



A Focus on Coronaviruses Infections in Animals: Review Article

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ABSTRACT

Coronaviruses are large, enveloped and single-stranded, non-segmented with positive sense RNA virus belong to Nidovirus, family Coronaviridae and included two subfamilies Orthocoronavirinae and Letovirinae. There are four genera variable in antigenetic characteristic and cross-reactivity (Alpha-coronavirus, Beta-coronavirus, Gamma-coronavirus and Delta-coronavirus) affect mammals and birds while Bafinivirus affect fish and cause different diseases in the vertebrate animals and human, so this review listed most important diseases in some animals which cause economic problems as in the avian cause infectious bronchitis (IB), in the bovine cause diseases in both bowl and respiratory system, Enteric form Disease in the equine, two forms of diseases have been occurred in the feline (feline enteric coronavirus and feline infectious peritonitis), in canine cause enteric and respiratory syndroms while in the porcine the diseases occur as are Transmissible gastroenteritis virus (TGEV), porcine epidemic diarrhoea virus (PEDV), and porcine deltacoronavirus (PDCoV). Also corona viruses affect aquatic animals and cause general clinical signs in fish. Some of these pathogens transmitted from camel and bates and causes diseases for human as SARS, MERS and SARS-2. From these review the conclusion is the hygiene practices and biosecurity are more important to prevent the emerging diseases in both human and animals cause by coronavirus.

Original Article:

DOI: <https://dx.doi.org/10.21608/javs.2020.117997>

Received :23 July, 2020.

Accepted :29 Aug., 2020.

Published in October, 2020.

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Keywords: Animals, Coronaviridae, Coronavirus, PEDV, SARS.

J. Appl. Vet. Sci., 5(4) : 25 – 36 .

INTRODUCTION

Coronaviruses (CoVs) are a large family of unsegmented, enveloped, positive sense ssRNA . that infect vertebrate animals and human. CoV causing the nervous, respiratory and digestive systems diseases of humans and other vertebrate (Chen and Guo, 2016; Unhale *et al.*, 2020) as in 2002 disease occur in human called SARS(severe acute respiratory syndrome) and the MERS(Middle East respiratory syndrome) in 2012,in these diseases the animals play as intermediat hosts for humans (Cui *et al.*, 2019) also recently coronavirus cause outbreak of severe pneumonia in human the International Committee on Taxonomy of Viruses (ICTV) called about the disease Severe Acute Respiratory Syndrome-Coronavirus-2 (SARSCoV-2) (Lu *et al.*, 2020; Gorbalenya 2020) and then the

World Health Organization (WHO) give its term “COVID-19” (Du Toit 2020; Gralinski and Menachery 2020).

Coronavirus are large, enveloped with protein projections, single stranded RNA related to Nidovirales belong to family Coronaviridae include sub-families: *Orthocoronavirinae* and *Letovirinae*. The *Orthocoronavirinae* involve genuses (Alpha-coronavirus, Beta-coronavirus, Gamma-coronavirus and Delta-coronavirus) which could affect mammals and bird and there was phylogenetic branches between these geneses (Fig.1), also there was Bafinivirus which related to *Torovirinae* and affect fish (International Committee on Taxonomy of Viruses ICTV 2019; de Groot *et al.*, 2012a). Woo *et al.*, (2010) are reported

the subgenera involvement in the Beta-coronavirus: Embecovirus, Merbecovirus, Nobecovirus and Sarbecovirus (involve SARS-2).

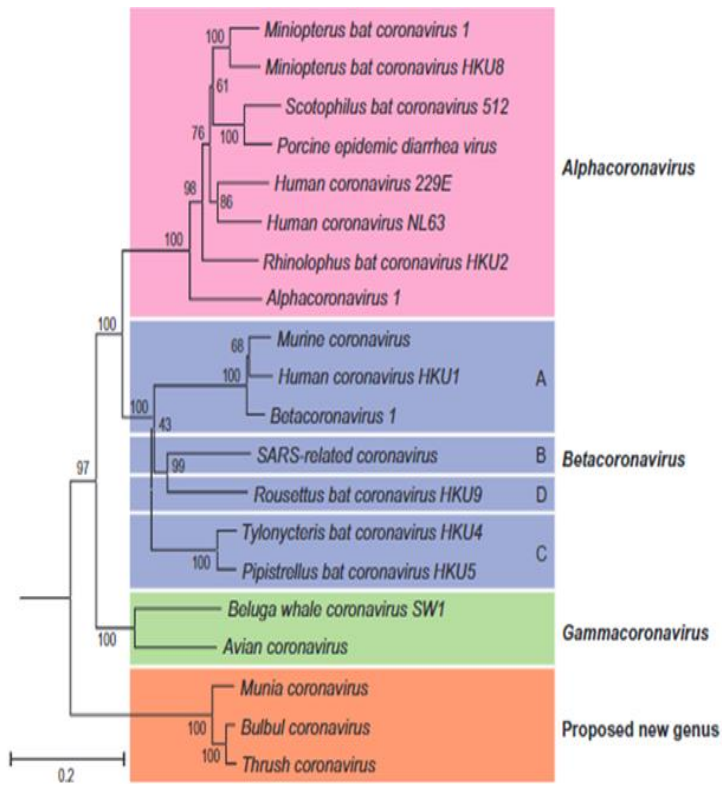


Fig.1: Phylogenetic analysis of genes of *Orthocoronavirinae* (ICTV, 2012).

The Viruses was firstly described the nidovirales in 1996 by the International Committee on Taxonomy ,the term coined in 1968, they have spherical in shape (120-160 nm) in diameters except Bafinivirus have baciliform (150-185 nm), “corona”-like or crown-like morphology, all five genera share in some characteristic as they single, positive stranded ribonucleic acid (RNA) approximately 30kb with 5' UTR replicase-SM-NUTR 3' (Lee *et al.*, 2003; de Groot, 2012b), unsegmented, polyadenylated, the structure was polycistronic capped with length 26–32 kb, have helical shape because the genome complexed with the basic nucleocapsid (N) protein also, envelope with large protein projections (80-120 nm),(Fig.2) these envelopes contain numeral variable membrane protein species which are important for binding with host cells ACE2 receptors and cause virion morphogenesis (Belouzard *et al.*,2012) and infectivity also preserved family -wide (S protein which is peplomers ,N-glycosylated and 1100- to 1600-aa class I fusion protein and triple-spanning NexoCendo integral membrane, 200- to 250-aa protein M 1)and a highly

hydrophobic and protein (E) which is slight membrane (Bond *et al.*, 1979).

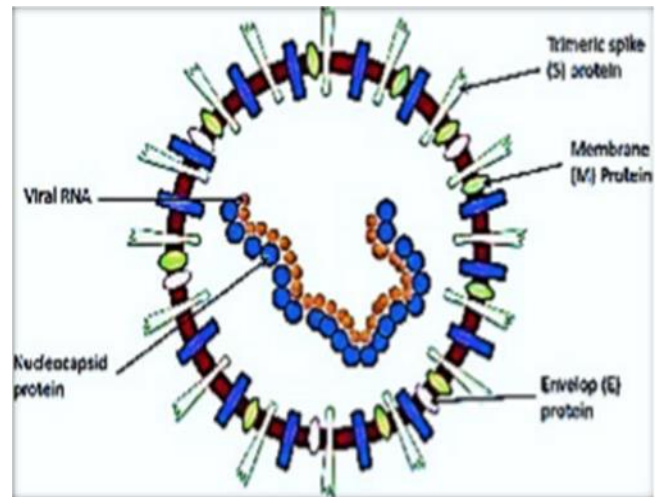


Fig.2: Coronavirus Structure (Meetakmal and Dwivedi,2020)

Coronavirus Diseases in different animal species

Coronavirinae include genus's variable according to genetic sequence, viral properties these viruses can grouped to animal species infection instead of their classification assignment mainly birds(Avian infectious bronchitis), cattle and horse(Bovine and Equine coronavirus), dog and cat(Feline Peritonitis and Feline enteric coronavirus), coronavirus in porcine , marine and fish coronavirus with laboratory coronavirus.Fig. (1)

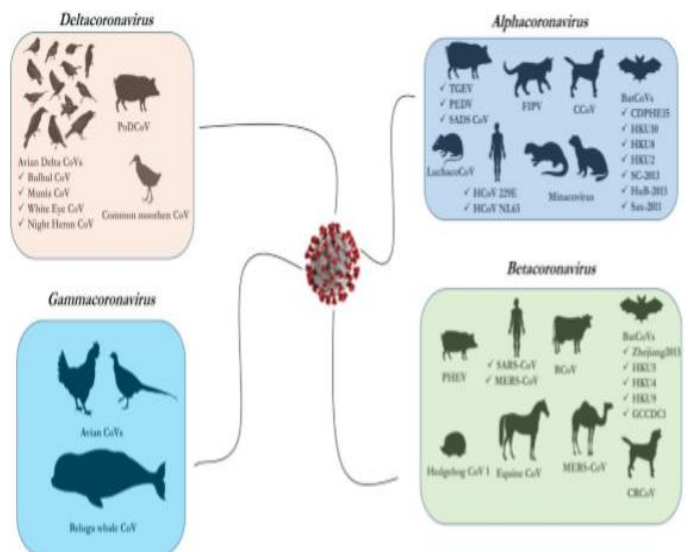


Fig.3: Coronaviruses genus's (*Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronavirus*) present in human and other as well as avian (Malik *et al.*, 2020)

1. Avian Coronavirus (Infectious Bronchitis IB)

The virus genus's was Gammacoronavirus; it is spread by aerosol so it cause economic losses to the poultry farms through affected respiratory, reproductive and urinary tracts (Dhama *et al.*, 2014). Avian coronaviruses are grouped in to infectious bronchitis (IB) which is highly contagious disease (Cavanagh, 2007) in chicken and closely genetically related to IBV- like viruses in pheasant and turkey and guinea fowls (Cavanagh, 2005; Weiss and Navas-Martin, 2005), it may isolated from wild birds which play vector in epidemiology and transmitted disease between domestic and wild bird (Milek and Blicharz-Domasnska, 2018).

The infectious bronchitis virus was firstly detected in 1930s in United State (Schalk, 1931) and cause economic problem IBV mainly affected epithelial of respiratory tract and may complicated with secondary bacterial and mycoplasma (Meulemans *et al.*, 2002; Matthijs *et al.*, 2003; Landman and Feberwee, 2004) .

This virus infect small aged animals and although it infect the bronchi, it also cause systemic problem as nephritis, cause defect to the oviduct lead to decline in the egg production and infect intestine (Saif, 2004a). Other genus of CoVs are Deltacoronaviruses include White-eye coronavirus HKU16, Muna coronavirus HKU13, Night- heron coronavirus HKU19 and Bulbul coronavirus HKU11 (Paim *et al.*, 2019).

1.1.Epidemiology and Clinical Signs

All ages are susceptible to infection with IBV, but small aged birds more susceptible and revealed high mortality and severe respiratory distress (Cook and Mockett, 1995). The period for incubation is take about 18-48hour, the clinical signs variable from moderate to severe diseases according to virulent strain, grading of immune system of the bird at the time of infection on age, and away of contact, dietary aspects (mainly calcium levels in the diet) and the presence of secondary bacterial infection, bad ventilation and decline temperatures all these factors considered as stress. Although primarily affecting the respiratory tract and the clinical signs variable from slight respiratory signs with low rates of both morbidity and mortality to severe respiratory distress characterized by wheezing, nasal exudate, coughing, sneezing, lacrimation and other respiratory disturbances with sinusitis.

In young chicks mortality is generally 25-30%, and may reach to 75% in cases of outbreak. Also, the virus may be infect oviduct of young female chickens and led to reduction in eggs product as a result of

cellular growth disturbances of the oviduct (Fan *et al.*, 2018). IBV demonstrates a varied tropism range for tissues, including the kidney and oviduct (Cavanagh, 2007 and Bande *et al.*, 2016).

1.2.Pathogenesis

The virus has a high affinity and firstly replicates in the ciliated epithelial cells of respiratory system; then viremia occur through 1-2 days of infection, in which virus spread to variable organs include the gastrointestinal, genital and urinary tracts. The pathogenesis of the disease variable according to the virus strain and system involved (Cavanagh, 2007).

2.Bovine Coronavirus (Beta Coronavirus)

BCoVs are mainly infect the intestinal and respiratory tracts of healthy cattle and diarrheic calves, in 1973 they were original stated in the United as a reason of diarrhea in calves, the diseases has including three clinical syndromes, respiratory infections with shipping fever, winter dysentery occur in adult and in small age animals the diseases called calf diarrhea in all age cattle the diseases are universal implications (Suzuki *et al.*, 2020) . Antigenically similar have been determined for both viruses cause enteric and respiratory distress in cattle (Saif, 2004b; Fulton *et al.*, 2015 and Gomez, 2017). In addition to infected domestic ruminant with Bovine-like coronaviruses the wild ruminants may also diseased with these viruses (Amer, 2018; Kim *et al.*, 2018).

2.1.Epidemiology and Clinical Signs

Two main factors affecting the wide spread distribution of BCoV: (1) the virus spread through via fecal-respiratory and oral routes (Decaro *et al.*, 2008) and (2) The feces of carriers animals considered as source for the virus mainly during stress environmental as cold period and parturition which represented the source of infection for neonatal.

The BOVs diseases occur in two forms, Enteric BCoV infection cause disease in both dairy and beef calf at early three weeks of aged and cause calf diarrhea (Boileau and Kapil, 2010), while in adult dairy cattle the virus cause winter dysentery lead to decline in milk production (Natsuaki *et al.*, 2007). The main investigation clinical signs of NCD was watery or yellow diarrhea, sometimes mixed with mucus or blood, is observed, lasting between 2 - 6 days with weakness and dehydration. Shipping fever occur in feedlot calve aged 2-16 weeks with respiratory problems (Saif, 2010), nasal and lachrymal discharge are the main signs of upper respiratory tract infection , while bronchopneumonia represented the sign of lower

respiratory tract infection, which may be associated with enteric forms of the disease. The severity of the clinical signs in NCD varies according to the level of maternal antibodies ingested by the calf which are usually occur after 5 days of age, when the level of virus-specific colostrum-derived antibodies decreases dramatically in the digestive tract.

2.2. Pathogenesis

The epithelial cells in the lung, trachea, and nasal turbinate's and enterocytes in the distal small and large intestines are chief positions of BCoV duplication (Park *et al.*, 2007). Other reports have documented that the virus shedding through two way, from respiratory tract after replication in the oropharynx or shedding with feces after swallowing the virus with mucus and reached to the stomach and intestine (Thomas *et al.*, 2006). A high viral load in the environment caused by a large number of animals excreting virus could probably also be a direct source of infection for the digestive tract.

3. Equine Coronavirus (Enteric Diseases, Beta coronavirus)

3.1. Epidemiology and Clinical Signs

The ECoVs are disease mainly characterized by diarrhea which occur as sporadic, mild cases in horses, the severe cases are rare and mainly affect young age animals, the ECoVs is firstly isolat in outbreaks from enteric disease in the US in 1991 also in Japan in 2011 from old aged horses (Guy *et al.*, 2000; Pusterla *et al.*, 2013 and Kooijman *et al.*, 2017).

The infection occurs through oral exposure and ingested feed and water contaminated with fecal, the incubation period was 48-72 hour and begin shedding the virus after 3-4 days of exposure (Pusterla *et al.*, 2018) the beta coronavirus that infect the equine lack the affinity to epithelial cell of respiratory tract and shedding the virus from nasal discharge is limited rather than the disease occur in cattle as two forms (enteric and respiratory) (Pusterla *et al.*, 2015). The morbidity ranges from 10-83% and the clinical signs were lethargy, fever, mild colic and neurological abnormalities the mortality range is rare and occur as a result of secondary infection and barrier damage of gastrointestinal tract and cause endotoxemia and septicemia with elevated concentration of ammonia in the blood a combined with encephalopathy (Pusterla *et al.*, 2018).

4. Feline Coronaviruses (Alphacoronaviruses)

4.1. Epidemiology and Clinical Signs.

The coronaviruses cause disease in feline in two forms Feline enteric coronavirus (FeCoV) is the causes of enteric disease which happen as benign and

infect respiratory and central nervous system which lead to death and infectious peritonitis (FIP) (Jaimes and Whittaker, 2018; Tekes and Thiel, 2016). Feces are the main source of transmission the FCoV, while the inhalation, saliva even transplacental transmission are very rare (Addie and Jarrett, 2001). In 1963 the feline infectious peritonitis was described as lethal, a common advanced and debilitating disease in both wild and domestic feline more common occur in depress immune status in all aged. Two forms of the disease will be occur (1) non-effusive (dry) form characterized by forming granuloma lesions with pus in the tissues (2) effusive (wet) form characterized by inflammation of blood vessels and accumulation fluid in the chest and abdomen (Kipar *et al.*, 2005).

There is a scientific agreement that the genetic mutation in S gene of FECVs lead to form FIPVs in the same environment and alters the tropism for macrophage (Harley *et al.*, 2013 and Rottier *et al.*, 2005), replication of FIPV begin in the bowel, respiratory and pharyngeal epithelial cells and travel the lymph nodes after tropism and infected macrophages more replication would be occur in the lymph nodes then spread to the organs and cause viremia which lead to nervous and ocular distress with inflammation of the thoracic and abdominal cavities (Addie, 2004).

5. Canine Coronaviruses

The disease was firstly reported in 1971 in German dogs, the CoVs occur in two genotype alphacoronavirus cause enteric syndrome (CCoV) was similar to transmissible gastroenteritis (TGVE) (Perlman and Netland, 2009) and beta-coronavirus cause respiratory syndrome (CRCoV) (Licitra *et al.*, 2014) which is similar to BoCoVs and describe in 2003 as respiratory illness called Kennel cough because injury to the ciliated respiratory epithelium (Erles *et al.*, 2007; Szczepanski *et al.*, 2019).

There is other classification according to tissue tropism as enterotropic cause maldigestion and malabsorption because destruction of enterocyte and intestinal villi and pantropic which the virus affect kidney, spleen, liver and CNS and the disease characterized by leukopenia, depression, diarrhea, anorexia, vomiting (Buonavoglia *et al.*, 2006).

6. Porcine Coronavirus

There are several porcine CoVs that are include Transmissible gastroenteritis virus (TGEV), porcine epidemic diarrhea virus (PEDV), and porcine delta coronavirus (PDCoV), Swine acute diarrhea (SADs-CoV) and hemagglutinating encephalomyelitis virus (PHEV), the variable stage and severity of porcine coronavirus describe as in Fig. (2).

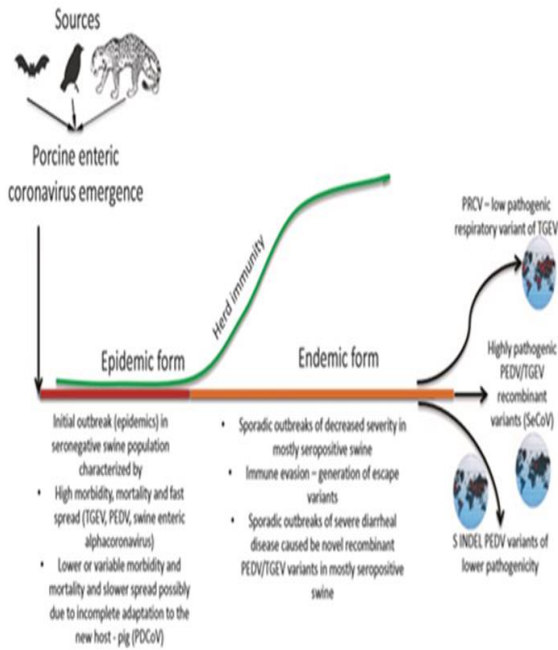


Fig.4: Variable phases of estimation of coronavirus as enteric disease in swine (Vlasova et al., 2020)

6.1. Pathogenesis and Clinical Signs

6.1.1. Transmissible gastroenteritis (TGVE)

It is worldwide spread disease was firstly described in 1946 as an extremely infectious disease occur as enteric forms in the swine (Weiss and Navas-Martin, 2005). Virus replication and targets the absorptive epithelial cells of villi and cause villous atrophy and severe necrosis to enterocyte of ileum and jejunum during twenty four hour after exposure to pathogen lead to disturbances in the enzyme activity, digestion and imbalance electrolytes led to accumulated the fluid in the lumen of the intestine , severe malabsorptive diarrhea (Moon et al., 1975 and Wu et al., 2020) severe TGVE are more common in small aged piglets and death uncommon after aged 2-3 weeks, the disease symptoms involved copious yellow watery diarrhea, vomiting, dryness and fast loss of body weight, vomiting animals was unusual but main clinical signs is the watery diarrhea, , the upper respiratory tract may often affect (Enjuanes et al., 1995).

6.1.2. porcine respiratory virus (PRVC)

PRCV is coronavirus that have been tropism and duplication in the pneumocyte type 1 and 2 and is isolated from epithelial cells of the upper and lower respiratory tract and seen in the alveolar macrophage (Atanasova et al., 2008), it can isolate from blood and tracheobronchial lymph nodes, it transmitted through mucus shedding the virus after 4-6 day of infection. The main clinical signs are lung and broncho interstitial pneumonia perivascular lymph histiocytic handcuffing (Jung et al., 2007 and Atanasova et al., 2008).

6.1.3. porcine epidemic diarrhea virus (PEDV)

Is a viral enteritis and a common in pigs cause high mortality rates in neonatal piglet, it was firstly identified and describe in the 1970s in Europe, in April 2013 in US the PEDV was occur as largest outbreaks with high mortality (Oldham, 1972 and Lee, 2015). The infection with PEDV occur through digestive and inhalation and take 1-4 days as incubation period, clinically similar with like pathogenesis of TGVE with it variation in the slower spread with in the herd association with low mortality (Sun et al., 2012; Song et al., 2015 and Lin et al., 2019), in very small aged piglet it causes vomiting, severe diarrhea, dehydration with high death rates and the diarrhea without vomiting are the main disease symptoms in a fattening growing pigs .

6.1.4. porcine delta coronavirus (PDCoV)

Delta coronaviruses is a new developing pathogen initially described in Hong Kong in 2012 (Woo et al., 2012a) as diarrhea in neonatal piglets, and spread to other countries including china, Thailand and United State (Zhao et al. 2019; Saeng-chuto et al., 2020 and Koonpaew et al., 2019), it take 1-3 day as incubation period and cause mild disease rather than other porcine coronavirus and the mortality rate reach to 40% during outbreak, (Ma et al., 2015 and Jung et al., 2016). PDCoV replicates and tropism to epithelial cell of the small and large intestine and lead to loss of enterocyte and cause malabsorption and the clinical signs similar to the TGVE and PEDV (Chen et al. 2015; Hu et al. 2016) The clinical signs of the disease represented by watery, acute, diarrhea, vomiting, loss body fluid , weight loss, lethargy and death, among suckling pigs mortality reach up to 40–80% (Anon 2014).

6.1.5. Swine acute diarrhea (SADs-CoV):

The disease detected in piglet in China as alphacoronavirus, cause enteritis and death, there was a sequence analysis similarity of SADs-CoV to bats (horseshoe) about 95-96% and was called KHU2-CoV (Zhou et al., 2018).

6.1.6. Porcine hemagglutinating encephalomyelitis virus (PHEV):

This virus is described in 1962 and classified as coronavirus in 1971, affected nervous and digestive system (Greig et al., 1962; Clarke and McFerran, 1971), (Mora-Dias et al. 2019). Early reported about the PHEV as neurotropic properties in pigs affected all age but cause high morbidity and mortality in piglets below four weeks age also, the disease occur as subclinical (Mora-Dias et al. 2019).

7. Aquatic Organisms

7.1. Marine organisms

In 1987, Alphacoronavirus was firstly isolated from dead harbor seals (*Phoca vitulina*) in Miami Sea aquarium and describe the disease as acute necrotizing enteritis (Bossart and Schwartz, 1990). A novel [BWCoV- SW1] is Gamma-coronavirus detected in 2008, was isolated by panviral microarray technology from hepatic tissue of white beluga whale (*Delphinapterus leucas*) (Mihindukulasuriya et al., 2008), also bottlenose dolphin CoVs (BdCoV)HKU22 was detected and isolated from the fecal samples of bottlenose dolphins (*Tursiops aduncus*), both BWCoV-SWI and BdCoV HKU22) are named Cetacean coronavirus (Woo et al., 2014).

7.2. Freshwater fish

In Germany, bacilliforms, bafinivirus white bream virus (WBV) has been isolated from healthy (*B. bjoerkna L.*) (Granzow et al., 2001). Also, in 1997 the virus was initial identification from diseased moribund fathead minnows (*P. promelas*) and called Fathead Minnow Virus (FHMNV) exhibited hemorrhage on the skin and eyes, in addition to renal, splenic and hepatic lesion, this pathogen considered second genus present in the Bafinivirus (Iwanowicz and Goodwin, 2002; Batts et al., 2012).

8. Camels Coronavirus

In Saudi Arabia in 2012 the diseased camels considered intermediated host for the Middle East respiratory syndrome (MERS) which is caused by coronavirus (CoV) and can transmitted to human cause fatality rate about of 35% (Hawkes, 2013).

9. Bat coronavirus

Coronaviruses infected bats are (alpha and beta), which is considered reservoirs for CoV and asymptomatic carrier (Fan et al., 2019) that cause diseases in human and animals include severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), porcine epidemic diarrhea (PED) and severe acute diarrhea syndrome (SADS), (Banerjee et al., 2019).

10. Zoonotic of Coronavirus

Coronaviruses have genus's (alpha-cov, beta-cov, gamm-cov and delta-cov) with twenty six species and there was cross-reactivity and genetic closely related with some of them (Paules et al., 2020), although CoVs consider veterinary microb but the genera alpha-CoV and beta-CoV have been affected human for at least many century ago and initiated in animals and bats (Chan et al., 2013), alpha-CoV cause endemic mild respiratory illness (HCoV-229, HCoV-OC43, HCoV-NL63 and HCoV-HKU1) and the disease of beta-CoV called epidemic severe acute respiratory syndrome SARS and middle east respiratory syndrome MERS (Skariyachan et al., 2019).

All CoV are originated from animal reservoir and transmitted from bats, mice, and domestic animals but there was limited zoonotic diseases transmitted from human to human (Weber et al., 2001 and Cotton et al., 2013) Fig. (5).

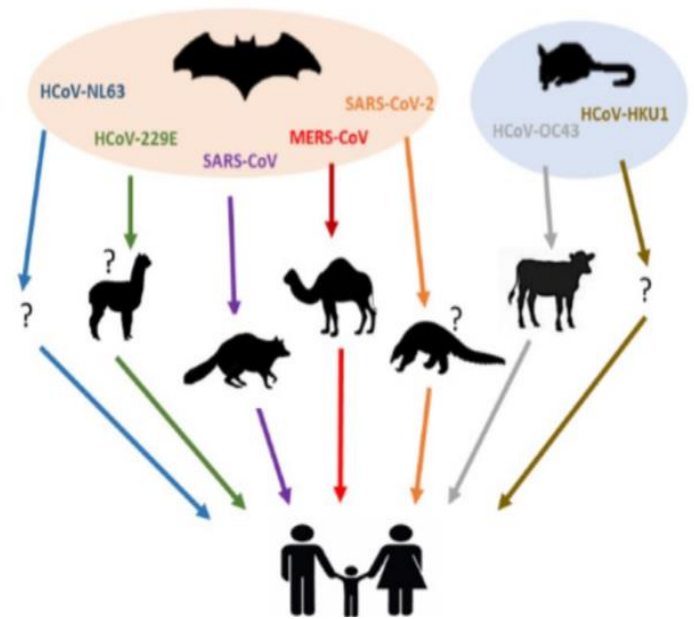


Fig.5: Origin of human CoVs and intermediated host (Ye et al., 2020)

Anovel CoV cause SARS (a typical pneumonia) was firstly reported in China Provinces in 2002 and then spread to Europe, Asia and North America (Peiris et al., 2003; Chen et al., 2007). Guan et al., (2003) suggested that racoon dogs and masked palm civets (*Paguma laravata*) are carrier for SARS, also horseshoe bats transmitted this disease (Ge et al., 2013; Fan et al., 2019). While epidemic MERS is reported in 2012 in Saudia Arabia, the disease transmitted through direct contact with disease dromedary camels and consumption milk and meat of illness camels (Durai et al., 2015 and Aleanizy et al., 2017).

Recently, in December of 2019 severe, cough, dyspnea and fetal pneumonia have been detected beginning in Seafood Market in Wuhan City in China, the disease called pandemic SARS-2 because it spread to worldwide with high mortality rate (Huang et al., 2019), SARS-2 is less pathogenic than SARS and MERS but more and rapid transmissible spread (Ye et al., 2020), animals considered origin as other CoV and intermediated host for human then transmitted between human (Hui et al., 2020; Nishiura et al., 2020). Bats (*Rhinolopus affinis*) is the origin of SARS-2 (Zhou et al., 2020b), in addition recent study suggested that Malayan pangolin (*Manis javanica*) play role as intermediated host for SARS-2 (Lam et al., 2019 and Xiao et al., 2020).

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Is SARS-2 has been reversible transmitted from human to animals?

Although that SARS-2 was origin from animals but there was variable susceptibility between the them (OIE, 2020), Shi *et al.*, (2020) reported result about the poorly SARS-2 replication in the chicken, dog, pig and ducks rather than ferret and cat, these efficient replication may due to similarity to human by possessing ACE2 receptors (Anderson *et al.*, 2020).

A few newly reports evidence that SARS-2 may transmitted from human to pet animals and cause mild respiratory illness (Malik *et al.*, 2020), recent knowledge for SARS-2 transmitted from human to animals was firstly reported in April, 2020 in which tiger called Nadia housed in Bronx zoo in New York show sneezing and dry cough with positive result for SARS-2 which transmitted from illness keeper house with SARS-2.

COVID-19 and Animals

Also the infection reported in pet dogs and cats United State, Hong Kong and Belgium, all these cases were direct contact with the infected owners but the clinical signs in these animals variable in severity from non- symptoms disease to mild respiratory syndrome with recovery status for all cases (Islam, 2020), many studies should be done in future to understand the mechanism of the pathogen transmitted from the human to the animals.

In general rapid diagnosis coronavirus and SARS-2 in both human and animals play an important roles to prevent spread infection and these will take traditional diagnostic methods as antigen detection and cell culture, ELISA, Immunofluorescence and more specific diagnosis methods depend on RT-PCR and genome sequence (Minakshi *et al.*, 2020). The prevention is efficiently than usage drug and therapy methods so the hygiene and biosecurity are more important to preventing the disease.

CONCLUSIONS

Coronavirus have been detected s emerging pathogen cause sporadic and outbreak diseases in animals and human as SARS-1, MERS and SARS-2 which are zoonotic diseases transmitted from animal to human. Recent disease SARS-2 has reversible transmission from human to pet animals, so it is important to make framework of biosecurity hygiene to protect human and animals from pathogen.

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How to cite this article:

Shahbaa K. AL-Tae, Hana Kh.Ismail, Al-Saidya A. M. and Al-sabaawy, H.B.2020. A Focus on Coronaviruses Infections in Animals: Review Article. *Journal of Applied Veterinary Sciences*, 5(4): 25 - 36.

<https://dx.doi.org/10.21608/javs.2020.117997>