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A Review on MERS-CoV Disease Globally and Ethiopian context

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SUMMARY

The emerging cases of Middle East respiratory syndrome (MERS), associated with infection by a novel Corona virus (CoV) was first publicly reported in the Kingdom of Saudi Arabia (KSA). Since then, laboratory confirmed MERS-CoV cases in human were reported in 27 countries of the world. At the end of September 2018, a total of 2260 laboratory confirmed cases of Middle East respiratory syndrome (MERS), including 803 associated deaths (case–fatality rate: 35.5%) were reported globally; the majority of these cases were reported from Saudi Arabia. Available evidences showed camels are the possible source of the virus to human infections. Once it establishes, human-to-human transmission has resulted in clusters of cases, some associated with multiple rounds of human-to-human transmission. MERS-CoV is enzootic in Dromedary Camel across the Arabian Peninsula and in parts of Africa, causing mild upper respiratory tract illness in its camel reservoir and sporadic, but relatively rare human infections. Precisely how virus transmits to humans remains unknown but close and lengthy exposure to infected camels appears to be the most important predisposing factor for zoonotic transmission.

Camels sera collected from a number of countries have been found to have antibodies to MERS-CoV and African countries are considered as a possible source for the establishment of MERS-CoV in Middle East. In Ethiopia, high sero-prevalence of MERS-CoV has been reported in camel population ranging from 93% to 97%. In spite of high seropositivity, only few studies were carried out in Ethiopia on viral isolation and molecular characterization of the virus from camel. Recently study confirmed that unlike the West African MERS-CoV virus the Ethiopian camel MERS-CoV showed a genetic and phenotypic similarity with isolates from camel of

Arabian Peninsula suggesting a potential significance for zoonotic transmission to high risk human population of Ethiopia. Thus the objective of this seminar review on the existing knowledge on epidemiology and MERS CoV virological characteristics and overview MERS-CoV status in Ethiopia in order to highlight the gap for future research.

Keywords: *Review, Globally, Ethiopia MERS-CoV, Dromedary camels, Bats*

1. INTRODUCTION

Middle East Respiratory Syndrome Coronavirus infection (MERS-CoV) became an evolving worldwide health concern. MERS-CoV originally reported in 2012 in Saudi Arabia (Zaki *et al.,* 2012). So far, 27 countries have reported human laboratory confirmed cases in four continents since 2012. At the end of September 2018, **a** total of 2260 laboratory-confirmed cases of Middle East respiratory syndrome (MERS), including 803 associated deaths (case–fatality rate: 35.5%) were reported globally; the majority of these cases were reported from Saudi Arabia (1882 cases, including 729 related deaths with a case–fatality rate of 38.7%) (WHO, 2018). In Middle East, Saudi Arabia is reflected as the epicenter of "MERS-CoV" infection. Saudi Arabia has unique cultural and religious practices; millions of Muslims come across from the globe travel to Saudi Arabia to perform Hajj and this could be the potential risk for global spread of the disease. (Zaki *et al.,* 2012).

The various regional appearances have provided favorable conditions for speedily transmitting viruses to appear. MERS-CoV triggered an occurrence of respiratory illness in the Middle East with secondary spread to Europe, Africa, Asia, and North America. The disease occurred mainly in the Middle East states with a highest cases of 88% followed by Asia 11%" "Europe 0.8%" and "USA 0.2 (Alaenazi *et al., 2018*).

MERS-CoV infection is transmitted from animals to humans and human to human. Phylogenetic analysis shows a close genetic relatedness between MERS-CoV and the group C Beta corona virus detected in insectivorous bats. (Woo *et al., 2012).*

This Evidence shows that bats aided as the original host species of MERS-CoV The interaction of humans with bats or their secretion is an occasional transitional to MERS-CoV,

and transmission from bat to human is unlikely. Available evidences showed that camels are the possible source of the virus to human infections. Once it establishes, human-to-human transmission has resulted in clusters of cases, some associated with multiple rounds of human-to-human transmission (Milne *et al*., 2014).

2. LITERATURE REVIEW

2.1 Epidemiology

2.1.1. Sero prevalence of MERS-CoV in camel and human

March 2012, autochthonous MERS cases have been detected only in the Middle East (Saudi Arabia, United Arab Emirates, Jordan, Qatar, Oman, Kuwait, Yemen, Lebanon and Iran). MERS cases have also been detected in other geographic areas with primary cases having travel connections to the Arabian Peninsula: in Europe (United Kingdom, Germany, France, Italy, Greece and the Netherlands), in Africa (Tunisia and Algeria), in Asia (Malaysia and Philippines) and in the Americas (USA). (Reusken et *al.,* 2014).

High percentages of animals seropositive for MERS-CoV were observed in Nigeria and Ethiopia; the overall seropositivity was 94% in adult dromedaries in Nigeria and 93% and 97% for juvenile and adult animals, respectively, in Ethiopia as indicated in Table 1. All provinces in which dromedaries were sampled in both countries showed high rates of seropositivity The overall seropositivity in dromedaries in Tunisia was 30% for animals ≤2 years of age and 54% for adult animals. (Woo. *et al*., 2012).

Seropositivity of 36% and 40% was observed in Sidi Bouzid and Sousse Provinces, respectively, and 100% of the dromedaries in the southern province of Kebili were seropositive. Array results were confirmed on a selection of positive and negative serum samples (n = 14 per country) in MERS-CoV neutralization tests performed as described in table 2 (Reusken *et al* ., 2014) . Serum samples from 72%, 82%, and 67% of the dromedaries from Nigeria, Ethiopia, and

Tunisia, respectively, reacted with the OC43 antigen, confirming common circulation of BCoV in camelids.

Table 1: Overview of serologic evidence for Middle East respiratory syndrome coronavirus among dromedary camels, Africa and the Arabian Peninsula **:**Reusken *et al* (2014)

Country	**Year**	**No. camels***	**% Middle East respiratory syndrome coronavirus antibodies†**
United Arab Emirates	2013	500 (A,J)	96‡,§,¶
	2013	59 (A)	97# , 100**, 98§
	2003	151 (A)	100§,‡
Egypt	2013	110 (A)	94§, 98††
	2013	17 (A)	82††
Spain (Canary Islands)	2012–2013	97 (A)	14¶,§
	2012–2013	8 (J)	13¶,§
Ethiopia	2010–2011	31 (J)	93¶
	2010–2011	157 (A)	97¶
Ethiopia, Sudan	2013	35 (A)	97††
Jordan	2013	11 (J)	100¶,§
Nigeria	2010–2011	358 (A)	94¶
Oman	2013	50 (A)	100¶,§
Qatar	2013	14 (A)	100¶,§
Saudi Arabia	2010–2013	65 (J)	72††
	2010–2013	245 (A)	95††
	2013	104 (J)	55‡‡
	2013	98 (A)	95‡‡
	2010	21 (J)	76‡‡
	2010	23 (A)	91‡‡
	2009	56 (J)	72‡‡
	2009	26 (A)	92‡‡
	2004	6 (A)	100‡‡
	1996	6 (A)	100‡‡
	1994	123 (A)	93‡‡
	1993	2 (A)	100‡‡
	1992	1 (A)	100‡‡
Tunisia	2009	46 (J)	30¶
	2009	158 (A)	54¶

*Camel age range indicated where known: J, juvenile ≤2 y of age ; A, adult >2 y of age.
†As determined by: ‡recombinant spike IFA.
§Neutralization test.
¶S1 micro-array.
#Nucleocapsid Western blot.
**Whole virus IFA.
††Pseudo particle neutralization test.
‡‡Complete virus infected cell ELISA.

Table 2: Background data and Middle East respiratory syndrome coronavirus serology results of selected camel serum samples from Nigeria, Ethiopia, and Tunisia **(**Reusken *et al*., 2014)

Country, Sample ID	Region	Age	Sex	MERS S1* (1:20)	MERS S1 (1:320)	MERS (1:640)	VNT
Nigeria							
1	Kano	7	M	63410	52,254	NT	640
2	Kano	2	F	63,022	10,998	4,585	320
3	Adamawa	6	M	63,146	41,200	20,627	1,280
4	Kano	2	M	63,213	63,331	63,353	1,280
5	Sokoto	2	F	63,123	8,215	–	80
6	Borno	7	M	63,173	13,873	7,471	160
7	Borno	6	F	63,065	63,065	NT	2,560
8	Sokoto	7	F	64,118	63,285	54,669	640
9	Borno	6	M	63,592	28,033	NT	80
10	Sokoto	6	F	64,176	63,427	35,190	640
11	Sokoto	2	F	–	NT	NT	<20
12	Adamawa	7	M	–	NT	NT	<20
13	Unknown	7	M	–	NT	NT	<20
14	Kano	7	M	–	NT	NT	<20
Ethiopia							
1	Somali	5	F	63,592	63,357	50,563	640
2	Afar	6	F	63,341	63,005	NT	2,560
3	Afar	13	F	63,366	63,205	63,467	1,280
4	Afar	10	F	63,206	63,299	NT	640
5	Afar	5	F	63,466	10,583	5,911	160
6	Fentale	<4	M	63,408	63,480	60,135	1,280
7	Afar	4	F	63,476	33,909	19,161	80
8	Afar	4	F	–	NT	NT	<20
9	Afar	2	M	–	NT	NT	<20
10	Afar	1	F	10,937	NT	NT	<20

Country, Sample ID	Region	Age	Sex	MERS S1* (1:20)	MERS S1 (1:320)	MERS (1:640)	VNT
11	Afar	3	F	18,269	NT	NT	<20
12	Fentale	>8	F	63,486	23,654	10,246	1,280
13	Afar	6	F	63,496	63,380	53,030	1,280
14	Afar	1	F	63,401	19,087	9,834	80
Tunisia							
1	Sidi Bouzid	8	F	–	NT	NT	<20
2	Sidi Bouzid	8	F	63,217	20,620	NT	80
3	Sidi Bouzid	6	F	–	NT	NT	<20
4	Sidi Bouzid	1	M	–	NT	NT	<20
5	Kebili	7	M	63,139	–	–	320
6	Kebili	4	M	63,113	–	–	160
7	Sidi Bouzid	1	M	–	NT	NT	<20
8	Sidi Bouzid	9	F	63,005	17,821	9,652	80
9	Sidi Bouzid	6	F	–	NT	NT	<20
10	Kebili	4	M	63,120	18,320	9,732	160
11	Sidi Bouzid	<1	M	–	NT	NT	<20
12	Sidi Bouzid	2	F	63,060	63,236	63,366	2,560
13	Sousse	13	F	63,220	50,510	26,575	320
14	Sidi Bouzid	5	F	–	NT	NT	<20

2.1.2 MERS-Cov in humans

Middle East respiratory syndrome in human was first identified in 2012, in Saudi Arabia and more than 1000 infection cases of the disease have been reported in May, 2015 and about 40% of those who were infected died due to the disease (Zaki *et al.,* 2012), accordingly, most cases have occurred in the Arabian Peninsula (Zumla *et al.,* 2015). HCoV-EMC/2012 is a strain of MERS-CoV that is detected in the first infected person in London in 2012, which was found to have a 100% identical viral sequencing to the strain identified in Egypt from tomb bats (Zaki *et al.,* 2012).The spread of MERS-CoV among humans has often been associated with outbreaks in hospitals, with around 20 % of all cases to date involving healthcare workers (Mackay *et al.,* 2015).

2.1.3. Susceptible hosts and Transmission

Many uncertainties still exist on the source of MERS-CoV and on the mode of transmission. This is typical of an emerging disease where there are often simultaneous possibilities, including

environmental, animal and human exposures. The continued detection of new MERS-CoV cases, the low estimated basic reproduction number of the infection (R0), and the detection of multiple distinct MERS-CoV genotypes suggest the existence of a persistent possible zoonotic source This is corroborated by the growing serological and molecular evidence that dromedary camels (Camelus dromedarius) are a host species for MERS-CoV (Al-Osail *et al* ., 2017).

Studies carried out in many Middle Eastern countries, including Saudi Arabia, Qatar, United Arab Emirates, and Oman, using samples from lung, nasal, and rectal swabs. Positivity for MERS-CoV by RT-PCR for the RdRp was observed in 1.6–61.5% of samples, mostly lung and nasal swabs . Analyses using anti-MERS-CoV antibodies have shown that 98–100% of camels are positive for MERS-CoV; consistent with this, the incidence of MERS-CoV in humans is 15 times higher in camel shepherds and 23 times higher in slaughterhouse workers than in the general population. The data supported that the main route of transmission from camels to humans is through the respiratory system (Hemida *et al.,* 2014).

2.1.4. The route of transmission

It is suspected that nasal mucous, sputum, saliva, milk or uncooked meat of infected camels are the main sources of transmission. However, the secondary infection can be through droplets or direct contact, and the virus may spread through the air or fomites. (Kenneth.*et., al* 2015)

2.1.5. Dromedary camels

Camels have been confirmed by several studies to be the reservoir of the MERS-CoV infection in humans. Zoonotic transmissions of MERS-CoV from dromedary camels to humans were reported in multiple occasions. MERS-CoV has never been reported as a disease in camels though in experimental infections MERS-CoV has been associated with mild upper respiratory signs. Positive PCR results for MERS-CoV or isolation of the virus from camels is notifiable to the OIE because MERS is an emerging disease with a significant public health impact (Kenneth. *et , al* 2018).

Camels as noted above, it is likely that it serve as hosts for MERS-CoV. The strongest evidence of camel-to-human transmission of MERS-CoV comes from a study in Saudi Arabia in which MERS-CoV was isolated from a man with fatal infection and from one of his camels; full-

genome sequencing demonstrated that the viruses isolated from the man and the camel were identical (Azhar *et a*l., 2014).

In study of camels there is growing serological and molecular evidence that the dromedary camel (Camelus dromedarius) is a host species for the MERS-CoV and that circulation of MERS-CoV or MERS-like CoV in dromedaries in Africa and the Arabian Peninsula were occurring well before 2012. (Reusken et al., 2014).

2.1.6. Bats

Corona virus as known to be a zoonotic virus; however, the MERS-CoV is a novel virus, and whether zoonotic transmission occurs is not clear yet. International studies carried out from 2012 to 2014 in Mexico, European countries (i.e., Germany, Ukraine, the Netherlands, and Romania), Ghana, and South Africa have examined whether bats may be carriers of MERS-CoV. These studies have tested bats mainly for the 329-bp fragment of RdRp using blood, fecal, and oral samples. The bat species that were tested in the study included *Pipistrellus*, *P. nathusii*, *P. pygmaeus*, Nycteris, and Neoromiciazuluensis, and 5.3–24.9% were found to be positive for MERS-CoV, with most positive results (> 70%) being identified in fecal samples with high viral loads (Memish *et al* ., 2013).

Thus, it may be possible for transmission to occur via bats; however, in Saudi Arabia, the species of bats that patients may have come in contact with are different from those tested. Thus, although there was a positive association between bats and corona virus infection, there was no association between bats and MERS-CoV. Therefore, these data have suggested that MERS-CoV is not transmitted through bats. (Graham *et al*., 2013).

On the other hand, the virus that causes Middle East Respiratory Syndrome (MERS) has been found in bats in Saudi Arabia, suggesting a potential origin for the disease .Researchers tested samples from bats living about 7 miles away from the home of the first person known to be infected with MERS in Saudi Arabia. (Mackay *et. al* ., 2015)

Investigations of samples from bats roosting in the vicinity of the first MERS CoV case in Bisha, Saudi Arabia, revealed the presence of a 190 nucleotide RNA fragment with 100% match to the

RdRp of MERS CoV in the feces of an Egyptian tomb bat (*Taphozous perforates*). Unfortunately, the short length of MERS like CoV sequences identified in bats limits the strength of phylogenetic analyses and subsequent conclusions about the origin of MERS CoV (Memish *et al*., 2013).

2.1.7. Other animals

In some countries of the Arabian Peninsula goats, cattle, sheep, water buffalo, swine, chicken and wild birds have been tested for antibodies to MERS-CoV, with no positive results. This indicate that the role of these animals in transmitting the disease or acting as a reservoir is not evitable. However it should be further studied to get clue information about the susceptibility. Because people often don't come in contact with bats, the researchers suspect that bats may infect other animals, which in turn, infect people. The researchers said they will continue to look for the virus in other domestic and wild animals in the region (Li *et al.*, 2005).

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2.1.8. Shedding of the virus and way of transmission

MERS-CoV virus is different than other corona viruses, including SARS-CoV, and had never been identified before 2012. MERS-CoV has been detected in camels in several countries but not in other livestock. It has been detected in camel meat, organs, milk and urine; infected camels may not be observably ill. The continued detection of new MERS-CoV cases, the low estimated basic reproduction number of the infection (R0), and the detection of multiple distinct MERS-CoV genotypes suggest the existence of a persistent possible zoonotic source This is corroborated by the growing serological and molecular evidence that dromedary camels (Camelus dromedarius) are a host species for MERS-CoV. Transmission from camel to camel is not well being described. The hypothesis that dromedary camels are hosts of MERS CoV has been proven by the viral RNA detection in different specimens collected from these animals in Qatar, Saudi Arabia, Oman and Egypt and the isolation of the virus from nasal and fecal samples (Cauchemez *et al* ., 2013).

MERS-CoV RNA has also been detected in the milk of camels actively shedding the virus. Whether infected camels excrete MERS-CoV directly into the milk or the milk is cross-contaminated during milking is unclear .Infection in dromedary camels has been reported to be either asymptomatic or associated with only mild respiratory signs with nasal discharge (Alaenazi et *al*., 2018).

The respective roles of human to human and zoonotic transmission in the current MERS CoV outbreak are not well understood. Conclusive evidence of human to human transmission of MERS CoV was first reported in a cluster of MERS CoV cases in the United Kingdom, when an adult male who had travelled to Saudi Arabia transmitted the virus to two of his family members (Health Protection Agency, 2013). Overall, MERS CoV human to human transmission chains have been self-limiting and irregular, and more than half of secondary MERS CoV cases have originated in a healthcare setting (WHO, 2014)

3. PATHOGENESIS

3.1. Animal Coronaviruses

Coronaviruses cause a large variety of diseases in animals, and their ability to cause severe disease in livestock and companion animals such as pigs, cows, chickens, dogs and cats led to significant research on these viruses in the last half of the 20th century. The pathogenesis of Middle East Respiratory syndrome corona virus infection is not well understood. (Fehr.*et al* ., 2015).

3.2. Human coronavirus

Coronaviruses cause more severe disease in neonates, the elderly, and in individuals with underlying illnesses, with a greater incidence of lower respiratory tract infection in these populations. Studies in both organ cultures and human volunteers show that corona viruses are extremely fastidious and grow only in differentiated respiratory epithelial cells. Infected cells become vacuolated, show damaged cilia, and may form syncytia. Cell damage triggers the production of inflammatory mediators, which increase nasal secretion and cause local inflammation and swelling. These responses in turn stimulate sneezing, obstruct the airway, and raise the temperature of the mucosa. (Fehr.*et al* ., 2015).

4. VIROLOGY OF MERS-COV

Coronaviruses are a group of enveloped RNA viruses of the family *Coronaviridae*. Their surface appearance resembles that of a crown under the electron microscopy, which has given rise to their scientific name (Latin “corona” meaning “crown” or “halo”). Coronaviruses able to infect humans are shown to emerge via cross-host transmission from animals. MERS-CoV is a lineage C *beta coronavirus* that is found in humans and camels. This virus is different from the other human *beta coronaviruses* (such as SARS-CoV). It is closely linked to some bat corona viruses (such as BtCoV-HKU4 or BtCoV-HKU5). This is why it is believed that MERS-CoV (like a plethora of other coronaviruses) originated in bats. (Al-Osail *et al*. 2017).

Dipeptide peptidase 4 (or DPP4) is a functional protein receptor for MERS-CoV that enables the infection, and it is found on the surfaces of non-ciliated epithelial cells in human bronchi. This receptor shows high level of amino acid sequence conservation between different species, including the bat cells. (Al-Osail. *et al., 2017*).

MERS-CoV is an enveloped, single-stranded, positive-sense RNA virus. The genome is approximately 30.1kb long and contains at least 10 predicted open reading frames (ORF), which are expressed from seven sub genomic mRNAs. These ORFs mainly include ORF 1a/1ab, which encode for large replicase polyproteins containing conserved functional domains and several non-structural (NS) proteins of CoV, the spike-surface glycoprotein (S), the small-envelope (E) protein, the matrix (M) protein, and the nucleocapsid (N) protein (Mackay *et al.,* 2015).

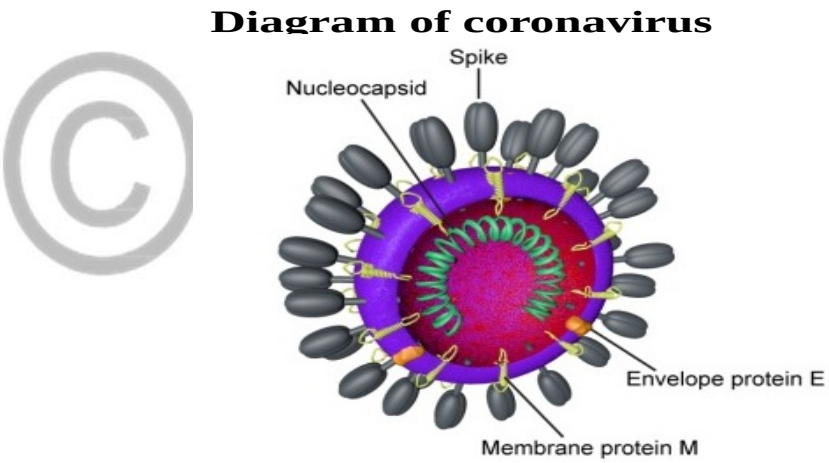

Figure 1: Diagram of coronavirus particle structure (Siddell et *al.*, 1983).

4.1. Viability of the virus

MERS-CoV remains viable at 48 hours at 20 °C and 40% relative humidity, comparable to an indoor environment on plastic and metal surfaces. The virions are sensitive to heat, lipid solvents, non-ionic detergents, oxidizing agents and ultraviolet light .In aerosol experiments, MERS-CoV retains most of its viability at 20 °C and 40% relative humidity. Viability decreases at higher temperatures or higher levels of relative humidity. In unpasteurized camel milk, MERS-CoV remains infectious beyond 72 hours after introduction to the milk but infectious viruses could not be found after pasteurization (van Doremalen *et al* .,2013) .

4.2. Genome Structure and Gene Functions

MERS-CoV, a lineage C Beta coronavirus (βCoVs), has a positive-sense single-stranded RNA (ssRNA) genome about 30-kb in size. As of 2016, phylogenetic analysis of MERS-CoV has been done on 182 full-length genomes or multiple concatenated genome fragments, including 94 from humans and 88 from dromedary camels. The MERS-CoV genomes share more than 99% sequence identity, indicating a low mutation rate and low variance among the genomes. MERS-CoV genomes are roughly divided into two clades: clade A, which contains only a few strains, and clade B, to which most strains belong (Al-Tawfiq *et. al.*, 2014).

As with other CoV genomes, the first 5′ two-thirds of the MERS-CoV genome consist of the replicase complex (ORF1a and ORF1b). The remaining 3′ one-third encodes the structural proteins spike (S), envelope (E), membrane (M), and nucleocapsid (N), as well as five accessory proteins (ORF3, ORF4a, ORF4b, ORF5 and ORF8b) that are not required for genome replication but are likely involved in pathogenesis . The flanking regions of the genome contain the 5′ and 3′ untranslated regions (UTR) . Typical of the coronaviruses, the MERS-CoV accessory proteins do not share homology with any known host or virus protein, other than those of its closely related lineage C βCoVs (Fehr *et al* ., 2015).

4.3. Genetic characterization

Nasal swabs samples collected from Morocco, Burkina Faso, Ethiopia and Nigeria camels positive with RT-PCR with high viral load were selected and attempted to maximize diversity in geography and sampling dates ,for full viral genome sequencing directly from the clinical specimen and for virus isolation. Three viruses from Burkina Faso, one from Morocco, nine from Nigeria and three from Ethiopia were fully sequenced and an additional virus from Ethiopia was sequenced from s2 gene region to the 3′ end of the genome (5,126nt). Genetic nucleotide identity was 99.17% within African camel virus genome,>99.26% with in human and camel MERS-Cov from the Middle East and 99.18-99.58% between viruses from the Middle East and Africa (GenBank accession no: MG923465-MG923481) (Chu Daniel *et al.*, 2018*).*

5. DIAGNOSIS

WHO provides recommendations for laboratory testing for MERS-CoV. These are based on, and updated according to, the latest scientific knowledge. The most recent recommendations can be found on the WHO Global Alert and Response webpage for coronavirus. Both upper and lower respiratory tract specimens should be collected. Lower respiratory tract specimens, such as bronco alveolar lavage, sputum and tracheal aspirates contain the highest viral loads and are to be preferred. If resources permit, further samples from feces and urine should also be collected and repeated sampling is highly recommended to gather further evidence on viral shedding and infectious periods. Appropriate handling of specimens during collection and transport is important (Kenneth *et al.*, 2018).

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Currently, confirmation of cases according to WHO standards is performed with detection of viral RNA by real-time PCR targeting upstream of the MRS-CoV E protein (upE) and then a secondary PCR assay targeting open reading frame (ORF) 1a or 1b. A negative secondary PCR

result would require further nucleotide sequencing of the viral RNA. Likewise, as an alternative to the secondary PCR assay, sequencing of the viral RNA together with a positive upE test can confirm a case. Target sites suitable for sequencing include the RNA-dependent RNA polymerase (RdRp) and (N) genes. WHO (2018).

Serology can be used to detect antibodies in patients or contacts when the direct detection (molecular methods) of MERS-CoV is negative in suitable specimens, as well as for human and animal surveys. However, interpretation of MERS-CoV serological results can be hampered by the widespread circulation of other human Coronaviruses such as HCoV-OC43, HCoV-HKU1, HCoV-NL63, and HCoV-229E. Different screening assays are used such as indirect immunofluorescence assay (IFA), ELISA, western blot, protein microarrays using the whole virus or recombinant spike and nucleocapsid proteins or a soluble S1 subunit of spike protein. A gold-standard neutralization test should be used for confirmation i.e. plaque reduction neutralization test or micro neutralization test or using pseudo particle virus). Serological testing has confirmed human cases in Germany and asymptomatic infection in the US. In Germany, two cases tested using IFA had high titres of antibodies and this was also confirmed by microarray testing and neutralization tests (Alaenazi *et al* .,2018).

6. THERAPEUTIC OPTIONS

Till date, there is no approved proper treatment or vaccine for MERS-CoV for both camel and human infection. In human, the challenge of devolving a pathogen specific intervention, in a relatively short time, has been a major difficulty. Management of this infection largely depends on diagnostic improvement, organs function preservation, and attention to prevent complications. (Alaenazi et al. 2018)

7. STATUS OF MERS-COV IN ETHIOPIA

Camels sera collected from a number of countries have been found to have antibodies to MERS-CoV and African countries are considered as a possible source for the establishment of MERS-CoV. In Ethiopia, high sero-prevalence of MERS-CoV has been reported in camel population. In an earlier study conducted by Reusken *et al* (2014) showed an overall MERS CoV sero-

positivity of 93% and 97% in juvenile and adult animals, respectively. Another study by Miguel *et al* ., (2017) showed MERS-CoV RNA detection of up to 15.7% and seropositivity as high as 99.4%. (Fekadu *et al*., 2017) also revealed 92.3 – 93.9% sero-prevalence and 7% viral detection in the country. In spite of high seropositivity, only few studies were carried out in Ethiopia on viral isolation and molecular characterization of the virus from camel. Recently published study confirmed that unlike the West African MERS-CoV virus from Burkina Faso and Nigeria, the Ethiopian camel MERS-CoV showed a genetic and phenotypic similarity with isolates from camel of Arabian Peninsula (Chu *et al.,* 2018); suggesting a potential significance for zoonotic transmission to high risk human population of Ethiopia.

8. CONCLUSION AND RECOMMENDATIONS

The recent epidemic MERS-CoV and the past outbreak of SARS-CoV, clearly demonstrate that new pathogens will emerge. As they are accelerated by globalization there is really no way to know when or where they might occur. What is more, there are no effective treatments or vaccines against these infections. Additionally, little is known about the zoonotic transmission of MERS-CoV, or even its origin, which hinder the progress of containing its spread to humans. MERS-CoV is highly pathogenic, exhibiting high fatality rate than the former human corona virus SARS. (36 vs. 10%), and can be obviously transmitted through several routes, with higher incidence in camel rearing populations like the pastoralist and in exposed healthcare workers in healthcare settings.

In Ethiopia, in spite of the high prevalence of MERS-CoV antibodies in camel, no human case has been reported to date, and only few ongoing studies has been carried out to investigate public health significance of MERS in highly exposed pastoralist community of Ethiopia who have close contact with camels and hence requires serious attentions for further surveillance both in camel and exposed human population . Thus, based on the above concluding remarks the following recommendations are forwarded:

- Continued epidemiologic surveillance and vigilance remains crucial in order to have preparedness in controlling emerging diseases like MERS-CoV in camel and human.
- Further in depth virological and molecular researches should be carried out to understand the virus characteristics, genomics, immunological reaction in hosts, transmission dynamics among susceptible hosts in order to design a feasible control strategies such vaccines for camels and human.
- Creation of awareness in the community about the clinical sign , transmission of the MERS-CoV , protecting themselves from the disease and system of reporting to Veterinarians, and human health care providers to reduce potential health hazard is crucial..

ABBREVATIONS

MERS	Middle East Respiratory Syndrome
Cov	Corona virus
KSA	Kingdom of Saudi Arabia
LRT	Lower Respiratory Tract
URT	Upper Respiratory Tract
RT-rtPCR	Reverse transcriptase real-time polymerase chain reaction
SARS	Severe Acute Respiratory Syndrome
BtCoV	Bat corona virus
HKU	Hong Kong University
DPP	Dipeptidyl peptidase
RNA	Ribo nucleic acid
DNA	Deoxy ribo nucleic acid

NSP	Non-structural protein
BCoVs	*Beta coronavirus*
RdRp	RNA-dependent RNA polymerase
ELISA	Enzyme Linked Immuno Sorbent Assay
IFA	Immuno Florescent Antibody

Declaration

Ethics approval and consent to participate

No need of ethical clearance

Consent for publication

No need of permission

Competing interests

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

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9. REFERENCES

1. Al-Osail, Aisha M., and Marwan J. Al-Wazzah. "The history and epidemiology of Middle East respiratory syndrome corona virus." *Multidisciplinary respiratory medicine* 12.1 (2017): 20.

2. Alaenazi, Mohammed, et al. "Emerging infectious diseases: MERS-COV, the new Betacoronavirus pandemic." *International Journal Of Community Medicine And Public Health* 5.2 (2018): 405-410.

3. Al-Tawfiq, Jaffar A., and Ziad A. Memish. "Middle East respiratory syndrome coronavirus: transmission and phylogenetic evolution." *Trends in microbiology* 22.10 (2014): 573-579.

4. Azhar, Esam I., et al. "Evidence for camel-to-human transmission of MERS coronavirus." *New England Journal of Medicine* 370.26 (2014): 2499-2505.

5. Bala, Mohamed Osman, Mohamad Abdel Halim Chehab, and Nagah Abdel Aziz Selim. "MERS: an emerging disease of the 21st century." *International Journal Of Community Medicine And Public Health* 4.7 (2017): 2202-2207.

6. Cauchemez S, Van Kerkhove MD, Riley S, Donnelly CA, Fraser C, Ferguson NM. Transmission scenarios for Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and how to tell them apart. *Euro Surveill*. 2013; 18(24).

7. Chu, Daniel KW, et al. "MERS coronaviruses from camels in Africa exhibit region-dependent genetic diversity." *Proceedings of the National Academy of Sciences* 115.12 (2018): 3144-3149.
8. Fehr, Anthony R., and Stanley Perlman. "Coronaviruses: an overview of their replication and pathogenesis." *Coronaviruses*. Humana Press, New York, NY, 2015. 1-23.

9. Fekadu, Getnet, Gelagay Ayelet, and Fufa Abunna. "Epidemiological investigation of Middle East respiratory syndrome corona virus (mers-cov) among dromedary camels in selected areas of Afar and Oromia region, Ethiopia." *Journal of Veterinary Medicine and Animal Health* 9.3 (2017): 47-54.

10. Graham, Rachel L., Eric F. Donaldson, and Ralph S. Baric. "A decade after SARS: strategies for controlling emerging coronaviruses." *Nature Reviews Microbiology* 11.12 (2013): 83.

11. Hemida, Maged G., et al. "MERS coronavirus in dromedary camel herd, Saudi Arabia." *Emerging infectious diseases* 20.7 (2014): 1231.

12. Islam, Ariful, et al. "Middle East Respiratory Syndrome Coronavirus Antibodies in Dromedary Camels, Bangladesh, 2015." *Emerging infectious diseases* 24.5 (2018): 926.

13. Kenneth McIntosh, Martin S Hirsch, Anna R Thorner “Middle East respiratory syndrome coronavirus: Virology, pathogenesis, and epidemiology”. This topic Literature review last updated: Oct 08, 2018.

.

14. Li, Wendong, et al. "Bats are natural reservoirs of SARS-like coronaviruses." *Science* 310.5748 (2005): 676-679.

15. Mackay, Ian M., and Katherine E. Arden. "MERS coronavirus: diagnostics, epidemiology and transmission." *Virology journal* 12.1 (2015): 222.

16. McIntosh, Kenneth. "Middle East respiratory syndrome coronavirus: Virology, pathogenesis, and epidemiology." Literature review current through http://www.who.int/emergencies/mers-cov/en/: Sep 2018. last updated: Oct 08, 2018.

17. Memish, Ziad A., et al. "Middle East respiratory syndrome coronavirus in bats, Saudi Arabia." *Emerging infectious diseases* 19.11 (2013): 1819.

18. Miguel, Eve, et al. "Risk factors for MERS coronavirus infection in dromedary camels in Burkina Faso, Ethiopia, and Morocco, 2015." *Euro surveillance* 22.13 (2017).

19. Milne Price, Shauna, Kerri L. Miazgowicz, and Vincent J. Munster. "The emergence of the Middle East respiratory syndrome coronavirus." *Pathogens and disease* 71.2 (2014): 121-136.

20. Nassar, M. S., et al. "Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection: epidemiology, pathogenesis and clinical characteristics." *European review for medical and pharmacological sciences* 22.15 (2018): 4956-4961.

21. Pathan Amanulla Khan, B. B., Naseerah Maryam, and Khateeja Sultana. "MIDDLE EAST RESPIRATORY SYNDROME (MERS): A SYSTEMATIC REVIEW." I. J. Of Pharmaceutical Sciences and research projected impact factor SJR 0.59 (2017).

22. Reusken CB, Messadi L, Feyisa A, et al. Geographic distribution of MERS coronavirus among dromedary camels, Africa. *Emerg Infect Dis*. 2014;20(8):1370-4.

23. Siddell, Stuart, Helmut Wege, and Volker Ter Meulen. "The biology of coronaviruses." *Journal of General Virology* 64.4 (1983): 761-776.

24. Tyrrell, David AJ, and Steven H. Myint. "Coronaviruses." **ncbi**.nlm.nih.gov (1996).

25. Van Doremalen, N., T. Bushmaker, and V. J. Munster. "Stability of Middle East respiratory syndrome coronavirus (MERS-CoV) under different environmental conditions." *Eurosurveillance* 18.38 (2013).

26. World Health Organization. "Middle East respiratory syndrome coronavirus (MERS-CoV)–update." *Saudi Medical Journal* 35.6 (2014): 633-634.

27. World Health Organization. Laboratory testing for middle East respiratory syndrome coronavirus: interim guidance (revised), January 2018. No. WHO/MERS/LAB/15.1/Rev1/2018. World Health Organization, 2018.

28. Woo, Patrick CY, et al. "Genetic relatedness of the novel human group *C beta coronavirus* to Tylonycteris bat coronavirus HKU4 and Pipistrellus bat coronavirus HKU5." *Emerging microbes & infections* 1.11 (2012): e35.

29. Zaki, Ali M., et al. "Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia." *New England Journal of Medicine* 367.19 (2012): 1814-1820.