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COVID-19 and vital organs of the body

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Abstract

corona virus is a genus belongs to corona viridae family with very small size of genomic single stranded RNA 30-32kb. There are three different types of corona viruses according to their mode of infection in different animals and size of genome. Every type is host specific and causes specific disorders. The three types alpha, beta and gamma corona virus having their unique properties of infection. It causes different respiratory disorders like severe acute respiratory syndrome (SARS), middle east respiratory syndrome (MERS), severe pneumonia as well as infects other organ system of humans and other animals. Recently emerged corona virus known as novel corona virus has been discovered in December 2019 in the Wuhan city of china. It has become the most deadlier virus of 21st century. Now the whole world is suffering with sever pneumonia and major respiratory disorders that's why it is declared pandemic named as covid-19. It attacks on the lungs of infected person and lungs filled with fluid that causes respiratory problem as death of patient occurs due to the severity of respiratory disorder.

Key words: Covid-19, SARS, MERS, HKU1, OC43, patients

Introduction

Corona virus is a genus belongs to *Corona viridae* family, that are enveloped viruses having spikes that are like a club and having large positive strand of genomic RNA. The size of genomic RNA is 27–32 kb, methylated capped and poly A strand. There are three different groups of coronaviruses according to serum diagnosis. Every group of belong to viruses are identified by their specific host and RNA sequence. Coronaviruses have been identified in rats, chickens, mice, turkeys, pigs, wild dogs, pets, domestic rabbits, horses, cattle as well as human serum, that viruses are responsible to cause a variety of severe infectious diseases especially respiratory tract diseases and gastroenteritis (Guy *et al.*, 2000).

In Wuhan, Hubei province of China during last days of December 2019 a novel coronavirus, known as 2019-nCoV which had previously not been detected in humans or animals causes severe respiratory problems in a group of patients with pneumonia of unknown cause were confirmed (WHO, 2020). Epidemiological studies showed that most of these patients had to visited Wuhan local seafood market and the gene obtain from bats and the sequence of RNA virus obtained from these patients was highly similar (Ji *et al.*, 2020)

Since January 2020 the migration and spreading novel corona virus 2019 has escalated and the virus has extended rapidly to china and in many other countries. As rough estimation of February 8-2020 a confirmed figure of 37589 native people of Wuhan and including 302 people across 24 other countries have been infected with Severe Acute Respiratory Syndrome Coronavirus type 2 all over the world (WHO, 2020).

Another human pathogen 2019-nCoV A novel coronavirus new virus was first discovered in 2019 when specimens from Chinese adult patients with unexplained severe pneumonia viral meta genomics was carried out on three bronchi alveolar lavage (Zhu *et al.*, 2020).

Coronavirus are mainly associated with severe effects like acute respiratory infections in humans, the pathogenicity of coronaviruses increases with the ability to infect multiple host species and a variety of diseases (Fung *et al.*, 2019). The human interaction with wild animals make them a common source of zoonotic infections. Middle Eastern Respiratory Syndrome Coronavirus and Severe Acute Respiratory Syndrome Coronavirus are pathogens that acts as zoonotic source and can cause severe respiratory diseases in mammals like humans (Luk *et al.*, 2019; Ramadan and Shaib, 2019).

The pathogenicity of Coronaviruses in birds and mammals, including humans are major host. The major genera of corona viruses are α-coronaviruses and β-coronaviruses mainly found in mammalian serum, on other hand Y-coronaviruses are detected primarily in the serum of birds. Detection of samples of coronaviruses in wild mammals paly a leading role in the discovery of a significant number of novel α-coronaviruses and β coronaviruses in mammals like bats (Poon, 2005; Tang, 2006; Woo, 2006).

Till to date no any effective antiviral vaccines are discovered for Severe Acute Respiratory Syndrome Coronavirus and, although many doctoral studies have been started, no licensed protective vaccine have been discovered. Severe Acute Respiratory Syndrome Coronavirus get entry into target cells by attachment of its cellular receptors, by using angiotensin-converting enzyme 2 with their spike at glycoprotein (Li *et al*., 2003). endosomal acidification such as ammonium chloride are main sensitive to inhibitors tostop infection (Simmons *et al.,* 2004; Hofmann *et al*., 2004; Yang *et al.,* 2004), Severe Acute Respiratory Syndrome Coronavirus requires a very low medium pH of body fluids for infection. There are other types of spikes protein can initiate cell to cell transmission at neutral pH at 07 (Li *et al*., 2003; Simmons *et al.,* 2004),

Novel coronavirus called as SARS-coronavirus are the major source for the speeding of severe acute respiratory syndrome. The signs of infection shown by Novel coronavirus are pneumonia with diffused alveolar damage with total mortality rate of _10% that ranges from 0 percent in children and at least 50% in persons from age 65-70 (Peiris *et al*., 2003). Attachment shown by Coronaviruses by binding to their glycoproteins receptors at 200 kDa spike at glycoprotein, with the viral envelope. Recognition of virus receptors can provide the insight into mechanisms of virus entry into, tissue as well as tropism, pathogenesis, and host ranges

Virus called Middle East Respiratory Syndrome Coronavirus are the major source of spreading of Middle East Respiratory Syndrome is an illness caused by a A novel coronavirus was first described in September 2012 causing severe respiratory infection (Omrani *et al*., 2013). First reported case of Middle East Respiratory Syndrome Coronavirus in September 2012 its samples obtained from a Saudi Arabian businessman who died due to the disease of acute respiratory and renal failure. Middle East Respiratory Syndrome affects the lungs and breathing tubes and whole respiratory system. Most patients developed severe acute respiratory illness with symptoms of fever, cough and shortness of breath are major signs due to transmission of Middle East Respiratory Syndrome (Memish *et al.*, 2013).

The main cause of spread of novel corona virus 2019 to have resulted from human to human transmission as noted by studies. In 26th January, 2020, cases of nCoV-2019 had registered in too many countries, including Wuhan province of China, Japan, The Republic of Korea, United States and Vietnam. Malaysia, Nepal, Singapore, Thailand, Hong Kong, Macau, Taiwan, Australia and France. Emergence process is the jump from animals to humans one of the key steps in transmission of many viruses. . Bats are known to be hosts for more than 30 coronaviruses with complete genomes sequenced and the origin of nCoV-2019 have been traced back to the seafood wholesale market in Wuhan, China given it has close similarity to bat coronaviruses. (Wong *et al.*, 2019).

Literature Review and method

Guo et al., (2008) concluded that the major source of severe morbidity and mortality in animals are severe acute respiratory syndrome viruses. The pathogens are not yet fully understood while its clinical manifestations have been extensively studied by researchers. The most severe damage of the lungs and the immune system caused due to these viruses studied by A limited number of autopsy. Other organs affected include the kidneys, brain, digestive tract, heart, liver, thyroid gland and urogenital tract. Those cells are the primary target cells having SARS-CoV receptor expressing angiotensin-converting enzyme 2 are pneumocytes and enterocytes. Cerebral neurons and epithelial cells of renal tubules and immune cells are also infected. Indirect injury and direct injury are main cause of spreading of these viral diseases. Indirect injury mainly results from immune responses, circulatory dysfunction, and hypoxia.

Memish *et al.* (2015) studied in September 2012 the primary detail of Middle East respiratory syndrome is include 1038 confirmed cases of coronavirus. Among these cases 460 death have been informed by Saudi Arabia. August 24 to September 3, 2013 total 397 patients were tested for coronavirus. Out of these patients about 5 % cases were reported from Al Madinah. We describe the findings, epidemiological and clinical features of this disease. In some cases health care workers were also affected from this disease. Almost 14 health care workers were suffering from this disease. The mortality rate due to coronavirus was almost 39%. About 6 cases were reported, that was spread due human to human transmission.

Cavanagh, D. (2007) analyzed that the foremost causes of economic loss within the poultry industry affecting the performance of both meat-type and egg-laying birds as well as in chicken *Gallus gallus* Infectious bronchitis virus the coronavirus are responsible. It can be detected in both faecal and respiratory material. In many tissues along the alimentary tract and elsewhere e.g. kidney, oviduct and testes but these virus replicates not only in the epithelium of upper and lower respiratory tract tissues. There is increasing evidence that birds other than the chicken are infected by IBV. Studies shows that IBV are Interestingly responsible for increase in breeds of chicken due to severity of infection. Probably the major reason for the high profile of IBV is the existence of a very large number of serotypes. Both live and inactivated IB vaccines are used extensively, the latter requiring priming by the former.

Chu *et al.* (2011) identified different coronaviruses in birds and wild animals. On the base of phylogenetic analysis these coronaviruses are classified as gamma-coronaviruses and delta-coronaviruses. These viruses cause different diseases in birds. Gamma-coronaviruses were found mainly in *Anseriformes* birds whereas the delta-coronaviruses were found in *Pelecaniformes* and *Ciconiiformes* birds. Observations show that gamma-coronaviruses could transfer largely in duck species. The delta-coronaviruses may have more specific host as compared to the gamma-coronaviruses. The avian coronaviruses and the mitochondrial DNA sequence of the host have resemblance which shows that these viruses are coevolved with the birds. But not all the coronaviruses are coevolved with the birds.

Chang *et al.* (2010) studied that pathogenic feline enteric coronavirus is a lethal virus which causes feline infectious peritonitis disease. Analysis showed that the 3-c gene is an infectious marker that infects cats. Investigation showed that functional 3-c protein expression is important for feline enteric coronavirus replication. The 3-c gene was mutant in majority of the population. Most cats with feline infectious peritonitis had no visible intestinal feline coronavirus and had apparently clear the main feline enteric coronavirus infection. The intestinal feline coronavirus always had an interaction with 3-c gene and appear to have been developed by feline enteric coronavirus.

The 3-c inactivated viruses do not replicate or poorly replicate in the gut.

Hasoksuz *et al*. (2002) studied the enteric bovine and respiratory coronavirus stains are different in antigenic, biological and genetic features. The present study is based on the analysis of the amino acid sequence and nucleotide sequence. The cleavage site for enteric bovine (n=3) and for respiratory (n=5), both were isolated from the same animals. Both were compared and stained. Bovine coronavirus when compared with Mebus stain shows spike of glycoprotein. Total 75 polymorphic nucleotides were recognized in bovine coronavirus. Each polymorphism has 42 amino acids changes at 38 different sites. Among these changes only 19 amino acids are involved which changes the surface probability and hydrophobicity of the proteins. The respiratory and bovine enteric clustered were isolated on the base of the phylogenetic analysis into two groups and two subgroups. Although the respiratory and bovine enteric cluster have a difference of few amino acids. The respiratory isolates have sequence diversity obtained from two different sources. The expected secondary structure of respiratory isolates shows significant changes in calf diarrhea and prototype winter dysentery when stained with bovine coronavirus. Amino acids variations are in 113, 115, 148, 501 and 531 of respiratory isolates. As a consequence, the adult winter dysentery and classical calf enteric stains are genetically different from the respiratory stains of bovine coronavirus.

Li *et al.* (2003) analyzed the angiotensin converting enzyme 2 is a receptor for the severe acute respiratory syndrome coronaviruses. Jeffers *et al.* (2004) discovered that human cellular glycoprotein are recognized as different receptors for the severe acute respiratory syndrome coronaviruses. Virus with genus pseudotyped retrovirus was separated from human lung and its cDNA was transformed into ovary cells of Chinese hamster. These ovary cells have ability to bind with acute respiratory syndrome coronaviruses and spike of glycoproteins S590 and S1180. Copies of transfer cells that bound to acute respiratory syndrome coronaviruses and glycoproteins increase in genomic viral RNA and detected by PCR. Human lung cDNA when inserted shows sequencing that the cloned cell line limited cDNA that coded human CD209L. The cells that express human CD209L glycoprotein became vulnerable to the infection acute respiratory syndrome coronaviruses. The histological studies show that CD209L in human lung is type 2 which contain endothelial and alveolar cells. Both these cells have ability for acute respiratory syndrome coronaviruses. Numerous others enveloped viruses use

CD209L as an entry in human body. These enveloped viruses include Sindbis and Ebola. The hepatitis C virus and HIV also attach to the CD209L on the cell membrane but these viruses cannot use it as entry site into the human body. Studies showed that the acute respiratory syndrome coronaviruses uses CD209L and angiotensin converting enzyme 2 in pathogenesis and virus infection.

Kahn and McIntosh (2005) purposed that the major source of a substantial proportion of upper respiratory tract infections in children a family of corona viruses were first identified in 1960 these are now a days called Human coronaviruses. The viruses causing severe acute respiratory syndrome and least 5 new human coronaviruses have been identified including the coronavirus, which caused significant morbidity and mortality since 2003. New Haven coronavirus and NL63, representing a group of newly identified group identified worldwide and another group I coronaviruses that includes NL also identified. These viruses are common human pathogens associated with both lower and upper respiratory tract syndromes. A newly identified group II coronavirus has not yet been established in the globe. Now a days Corona virology has advancement significantly in the past few years to analyze severe acute respiratory syndrome epidemic put the animal coronaviruses at the main focus to scientists.

CORONAVIRUS GENOME AND STRUCTURE:

In electron micrograph there is a distinctive appearance of coronavirus as RNA virus in negatively stained processes. Nucleic acid is one strand and polyadenylated. The length of nucleic acid is 30 kb. Genome of corona virus is based on RNA and different types of proteins. In OC43 and other group II coronaviruses different types of protein are cut through enzymes. The enzymes use in this process are ATPase helicase, RNA dependent RNA polymerase and surface protein hemagglutinin-esterase.

The S glycoproteins are present on the surface which forms petal like projections on the surface, E protein form small envelop, M glycoprotein are present on membrane and N protein present for nucleocapsid and it make compound complexes with RNA. Many open reading frames could not be code clearly. Basic mRNAs and polyadenylated 3-ends are taken as common strategy for the replication of viruses, the specific parts of 5-end are translated (Lai and Holmes, 2001). Mutations could be taking place naturally. The two corona viruses have ability to make genetic recombination, if they both attacked the cell at same time (Kahn and McIntosh, 2005).

The coronaviruses are developed in the form of vesicles budded from the endoplasmic reticulum in the cytoplasm of infected cell (Fig. 2). These vesicles are releasing from the cell after its lysis.

229E are member of group 1 coronavirus and its receptor on cell that is human aminopeptidase N. Group II corona virus included MHV (Mouse Hepatits Virus) and its receptor are carcinoembryonic antigen family. The OC43 receptors are not yet recognized but HLA-I molecule and 9-*O*-acetylated neuraminic acid considered to be its receptor.

History:

Human corona viruses are firstly not believed to be harmful for human and have mild symptoms of infections and mostly caused infection in the lower part of respiratory tract. But in 2003 after the outbreak of SARS and in 2012 after the outbreak of MERS-CoV, corona virus considered to be important for public health issues. After 2004 severe acute respiratory syndrome corona virus could not be found in humans but MERS-coronavirus spread to most of the countries and have high ability to infect humans easily. By studying Corona virus at cellular level its mode of action, transmission, prevention and control could be determined. Human corona virus (HCoV) was becoming the emerging problem now a day.

NEWLY IDENTIFIED GROUP I HUMAN CORONAVIRUSES:

Five human corona virus cases have discovered since 2003. Three of them belong from group 1 corona virus family and have same species of virus. Hoek, in 2004 observed the 7-month-old girl having bronchiolitis, coryza, fever and conjunctivitis and isolated a new type of corona virus, NL63. The investigators could sequence the whole genome of the virus by using the new genome amplification technique. It is contagious gastroenteritis virus of pigs and related to the 229F corona virus group 1 shown by phylogenetic analysis. Data has been taken since December 2002 to April 2003, 614 respiratory samples have been screened and 7 more peoples have positive test for NL63. All of them have respiratory disorder of both upper and lower respiratory tract (Hoek et al., 2004).

NEWLY IDENTIFIED GROUP II HUMAN CORONAVIRUSES:

In 2001 January, in Hong Kong a 71 years old man is identify with fever and prolific cough, he is recently returned from the shen-zhen, China a place previously hit with epidemic of SARS. His SARS screening test is not positive but by using reverse transcriptase-polymerase chain reaction, a new group II corona virus have been identified by using the primer of the conserved part of replicase gene of virus. This new corona virus is named as HKU1. This new corona virus is genetically highly different from another corona virus of group II and OC43. This virus cannot propagate in cell culture. Serological studies which are based on the reaction of antibodies with recombinant HKU1 nucleocapsid showed that HKU1 infection to humans could be common. It is very uncertain that, the Western blot assays and ELISA that are using for the detection of HKU1 antibody can be used for OC43 antibody and other corona viruses of humans (Woo et al., 2005).

Coronavirus belong from the enveloped viruses' family. It mostly replicates in host cell's cytoplasm (Fields et al., 2001). Corona virus can be distinguished by the presence of single strand positive sense RNA genome. It has genome of 30 kb length and have 3-polyadenylation tract and 5-cap structure.

When healthy cell is infected by corona virus, large poly proteins are formed by the translation of viral 5-open reading frame. These polyproteins are then cleaved by the viral proteases and releases many non-structural proteins like, adenosine triphosphate helicase and RNA dependent RNA polymerases. Viral genome replication is aided by these proteins and they also help in the formation of transcript which aid in the formulation of viral proteins. The mechanism of formation of viral genome messenger RNA is not yet understood.

The discontinuous transcription of viral messenger RNA is regulated by the transcription regulating sequence that are present in the end of every gene. The transcription regulating sequence have some conserved sequences in virus is 5-CUAAAC-3. There are two possible models for the discontinuous transcription in arterioviruses and coronaviruses. After the discovery of transcriptionally active, viral negative strands having anti leader sequence and intermediates of transcription plays important role in the formation of messenger RNAs. Formation of negative strand, favours the discontinuous transcription model (Sawicki et al., 2001).

The proteins of virus membrane that includes membrane and spike proteins are moved to ER and then the middle compartments of golgi apparatus and complete replicated positive strand of RNA arranged with nucleocapsid proteins. This complex of RNA and proteins are combined with the membrane proteins of endoplasmic reticulum; this complex is then budded off into the lumen of endoplasmic reticulum. The virus moves to the Golgi bodies and leave the cell through exocytosis (Fields et al., 2001).

The place of attachment of viruses is present within S proteins.

According to the genome phylogeny corona virus are divided into four genera, alpha-, beta-, gamma- and delta coronavirus (Woo et al., 2012).

Targeted Organs

1. Respiratory system

According to diagnosis the lungs of patients that are infected with severe acute respiratory syndrome were heavier than normal people lungs (Gu et al., 2005). Pleural effusion and hepatization hasbeen found on gross examination with Severe lung consolidation and edema (Ding et al., 2003; Gu et al., 2005).

2. Immune system

Severe acute respiratory syndrome (SARS) has antagonistic influence off immunity. Consequences of SARS is Hemorrhagic necrosis .This type of necrosis is occur in lymph nodes and spleen .In certain lymph nodes,specifically pulmonary hilar lymph nodes are effected. Germinal ceters of pulmonary hilar lymph nodes is damag .This lymph node is malfunction for filtration process (Ding et al., 2003; Lang et al., 2003).

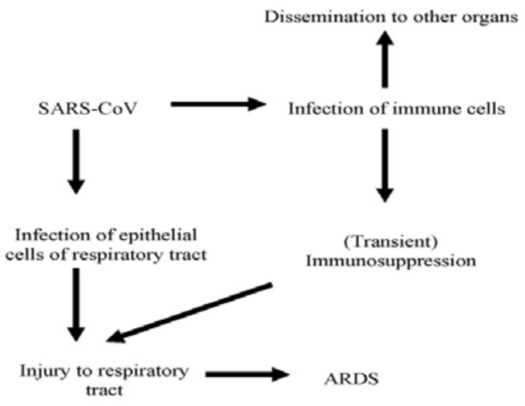

Fig. Diagram depicting the role of infected immune cells in the pathogenesis of SARS.

In SARS patients CD4 and CD8 cells have been reduced in specific amount although CD4/CD8-ratios persisted standard. T-lymphocytes ares begin to decrease from standard value after the infection of two weeks(Cui et al., 2003; Gu et al., 2005).

3. Bone marrow

In bone marrow biopsies the digestion of solid things has detected by SARS, whereas this information is absent in any other places. (SARS Research Group, 2004; Ng et al.,200) There is no any indication of hypoplastic bone marrow (Wong et al., 2003).. The negative impact of Reverse transcriptase polymerase chain reaction and In-situ hybridization is observing on bone marrow specimen (Ding et al., 2004; To et al., 2004).6

4. Digestive tract

Usually, there is no change observe in the processes work of digestive system. In few absolute cases of SARS, minute destruction in esophagus and inflammatory disorders together with self- digestion start (Gu et al., 2005)

5. Liver

Mitoses of liver cells, degradation of liver cells and minor or severe lymphocytic blockage observed in SARS auto-digested hepatocytes. Damages of fatty layers and damages at central point have been reported. Sudden death has confirmed in all the cases. SARS infection is proved by RT-PCR in liver tissues while ISH and EM cannot be detected the viral genome and viral particles (Chow etal., 2004; To et al., 2004).

6. The nervous system

This type of viral attack causes the infection of nervous tissue. In which infection the brain tissues start to disintegration and death of neurons and also demaged the gelial cells and nerve impulse pathway. (Xu et al., 2005).

7. The endocrine system

To check the effect on endocrine system, extract the thyroid gland from 5 patients which have infection by severe acute respiratory syndrome. Their Thyroid gland is suffering to planed cell death have shown by terminal deoxynucleotidyl transferase-mediated nick end labeling .in situ hybridization are used to know the viral genomic sequences. Viral genome sequences are not clearly known in thyroid cells estimate by in situ hybridization (Ding et al., 2004; Gu et al., 2005). SARs-cov

8. The reproductive system

Reproductive system is effect by severe acute respiratory syndrome. Germs cells of testes is damage in SARS patient. Spermatozoa in the seminiferous tubules are damage in this way thickness of basement membrane decrease. viral entities and thier genomic sequences does not cleary seen in the testes by in situ hybridization and electrone microscope (Ding et al., 2004; Xu et al., 2006

Status of Covid-19 in Pakistan

The number of confirmed COVID-19 cases in Pakistan has risen to 108,317 as of 09 June. Increase of 4,646 new cases and 105 deaths in the last 24 hours. The most affected province due to COVID-19 pandemic is Punjab 40,819 followed by Sindh 39,555. Prime Minister Imran Khan said the government expects coronavirus cases in the country to peak by end of July or early August. The Government decided in the NCOC meeting that the federal government would ensure increase of 1,000 beds with oxygen supply capability in the major cities of the country within the month of June. Khyber Pakhtunkhwa has recorded co-morbidities in 85 per cent of the people, who died of Covid-19, compared to 74 per cent among the nationwide deaths happened due to the pandemic. Now in January 2021 a new strain of corona virus has been emerged for UK and also shifted to Pakistan by international travelers and 4 confirmed cases from Karachi Pakistan has been registered

Preventions and measures

- The illness continuum varies from asymptomatic to cough, minor respiratory disorder, extreme pneumonia, or acute respiratory distress syndrome (ARDS).
- Big forms of spreading include touch from animal to object, from object to person, and from human to human.
- The risk of infection with Coronavirus shall be recognized in patients with Temperature, cough, shortness of breath AND heaviness
- wash hands frequently (While feeding or frying, after using the toilet and in soiled condition)
- healthcare workers must strictly adhere to the following moments of hand hygiene: before and after touching a patient, before clean or aseptic procedures, after coming in contact with patient surroundings and body fluids)
- Try adding tissue paper placed in bins forbid from spitting around you and use waste containers
- Care to avoid close contact with respiratory sufferers
- Avoid using unwashed hands to touch your eyes, nose or mouths.
- There are many companies claiming to provide effective vaccines but Pfizer antiviral vaccine is used in trials world widely since November 2020.

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