MERS-questions of public health importance: The “known unknowns”

Malik Peiris
School of Public Health
The University of Hong Kong
malik@hku.hk
MERS CoV: Geographic virus distribution in camels

Reusken et al EID 2014; Perera et al EID 2013; Hemida et al 2014; Chan et al 2015; Miguel et al EID 2015; Miguel et al Eurosurveillance 2017; Chu et al Eurosurveillance 2015

Why no zoonotic MERS disease in Africa?

77% of global dromedary population

4% MERS-CoV active
Why “no” zoonotic MERS disease in Africa?

Hypotheses

Exposure → Infection → Disease → Medical attention → Diagnosis

- Infected animals
- Behavioural factors

- Viral genetics
- Host genetics

- Recognition
- Diagnostics

So et al Eurosurveillance 2018
Abbad et al Eurosurveill 2019
Is human infection taking place in Africa?

Seroprevalence:
- 0.8% of 379 camel exposed humans (Nouriil et al. 2019)
- 0% of 179 camel abattoir workers (Hemida et al. 2014)
- 0% of 260 camel abattoir workers (So et al. 2018)
- 0% of 760 camel exposed people (Munyua et al. 2017)
- General population: 0.18% of 1222 (Liljander et al. 2016)
- Camel handlers: 4 (4.3%) of 93 (Kiyong et al. 2020)

RNA:
- 3 (1.2%) of camel exposed humans, concurrent with virus infection in camels (Ngere et al. 2022)
Is human infection taking place in Africa?

Seroprevalence: 0.8% of 379 camel exposed humans (Nouril et al. 2019)

Seroprevalence: 0% of 179 camel abattoir workers (Hemida et al. 2014)

Seroprevalence: 0% of 260 camel abattoir workers (So et al. 2018)

Seroprevalence: 0% of 760 camel exposed people (Munyua et al. 2017)

Seroprevalence: General population: 0.18% of 1222 (Liljander et al. 2016)

MERS-CoV specific T cell responses may be detectable in infected sero-negative individuals in Saudi Arabia (Perlman et al. 2017)

Seroconversion in RT-PCR confirmed mild or asymptomatic infection is poor (Choe et al. 2017; Zhao et al. 2017; Ko et al. 2017)

RNA: 3 (1.2%) of camel exposed humans, concurrent with virus infection in camels (Ngere et al. 2022)

18 (30%) of 61 camel abattoir workers in Nigeria had MERS-CoV specific CD4+ or CD8+ T cell responses, even though they were MERS-CoV antibody negative. In comparison, none of control population had MERS-CoV specific T cell responses (Mok CKP.. Oladipo J, Kuranga S .. et al 2021)

Needs confirmatory studies
Why “no” zoonotic MERS in Africa? Hypotheses

- **Exposure**
  - Infection
    - **Disease**
      - **Medical attention**
        - **Diagnosis**

- • Infected animals
- • Behavioural factors
- • Viral genetics
- • Recognition
- • Diagnostics

So et al Eurosurveillance 2018
Abbad et al Eurosurveill 2019
Phylogenetics of MERS coronaviruses

>99% nucleotide identity

<table>
<thead>
<tr>
<th>Clade</th>
<th>Strain</th>
<th>Species</th>
<th>Country</th>
<th>Sampling date</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>EMC/2012</td>
<td>Human</td>
<td>Saudi Arabia</td>
<td>13/6/2012</td>
</tr>
<tr>
<td>B</td>
<td>AH13</td>
<td>dromedary</td>
<td>Saudi Arabia</td>
<td>30/12/2013</td>
</tr>
<tr>
<td>C1.2</td>
<td>C270</td>
<td>dromedary</td>
<td>Egypt</td>
<td>2013</td>
</tr>
<tr>
<td>C1.1</td>
<td>BF785</td>
<td>dromedary</td>
<td>Burkina Faso</td>
<td>18/3/2015</td>
</tr>
<tr>
<td>C1.1</td>
<td>Nig1657</td>
<td>dromedary</td>
<td>Nigeria</td>
<td>3/2/2016</td>
</tr>
<tr>
<td>C1.1</td>
<td>MOR213</td>
<td>dromedary</td>
<td>Morocco</td>
<td>3/3/2015</td>
</tr>
<tr>
<td>C2</td>
<td>CAC9690</td>
<td>dromedary</td>
<td>Ethiopia</td>
<td>24/11/2019</td>
</tr>
<tr>
<td>C2</td>
<td>CAC10200</td>
<td>dromedary</td>
<td>Kenya</td>
<td>19/3/2020</td>
</tr>
</tbody>
</table>

* Virus strains phenotyped in this study

Compared with clade A & B MERS-CoV from Saudi Arabia, viruses from Africa (clade C) (Burkina, Ethiopia, Kenya, Nigeria, Morocco) have lower replication competence ex-vivo cultures of human lung (and Calu-3 cells).


Also for Nigerian, Moroccan and Egyptian isolates
Lower viral replication competence of MERS coronaviruses from Africa (Burkina, Ethiopia, Nigeria, Morocco, Egypt) in mouse model

Humanising exons 10-12 of mouse DPP4 provided by Stanley Perlman

Li K et al PNAS 2017

Also for Nigerian, Moroccan and Egyptian isolates

Zhou et al PNAS 2021
What are implications for viral genetic diversity for infection in dromedary camels?

- Clade C: viral replication levels in naturally transmitted animals was lower. Transmission efficiency also lower (Rodon .. Segales et al EID 2023)
- Suggests that fitness in camels of clade B > clade C
- Explains why clade C virus does not get established in Arabian Peninsula in spite of repeated importations of dromedaries (and virus) from Africa.
- Danger: If Clade B virus gets introduced into Africa, it will potentially become dominant in Africa? → Implications for zoonotic potential?

Experimental infection and transmission clade B vs clade C virus in Llamas (a surrogate for camels)

Clade B (Qatar15/2015)
Clade C (Egypt/2013)

Camel density and trade routes
25,000/year

(Younan et al., 2016; Azhar et al., 2014; FAO, 2017; Anthony et al., 2017; Moreno et al., 2017)
Why “no” zoonotic MERS in Africa? Hypotheses

Exposure → Infection → Disease → Medical attention → Diagnosis

- **Exposure**
  - Infected animals
  - Behavioural factors

- **Infection**
  - Viral genetics

- **Disease**
  - Recognition
  - Diagnostics

Viruses from Africa (clade C)
- Genetically distinct (Zhou et al 2021)
- May partially explain why severe human disease is not prominent?
- But repeated exposure and unsuspected infection in large numbers of people may lead to virus adaptation to humans → pandemic emergence.

So et al Eurosurveillance 2018
Abbad et al Eurosurveillance 2019
Diverse genome deletions and insertions in MERS-CoV genomes in dromedary camels in Africa

- MERS-CoV in African camels genetically unstable (Zhou et al Emerging Microbes & Infections 2023)

- ORF8 deletion of SARS-CoV-1 was associated with the emergence of the SARS epidemic in 2003 (Guan et al 2003)
MERS CoV: Geographic virus distribution in camels

What is viral lineage in Central Asia?

Lack of sequence data from Central Asia?

77% of global dromedary population

4%

MERS-CoV active

Reusken et al EID 2014; Perera et al EID 2013; Hemida et al 2014; Chan et al 2015; Miguel et al EID 2015; Miguel et al Eurosurveillance 2017; Chu et al Eurosurveillance 2015
Why “no” zoonotic MERS in Africa?

Hypotheses

Exposure

• Infected animals
• Behavioural factors

Infection

• Viral genetics

Disease

Medical attention

• Recognition
• Diagnostics

Diagnosis

Human respiratory surveillance & Health care workers in Africa:

• How aware that MERS-CoV may be causing mild or severe respiratory disease in camel herding regions of East, West and North Africa?

• How many ILI/SARI surveillance sites are situated in proximity to camel exposed populations?

• How many ILI and SARI surveillance specimens in camel herding / exposed areas are being tested for MERS-CoV?
Summary of knowledge gaps

• Transmission within health care facilities can be efficient (more so that for avian flu H5N1, H7N9 etc.), but less efficient in the community? Can that change?
• Majority of MERS-CoV infected dromedaries are in Africa but no reported zoonotic disease there?
• Need more surveillance at the camel-human interface in camel-herding regions of Africa?
• Gaps in surveillance and sequence data from Central Asia
• Few recent MERS-CoV sequences in public databases
• MERS remains a pandemic threat and development of counter-measures are a priority
Thank you for your attention
... and to many research collaborators in Africa

Phenotypic and genetic characterization of MERS coronaviruses from Africa to understand their zoonotic potential


1School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong (HKU), Pokfulam, Hong Kong Special Administrative Region, People’s Republic of China; 2HKU-Postdoc Research Pole, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, People’s Republic of China; 3National Veterinary Institute, Debre Zeit, Ethiopia; 4Ministry of Defense Health, Ethiopia; 5Vietnam National Institute of Hygiene and Epidemiology, Hanoi, Vietnam; 6The University of Hong Kong, Hong Kong, China; 7Food and Agriculture Organization, Emergency Centre for Transboundary Animal Diseases, Addis Ababa, Ethiopia; 8Food and Agriculture Organization, Emergency Centre for Transboundary Animal Diseases, Nairobi, Kenya; 9Food and Agriculture Organization, Rome, Italy; 10Centre de Coopération Internationale en Recherche Agronomique pour le Développement, Université Montpellier, Montpellier, France; 11Laboratoire de Biologie et Santé Animale, L’institut de l’Événement et de Recherches Agricoles du Burkina Faso; 12Centre National de la Recherche Scientifique et Technologique, 04 BP 8665 Ouagadougou 04, Burkina Faso; 13Institut Agronomique et Vétérinaire Hassan II, B.P. 6020 Rabat-Instituts, Rabat, Morocco; 14State Key Laboratory of Respiratory Disease, National Research Center for Respiratory Disease, Guangzhou Institute of Respiratory Disease, First Affiliated Hospital of Guangzhou Medical University, Guangzhou, People’s Republic of China; 15Department of Pathology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Pokfulam, Hong Kong Special Administrative Region, People’s Republic of China; and 16The Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong Special Administrative Region, People’s Republic of China.

Genetic diversity and molecular epidemiology of Middle East Respiratory Syndrome Coronavirus in dromedaries in Ethiopia, 2017–2020


Emerging Microbes and Infections 2023

Proceedings of National Academy of Science, 2021