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Micro-elimination of Hepatitis C Virus in the Middle East

Report of an expert workshop

The EASL International Liver Foundation in association with:

**World|Hepatitis
Alliance**

This report reflects the discussions that took place at a workshop in Dubai on 28th September 2019.

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Background

The EASL International Liver Foundation in association with local medical societies and international organization held a workshop in Dubai on 28th September 2019 to review the hepatitis micro-elimination policies and strategies of the Kingdom of Saudi Arabia (KSA), Kuwait and the United Arab Emirates (UAE). The workshop aimed to identify bottle necks and knowledge gaps, and to develop action plans to aid these countries in their efforts to achieve elimination of hepatitis C virus (HCV) by 2030. The workshop had the following specific objectives:

- Review the status of HCV elimination efforts in KSA, Kuwait, UAE and identify key barriers to progress
- Develop a list of populations suitable for HCV micro-elimination
- Prioritize key activities to accelerate action toward HCV micro-elimination in the priority populations

Hepatitis C in the Kingdom of Saudi Arabia, Kuwait and the United Arab Emirates

In the WHO Eastern Mediterranean Region, it is estimated that a total of 22 million persons are infected with HCV, among whom around 15.4 million are chronically infected. According to WHO, the prevalence of HCV is estimated to be between 0.6 –2% in the KSA, while it is estimated to be less than 0.5% in the UAE and Kuwait.

The WHO has set the goal of eliminating hepatitis B virus (HBV) and hepatitis C virus (HCV) by 2030. To support the achievement of this goal the WHO has also developed a health sector strategy, which was endorsed by the 69th World Health Assembly in 2016. The WHO strategy has guided many countries in the development of national hepatitis elimination plans. However, according to the Regional Action Plan for the Implementation of the Global Strategy for Viral Hepatitis 2017-2021, *“programs targeting HCV infection are still lagging in most countries”* and *“implementation of the interventions is still not to scale, and approaches are not standardized across the countries.”*

In recent years the Middle East has taken significant strides towards the elimination of HCV with KSA, the UAE and Kuwait all having national policies and strategies to guide their elimination approaches. The experience of HCV elimination in the Middle East is however unique, with KSA, the UAE and Kuwait all having large expatriate population that outnumber the indigenous populations. There are also differences in the health systems that indigenous and expatriate

populations have access to. The dynamic population and health system structure makes approaches to identifying and targeting populations in K.S.A., Kuwait, and U.A.E. complex.

Many countries have focused programmatic efforts on a specific subpopulation which traditionally have a higher risk of contracting viral hepatitis. This approach, commonly termed micro-elimination, is proven to be highly effective at eliminating hepatitis in subpopulations while also requiring fewer resources to implement than broader approaches. By engaging health leaders and building necessary capacity, micro-elimination can be a bridge toward national-level elimination. Micro-elimination has been suggested as an approach to mobilize the HCV treatment agenda in the Middle East

Overview of micro-elimination program and micro-elimination success stories

Prior to exploring the micro-elimination program in KSA, the UAE and Kuwait, an overview of micro-elimination program was provided, along with examples of successful micro-elimination models from different countries.

The path toward micro-elimination has been described by Lazarus and colleagues^{1,2}. The majority of successful micro-elimination program will generally have the following components.

- A clear plan that will help to overcome known barriers and challenge in order to achieve high levels of diagnosis and treatment
- Clear annual targets for treatment and diagnosis which dictate the progresses needed to achieve the ultimate goal of elimination
- A multi-stakeholder process for developing and implementing the plan, which includes all key stakeholders
- A clear plan for monitoring and sharing the progress and outcomes of the micro-elimination program

An important step in developing a micro-elimination plan is to select an appropriate population. Selection of populations suitable for micro-elimination will depend on local characteristics including the prevalence of HCV, the size of the population group, and their access to medical care.

¹ Lazarus JV, Wiktor S, Colombo M, Thursz M. Micro-elimination - A path to global elimination of hepatitis C. *J Hepatol.* 2017;67(4):665-6.

² Lazarus JV, Safreed-Harmon K, Thursz MR, Dillon JF, El-Sayed MH, Elsharkawy AM, et al. The Micro-Elimination Approach to Eliminating Hepatitis C: Strategic and Operational Considerations. *Semin Liver Dis.* 2018;38(3):181-92

Population that are commonly selected for micro-elimination programs include people with cirrhosis, incarcerated individuals, Persons Who Inject Drugs (PWID), people living with HIV and HCV co-infections, veterans and people with chronic kidney disease.

The process of selecting population to be included in micro-elimination program's is challenging with health planners needing to balance a number of considerations, and with decisions often being made in the absence of data about specific populations, such as the HCV prevalence. Table 1 provides an overview of the considerations that health planner must make in the selection of populations for micro-elimination programs.

Table 1: Considerations to assist health planners in selecting the most appropriate populations for micro-elimination

Population defined by:	Example	HCV Prevalence	Ease of access to care	Political acceptability
Risk behavior	Prisoners, PWID, HIV-coinfected	Very high	Poor	Poor
Other health condition	Dialysis, hemophiliac, thalassemia	High	Good	Good
Demographics	Birth cohort	Moderate	Poor (not well defined)	Fair
Geography	City, Region, hospital	Low	Fair	Good
Other	Migrant	Moderate	Poor	Poor

Successful HCV Elimination Models

- **Scotland:** The Tayside region of Scotland uses an integrated combination of pathways to target all groups infected with HCV, especially focusing on the treatment of PWIDs who are in needle and syringe programs, to prove the concept of “*treatment as prevention*”. They are on the pathway to achieving micro-elimination by decentralizing healthcare to simultaneously increase accessibility and decrease stigmatization.
- **Egypt:** An eminent grass-root initiative in Egypt launched the country towards achieving elimination in this decade. Health workers go door-to-door in rural areas where the HCV prevalence is high and work with the community to implement accessible and comprehensive treatment, care, and follow-up services. By 2018, 63 villages were declared free from HCV after testing up to half a million people and linking all diagnosed cases to care. In addition, the Presidential initiative and school screenings have increased the screening numbers significantly.

- **Slovenia:** By following up with patients with congenital bleeding disorders who were screened positive for HCV in the 1990s, 98% of the cohort were successfully cured following the micro-elimination approach.
- **Cherokee Nation, U.S.A:** The indigenous Cherokee population in the United States implemented a HCV testing policy in 2012, with an auto-generated reminder on electronic medical records, urging doctors to screen each individual patient of Cherokee decent. This micro-elimination initiative caused overall testing to increase five-fold.
- **Prisons:** The Hepatitis C Trust in the United Kingdom conduct micro-elimination projects across UK prisons. Their model uses people with lived experiences to share their stories to others to encourage them to take up testing and treatment. Peer models are often used in micro-elimination efforts as the target populations are often some of the most underserved populations who are marginalized by health systems. Peers play a vital role in bridging the gap between health systems and the target population.

HCV Micro-elimination Workshop Outcomes

United Arab Emirates

With a decentralized healthcare system, there is an independent Ministry of Health in all seven Emirates, each aligning with the various needs of the populations across the country. With the advent of Direct Acting Antivirals (DAAs) for treating HCV, HCV patients across the U.A.E. were primarily directed to specialists at referral centers (*e.g. Dr. Mohamed Al Zaabi at Zayed Military Hospital or at the Cleveland Clinic*). In Dubai, thalassemia centers have treated approximately 800 patients in recent years, demonstrating the feasibility of micro-elimination in targeted cohorts.

HCV treatment is free for all nationals across the seven Emirates, as for expats, accessibility to HCV treatment has increased significantly as it is now covered by medical insurance. The greatest challenge faced by the U.A.E. is the lack of an official database to track patients that have been screened, diagnosed and treated. With about 80% of the country's population comprising of expats, quantifying elimination appears complex due to the fluidity of the population entering and exiting the country intermittently. The U.A.E. is one of the only countries in the GCC region with open borders to expats with Hepatitis B and C, allowing hepatitis positive patients to enter the workforce, with the exception of certain professions. Physicians find that most expats hail from countries where the cost of HCV treatment is much lower than in the U.A.E., yet the majority prefer to be treated within the country due to the high quality of healthcare in the region.

High-risk Populations

Prisoners who are citizens of the U.A.E. are treated with allocated funding from the Ministry of Health, while expat prisoners are under the jurisdiction of the Ministry of Interiors. PWIDs typically seek out or are mandated treatment from courts, prisons, or rehabilitation centers. At-risk groups such as the prison population and PWIDs have the highest prevalence of HCV but face unique challenges to access adequate treatment and care. Bridging the gap between the prison population and referrals to healthcare professionals (HCPs) is a crucial step in tackling the high rates of HCV among this sub-population.

Thalassemia centers have seen the greatest success of HCV micro-elimination so far in the U.A.E. Dr. Maryam Al Khatri and colleagues at the RAK hospital, have recently included HCV testing as part of routine screening for other medical conditions (e.g. diabetes) stressing that obtaining verbal consent from a patient is sufficient, and thus increases the likelihood of the patient consenting to HCV testing.

HCV testing occurs in the setting of pre-marital, pre-employment, and national service screening, which includes a sizeable portion of the younger population. There is a need to target certain households, with the goal of identifying the population that have received blood transfusions before 1992, when blood used to be imported from G1 countries prior to HCV screening.

Mobile van screening has been tried and tested in Abu Dhabi but has not met with much success as the high level of stigma within local tribes and communities prevented national patients from openly seeking treatment. HCV testing is still met with stigmatization within existing regions of the U.A.E., despite widespread media awareness. Patients from certain populations tend to become fearful and anxious of drawing attention, subsequently denying themselves treatment. Physicians have extensively emphasized on the need for hospitals and clinics to offer HCV testing, under a general screening or test (e.g. cholesterol, blood pressure, diabetes) which allows the patient to be routinely screened without scrutiny. A potential mandate by Ministry of Health, calling all nationals over the age of 50 across the U.A.E. to volunteer for screening could help physicians identify and treat this specific age cohort.

Advancing Engagement

The Department of Health in each Emirate would need to work hand-in-hand with the Ministry of Health to establish a comprehensive system to track and monitor the population of the U.A.E. Physicians considered approaching the local majlis to spread awareness, a grass-rooted effort to communicate directly with the community, an endeavor commonly practiced by The Royal Family. This approach was met with some hesitation, however the majority of physicians agreed

that overall it would be a noble effort. Patient outreach by practitioners is a powerful tool which could effectively draw attention and treatment to high-risk facilities such as rehab centers and prisons. On the other hand, civil society engagement in the U.A.E. is challenging given the existing level of stigma surrounding HCV. The current level of education on the disease is relatively low, creating an urgent need for patient advocacy groups to eradicate widespread of misinformation and urge infected populations to readily seek treatment.

There is shared sentiment among local physicians that HCV prevalence in the local population of U.A.E. may have been overestimated, because the prevalence estimates were derived from populations that are not wholly representative of the general population. Most physicians considered the prevalence of HCV in the general population (0.2-0.3%) to be too low to warrant general physicians to treat HCV patients. There is unanimous agreement on effectiveness and reach of HCV micro-elimination efforts, however physicians also concluded that along with individual effort, the U.A.E. simultaneously requires a top-down initiative from the majority stakeholders to reach elimination.

With the support of the ministry and government, the U.A.E. needs proactive engagement and action from health care providers to urge blood banks, clinics, hospitals, courts, rehabilitation centers to unify in a collaborative effort to achieve HCV micro-elimination within the high-risk populations.

Kingdom of Saudi Arabia

Out of a population of 32 million, it is estimated that approximately 100,000 individuals (<0.5%) in KSA are infected with HCV, out of which 20% have been diagnosed or treated. The remaining 80,000 infected individuals remain either undiagnosed or untreated.

Due to the low prevalence of this disease, there is a reduced incentive to implement policies and funding by authorities in K.S.A. There are currently 70 primary health care centers that provide HCV treatment across K.S.A., which will soon be expanding to 120. Patients are able to search for centers nearest to them with the help of web tools.

Until 2016 only hepatologists were able to treat HCV patients in K.S.A., and at this time there were only four hepatologists at the Ministry of Health in Riyadh. As of 2018, most primary health care providers have the ability to treat HCV patients, inclusive of point of care, testing and treatment. All nationals can be screened and treated at no cost in KSA. Since 2018, any expats legally present in the country are able to seek treatment under insurance, however, this number is small.

Although, stigmatization of hepatitis remains the greatest challenge in expanding HCV treatment in K.S.A., there are philanthropic societies and NGOs in Riyadh and Mecca, providing medication for those who cannot afford it. Primary health care providers have been proactive in assuring HCV treatment is highly accessible, with increased task-force initiatives and funding, yet the population remains hesitant in seeking out treatment due to lack of awareness, misinformation, and stigma.

The engagement of patient associations remains low, with many physicians attributing this lack of motivation to the low prevalence of HCV in the population as well as misconceptions about the disease. Comparatively, Egypt's population is three times as large as the population of K.S.A. and is a flagship example of HCV elimination. Egypt's high rate of HCV infection (>4%) helps explain the high level of motivation from all communal and governing bodies to achieve elimination, while contrastingly, the low rate of HCV infection (<0.5%) in K.S.A. rationalizes the low level of prioritization of HCV treatment in the country. There is a shared sentiment among physicians that HCV prevalence in the local population of K.S.A. may have been overestimated. There has also been a decline in patients seeking treatment in recent years. In 2016, approximately 2,110 patients sought treatment, while as of August 2019, this number declined to 1,285 individuals. Most (80%) of these patients are treated in the public sector (*i.e. Ministry of Health*), while the remainder are treated in the private sector.

High-risk Populations

In Jeddah, physicians screen the prison population for HBV and HCV, providing treatment for those testing positive. Until 2018, prisoners received up to 40,000 SAR (*AED 39,177*) in medical coverage and were directed to government hospitals to receive treatment. This population is deemed low priority for treatment but can be effectively targeted to achieve micro-elimination.

Patients with blood disease such as sickle cell, thalassemia, and hemophilia are considered high priority and quite feasible for micro-elimination. Patients undergoing renal dialysis can be monitored and targeted at the centers, while those undergoing transplants through the Ministry of Health can be linked through a similar system. Physicians considered targeting the diabetic population as this cohort could be tracked through an existing registry, but this approach was eventually deemed unfeasible due to the size of this population.

Pre-marital and pre-employment screening needs to be enhanced by introducing a recall strategy for patients that test positive for HCV, to ensure follow-up and treatment. An existing registry for both these cohorts makes it a viable target in an effort of micro-elimination. In addition, 81% of

HCV-infected individuals are men and women above the age of 40 years, suggesting that a mandate by the Ministry of Health could catalyze the population's effort to be screened.

The National Guard recently received approval for funding to treat members of the National Guard and their families. A potential screening mandate at relevant primary health care facilities could screen any member of the National Guard or individual above the age of 40 years for HCV. Previously, residents requiring any work or vehicle license would need to be screened for hepatitis, but this initiative was stopped as it was deemed 'politically incorrect'. The HCV disease burden is almost exclusively (99%) among the local population, as all expats residing in K.S.A. are tested for HCV under strict regulations before being granted a visa and employment.

Advancing Engagement

Physicians suggested setting up a network of referrals between blood banks and clinics; possibly following up with prior positive cases from blood banks to ensure the individual has received due treatment. Physicians also suggested a possible link between the National ID and HCV screening and testing, establishing a national registry may not directly be an effort in micro-elimination, but lays the foundation in quantifying a precise goal, toward which micro-elimination can be targeted.

Assembling a taskforce of physicians and advisors within the Ministry of Health could help push for increased prioritization, funding and logistical support, and treatment. The power of media can be used to galvanize the current landscape of misbeliefs and stigma that results in patients withholding from seeking treatment in K.S.A. It was suggested to publish a televised or viral clip of a patient speaking out about their life with HCV, to push the envelope to involve and inform the younger populations. Targeting treatment to the prison population, military hospitals and primary healthcare centers is a feasible task, but this approach will require increased support and a shift in priorities from the Ministry of Health.

Kuwait

Kuwait seeks to align with WHO's agenda to reduce new cases of HCV by 90%, reduce mortality by 60%, and treat 80% of HCV patients. An HCV committee of Kuwaiti health care providers gathered in December 2018 to identify successes, barriers, and gaps to resolve, in order to empower elimination of HCV. With a population of approximately 4 million, HCV prevalence is 0.8% among nationals and 5.4% among expats; with a significant proportion of the expatriate community come from Egypt and Pakistan, both of which have high HCV prevalence. With a smaller geography and centralized healthcare system, it is deemed highly achievable for Kuwait

to reach HCV elimination before 2030. A national hepatitis elimination plan is being developed by representatives of health care providers under the Ministry of Health.

High-risk Population

In principle, the entire prison population of Kuwait is screened and treated for HCV; however, there is no available data to evaluate the effectiveness of the program. Records of positive HCV antibody and PCR tests are stored in hard-copy and destroyed every three years. There is need to transition to an electronic record system and to transfer all current paper records onto an online database for efficient management.

Strengthening of the PWID program is seen as the foremost and most feasible step in the direction of micro-elimination with the populations being targeted through drug treatment centers. Upon establishing a registry centers can approach family members of the PWID to encourage screening through on-site or at-home tests (finger or saliva test). Stigma around HCV can be mitigated by testing the family as part of "*routine testing for family member of PWID*" rather than a targeted test for families of HCV patients. The main stakeholders for PWIDs are PWIDs themselves, peers, psychiatrists and physicians. The juvenile population could potentially be treated along-side, with the collaborative effort of social services.

There are currently two NGOs in Kuwait - one religious and one secular - that screen and treat PWIDs. All hemodialysis patients in centers are screened and referred for treatment. Before DAAs, HCV prevalence among hemodialysis patients was at 20%, this was subsequently reduced to 4% as a result of improved infection control. There are approximately seven hemodialysis centers in Kuwait - one stand-alone, the rest adjunct to hospitals - yet as of 2019 they rarely see new patients.

With a large and growing diabetic population, physicians consider this population would be suitable for provider-initiated screening. Pre-marital screening is tracked on a registry, yet there needs to ensure that persons diagnosed with HCV are linked to care. As the older population is was not covered by premarital and pre-employment health screening, the prevalence of HCV in this population is likely higher than the younger population, thus making it a candidate group for targeted screening.

Currently donors whose blood is rejected at blood banks are not contacted or followed-up if they are found to be HCV positive. These individuals are only linked to care if they return for a repeat donation. HCV positive blood donors represent an ideal target for patient follow-ups to eliminate the virus this specific cohort.

A large number of undocumented and stateless individuals (60,000) live in Kuwait, unable to be deported to their home countries. Undocumented and stateless individuals diagnosed with HCV are screened and funded by the government, making it another cohort in which micro-elimination can be achieved.

Advancing Engagement

Physicians recommend their peers to approach private insurance companies with an improved business model to increase HCV treatment coverage. Mass screening was attempted in Kuwait with the support of Gilead and Abbvie, but the desired population was unresponsive. The younger age range of 22-40 years were seen to be highly engaged in education and screening, yet the higher risk population (above 40 years) proved difficult to retain.

It is a commonly held belief by practitioners in Kuwait that any and all patients that walk into a clinic for a routine checkup should be offered HCV screening. Physicians consider the local population of Kuwait to be generally unresponsive in seeking treatment, compared to the expat population. However, while nationals are typically covered by medical insurance, expats more likely have to pay out of pocket for HCV medication if their private insurance does not provide coverage. A more impassioned and strategic appeal for “work-place wellness programs” to educate about and screen for HCV among private and public companies is needed.

To formulate an action plan to directly approach ministers, there is need to assemble a core team, of hepatologists and physicians, but also individuals from eclectic backgrounds (*lawyers, entrepreneurs, philanthropists*). Overall, the efforts of a core team can only be successfully executed with the support of key opinion leaders in the region, chief executives, and policy makers. Physicians believe that the Ministry in Kuwait is highly impassioned yet does not have the tools necessary to embark on a plan of action, nor are they inclined to shift focus to HCV, without a reassuring push from the core-team. It will be key to form a platform for multi-stakeholder engagement that can fill knowledge gaps and advance the national discourse.

Conclusion

The three countries to participate in the workshop, K.S.A., Kuwait, or U.A.E., all aim to achieve national elimination of HCV before 2030. Various jurisdictions in these nations are working in silos under a healthcare plan, creating a necessity to integrate the involved governing agencies and authorities, in a multi-disciplinary effort to streamline micro-elimination in each country.

It is evident that establishing a national registry or database is a fundamental step to quantifying elimination. Concurrently, physicians suggest grass-roots efforts are needed to accelerate micro-

elimination by targeting certain populations or geographic regions within each country in order to screen and declare these as HCV-free (*undocumented refugees, blood banks, geriatric cohort, diabetes, blood disease, transplant patients*).

Individual effort by physicians, such as offering HCV screening to targeted patients would be highly effective and impactful, as patients are more likely to accept screening and treatment in these circumstances.

A shift in focus towards high-risk populations such as the prison population and PWIDs is required due to high proportion of infected population falling in these sub-populations. The unique challenge of a fluid expat population in this region can be ultimately overcome by utilizing technology to consolidate and maintain online records. Practitioners play a substantial role, not only in raising awareness and educating the public, but also in outreach to physicians from adjacent disciplines that might be lesser informed of the treatment process of HCV.

Increased media awareness can also be a power tool to combat the stigma around hepatitis, the lack of awareness and the spread of misinformation. Along with civil society engagement, a simultaneous top-down approach involving all stakeholders and KOLs is essential to sustain any efforts of micro-elimination. Although HCV has significantly lower mortality rates than heart disease; its transmissible nature, expensive treatment, and high rates of psoriasis, should elevate it to a top priority in healthcare, as it is notably, a highly treatable disease.

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