

The role of UAE in supporting COVID-19 genomic surveillance across the EMRO for complex emergency countries

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Abstract

Introduction The Eastern Mediterranean region was highly exposed to COVID-19 due to diverse challenges and lack of laboratory resources and relevant expertise in these countries limited the quality of detection and surveillance of circulating strains. UAE, through the Reference Laboratory for Infectious Disease-Abu Dhabi (RLID-AD), played a central role in providing genomic support to these countries. **Methods** SARS-CoV-2 samples were transported to RLID-AD with support from WHO/EMRO, then sequenced primarily using the Midnight workflow and GridION from Oxford Nanopore Technology and the data were analysed using the CLC platform from Qiagen, and lineages assigned using Pangolin. **Results** Between April 2021 and March 2022, RLID-AD received 170 COVID-19 samples from Syria, Yemen and Lebanon for genomic analysis. Of these , 159 were successfully sequenced (93.5%) with >90% coverage and 30x depth, with lineages being successfully assigned through Pangolin. The lineages discovered were predominantly alpha, beta, and delta variants, largely consistent with the global waves at the time. Turnaround time from receipt at the lab to result sharing with member states was 2-3 weeks. **Conclusion** The implementation of a hub-and-spoke model for sequencing support was a key aspect to the COVID-19 response in the EMRO region. UAE played a critical role in supporting genomics surveillance in the region, despite the logistic challenges faced with transport and importing of samples to UAE. The challenges faced during COVID19 pandemic clearly demonstrates the need for implementation of national-level sequencing laboratories that contribute data to the region, with hubs acting in technical and emergency support.

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Conclusion

The implementation of a hub-and-spoke model for sequencing support was a key aspect to the COVID-19 response in the EMRO region. UAE played a critical role in supporting genomics surveillance in the region, despite the logistic challenges faced with transport and importing of samples to UAE. The challenges faced during COVID19 pandemic clearly demonstrates the need for implementation of national-level sequencing laboratories that contribute data to the region, with hubs acting in technical and emergency support.

Key words: UAE, COVID19, Genomic Surveillance, sequencing, Hub-spoke model, EMRO

Introduction

The COVID-19 pandemic presented an unprecedented challenge to the already strained health system in the Eastern Mediterranean region (EMR), with many countries already struggling with complex emergencies, such as regional or national conflict, political struggles, existing outbreaks, population displacement, poverty and more¹. Many countries lacked the capacity to rapidly implement diagnostic or genomic support, which limited their ability to assess the national burden of COVID-19 and identify circulating variants of concern, making their informed decisions regarding vaccination and public health interventions more challenging^{2,3}.

COVID-19 came to the Middle East and North Africa (MENA) region early, with the first instances occurring in the United Arab Emirates (UAE) in January 2021, followed by Iran recording its first case in February 2020, and Yemen the last country to record its first case in April 2020. The World Health Organization's Regional Office for the Eastern Mediterranean (WHO/EMRO), which includes the majority of MENA states, reported 12.6 million cases and 236 thousand fatalities in early August 2021, and the total vaccination rate was less than 6.0% at the time^{1,4}.

UAE recognised the seriousness of the situation and rapidly operationalised and implemented a nationwide COVID-19 diagnostic laboratory network, building on existing capacity for SARI/ILI surveillance programs. Molecular diagnostic capacity for SARS-CoV-2 was validated and made ready for testing in January 2020, before the pandemic was declared. To date, the country has tested an astonishing 168 million samples, identifying 1,055,334 positive cases (0.5% positivity). The country has recorded 2,349 deaths due to COVID-19 (CFR 0.25%), which is comparable to or lower than most developed countries. This is largely due to the

timely and higher detection capacity, healthcare capacity and available ICU beds, and widespread vaccination campaigns implemented to respond to the virus⁵.

UAE also recognised the importance of assessing circulating variants in the region, as the strains can directly impact the virus's spread, diagnostic sensitivity, case fatality and vaccine response and efficacy. Through RLID-AD, and with funding from Abu Dhabi Public Health Center (ADPHC), the country invested in and implemented whole genome sequencing of SARS-CoV-2 on a number of platforms, including the Oxford Nanopore Technologies Nanopore, Illumina MiSeq and Sanger sequencing platforms, to ensure variants were monitored and assessed as they emerged. As of the end of March 2023, UAE has shared 7,214 sequences through the Global initiative on sharing All avian data (GISAID) platform, covering 5 waves of infection. The investment in this capacity also allowed the country to perform research and developmental studies into vaccine efficacy, with publications shared or in preparation^{6,7}.

RLID-AD facility was rapidly designated by WHO/EMRO as one of three regional hubs for COVID-19 (Fig.1), providing support to countries in the region with less technical or logistical capacity for molecular diagnostics. WHO/EMRO, with the support of UNHAS and other stakeholders, provisioned logistical networks to transport samples from some of these countries to UAE, in support of both molecular diagnostics and genomics despite the anticipated challenges.



Figure 1. Location of regional sequencing reference hubs, providing support to complex emergency countries for genomic surveillance.

Methods

Collection and transport of samples

One hundred seventy nasopharyngeal samples were collected from primary, secondary and tertiary public health facilities from Syria, Yemen and Lebanon for analysis between January and June 2021. Sample storage conditions are unknown, as transport took several weeks, and temperature logging was not operational then. Upon receipt at RLID-AD samples were stored at 4°C until extraction or were extracted immediately upon arrival.

Sample extraction and library preparation

On arrival, samples were extracted using the Qiagen QiaAmp (QIAGEN GmbH, Germany) or MagNA Pure 96 DNA and Viral NA Extraction kit (Roche Diagnostics GmbH, Switzerland) as per the manufacturer's instructions, then submitted for quantification by PCR, detecting orf1ab, E and N genes to ensure the Ct

values were within a range that would support high-quality sequencing (Ct15-30). Samples not within this range were not sequenced to limit on cost and preserve reagents already in high demand.

Sequencing and bioinformatics analysis

Libraries were prepared using the Oxford Nanopore Technologies Midnight Protocol, following the manufacturer’s instructions. Briefly, cDNA was generated from the extracted viral RNA using the NEB LunaScript RT mastermix, then split into two pools for PCR with the midnight primers, generating 1200bp amplicons^{8,9}. Amplicons were pooled and then cleaned up using AmpureXP magnetic beads (Beckman Coulter, USA) before being quantified by fluorimetry using the Qubit 1X HS dsDNA quantification kit and a Qubit 4 platform (Thermo Fisher Scientific, USA). Samples were then barcoded using the rapid barcoding kit (SQK-RBK110.96) following the protocol instructions before another round of AmpureXP cleanup and quantification. Samples were normalized, then adaptor-ligated ready for loading into R9.4.1 nanopore flow-cell. Basecalling and demultiplexing were performed by Guppy (Version 5.1.11), integrated with MinKNOW (Version 21.05.8), and the runs allowed to continue for 48 hours to collect as many reads as possible. Consensus was generated using the in-house workflow with a minimum coverage of 30x on Qiagen CLC workbench, and lineages assigned using the Pangolin software.

Results

Transportation challenges limited the utility of the hub-and-spoke model during the COVID-19 pandemic, taking 3-6 months to move samples between countries in EMR.

Complex emergency countries such as Yemen, Syria and Lebanon face extreme challenges in both importing and exporting reagents and samples⁴⁴. It is estimated during the COVID-19 pandemic that, the cost of acquiring reagents and importing them into these countries was 5-7x higher than those found in other regions^{5,10}. While this is partially due to geographical challenges with moving samples from conflict zones, it is also likely partially due to challenges with import and export embargoes imposed by suppliers and other countries in response to the situations in these countries¹¹. A lack of courier networks and stable cold-chain logistics also impacts the time taken to move samples between countries. Despite the best efforts of UNHAS, WHO/EMRO and other stakeholders, it took 3-6 months to move samples from each country to RLID-AD for analysis. Import and export challenges were also faced, holding the samples up further and impacting the quality of testing that could be performed downstream. Samples were collected between 07/01/2021 and 10/06/2021, with sequencing and results performed in March and April 2022 upon receipt at RLID-AD, almost 12 months after collection in some cases. In spite of this, 170 samples were received intact at SKMC for further analysis.

Sequencing identifies predominantly Delta lineages circulating in Syria, Yemen and Lebanon.

Using the Oxford Nanopore midnight protocol, RLID-AD was able to successfully sequence 154/170 samples received (90.5% success rate, Table 1). Of the samples that failed, those that were sent as extracted RNA were more likely to fail, 6 out of 10 extracted RNA failed (60% failure), which is likely due to RNA degradation from the time the samples were extracted in March/April 2021 in Syria, to the time they were sequenced in March/April 2022 in UAE. Of the samples transported in VTM, the majority of failures were in samples with higher Ct (~Ct30) which is not unexpected. Even with the limited number of samples sequenced, it was possible to observe lineage switching over time, with the majority of samples collected in Q1 of 2021 showing the Alpha lineage in both Syria and Yemen, while in Q3 a switch to the Delta lineage was apparent. This was in general agreement with global trends, with Delta becoming the primary lineage in circulation in late 2021 (Figure 2).

Table 1. Total number of samples received from Syria, Yemen and Lebanon and the number of samples sequenced successfully (success rate) with the lineage of SARS-CoV-2 assigned

Sequencing Run	Country	Pathogen	Date	Samples Received	Successfully Sequenced	Success
1	Syria	SARS-COV-2	22/02/2022	60	59	98.3

Sequencing Run	Country	Pathogen	Date	Samples Received	Successfully Sequenced	Success
2	Syria	SARS-COV-2	30/04/2021	30	25	83.3
3	Yemen	SARS-COV-2	07/07/2021	40	28	70
4	Syria	SARS-COV-2	25/07/2021	20	20	100
5	Lebanon	SARS-COV-2	25/07/2021	20	17	85
Total				170	149	87.6

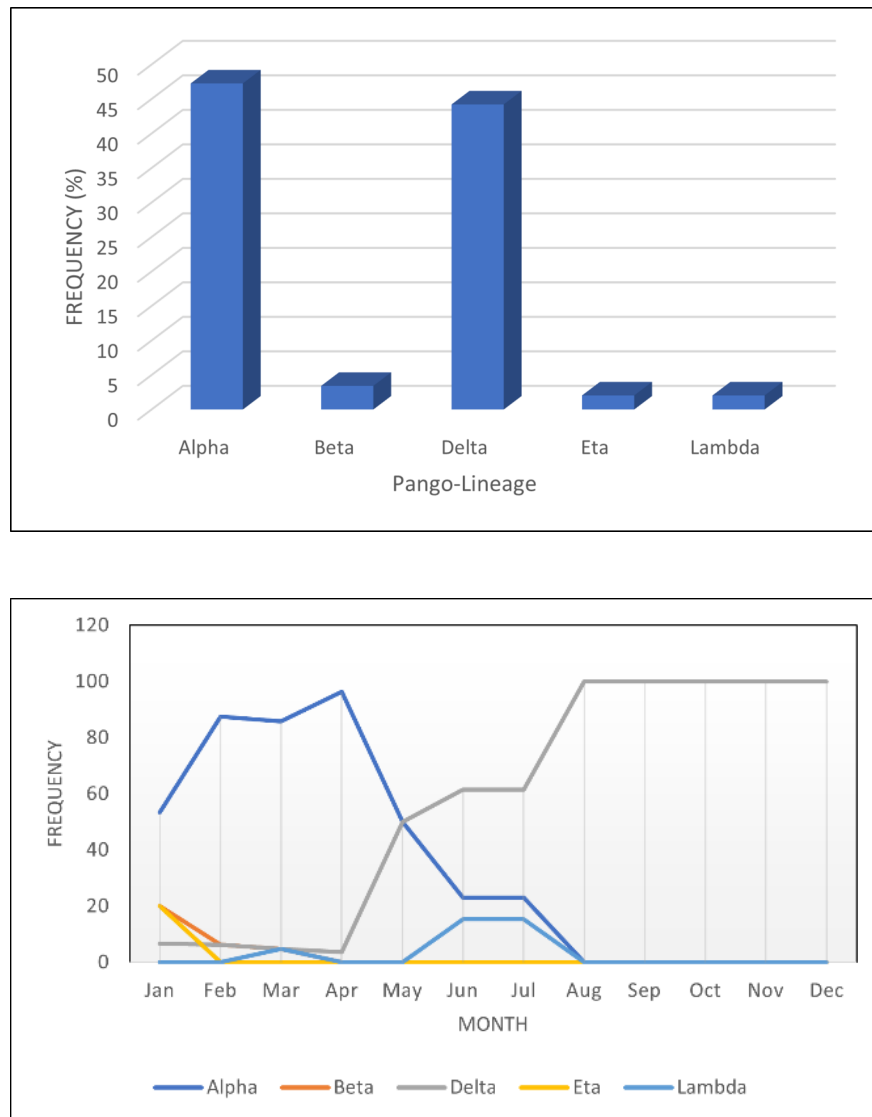


Figure 2. A. Monthly distribution of the SARS-CoV-2 variants received and sequenced in UAE hub; B. lineage frequency

Discussion

The pandemic was a challenge in the MENA region as some of which are weak, fragile and conflict-affected countries, however, the situation is not same in all the Gulf countries. In conflict-affected areas, where

health systems are already fragile and medical resources are scarce. The common challenges faced in the EMR countries specially Lebanon, Syria and Yemen were strained healthcare system due to various social and economical issues^{12,13}. In Syria, the WHO estimates that 70% of health care workers have left the country as migrants or refugees¹⁴. Lebanon had initially managed to contain the first COVID-19, but following the explosion in the port of Beirut destroyed medical centres and the health situation has gotten largely out of control^{15,16}. Moreover, the lack of testing capacity has resulted in months of under-reporting, in particular in Syria and Yemen^{17,18}. At the same time, the region suffers from a drop in demand at the regional and at global levels, while most supply chains are disrupted. International organisations have also mobilised to help the most fragile countries in the region in strengthening their capacity to respond to the crisis¹⁹. UAE's role in swift diagnosis of COVID-19 and further strengthening its healthcare system specially to increase the diagnostic capacity helped to tackle the pandemic successfully. Furthermore, the UAE's support to other countries in EMR in identifying circulating strains was significant.

Genomics is a key tool that provides critical data to advise public health responses, which has been illustrated throughout the COVID-19 pandemic²⁰. Novel variants have emerged and become dominant on no fewer than five occasions during the pandemic, with each variant having differences in sensitivity to vaccination, transmission frequency, and molecular detection²¹. Multiple demonstrations have occurred throughout the pandemic, including the loss of sensitivity of PCR testing due to S-gene mutation (SGTF) when the delta variant emerged^{22,23} and the rapid expansion of cases when the Omicron variant became dominant in 2021/2022^{24,25}. In each case, the wide availability of sequencing data was a key that allowed public health responses to be tailored to each situation.

The limited capacity of health systems and the lack of bioinformatics expertise and trained laboratory personal to perform the sequencing were the major constrained faced by most of the countries around the world²⁶. Logistics and capacity to rapidly commence sequencing, added to lack of expertise, are the primary challenges with these countries. This was further worse in the EMR countries due to the economical and logistical issues posed great challenge in implementing genomics surveillance²⁷⁻²⁹. In these situations, a hub-and-spoke model can be adopted to ensure that some data is obtained for these countries to allow for global awareness of the situation being faced. In the case of the EMR, three hubs have been established by WHO-EMRO, selected for their geographical location, capacity and expertise in laboratory procedures (Figure 1). Under this hub-and-spoke model, samples are collected in different location throughout EMR, and then sent to the three central hubs for the final processing of genomic sequencing and subsequent retrieval of the results to the country where the samples are received from for the subsequent necessary action. However, there were potential time gap in moving samples from conflict affected countries to the sequencing hubs, which delayed the sample receipt, processing and the report sharing. The success of this sequencing hubs is depending on the scientific infrastructure and from sample acquisition through reporting the results, meets or exceeds the high-quality standards of the international community. Moreover, this genomic hub-spoke model, need to have a schematic system to collect, receive, store the samples and timely delivery of the results. Also, adding a global unique identifier and a common data element to ensure that the relevant data is collected enable data to be used across multiples studies³⁰.

The hub and spoke model was successfully adopted in several developed and developing country to provide support to the far reached areas of the country and provide necessary expertise in times of need interms of medical, surgical support and vaccine distribution during COVID-19³¹⁻³³. Genomic testing in the NHS England is being provided through a national testing network, a hub-and-spoke model consolidating and enhancing the existing laboratory provision to create a world class genomic testing resource for the NHS and underpin the NHS Genomic Medicine Service. The national genomic testing service is delivered through a network of seven Genomic Laboratory Hubs (GLHs), each responsible for coordinating services for a particular part of the country³⁴.

RLID-AD in UAE is one of these hubs, with a wide array of diagnostic and molecular capacity available on multiple platforms. During the COVID-19 pandemic, provision of genomic and diagnostic support to emergency countries was a key aspect of the regional public health response, and UAE, as a hub directly

supported Yemen, Syria and Lebanon with sequencing capacity while efforts were made to operationalize genomics directly in-country. The primary challenge faced was logistical, taking around 3-6 months to move the samples into the country, with transport challenges at the country end and import issues faced in bringing samples into the country. These delays in the critical information required by the counties directly impact the quality of the data that can be provided to support public health, and WHO/EMRO is working with both member states and hubs to facilitate a more streamlined transfer of samples in future.

Conclusion

While the hub-and-spoke model is necessary to ensure expertise is available at all times during an outbreak, the main goal of WHO/EMRO is to ensure that in-country capacity is adequate to meet the needs of testing. The UAE hub continues to support this goal by providing training courses and facilities to support member states as they expand from COVID-19 into other pathogens of concern. This collaborative network has been one of the important success stories during the pandemic and will inform ongoing diagnostic laboratory infrastructure moving forward.

Author Contributions

AF, FAH, MAM, LW, BA: Study conception and design; Data collection: AF, LM, BA, ALS, AS; Analysis and interpretation: AF, FAH, MAM, LW, BA, ALS; Data generation: AKS, AS,FA; draft manuscript preparation: AF, LM, BA

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Conflict of Interest

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

Ethics Statement

This study was approved by Institutional Review Board, Department of Health Abu Dhabi, UAE

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