acute diarrhoea syndrome caused by an HKU2-related coronavirus of bat origin. *Nature*. 2018; 556: 255–258.
81. Huang YW, Dickerman AW, Piñeyro P, et al. Origin, evolution, and genotyping of emergent porcine epidemic diarrhea virus strains in the United States. *M Bio*. 2013; 4: e00737–00713.
82. Liu C, Tang J, Ma Y, et al. Receptor usage and cell entry of porcine epidemic diarrhea coronavirus. *J Virol*. 2015; 89:6121–6125.
83. Simas PV, de Souza Barnabé AC, Durães-Carvalho R, et al. Bat coronavirus in Brazil related to appalachian ridge and porcine epidemic diarrhea viruses. *Emerg. Infect. Dis*. 2015;21: 729–731.
84. Lacroix A, Duong V, Hul V, et al. Genetic diversity of coronaviruses in bats in Lao PDR and Cambodia. *Infect Genet Evol*. 2017; 48:10–18.
85. Guan Y, Zheng BJ, He YQ, et al. Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China. *Sci*. 2003; 302: 276–278.
86. Lau SK, Woo PC, Li KS, et al. Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats. *Proc Natl Acad. Sci*. 2005;102: 14040–14045.
87. Kan B, Wang M, Jing H, et al. Molecular evolution analysis and geographic investigation of severe acute respiratory syndrome coronavirus-like virus in palm civets at an animal market and on farms. *J Virol*. 2005; 79: 11892–11900.
88. Tu C, Crameri G, Kong X, et al. Antibodies to SARS coronavirus in civets. *Emerg Infect Dis*. 2004;10: 2244–2248.

89. Wang M, Xu HF, Zhang ZB, et al. Analysis on the risk factors of severe acute respiratory syndromes coronavirus infection in workers from animal markets. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2004; 25: 503–505.
90. Xu HF, Wang M, bin Zhang Z, et al. An epidemiologic investigation on infection with severe acute respiratory syndrome coronavirus in wild animals traders in Guangzhou. *Zhonghua Yu Fang Yi Xue Za Zhi*. 2004; 38: 81–83.
91. Song HD, Tu CC, Zhang GW, et al. Cross-host evolution of severe acute respiratory syndrome coronavirus in palm civet and human. *Proc Natl Acad Sci*. 2005;102: 2430–2435 (2005).
92. Li W, Shi Z, Yu M, et al. Bats are natural reservoirs of SARS-like coronaviruses. *Sci*. 2005; 310: 676–679.
93. Hu B, Zeng LP, Yang XL, et al. Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. *PLOS Pathog*. 2017;13: e1006698.
94. Lacroix A, Duong V, Hul V, et al. Genetic diversity of coronaviruses in bats in Lao PDR and Cambodia. *Infect Genet Evol*; 48: 10–18.
95. Ren W, Li W, Yu M, et al. Full-length genome sequences of two SARS-like coronaviruses in horseshoe bats and genetic variation analysis. *J Gen Virol*. 2006; 87: 3355–3359.
96. Drexler JF, Gloza-Rausch F, Glende J, et al. Genomic characterization of severe acute respiratory syndrome-related coronavirus in European bats and classification of coronaviruses based on partial RNA-dependent RNA polymerase gene sequences. *J Virol*. 2010; 84: 11336–11349.
97. Lau SK, Li KS, Huang Y, et al. Ecoepidemiology and complete genome comparison of different strains of severe acute respiratory syndrome-related *Rhinolophus* bat coronavirus in China reveal bats as a reservoir for acute, self-limiting infection that allows recombination events. *J Virol*. 2010; 84: 2808–2819.
98. Rihtaric D, Hostnik P, Steyer A, et al. Identification of SARS-like coronaviruses in horseshoe bats (*Rhinolophus hipposideros*) in Slovenia. *Arch Virol*. 2010;155: 507–514.
99. Yuan J, Hon CC, Li Y, et al. Intraspecies diversity of SARS-like coronaviruses in *Rhinolophus sinicus* and its implications for the origin of SARS coronaviruses in humans. *J Gen Virol*. 2010;91: 1058–1062.
100. Balboni A, Gallina L, Palladini A, et al. A real-time PCR assay for bat SARS-like coronavirus detection and its application to Italian greater horseshoe bat faecal sample surveys. *Sci World J*. 2012; 989-514.
101. Yang L, Wu Z, Ren X, Yang F, et al. Novel SARS-like betacoronaviruses in bats, China. *Emerg Infect Dis*. 2013; 19: 989–991.
102. He B, Zhang Y, Xu L. et al. Identification of diverse alphacoronaviruses and genomic characterization of a novel severe acute respiratory syndrome-like coronavirus from bats in China. *J Virol*. 2014; 88: 7070–7082.
103. Gouilh MA, Puechmaille SJ, Gonzalez JP, et al. SARS-coronavirus ancestor's footprints in South-East Asian bat colonies and the refuge theory. *Infect Genet Evol*. 2011; 11: 1690–1702.
104. Wacharapluesade S, Duengkae P, Rodpan A, et al. Diversity of coronavirus in bats from Eastern Thailand. *Virol J*. 2015;12: 57.
105. Tong S, Conrardy C, Ruone S, et al. Detection of novel SARS-like and other coronaviruses in bats from Kenya. *Emerg Infect Dis*. 2009; 15: 482–485.
106. Ge XY, Li JL, Yang XL, et al. Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature*. 2013;503: 535–538.
107. Wang MN, Zhang W, Gao YT, et al. Longitudinal surveillance of SARS-like coronaviruses in bats by quantitative real-time PCR. *Virol Sin*. 2016; 31: 78–80.
108. Hon CC, Lam TY, Shi ZL, et al. Evidence of the recombinant origin of a bat severe acute respiratory syndrome (SARS)-like coronavirus and its implications on the direct ancestor of SARS coronavirus. *J Virol*. 2008; 82: 1819–1826.
109. Wu Z, Yang L, Ren X, et al. ORF8-related genetic evidence for chinese horseshoe bats as the source of human severe acute respiratory syndrome coronavirus. *J Infect Dis*. 2016; 213: 579–583.

110. Nagy PD, Simon AE. New insights into the mechanisms of RNA recombination. *J Virol.* 1997; 235: 1–9.
111. Rowe CL, Fleming JO, Nathan MJ, et al. Generation of coronavirus spike deletion variants by high-frequency recombination at regions of predicted RNA secondary structure. *J Virol.* 1997;71: 6183–6190.
- How to cite this article: Kaur N, Sethi A, Patil HC et.al. Origin and evaluation of pathogenic coronavirus: a literature review. *Int J Health Sci Res.* 2020; 10(7):207-217.
