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REVIEW ON MIDDLE EAST RESPIRATORY SYNDROM CORONAVIRUS IN CAMELS OF AFRICA

Ayelech Mulneh[1], Gezahegne Mamo[2]

1. National Animal Health Diagnostic and Investigation Center (NAHDIC),Ethiopia

2. Addis Ababa University College of Veterinary Medicine and Agriculture (AAU), Ethiopia

ABSTRACT

Middle East respiratory syndrome (MERS) remains a disease of global public health concern. Many human infections in Middle East are zoonotic in origin, but some result from clusters of human-to-human transmission, especially within hospitals and health care facilities. Zoonotic disease has been reported from the Arabian Peninsula, and dromedary camels are the only confirmed source of zoonotic infection. Droplet transmission or direct contact with infected camels may be one way of transmission, the other possible way includes through food-borne transmission, consumption of unpasteurized camel milk/raw meat and the medicinal use of camel urine were common culture of the people. Globally,23 countries reported confirmed cases of camels MERS CoV/serologically and few of them characterized the virus. According to FAO, 2018 there are about 27 countries reporting human cases of MERS-CoV most of them caused with travel history from Middle East. Africa harbors more than 60% of the world population of the dromedary camels, in several African countries sero surveillance was done and in average more than 85% of the camels was found positive. In Africa, in spite of high sero positivity for MERS-CoV in camels, un like middle east there were no zoonotic report from Africa, the zoonotic significance of the diseases especially to high exposed groups of population were not well studied. Nowadays only few attempts to isolate the virus and perform molecular characterization of MERS-CoV in camel of Africa were seen. Hence, the objectives of this seminar are to review the prevalence of MERS-CoV in camels of Africa with particular emphasis on camels of East Africa and highlight the existing knowledge gaps in epidemiology, virology and potential zoonotic risk of MERS-CoV in the animal human interface.

Keywords: Africa, Diagnosis, Dromedary camels, MERS-CoV, Public health, Zoonotic

1. INTRODUCTION

Middle East Respiratory Syndrome corona virus (MERS-CoV) was first found in the Middle East, in 2012(Zaki *et al.,* 2012, Zumla *et al*., 2015; De Groot *et al* 2013). Given the diversity of animal corona viruses, it was not surprising when another human Corona virus was isolated from a patient presenting with severe respiratory illness in June 2012.The first victim, the 60-year-old man died as a result of renal and respiratory failure 11 days after admission to a hospital in Jeddah, Saudi Arabia (Zaki *et al*., 2012).

MERS-CoV is one of six known human corona viruses that cause respiratory disease in humans and, with a mortality rate >35% (WHO, 2016). MERS CoV is a lineage C beta corona virus with a genotype that is very closely related to bat corona viruses from the same lineage, such as BCoV-HKU4 and BCoVHKU5, though its evolutionary pathway is still unclear (Boheemena *et al.,* 2011). It is the first highly pathogenic human corona virus to emerge since the global threat caused by the severe acute respiratory syndrome corona virus (SARS-CoV) in 2002-2003.Kingdom of Saudi Arabia, the focal point of an ongoing MERS-CoV outbreak, the large number of religious pilgrims congregating annually in Saudi Arabia drastically increases the potential for the uncontrolled global spread of MERS-CoV infections (Gautret *et al*., 2013).

In fact, Human infections have already been reported in more than 27 countries across the Middle East, Europe, North Africa and Asia (Warner *et al*., 2015; Pas *et al*., 2016; Bin *et al*., 2016; Kraaij *et al*., 2014). Between 2012 and May, 2019, 2434 laboratory-confirmed cases of Middle East respiratory syndrome-coronavirus (MERS-CoV) infection were reported to WHO, 83% of whom were reported by the Kingdom of Saudi Arabia. Human cases reported countries were Middle East, North Africa, Europe, the United States of America, and Asia. Males above the age of 60 with underlying medical conditions, such as diabetes, hypertension and renal failure, are at a higher risk of severe disease, including death. Since 2012 to May 2019, 876 (35.5%) individuals have died (FAO, May 2019).

MERS-CoV uses dromedary camels as an intermediate host Archived camel sera (1983–1997) showed the presence of neutralizing antibodies suggesting long-term MERS-CoV circulation among camels (Muller *et al*., 2014). Zoonotic cases have been reported from the Arabian Peninsula and hence dromedary camels are the only confirmed source of the zoonotic infection, the origin of the virus and the extent of its involvement in both human and animal populations remain hot topics that are being explored with phylogenicity and surveillance studies (Haagmans *et al*, 2014).

The world camel population is estimated to be 26,989,193 of which 89% are single-humped dromedary and 11 % are Bactrian (two-humped). Africa has 85% estimated to be 24 million of the world's camel population; More than 60% of the world's camel population is found in the Horn of Africa region (FAO STAT, 2015). Dromedaries play a vital role in the livelihoods and survival of majority of the nomadic pastoralists in Africa. They generate income for their owners through provision of milk, meat, draught power, and transport (Marshall *et al*., 2014).

MERS-CoV is endemic in dromedaries in Africa including Ethiopia, and a number of reports indicated that a seroprevalence of camels MERS CoV reported 94% in -Ethiopia (Reusken Miguel *et al,2017*) in Kenya 60.8% (Deem *et al*., 2015) and in Tunisia 42% (Ruesken *et al*.,2014); Egypt 92.3% (Daniel *et al*.,2014). However; zoonotic infections have not been reported from Africa (Ruesken *et al*., 2016; Chu *et al*., 2014; Chu *et al*., 2015; Miguel *et al*., 2017).

Molecular characterization of RNA in African countries tends to follow some Phylogenetic differences in the continent according to chu *et al*., 2014 the Egyptian camels virus strain has an overall nucleotide similarity of 98-100% to ORF gene of human MERS CoV (EMC), in the sequence MERS CoV NRCE they found 12 aa differences in the nucleotide of the spike protein, but these aa have no impact on the binding domain of the virus .the other new findings were from Nigeria ,by sequencing those MERS CoV RNA positive specimen, they found that Nigerian strain genetically distinct from viruses found in the middle east and the strain of MERS CoV so far detected in human(Chu et al.,2014; Chu et al., 2015).

In previous study report, MERS-CoV from Egypt and Nigeria appears to be phylogenetically distinct from those currently circulating in the Arabian Peninsula (Chu *et al*., 2014; Chu *et al*., 2015). In another recent whole-genome sequence-based study report by Chu *et al*., (2018), which was conducted in four African countries (Ethiopia, morocco, Bukina faso and Nigeria) support the previous finding in that there was phylogenetical difference between Africans virus strain with each other and with Arabian Peninsula.

In this study positive specimen with high viral load selected and sequenced. Phylogenetic analysis was done for each PCR positive specimen from each country, the overall findings exhibit phylogenetic differences between two locations of the East and West Africa. In the three country: Burkina Faso, Morocco and Nigeria had signature deletion of the MERS CoV at ORF 4b and /or ORF3 gene region, in Burkina

Faso the length of ORF 4b gene truncated from EMC 246aa to 14 aa ,In the same way Nigerian viral isolate of ORF4b decreased in the length from EMC 246aa to 71aa,these deletion disrupt the PDE catalytic site .additionally the amino acide residue e in the receptor binding domain of the spike protein of AH13,Nigeria and Burkina Faso had Amino acid substitution, especially the Nigerian strain gene substitution may influence with interacting interface of the receptor binding domain with the host, hence the west Africans strain exhibit gene differences with the prototype strain of EMC AH13.and this phylogenetic difference may support the absence of zoonotic causes in Nigeria (west African country), while this differences not supported by antigenic test of the strains this means all strains in Africa remain antigenically similar by neutralizing sera produced by the strain of EMC spike vaccine. While virus from Ethiopia revealed similarity with Arabian Peninsula MERS-CoV, suggesting a potential significance for zoonotic transmission.

Therefore, the objectives of this review are:

- To review the prevalence of MERS-CoV in camels of Africa and highlight the existing knowledge gap in epidemiology, virology and potential zoonotic risk of MERS-CoV in the animal–human interface in Africa.
- To assess the availability of diagnostic techniques in MERS-CoV investigations.

2. AN OVERVIEW OF MERS-CoV

2.1. History of MERS-CoV

A novel CoV (named MERS-CoV) was isolated from the sputum of the patient and was identified as the causative agent of Middle East respiratory syndrome (Zaki *et al*., 2012). Since then, MERS-CoV has been an epidemic in the Middle East, and travel-associated cases have been reported in a number of countries outside the Middle East.

Up to 100 % MERS-CoV antibody sero positivity has been found in archived camel sera, demonstrating endemic presence of MERS-CoV in camel populations in Somalia since 1983, in Sudan since 1984, in Egypt since 1997, in Kenya from 1992 to 2013 (Muller *et al*., 2014; Corman *et al*., 2014), in the KSA since 1992/1993 (Alagaili *et al*., 2014) and in the UAE for at least one decade (Meyer *et al*., 2014; Alexanderson

et al., 2014). MERS antibody-positive camels are also reported from Oman, Nigeria, Tunisia, Ethiopia, Jordan and the Canary Islands (Reusken *et al*., 2014a, Reusken *et al*., 2014b).

Sero negative dromedary camel populations have so far only been found in Australia (Crameri *et al*., 2015) and in Kazakhstan No information on MERS in camels has been published from Afghanistan, or India, despite the fact that these countries have significant dromedary camel populations (Miguel *et al*., 2016).Screening of trade camels by PCR at Kingdom of Saudi Arabia (KSA) markets revealed a higher MERS-CoV carrier rate in local Kingdom of Saudi Arabia camels as compared to camels imported from Sudan and Somalia (Sabir *et al*., 2016). Anti-MERS-CoV antibodies were detected in archived serum samples from dromedary camels obtained in Saudi Arabia in 1993, and the United Arab Emirates in 2003 (Hemida *et al*., 2014; Meyers *et al*., 2013). Furthermore, many camels in Saudi Arabia are imported from East Africa (Woo *et al*., 2007; Wang *et al*., 2014; Yang *et al*., 2014; Drosten *et al*., 2014; Hemida *et al*., 2014; Corman *et al*., 2014; Muller *et al*., 2014; Muller *et al*., 2015). This showed that serum samples from camels in east, west, and North Africa were positive for MERS-CoV as early as 1992, indicating widespread circulation of MERS-CoV in camel populations for many years.

2.2. Virology

Corona viruses are species of virus belonging to the subfamily Coronavirinae in the family Coronaviridae, in the order Nidovirales (deGroot *et al*., 2011; ICTV, 2010). Coronaviruses are enveloped viruses with a positive-sense single-stranded RNA genome and with a nucleo- capsid of helical symmetry.

The genomic size of coronaviruses ranges from approximately 26 to 32 kilo bases; it is the largest for an RNA virus (Masters and Perlman, 2013). The name "coronavirus" is derived from the Latin corona, meaning crown or halo, and refers to the characteristic appearance of virions under electron microscopy (E.M.) we can appreciate it in Figure 1 with a fringe of large, bulbous surface projections creating an image reminiscent of a royal crown or of the solar corona. This morphology is created by the viral spike (S) peplomers, which are proteins that populate the surface of the virus and determine host tropism.

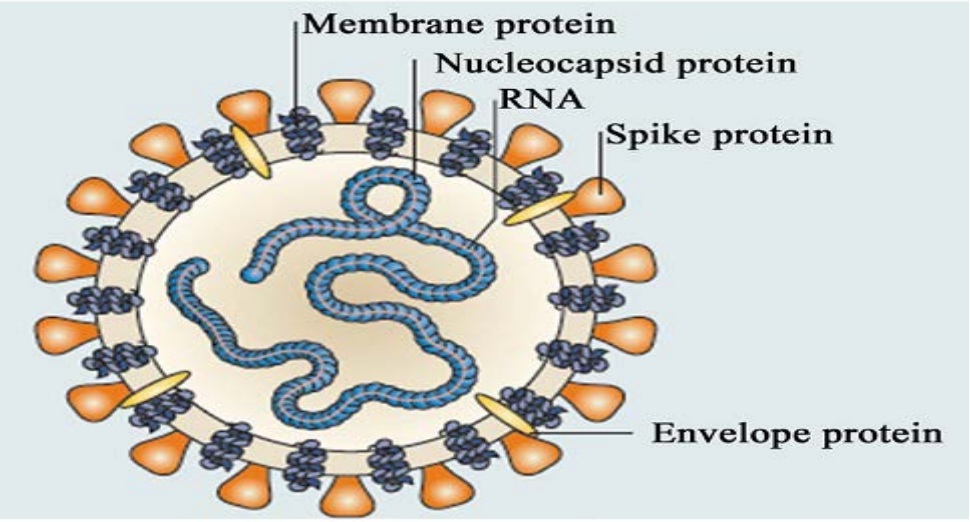

Figure 1. Genomic **s**tructure of corona virus. Source: (Graham *et al*., 2013).

Proteins that contribute to the overall structure of all coronaviruses are the spike (S), envelope (E), membrane (M) and nucleocapsid (N). In the specific case of the SARS coronavirus a defined receptor-binding domain on S mediates the attachment of the virus to its cellular receptor, angiotensin-converting enzyme 2 (ACE2)(Li *et al*.,2005) Some coronaviruses (specifically the members of Beta corona virus subgroup A also have a shorter spike-like protein called hemagglutinin esterase (HE)(de Groot et al .,2011).Coronaviruses have high rates of mutation and recombination and a propensity to cross host species (Masters *and* Perlman 2013).

2.3. Tissue Tropism

Originally, CoVs were thought to be limited to individual species and a narrow organ tropism in a given species (Kuo *et al.*, 2000; Li, 2008; Zhang *et al.*, 2006). The spike receptor protein, a very strong determinant of tissue and species tropism, binds to its cognate receptor and initiates viral entry into a host cell. To enter host cells, MERS-CoV attaches its receptor, dipeptidyl peptidase (CD 26) clearly stated in Figure 2. Protease cleavage of the S protein is then required for virus–cell fusion and release of genomic RNA into the cytoplasm.

There are also viral accessory genes that are thought to aid in immune evasion and viral replication in target species and tissues. Since the SARS-CoV outbreak, and the resulting population studies, it has been postulated that cross-species events occur more often than hypothesized originally (Rest & Mindell, 2003). The more recent 2012 emergence of the Middle East respiratory syndrome (MERS)-CoV underscores the potential for zoonotic spread of animal CoVs to humans. Thus, there is a continuing need for animal models of severe CoV disease (Assiri *et al.*, 2013; Memish *et al.*, 2013), the following picture indicates the MERS CoV receptor (DPP4) in camel and Human being is identical.

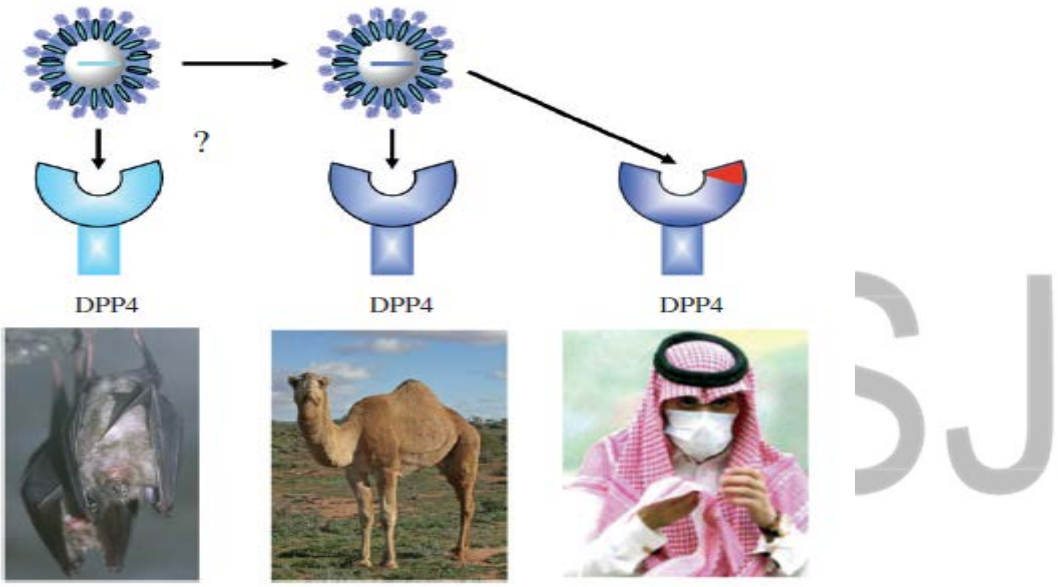

Figure. 2. MERS corona virus infection in humans and animals Source: (Judith et al., 2015)

MERS-CoV bind to a (DPP4) to enter cells, binding to the host-cell receptor is a major determinant of pathogenesis, since no infection occurs in its absence (Raj *et al*., 2013; Li *et al*., 2003). In humans, the virus has a strong tropism for nonciliated bronchial epithelial cells, and it has been shown to effectively evade the innate immune responses and antagonize interferon (IFN) production in these cells. This tropism is unique in that most respiratory viruses target ciliated cells; the amino acid sequence of DPP4 is highly conserved across species and is expressed in the human bronchial epithelium and kidneys (chan et al., 2014)

2.4. Classification

The classification of Coronaviruses has been based on genomic organization, similarities in genomic sequence, antigenic properties of viral proteins, replication strategies, and structural characteristics of virions, pathogenic, cyto pathogenic and physicochemical properties.Acordingly they have been divided in to Order, Family,subfamily and genus Figure 3 (Lai *et al*., 1997). The following Figure shows the order, Family, sub family and genus of Nidovirales including Corona virus.

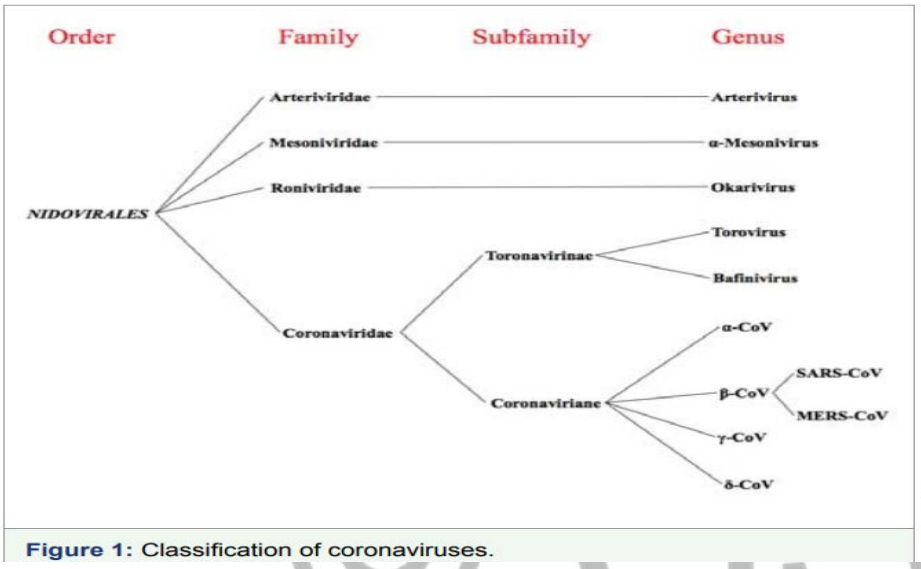

Figure.3: Classification of coronavirus Source: Tok, (2017)

2.5. Epidemiology

Dromedary camels are common animal of the Arabian Peninsula and also found in great numbers in many countries of the African continent. Camels are widely spread throughout the world, mainly in arid and semi areas, and serve important economic, livelihood, nutritional and social purposes. Camels are thought to be a natural reservoir of MERS-CoV and can be a source of CoV transmission (FAO, 2017).

Globally more than 23 countries from different continent reported the prevalence of MERS-CoV in camels (FAO, 2018; Omrani et al., 2015). Additionally, 27 countries have reported human cases of MERS-CoV in the Middle East, Africa, Europe, Asia and United State of America (FAO, 2018). Nevertheless, the majority of cases have so far occurred in Saudi Arabia. Where active cases continuing to kill people.

according to some studies MERS-CoV has been circulating in dromedary camels figure 4, since at least 1992 . All cases and outbreaks outside of this region can be traced back to someone who travelled from the Middle East (FAO , 2017). The virus has crossed from dromedaries to humans in the Arabian Peninsula, but this hasn't been observed in any African countries (FAO, 2018).

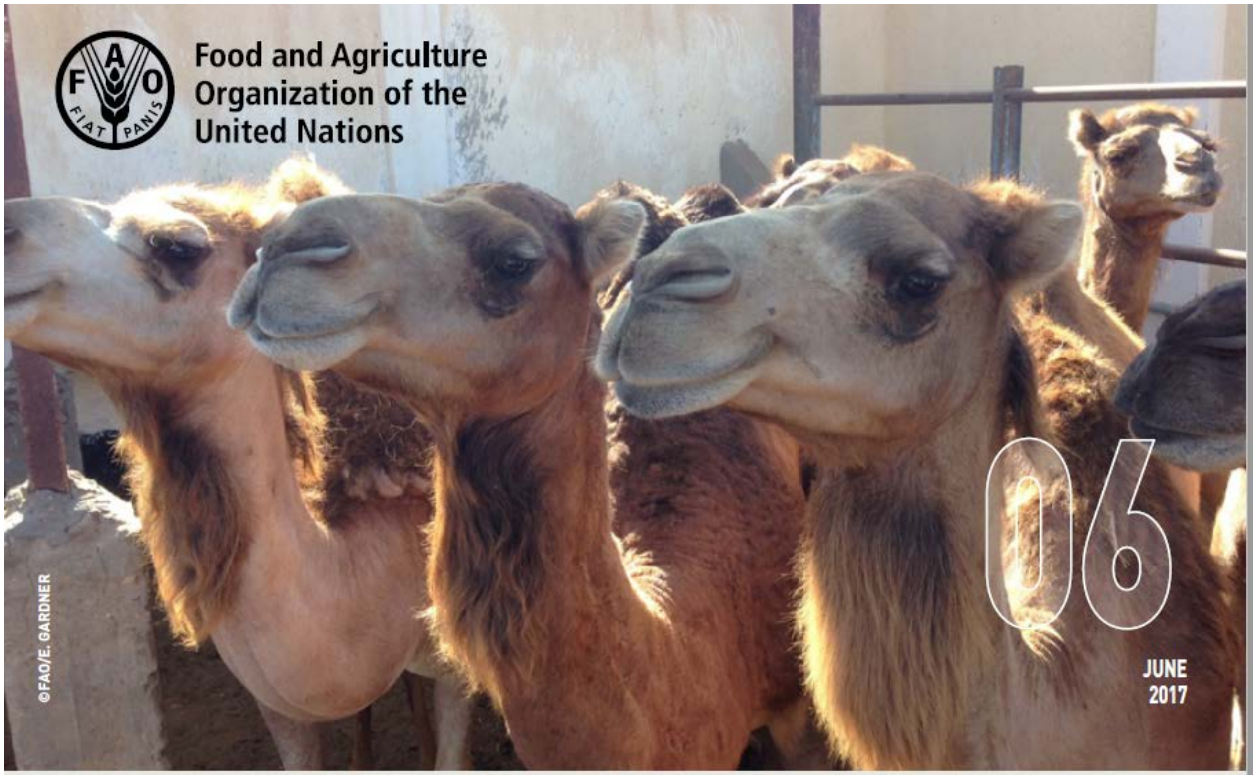

Figure.4: Dromedary Camels, Source: FAO, (2017)

2.5.1 Epidemiology of MERS-CoV in camels based on Serology and/or Virology

Based on FAO update the following countries have confirmed and published Animal cases in the world organized in table 1: Bangladesh, Burkina Faso, Chile, Egypt, Ethiopia, Iran, Israel, Jordan, Kenya, Kuwait, Mali, Morocco, Nigeria, Oman, Pakistan, Qatar, Saudi Arabia (KSA), Somalia, Spain (Canary Islands), Sudan, Tunisia, United Arab Emirates (FAO,2018). From these countries, only few of them are able to characterize and studied the virology and the sero epidemiology of the disease.

Table.1: The table shows the countries conducted Virology/serology test on camels and the technique they use.

No	Country	Virology/Serology	No	Country	Virology/Serology
1	KSA	Both	12	Nigeria	Both
2	Qatar	Both	13	Sudan	Serology
3	UAE	Both	14	Oman	Both
4	Jourdan	Both	15	Somalia	Serology
5	Egypt	Both	16	Kenya	Serology
6	Tunisia	Serology	17	Ethiopia	Both
7	Morocco	Both	18	Israel	Serology/virology
8	Bangladesh	Serology	19	Pakistan	Serology
9	Burkina Faso	Both	20	Spain	Serology
10	Chile	Serology	21	Mali	Serology
11	Iran	Serology/virology			

Source: Chu *et al*., (2014); Chu *et al*., (2015); Fekadu *et al*., (2016); Miguel *et al*., (2015); Deem *et al*., (2015).

2.5.2 Global distribution of Confirmed human MERS-CoV

According to the current update of FAO, Between 18 July and 24 August 2018 (table 2), seven new human cases have been reported, six in Saudi Arabia, including two fatalities, and one in the United Kingdom (FAO,2018).

Table.2: The table shows globally confirmed human MERS Cov

No	Country	No	Country	No	Country
1	Jordan	10	German	19	Turkey
2	Saudi Arabia	11	Italy	20	Austria
3	Qatar	12	Tunisia	21	Greece
4	UAE	13	Malasia	22	Korea
5	Oman	14	Philipins	23	Chaina
6	Yemen	15	USA	24	Thailand
7	UK	16	Lebanon	25	Bahrain
8	France	17	The Netherlands	26	Egypt
9	Iran	18	Algeria	27	Kuwait

Source : (FAO, 2018)

2.5.3 Abattoir workers Serological result in Africa

In some Studied African camels there were positive findings for Viral RNA and serum antibody, as camels are the source of infection for humans, attention is not well given for public health status especially for those peoples having intimate contact with these animals in Africa. Only there are few reports from the continent, concerning MERS CoV in public health, it is a good start and should be appreciated. The first one is from the east African country Egypt: 179 sera samples were collected in Egypt Cairo from peoples working in camel abattoir specially from those having intimate contact with MERS CoV positive camels,they tested for MERS CoV specific antibody and the laboratory result showed all were Negative (Daniel *et al*., 2014).

The other report was from west African country Nigeria, 261camel abattoir workers tested for MERS CoV specific antibody, the history of these peoples were they have repeated occupational exposure to camels at an abattoir in Kano, Nigeria, many of whom also reported drinking fresh camel milk (n = 138) or eat raw meat (n = 94) or using camel urine for medicinal purposes (n = 96),The laboratory Results showed that none of the abattoir workers with exposure to camels had evidence of neutralizing antibody to MERS-CoV (So *et al*., 2018). From these report we can understand that there are same knowledge gaps about the character of

the virus especially in east Africa which need extensive research on the MERS CoV strain circulating in the region.

2.6 Host range

Even though Corona viruses are widespread in the animal kingdom MERS-CoV seems to have a narrow host range (Woopc *et al*., 2012). In the last few years, a large spectrum of domestic species has been tested and found negative for MERS-CoV antibody; it included horses, cattle, pig, water buffalo, chickens and goats (Perera *et al*., 2013; Reuskan *et al.,* 2013; Miguel *et al*., 2016; Hemida *et al*., 2013). This indicates that the host range of MERS CoV currently limited to Dromedary camels from domestic animal.

Corman and colleagues characterized the full genome of an African bat virus closely related to MERS-CoV and showed that human, camel, and bat viruses have phylogenetic relationships although these bat viruses are not closely similar to MERS-CoV. They suggest that, according to available serologic data on camels and humans since 2012 and molecular investigations of known cases, MERS-CoV moved from bats to camels in sub-Saharan Africa (Corman *et al*., 2014).

Camelids could be the “mixing vessels” for MERS-CoV and other mammalian CoVs and that the virus can be transmitted between humans and camels (Corman *et al*., 2014). Up to now, MERS-CoV-like viruses have not been detected in any domestic animal species other than camels while from wild animal an unconfirmed report of the detection of a very small fragment of MERS-CoV-like RNA in a specimen from a *Taphozous perforatus* bat collected in Saudi Arabia was reported by Memish *et al*., (2013).

2.7 Reservoir Animals

2.7.1 Bats as Putative Origin of MERS-CoV

Bats are known natural reservoirs for several emerging viral infections in humans including rabies, Nipah virus, Hendra virus and Ebola virus (Han *et al*., 2015). Several features enable bats to be efficient sources of emerging human viral infections. MERS-CoV belongs to *Beta corona virus* Lineage c, along with bat corona viruses HKU4 and HKU5 (Woo *et al*., 2007; Corman *et al*., 2014). It is therefore not surprising that initial efforts to identify the origins of MERS-CoV focused on bats (Drexler *et al*., 2014; Omrani *et al*., 2013).

Throat swabs, urine, faces and serum samples were collected from wild bats in Saudi Arabia including the area where the first MERS-CoV patient had lived and worked. Several corona viruses were identified in 227 of 1003 samples. A 190-nucleotide fragment of the RNA-dependent RNA polymerase (RdRp) region of MERS-CoV genome was detected in one fecal pellet from an Egyptian tomb bat (*Taphozous perforates*) (Memish *et al*.,2013). The sequenced amplification product was identical to that of the MERS-CoV sequence obtained from the first index human case (Zaki *et al*., 2012; Memish *et al*., 2013).

Away from the Arabian Peninsula, novel MERS-CoV related corona viruses were detected in slit-faced bats (*Nycteris gambiensis*) from Ghana and pipistrelle bats (*Pipistrellus pipistrellus, P. kuhlii, P. nathusii, P. pipistrellus and P. pygmaeus*) from Germany, the Netherlands, Romania and Ukraine (Annan *et al*., 2012). The 816-nucleotide RdRp amino acid sequence of the novel *Pipistrellus* and *Nycteris* bat viruses differed from that of MERS-CoV by only 1.8%and 7.5%, respectively.

Novel beta corona viruses closely related to MERS-CoV have also been identified from Asian parti-colored bats (*Vespertilio superans*) in China, serotine bats (*Eptesicus serotinus*) in Italy and broad-eared bat (*Nyctinomops laticaudatus*) in Mexico, in addition to bat guano fertilizer from Thailand (Yang *et al*., 2014; Wacharapluesadee *et al*., 2013). In another study, a novel beta corona virus named Neo CoV was identified in a vesper bat (*Neoromicia capensis*) from South Africa. The sequenced 816-nucleotide RdRp fragment from Neo CoV differed from that of MERS-CoV by only one amino acid (Ithete *et al*., 2013).

Recent study in kenya reveals alsoThe detection of distinctive HCoV -NL63 -like and HCoV -229E -like sequences in bats shed s new light on CoV evolution. In particular, it provide strong evidence that HCoV -NL63 has a zoonotic recombinant origin. Although the majority of the HCoV -NL63 genome originate s from the viruses circulating in Triaenops afer bat s , its spike protein gene is derived from a 229E -like virus

circulating in Hipposideros sp p. bats . However, despite the strong signal for recombination, both putative parental strains show substantial genetic distancess from human CoVs. This most likely reflects extensive post -recombination sequence divergence, which in turn suggests that the recombination event has occurred prior to the emergence of HCoV -NL63 in humans(Ying Tao et al .,2017).

The close relatedness of MERS CoV and various bat viruses allows speculation that its ancestors might exist in Old World bats (Corman *et al.*, 2013). Though S protein of the bat corona virus HKU4 can recognize human DPP4, it is not activated by human proteases and therefore cannot mediate viral entry into human cells (Yang *et al.*, 2014; Wang *et al.*, 2014).

2.7.2 Dromedary Camels as Reservoirs for MERS-CoV

Multiple lines of evidence implicate dromedary camels in the emergence and transmission of MERS-CoV. Firstly, MERS-CoV antibodies are highly prevalent in dromedary camels from across the Arabian Peninsula, North Africa and Eastern Africa (Reusken *et al*., 2013; Hemida *et al*., 2013; Alexanderson *et al*., 2014).

Another evidence to link MERS-CoV to dromedaries was found after two human cases of MERS-CoV infection, diagnosed in October of 2013, and were linked to a farm in Qatar (Haagmons *et al*., 2013). In response, all the 14 dromedary camels on that farm were tested with RT-PCR; eleven dromedary camels had positive nasal swabs for MERS-CoV. The nucleotide sequence of an ORF1a fragment and a 4.2 kb concatenated fragment of three dromedary camel samples were very similar to the sequence from the two human cases linked to that farm (Haagmans *et al*., 2013).

Another study from Saudi Arabia described a 43 year old man who owned nine dromedary camels and who have direct contact with them up, until he was diagnosed with MERS-CoV infection in November 2013, four of his dromedary camels were slightly sick before his symptoms started. Cell cultures from a laboratory confirmed dromedary camel and the patient grew genetically identical MERS-CoV viruses (Azhar *et al*., 2014). The above evidence suggests that dromedary camels are reservoir of the virus.

Another study by (Chu *et al*., 2018), implicate that Ethiopian camels carried MERS CoV isolate Phylogenetically and antigenically similar with the isolate of Arabic peninsula(Figure 5), even though there was no any zoonotic report, but it indicates that the camels are the carrier of the virus without apparent infection sign on them. Those Ethiopian isolates taken from the phylogenetic tree are the following (Chu *et al*., 2018).

1. MERS-CoV camel/Ethiopia/AAU-EPHI-HKU4412/2017(Eth4412),
2. MERS-CoV camel/Ethiopia/AAU-EPHI-HKU4448/2017(Eth4448) and
3. MERS-CoV camel/Ethiopia/AAU-EPHI-HKU4458/2017(Eth4458).

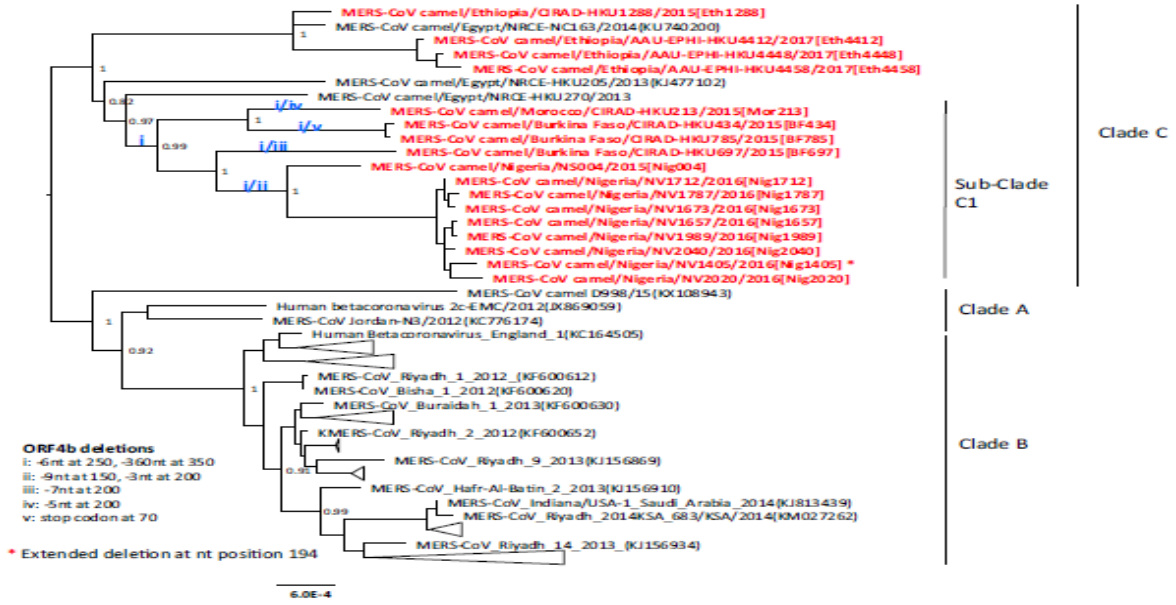

Figure. 5: African camel MERS CoV isolate Phylogenetic tree, source: Chu et al., (2018) 3. TRANSMISSION

3.1. Transmission from camels to humans

Experimental camel infected with MERS CoV for research purpose confirmed susceptibility, with a large quantity of virus shedding from the upper respiratory tract (Adney *et al*., 2014). Therefore, droplet transmission or direct contact with infected camels(figure 6) may be the most likely mode of camel-to-human transmission of MERS CoV (Memish *et al*., 2014; Azhar *etal*.,2014).

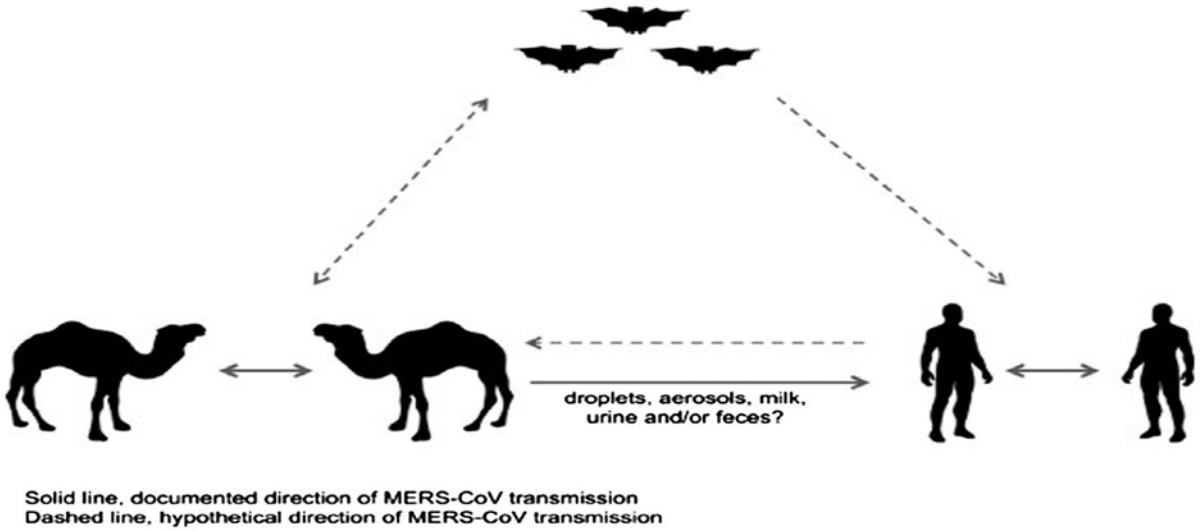

Figure. 6: Inter and Intra Species transmission of MERS CoV Source: Omrani *et al*., (2015)

The epidemiology of many human MERS-CoV infections could not be correlated to the contact with diseased humans and therefore it was suspected that these patients might have been infected from other sources, since many infectious diseases have their origin in animals (Wool *et al*., 2012; Wool and Gowtage, 2005).

The route of transmission from animals to humans is not fully understood, but dromedary camels are a major reservoir host for MERS-CoV and an animal source of infection in humans. Strains of MERS-CoV that are identical to human strains have been isolated from dromedaries in several countries, including Egypt, Oman, Qatar, and Saudi Arabia (Perera *et al*., 2013; Reusken *et al*., 2013).

In one study where livestock species such as dromedary camel, goat, sheep and cattle have been investigated together, only the livestock species dromedary camel harbored neutralizing antibodies against MERS-CoV (Reusken *et al*., 2013a, Reusken *et al*., 2013b). This and other findings indicated that, infected dromedary camel acts as donors of the viruses for humans rather than the other way around (Corman *et al*., 2014a).

3.2. Transmission between infected and non-infected humans

Transmission of MERS-CoV has been reported via two routes, between infected and non-infected humans and between dromedary camels and humans. The existence of clusters of infected medical staff and families play great role in the potential of the virus to spread between humans. Aerosol transmission and direct

contact is the main route of transmission in hospitals as well as in the environment (Memish *et al*., 2013; Assiri *et al*., 2013). The basic reproduction number (R0), which is a measure to determine the contagious nature of the pathogen has been determined to be <1 in MERS CoV and is relatively low compared to highly infectious diseases (such as Measles, which has an R0 >15) (Cotten *et al*., 2014). Therefore, the current MERS-CoV has a very low potential to cause a pandemic. But since coronaviruses mutate constantly has the potential to cause a pandemic if a mutation leads to a highly transmissible and virulent virus (Cotten *et al*., 2014).

The transmission of the MERS-CoV has been shown between humans; many humans that have been infected were male above 50 years of age and had underlying diseases such as diabetes or liver disease (Zumla *et al*., 2015). The exact mechanisms of infection and the minimal infectious dose are not fully understood at the moment; however, MERS-CoV infections that lead to clinical signs have been shown to have a high rate of mortality of about 40 % (Cotten *et al*., 2014).

The virus does not pass easily from person to person unless there is close contact, such as providing unprotected care to an infected patient. There have been clusters of cases in healthcare facilities, where human-to-human transmission appears to have occurred, especially when infection prevention and control practices are inadequate or inappropriate. Human to human transmission has been limited to date, and has been identified among family members, patients, and health care workers. While the majority of MERS cases have occurred in health care settings, thus far, no sustained human to human transmission has been documented anywhere in the world (FAO, 2018).

4. CLINICAL SIGNS

4.1. Clinical Signs of MERS CoV in inoculated Dromedary Camels

The fact that significant clinical disease is not recognized in relation to MERS-CoV in dromedary camels indicates a well-established balance between the camel host and the MERS CoV. A limited experimental infection of naive camels with MERS-CoV produced only mild symptoms (Figure 7) (Adney *et al*., 2014).

MERS-CoV infections in dromedary camels are often asymptomatic or associated with short periods of nasal discharge (rhinitis). Only experimentally inoculated camel showed minor clinical signs like consisting of rhinorrhea, slight increase in temperature yet no other clinical signs were observed.

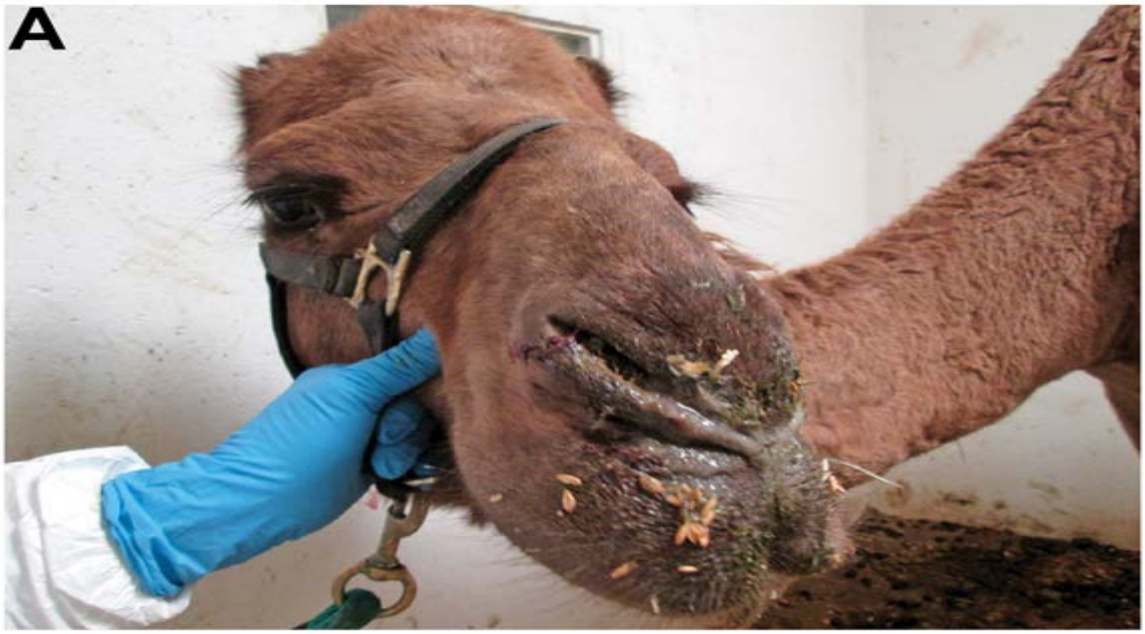

Figure.7: Clinical signs of MERS-CoV inoculated camel Source: Adney *et al*., (2014).

Rhinorrhea developed in inoculated camels and persisted less than two weeks. The nasal discharge drained from both nares varied in character from serous to purulent; minor hemorrhage was also observed on some occasions, hence MERS-CoV sequences have been detected more commonly in nasal swabs than in rectal specimens of camels (Alagaili *et al*., 2014; Hemida *et al*., 2014).

4.2 Clinical signs in humans

Corona virus can cause respiratory and enteric infections and therefore the patients can present with varying symptoms such as high-grade fever, non-productive cough, and shortness of breath, headache, myalgia, nausea, vomiting and diarrhea (Sharif *et al*., 2014). Development of Acute renal failures (ARF) is associated with underlying conditions such as diabetes, chronic cardiac disease, chronic renal disease, chronic lung disease and immune-compromised persons including pregnant females and infants (WHO, 2015; Mailles *et al*., 2013; Eckerle *et al*., 2013).

The number of patients who died was significantly higher among source case-patients (2/3, 67%); than among healthcare-associated case-patients (2/27, 7%) Most of the patient died due to respiratory and kidney failure (Hunter *et al*., 2016).

5. DIAGNOSIS

There are different types of laboratory tests which are found for screening and confirmation of MERS CoV.Most Serological assays have improved and sensitivity and specificity have increased (Dorsten *et al*., 2014; Hemida *et al*., 2014; Perera *et al*., 2013).

5.1. Virus Isolation

Cell culture for propagation and identification of viruses is an important component of the clinical virology laboratory. Since viruses are obligate intracellular parasites, they require living cells to replicate. In general, diagnostic tests can be grouped into three categories: direct detection, indirect examination (virus isolation), and serology. In direct examination, the clinical specimen is examined directly for the presence of virus particles, virus antigen or viral nucleic acids. In indirect examination, the specimen will be inoculated into cell culture, eggs or animals in an attempt to grow the virus: this is called virus isolation (Coleman and Frieman, 2015).

Cell culture: Monolayer cultures of primary, diploid, and continuous cell lines are the hosts of choice for virus isolation. Quality cell cultures are available commercially and are conveniently maintained in the laboratory. After proper decontamination and purification, each clinical sample is inoculated into several types of cell cultures; the preferred lines vary from virus to virus (Leland and French, 1988).

Growth of MERS-CoV: MERS-CoV productively infects a number of cell lines; new stocks of MERS-CoV can becreated by simple infection and collection of supernatant. However, it is important to note that different strains of MERS-CoV may grow at different rates, which affects the point at which supernatant should be harvested for maximum yield. MERS-CoV causes damage to and, ultimately, death of infected cells, therefore a good guide to the success of the virus growth is observation of cell death, termed the cytopathic effect (CPE) once the virus has multiplied it is possible to conduct different serological and molecular technique to study the characteristics of the virus(Coleman and Frieman,2015).

The appearance of CPE (Figure 8) can be strain specific or dependent on the starting titer of the seed stock. One can observe significant CPE with MERS-EMC at 48 hours post-infection, and significant CPE with MERS-Jordan at 72 hours post-infection. We would recommend checking the flask daily from 48 hours post-infection onwards. Collect supernatant from the infected flask and centrifuge at 500g for 5 minutes to remove any cellular debris. Aliquot appropriate volumes (100µl–1ml) of the clarified supernatant into 1.5ml screw cap tubes and store at −80°c until needed (Coleman and Frieman, 2015).

CAUTION: MERS-CoV is a Biosafety Level 3 (BSL-3) pathogen. Follow all appropriate guidelines for the use and handling of pathogenic microorganisms.

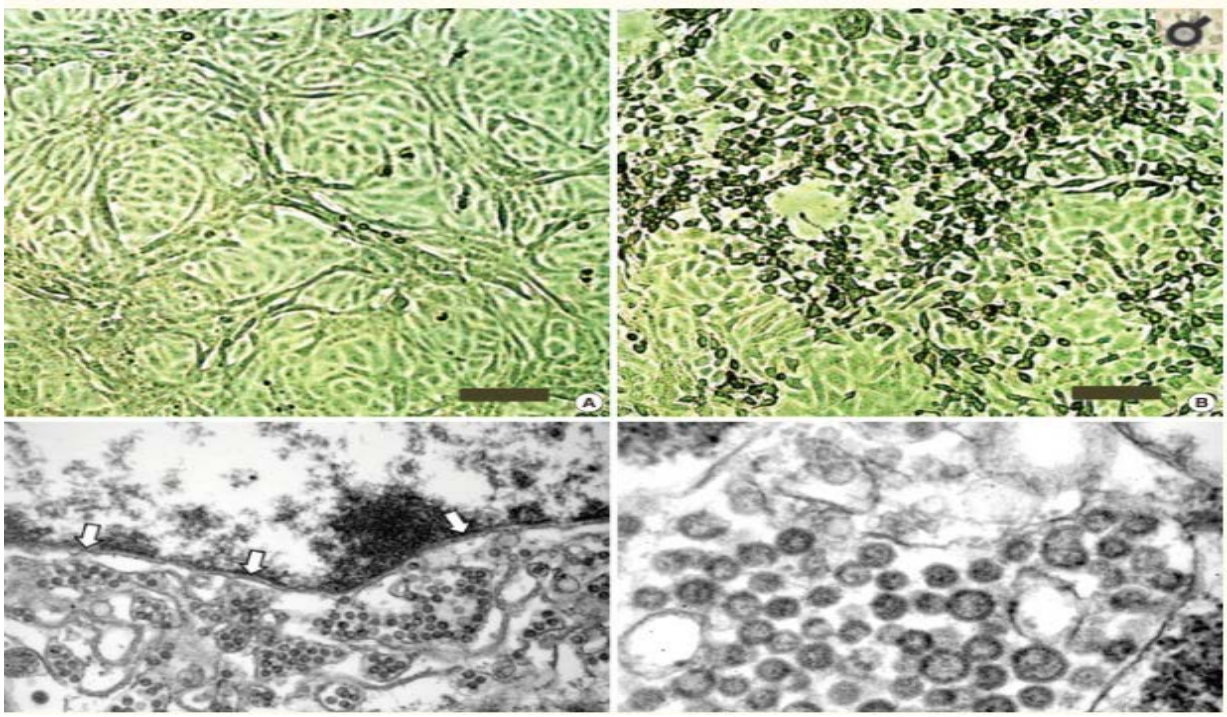

Figure 8: Cytopathic effect of MERS CoV on vero cell. Source: Park et al.,(2015).

Cytopathic effects of MERS-CoV in Vero cell cultures and Electron microscopy image of MERS-CoV. Vero cells were inoculated with oropharyngeal swab sample. (A) Vero cell cultures in negative control. (B) Cytopathic effects (rounding and detachment of cells) in Vero cell cultures 3 days after inoculation of the sample.

5.2 Detection of Virus Antibody

Regardless of the method of cultivation, once a virus has been introduced into a whole host organism, embryo, or tissue-culture cell, a sample can be prepared from the infected host, embryo, or cell line for further analysis under a bright field, electron, or fluorescent microscope or by other molecular and serological techniques. Cytopathic effects (CPEs) are distinct observable cell abnormalities due to viral infection**.**

5.2.1 Micro neutralization test

The micro neutralization assay is a highly specific confirmatory test used to measure neutralizing antibodies, or antibodies that can neutralize virus. This method is considered the "gold standard" for detection of specific antibodies in serum samples. And neutralization tests set up using susceptible cell lines and whole virus particles these assays require biosafety level III facilities to work with the infectious MERS-CoV in-vitro, limiting their usage. (Dorsten *et al*., 2014; Aburizaiza *et al*., 2014).

Sera which contain antibodies to the virus in question are able to neutralize the aliquot of virus used in the test, thus preventing infection of the cells when they are added to the plate. Where high concentrations of antibody to the virus in question are present in the serum sample, virus neutralization will occur even at high serum dilutions. Conversely, where little or no antibody to the virus is present in the test sample, it will be unable to neutralize the aliquot of infectious virus at the first dilution used in the test. The result of the test is the point at which the serum sample has been diluted such that it is no longer able to neutralize the virus in the test. This dilution, or its log equivalent, is reported as the titer of the serum tested, for MERS study all procedure should be conducted in BSC level III (Park *et al*., 2015).

5.2.2 Pseudo particle virus Neutralization Test

For those pathogens classified to be handled in a bio safety level 3 or 4 (BSL-III or IV) at high level biosafety settings, Due to these stringent biosafety requirements, options for clinical diagnosis or epidemiological studies of these diseases by a pseudo viral particle neutralization (PPNT) assay was developed that can detect neutralizing antibody to MERS COV virus in BSL-2 containments. Methods for

the pseudo viral particle production and VNT assay were essentially identical (Perera *et al*., 2013) and The MERS S ppNT is a sensitive and specific assay used for detecting NAbs against MERS-CoV (Wang *et al*, 2016).

Principle of the test: A codon-optimized GP sequence of MERS CoV was chemically synthesized (Descript) and sub cloned into a protein-expressing vector, pcDNA3.1. The resulting pseudo viral particle is capable of achieving only a single-round infection and contains a luciferase reporter gene that can be expressed in infected cells. Anti-GP neutralizing antibodies can inhibit the entry of this pseudo viral particle into cells, thereby inhibiting the expression of luciferase in the assay (Garcia *et al*., 2009; perera *et al*., 2013*).*

Pseudo virus expressing the MERS-CoV S protein was prepared using the Env-defective and luciferase-expressing HIV-1 genome, and the ppNT was performed as described by (Gierer *et al*., 2013).

A lent virus-based MERS-CoV S pseudo virus was pre-incubated with serially diluted serum samples from the patients with MERS-CoV at 37 °C for 1 h, and the mixtures were distributed into 96-well plates containing monolayers of Huh7.5 cells. After 24 h of incubation, fresh medium was added, followed by incubation for an additional 48 h. The cells were washed with PBS and then lysed using the lysis reagent included in the Luciferase Kit (Promega, Madison, WI, USA). Aliquots of cell lysates were transferred to 96-well Costar flat-bottomed luminometry plates (Corning Costar, Corning, NY, USA), followed by addition of the luciferase substrate (Promega). Relative fluorescence intensity values were immediately determined using a Gaomax illuminometer (Promega) (Garcia *et al*., 2009; perera *et al*., 2013*).*

The luciferase activity of Huh7.5-CD81 cells treated with pseudo virus alone (reference group) was defined as 100% infection. Cells not treated with pseudo virus were included as a background control. The results were expressed as the percentage of infection compared with those of the control group (Huh7.5 cells treated with only pseudo virus preparations).

Fifty percent reductions in relative fluorescence intensity were used to calculate MERS-CoV-specific neutralizing antibody (NAb) titers in the sera. The NAb titers were defined as the highest serum dilutions that resulted in a 50% reduction in luciferase activity. NAb titers lower than 1:100 were considered negative (Garcia *et al*., 2009; perera *et al*., 2013*).*

5.2.3 Enzyme Linked Immune Sorbent Assay

Principle of Indirect ELISA EUROIMMUN MERS CoV antibody test: The ELISA test kit contains micro titer strips each with 8 break off reagents wells coated with purified S1 antigen of MERS coronavirus (MERS-CoV S1). In (Figure 9) the first reaction step, diluted samples are incubated in the wells. In the case of Positive samples, specific IgG antibodies (also IgA and IgM) will bind to the antigens (Test instruction for MERS CoV, 2017).

to detect the bound antibodies, a second incubation is carried out using an enzyme-labeled anti-camel IgG (Enzyme conjugate) catalyzing a color reaction, the addition of substrate will produce color in those positive wells, the color production in the wells are directly proportional to the presence of specific antibody against MERS CoV. The intensity of color will be measured by spectrophotometer at 450 nm (Test instruction for MERS CoV, 2017).

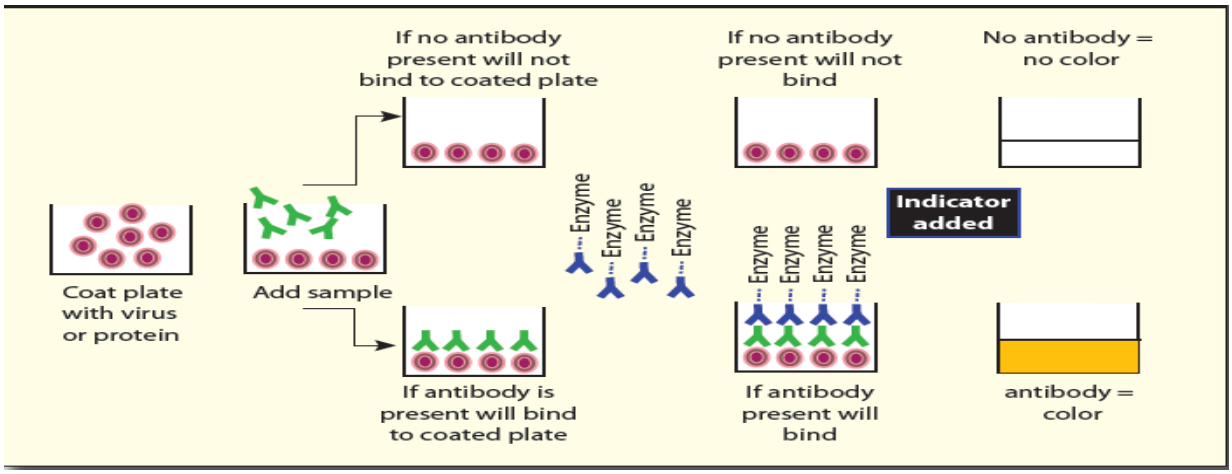

Figure .9: Principle of indirect ELISA Source: *Virology Techniques, Chapter 5 - Lesson 4*

5.3 Molecular characterization

5.3.1 Real-time reverse-transcription polymerase chain reaction (RT-rtPCR)

Reverse Transcription PCR (RT-PCR) is used to amplify DNA from RNA. The Enzyme Reverse transcriptase reversely transcribes RNA into cDNA, which is then amplified by Real Time Quantitative PCR

(RT-qPCR.PCR technology has a number of advantages. It is fairly simple to understand and to use and produces results rapidly. Real-time reverse transcription PCR (RT-PCR) targeting upstream of E gene of MERS-CoV was used for screening (Figure 10). The open reading frame (ORF) 1a gene was used for confirmation as recommended by the World Health Organization (Corman *et al*., 2012; WHO, 2013).

The technique is highly sensitive with the potential to produce millions to billions of copies of a specific product for sequencing, cloning, and analysis. (Corman *et al*., 2012). In MERS CoV diagnosis it is one of the most reliable laboratory technique used as confirmatory test. The first probe and primer sets for MERS-CoV detection by RT-rtPCR were developed shortly following the first reports of the disease (Corman *et al*., 2012).

The primers used include for upE target includes forward (Fwd) (GCAACGCGCGATTCAGTT), UpE reverse (Rev) (GCCTCTACACGGGACCCATA), and 200 nm of probe upE-Prb (6 carboxy fluoresce in (FAM) CTCTTCACATAATCGCCCCGAGCTCG 6 carboxy N, N, N, N' tetramethyl rhodamine (TAMR); Primers for ORF1b includes Fwd (TTCGATGTTGAGGGTGCTCAT), ORF1b Rev (TCACACCAGTTGAAAATCCTAATTG), and probe ORF1b Prb (6 carboxy fluoresce in [FAM]) CCCGTAATGCATGTGGCACCAATGT-6 carboxyN, N, N, N'-tetramethyl rhod amine (TAMRA). The primers for ORF1a include Fwd (CCACTACTCCCATTTCGTCAG), ORF1a Rev (CAGTATGTGTAGTGCGCATATAAGCA), and probe ORF1a Prb (6 carboxy fluoresce in (FAM) TTGCAAATTGGCTTGCCCCCACT-6-carboxy-N, N, N, N'-tetramethylrhodamine (TAMRA)). Thermal cycling involves 55˚C for 20 minute (min), followed by 95˚C for 3 min and then 45 cycles of 95˚C for 15 seconds (s), 58˚C for 30 s, 72˚C for 30 s (Corman *et al*., 2012).

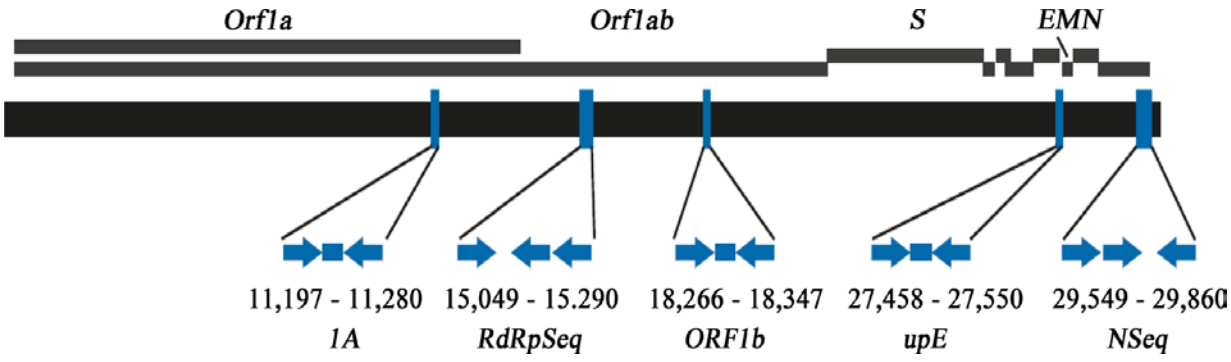

Figure. 10: RT-rtPCR target regions for screening, confirmation and sequencing of novel human corona virus (HCoV-EMC). Source: Corman *et al*.,(2012).

For detection of MERS CoV the target regions are the upstream of the E protein gene (upE), ORF1b, and ORF1a are the recommended site for amplification and detection (Corman *et al*., 2012).

5.3.2 Ssequencing

DNA sequencing is the process used to determine the order of nucleotides in a specific DNA/cDNA molecule. This information is useful for researchers in understanding the type of genetic information that is carried in the DNA, Specially in MERS COV it is currently used for comparison of genetic difference between viral isolates.

Two different RT-PCRs to produce amplicons for sequencing were designed. One amplicon was from the *RdRp* gene, a common target for CoV detection and a genome region where sequences for most coronaviruses are available (*RdRpSeq* assay). The assay was designed to provide broad detection of *Betacoronavirus* clade C sequences including hCoV-EMC as well as related viruses from animal sources such as bats (unpublished observations). The other amplicon was from a highly specific fragment within the hCoV-EMC *N* gene (*NSeq* assay) This region was chosen because it comprised a two amino acid (6 nt) deletion in the corresponding sequence published from a patient treated in London, United Kingdom . both amplicons were sensitive enough to detect cell culture-derived virus at very low concentrations. Both assays also yielded amplification products from the bronchoalveolar lavage sample from the Essen patient, in spite of its very low RNA concentration (Corman et al.,2012).

Procedure: The first and most important factor in automated DNA sequencing is clean, pure template. Once a pure and clean PCR product is available it is ready to perform a sequencing reaction. For a sequencing reaction to be successful all excess primers, dNTPs, salts and residual RNA and proteins must be removed from the sample. Most laboratories routinely use Qia Quick PCR clean up columns from Qiagen. Once PCR reaction has been cleaned, it is always a good idea to run it on an agarose gel to assure purity. Quantization of your PCR products after clean up is also helpful since no clean-up protocol results in 100% yield.

Purified PCR amplicons were sequenced with the PCR primers in both directions on an ABI Prism 3130 Automated Capillary Sequencer (Applied Bio systems Foster City, CA, USA) using Big Dye 3.1 cycle sequencing kits (Life Technologies, Carlsbad, CA, USA). The Sanger sequence data were analyzed using Sequencer 5.0. Ends and low-quality regions were trimmed manually, Contigs and consensus sequences were generated (Yusof *et al*., 2017).

In human MERS CoV Genetic sequencing was performed on a subset of isolates from PCR confirmed cases.Full genome sequencing from original respiratory samples was better determined by using the Sanger method (direct genome walking PCR). And next-generation sequencing approaches (IlluminaMiSequencer,http://www.illumina.com/systems/miseq.html) (chu *et al*., 2014). Sequences were aligned by using muscle (Edgar *et al*., 2004). Within the MEGA5 program (Tamura *et al*., 2011).

Therefore the two target sites on the novel coronavirus genome suitable for sequencing using RT-rtPCR assay are the RNA dependent RNA polymerase gene (RdRp Seq assay) and nucleocapsid protein gene (N gene) (NSeq assay) (Cotton *et al*.,2013).

5.3.3 Phylogenetic Analysis

Molecular sequencing technologies and phylogenetic approaches can be used to learn more about a new pathogen. This includes finding out about which species the pathogen is related to and subsequently the likely source of transmission. This can lead to new recommendations for public health policy. Phylogenetics is needed to add biological meaning to the data.

Phylogenetics is the area of research concerned with finding the genetic connections and relationships between species. The basic idea is to compare specific characters (features) of the species or strains, under the natural assumption that similar species (i.e., species with similar characters) are genetically close. The term phylogeny refers to these relationships, usually presented as a phylogenetic tree.

6. MERS-CORONA VIRUS IN AFRICA

6.1 MERS-CoV in African Camels

Dromedary camels in the Middle East have a high seroprevalence for MERS-CoV and MERS-CoV RNA has been consistently detected in these animals, especially in settings such as camel abattoirs, where camels from multiple origins are assembled Camels are thus identified as a potential source of zoonotic MERS. More than 60% of the global population of dromedary camels is distributed in African countries. Some of these countries are important camel exporters to the Arabian Peninsula (Faye *et al*., 2012).

According to Omrani *et al* 2015 the prevalence of MERS-CoV antibodies in more than 7 African countries (Table 3), indicated the existence of the virus in dromedary camels long before the Arabian outbreak of 2012 and these positivity ranges from 29 % in Kenya up to the highest score 95 % in Ethiopia (Reusken *et al*., 2014). However, zoonotic human disease has so far reported only from countries in the Middle-East. The reason for the absence of zoonotic disease in Africa is unclear recent study by Cho et al, (2018) revealed same indication for genetic variation between some of viral strain of African MERS COV with the prototype strain of Arabic peninsula.

Table. 3: The following table shows some of African Countries with MERS CoV positive camels and laboratory Technique they used to detect the infection**.**

Country	Sampling year	Type of test	Positivity %
Ethiopia	2010-2011	ELISA/PPN	93.97
Egypt	1997-2013	ELISA/PPN	81-92
Somalia	1983-1984	ELISA/PPN	83.7

Sudan	1984	ELISA/PPN	86.7
Kenya	1992-2013	ELISA/PPN	29.5
Nigeria	2010-2011	ELISA/PPN	94
Tunisia	2009	ELISA/PPN	30-54

Source Omrani *et al., (*2015)

6.2. Status of MERS COV in ETHIOPIA

In Ethiopia, camels represent a subset of major livestock resources with a population estimated at 1.209,321 (CSA, 2016/17). The Ethiopian most dromedaries are found in East, south eastern and north eastern arid and semi arid regions of the country, such as Somali, Afar, and Borena and others (Simenew, 2013).

Since the discovery of MERS-CoV in 2012, accumulative serological and molecular study had taking place in different part of the country. In Ethiopia an earlier study conducted by Reusken *et al*., 2014 showed an overall MERS CoV sero positivity of 93% in adult and 97% in juvenile. Another study revealed 92.3-93.9% sero prevalence and 7% viral detection in the country (Fekadu *et al*., 2016). Another study by Miguel *et al*., 2017 indicated MERS CoV RNA detection of up to 15.7% and sero positivity at high as 99.4%.

Recently, genetic and phenotypic characterization MERS-CoV from dromedaries sampled in four African countries (Table 4), Ethiopia, Morocco, Nigeria and Burkina Faso, demonstrated the viral strain genetically and phonotypical difference between West and East Africa (Chu *et al* 2018). The Ethiopia MERS-CoV isolates showed a very close similarity with viruses from camels in Arabian Peninsula suggesting the potential hazard for zoonotic transmission to the pastoralist of Ethiopia and warrants further study in the area. In this study have successfully carried out a whole genome sequence of three MERS-CoV isolates.

According to chu *et al*., (2018), the Sero positivity and viral RNA detection rates were higher in Ethiopia , as compared with Burkina Faso and Morocco and Nigeria. The following figures were taken from the article published online March 5, 2018.

Table 4: Research findings of African Country

Findings	Ethiopia	Morocco	Burkina Faso	Nigeria
Serology Result	85-99.4%	48.3-100%	73.2-84.6%	95%
PCR result	0-15.7%	0-7.6%	0 -12.2%	11%

Source: Chu et al., (2018)

The viral detection and the sero prevalence of MERS CoV in Ethiopia is higher than other African countries it indicates that disease is more endemic in East Africa Table 5.

Table 5: The highest prevalence of MERS CoV RNA positive region is Afar

Findings	Akaki Abattoir	Assaita	Melka worer	Metehara	Yabello
Serology	99.3%	85.5%	99%	99.4%	85.1%
PCR	5.5%	15.7%	14.9%	9.8%	0%

Source: Chu et al., (2018)

7. CONCLUSIONS

Africa has high population of camels which accounts to 60% of the total camel population of the world and there are many peoples in Africa whose lives are totally dependent on these animals as a source of food and transportation. As some studies indicated, there were evidences that showed the circulation of MERS-CoV in African camels even before the outbreak occurred in 2012 in the Middle East. Currently On those African countries where survey conducted on average around 85% of the camels were serological positive MERS CoV and few countries were also characterized the virus which clearly indicated the high circulation of the virus in the continent.

These findings prove that the camels are the carrier for MERS CoV, In the Middle East this carries animals are the source of infection and deaths for many people's but in Africa this condition is not clear. In recent few studies there are some findings which indicate there are genomic differences in the viral isolate of Africa and Middle East. Still it needs further investigation. Generally, these peoples who are living intimately with these animals, and use their bi products as a source of food and a medicine, are exposed to high level for MERS CoV, So further the sero epidemiological and virological test for the camels and for the peoples should be addressed.

Well-developed diagnostic techniques which are capable of detecting and characterizing the virus were invented, published and established immediately after the outbreak of MERS CoV in the Middle East. So those African countries should adapt the technologies and the knowledge required for investigate the status of the disease in each Africa country and design a means of controlling and prevention strategy of MERS CoV from the continent.

8. RECOMMENDATIONS

It is already confirmed that the circulation of MERS CoV in eastern and other parts of Africa This kind of disease has great impact on the lives of the nomadic people, hence further extensive and systematic research study should be conducted by taking the previous and recent research works as ground, jointly with all Africans exposed country and the middle east , to get more conclusive findings that will improve the risk level of the continent and the world to decrease impact on the economic viability of each country, specially east Africans since it affects our export market.

One health approach between public health and veterinary field should be implementing in the survey and research work of MERS CoV in Ethiopia.

Camel is the live of Ethiopian farmers especially in arid and semi arid areas of the country, if this virus changes it characteristic and become outbreak, the damage it causes will be intolerable, designing an effective vaccine should be encouraged and supported, Government and international collaborators should support human and laboratory Capacity building of research and academic institutes on viral isolation and Molecular diagnosis of MERS-CoV and other emerging viruses in African and Ethiopia

Regular surveillance of MERS-CoV in camels and identification of the virus and researching on the potential zoonotic significance should be initiated.

LIST OF ABBREVATION

BSL	Bio Saftey Level
CDC	Center for Diseas Control and prevention
DNA	Deoxyribose Nucleic Acid
DPP4	Deoxyribose Nucleic Acid
ELISA	Enzyme Linked Immuno Sorbent Assay
FAO	Food and Agriculture Organization
HCoV	Human Corona Virus
HKU	Honk Kong Universty
KSA	Kingdom of Saudi Arabia
Kb	Kilo base
MERS-CoV	Middle East Respiratory Syndrome Corona Virus
NAHDIC	National Animal Health Diagnostic and Investigation Center
OIE	International Office for Epizootics
PCR	Polymerase Chain Reaction
RdRP	RNA dependent RNA Polymerase
RNA	Ribo Nucleic Acid
RTrPCR	Reverse Transcriptase real time Polymerase Chain Reaction
SARS CoV	Severe Acute Respiratory Syndrome Corona Virus
PPNT	Pseudo Particle Neutralization Test
WHO	World Health Organization

Declaration

Ethical approval and consent to participate

No need of ethical clearance

Consent for publication

No need of permission

Availability of data materials

The data and materials are available

Competing interest

None of the authors of this paper have financial or personal relationship with other people or organization that could inappropriately influence or bias the content of this paper by any means.

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Author Contribution

Ayelech and Dr Gezahegne contributed equally in the entire work of the review paper

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