

REVIEW



# Emerging from the screening of 57 million citizens and treating 4 million patients: future strategies to eliminate hepatitis C from Egypt

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## ABSTRACT

**Introduction:** Egypt succeeded in establishing a successful model of care for hepatitis C virus (HCV) management in the country with the highest worldwide disease prevalence. The Egyptian ministry of health announced an optimistic goal of near disease elimination. More steps are still required to achieve such a goal.

**Areas covered:** This review covers the efforts made in treatment and prevention of HCV by the Egyptian National Committee for the Control of Viral Hepatitis (NCCVH) with emphasis on the extensive screening program that was able to screen more than 57 million citizens, and future strategies implemented to ensure eradicating the virus from the country.

**Expert opinion:** Despite the great efforts and the proven success in controlling the HCV epidemic in Egypt, some facets of the Egyptian program still need to be upgraded to reach the HCV elimination goal. A significant workload with follow up programs for those who were successfully treated, and treatment failure cases are existing. More enhancement for the currently performed prevention and control measure is missing. Also, we strongly recommend conducting a recent nationwide survey to document the actual infection rates of HCV after all these efforts.

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## 1. Introduction

Hepatitis C virus (HCV) is a major global health challenge with more burden in some countries like Egypt, which was always considered to have the world's highest prevalence rates for HCV [1,2]. This extraordinary prevalence of HCV in Egypt is mostly due to the long-lasting treatment campaigns against schistosomiasis conducted by the Egyptian Ministry of Health (MOH) during the period from 1950–1980 [3,4]. The use of poorly sterilized non-disposable needles in these campaigns could explain the spread of HCV in Egyptian rural areas [5]. To combat such an epidemic, the Egyptian MOH launched the National Committee for Control of Viral Hepatitis (NCCVH), to take the responsibility of managing the HCV epidemic in the country [6,7]. During the interferon era in the management of HCV, the prevalent genotype in Egypt (genotype 4), was always one of the obstacles that prevent securing an effective therapy for HCV in Egypt, in addition to the treatment cost and lack of infrastructure [6,8,9]. After the introduction of directly acting antivirals (DAAs) in the management of HCV, and because of the high success rates and excellent safety profile of these drugs, a great revolution occurred in the field of HCV worldwide [10,11]. With DAAs use, Egypt was able to treat millions of patients from HCV with high success rates for the mainly locally produced medications [12–15].

## 2. Egyptian achievements in the battle against HCV

Since its launch in 2006, the Egyptian NCCVH took the lead in putting the strategies and adopting policies to face the HCV epidemic in Egypt. Among such strategies was the moderation

of the Egyptian national treatment program and the conduction of screening programs.

### 2.1. HCV national treatment program

In Egypt, before October 2014, the only available treatment for chronic HCV patients was the combination of pegylated interferon (alfa 2a or alfa 2b) and ribavirin (Standard of Care) for 48 weeks. The broad list of contraindications for this treatment regimen prevented a sizable group of patients from receiving the only available treatment at that time. This list included advanced liver cirrhosis, decompensated liver disease, co-infected patients with HIV, patients with severe psychiatric disease, and patients with co-morbid severe conditions. Sustained virological response (SVR) did not exceed 60% with this treatment that had many side effects like hematological abnormalities as anemia, neutropenia, leukopenia, and thrombocytopenia, in addition to hair loss, reactions at the injection site, and flu-like symptoms [8,9,16]. With the approval of Sofosbuvir (SOF) internationally, NCCVH and MOH made all their efforts to make the drug available for all patients in reasonable prices through negotiations with the manufacturing companies, and they succeeded to have the drug with a price that is lower than its cost in any other country [1,2,6]. In October 2014, SOF became available but still expensive and with limited supplies that cannot withstand the high demand for a country like Egypt. Based on these facts, the priority of treatment was given at this time to those with advanced fibrosis and cirrhosis, as they are more prone to complications shortly. During this period, there were two available regimens, either

**Article highlights**

- Egypt succeeded in establishing a useful model of care for HCV management in the country with the highest worldwide disease prevalence that was able to treat about 4 million patients.
- The sizeable Egyptian program relied on establishing a network of specialized viral hepatitis treatment facilities that provide integrated care for HCV patients
- A sizeable nationwide screening program ‘100 Million Health campaign’ was conducted in Egypt over six months to screen more than 57 million citizens for HCV serology.
- One of the significant challenges facing Egypt after the successful HCV screening and treatment programs is the need to maintain this success by making more efforts towards prevention. Despite the implemented great efforts in the field of HCV management in Egypt, some limitations could delay the complete elimination of the disease.

dual therapy (SOF-RBV) for those with advanced fibrosis and cirrhosis or triple therapy (SOF-PEG-RBV) for those who were eligible for interferon treatment [17]. By May 2015, it was confirmed that the prioritization strategy was not the best and that it leads to very long waiting lists of HCV patients. At that time, the NCCVH was sure that this strategy must change to have more patients cured and to achieve the desired target. Therefore, they changed the protocol of treatment, giving a chance to all chronic HCV patients whatever the stage of fibrosis (F0-F1) to receive treatment, and other types of DAAs were introduced to the Egyptian market as Simeprevir [13].

The use of SOF-PEG-Ribavirin was a transition until Egypt succeeded in producing the generic drugs, and the protocol changed again to be totally interferon-free regimens with generic Sofosbuvir and Daclatasvir (SOF-DCV). Patients with Child-Turcotte-Pugh (CTP) B were included in the treatment protocol in December 2015. **Phases of the Egyptian nationwide HCV management program** is summarized in Table 1. Regarding Child C patients, they were not treated in the viral hepatitis specialized treatment centers as they need extra care and in need of a ready transplant center and to be put on the transplant list to manage once any complication occurs [18]. The presence of a web-based registry system was significant during

**Table 1.** Phases of the Egyptian nationwide HCV management program.

Time	Action
2006 – 2014	<ul style="list-style-type: none"> <li>• PegIFN/Ribavirin (SVR less than 60%).</li> <li>• Introduction of:               <ol style="list-style-type: none"> <li>(1) Sofosbuvir/RBV (SVR 82.7%)</li> <li>(2) Sofosbuvir/PegIFN/RBV (SVR 93.9%)</li> </ol> </li> </ul>
May 2015	<ul style="list-style-type: none"> <li>• Prioritization of advanced fibrosis and cirrhosis patients.</li> <li>• Introduction of Simeprevir/sofosbuvir (SVR 94–98.5%)</li> <li>• All stages of liver fibrosis are eligible for treatment, no more prioritization.</li> </ul>
December 2015	<ul style="list-style-type: none"> <li>• Introduction of generic drugs.</li> <li>• Main line of treatment is Sofosbuvir/Daclatasvir with/without RBV (SVR 94.7–95.4%).</li> </ul>
October 2018	Launch of the Nationwide Screening Program

Peg IFN: pegylated interferon; SVR: sustained virological response; RBV: ribavirin  
NB:

- In September 2015, Paritaprevir/Ombitasvir/Ritonavir with ribavirin was introduced (SVR 91 – 100%) and was prioritized for renal impairment patients.
- In December 2015, sofosbuvir/Ledipasvir was added to lines of treatment but minor number of patients were treated using this line.

all these steps. It has a great role in arranging appointments, giving dates to patients, and registration of all data with connections between treatment centers and the registry.

Moreover, the number of centers increased, reaching more than 50 centers all over the country [2,6]. To facilitate the inclusion process, many changes have been made to the protocol. Fibroscan examination was routine in the beginning; then, with the increased number of patients that overcame the capacity of the centers, it was replaced by FIB 4 as an indicator for fibrosis stage [1].

Also categorizing patients to ‘easy-to-treat’ group that included non-cirrhotic, naive patients, who were treated with SOF-DCV for 12 weeks, and ‘difficult-to-treat’ group that included experienced cirrhotic patients who received SOF-DCV-RBV for 12 weeks, enabled easy inclusion and treatment of patients according to their category [13].

Sustained virological response varied among different treatment regimens being the lowest (82.7%) with SOF-RBV (93.9%) with SOF-PEG-RBV (97.4%) with SIM-SOF and increased to (98.5%) with the use of SOF-DCV [13,14,17].

With all these achievements, it was the proper time to go through the complete elimination of HCV, and the primary tool was to screen as many people as we can.

## 2.2. Before the national screening stage

### 2.2.1. Limited screening initiatives

In 2018, Shiha and his colleagues provided a prototype model for the potential adoption of an ‘educate, test, and treat’ program. This initiative was performed in a rural Egyptian village. Within one year, they succeeded in screening 89% of eligible villagers and treat all discovered HCV patients [19]. In 2019, they published a larger-scale experience that included 73 villages with a successful 84.6% coverage of eligible villagers. Sustained virological response at 12 weeks following treatment (SVR12) was achieved in 98.3% of treated patients, and the authors provided a feasibility model for the sizable community-based program in more than 200 thousand people [20].

In the same year (2019), Soliman et al. published their results for a mass screening program for both hepatitis B and C viruses in Southern Upper Egypt. Within a year, the investigators screened more than 67 thousand persons and found 14.5% and 4.4% of patients to be positive for HCV and HBV, respectively. They provided costs, turnouts, and logistical issues that could be valuable information for the more substantial national mass screening and treatment programs [21].

### 2.2.2. SWOT analysis for the national program of HCV treatment

Under the patronage of a Knowledge and Technology Alliance (KTA) supported by the Egyptian Science and Technology Development Fund (STDF), a technical workgroup that was derived from Central Administration and Health Development (MOH), developed a fundamental and comprehensive SWOT analysis in conjunction with eminent Egyptian hepatologists as well as stakeholders from the NCCVH. Based on the data of the national HCV treatment program, the report analyzed the current national projects, opinions of relevant stakeholders, innovative hubs, and centers of excellence for managing HCV. This report helped in guiding researchers,

policymakers, academic institutions, and health development partners and highlighted best practices at the national level that tackled identified weaknesses and threats.

### 2.2.3. Brand and generic DAA drugs

One of the crucial elements for the feasibility of the significant health campaign was the cost and availability of enormous amounts of DAA drugs. By October 2014, the brand SOF (Gilead company) was first approved and introduced by NCCVH for nationwide treatment at 1% of its international price [22]. Still, this cost was remarkably high for mass screening and treatment programs. The production of local manufacturers for highly efficient DAA drugs at a much lower cost and considerable productive amounts was the plummet to open the gate for the '100 million Health' campaign. Different studies reported the same and comparable safety and efficacy of generic and brand drugs [12,23]

### 2.2.4. The goal of HCV elimination

In 2017, El Akel et al. demonstrated the Egyptian treatment program of HCV management as an HCV model of care and delineated the robust infrastructure for controlling viral hepatitis in Egypt. By that time, more than one million Egyptian patients were eventually evaluated, and more than 850 thousand people received treatment [6]. Omran et al. addressed the Egyptian experience toward HCV elimination. They importantly highlighted the necessity of applying different preventive measures and awareness campaigns to reduce rates of HCV transmission in parallel to HCV treatment and described the barriers and limitations for HCV elimination [2].

Another main issue was concerned with the planning and prioritization of DAA treatment for HCV patients in countries with low income and resources. The Egyptian program started with the management of advanced fibrosis patients then soon included all stages of fibrosis (F0-F4). Inclusion of all HCV patients in treatment could be a key-player factor to manage HCV reservoir and reduce rates of transmission. Hill et al. analyzed the rates of cure versus new infections in 91 countries and concluded that ten countries, including Egypt, had at least five times more people reaching SVR rates than new HCV infections [24].

## 2.3. The nationwide screening program (screening everyone for HCV)

The huge nationwide screening program '100 Million Health campaign' started in October 2018 and involved nine governorates in its first phase, where more than 13 million people were screened. The second phase started three months later and involved 11 governorates. The last phase was enrolled in March 2019 and lasted for another three months in the last seven governorates. Phase 2 and 3 screened more than 18 million and 19 million, respectively. Egyptian MOH announced that a total number of 57 million people were screened. Media campaigns were done in concordance with the national screening program and involved TV ads, press conferences, and daily press coverages. Social media played a tremendous additional role.

At the start of the screening program, 165 centers (in both NCCVH and Health Insurance centers) were well established and were working according to the national guidelines. For better coverage, the number of centers effectively increased to reach 302 centers by the end of the campaign. Besides, 5820 testing sites (including 1079 mobile units) performed the initial screening. The workforce included 20423 in all phases. NCCVH human resources included 98 University staff hepatologists, 1842 medical doctors and nurses, and 1704 administrative staff members.

All screening sites were connected to an online database to reach for the status of the screened person through his national ID, whether he was previously treated or not. Laboratory results were added at the same online system, and the patient was referred to the nearest treatment center with a set date if HCV Ab tested positive. All the investigations were done free of charge. Governmental support covered the whole program, and the cost per screening person was 0.62 USD (included screening test and blood glucose test). If the patient proved to be HCV antibody positive, laboratory tests cost 25 USD while treatment (using sofosbuvir and daclatasvir for 12 weeks) cost 45 USD. Apart from screening for HCV, every citizen was screened for non-communicable diseases (diabetes and hypertension) and checked for BMI. Special initiatives were performed for refugees, renal patients, HIV patients, prisoners, University students, blood donors, and school children.

## 3. Required future strategies and policies to ensure disease control and elimination from the country

Despite the huge work of the NCCVH during the past few years in the field of HCV management, there is still a room for more advanced steps to achieve complete and rapid elimination of the disease:

### 3.1. HCC surveillance in treated patients

Recently, a significant debate evolved about the incidence of de-novo and recurrent hepatocellular carcinoma (HCC) post DAA therapy in cirrhotic patients [25,26]. Some reports from Egypt raised the possibility of an existing relation between HCV treatment with DAAs and the recurrence of previously treated HCC [27]. Tumor behavior post DAA therapy was also more aggressive as regards the development of portal vein thrombosis, malignant lymphadenopathy, and HCC imaging characteristics in another Egyptian study [28].

Previous studies necessitated the adoption of a special follows up the program for cirrhotic patients who received DAA treatment for the management of HCV. Accordingly, the targeted population includes ~400 thousand cirrhotic patients. As the program is very recently applied, coverage is still around 10% after three months of the launch of the program. Cirrhotic patients are requested to perform abdominal ultrasonography and alpha-fetoprotein every four months. Patients are followed up by skilled hepatologists and radiology specialists. The program includes 92 screening centers, 63 radiology centers, 20 MRI centers, and 20 HCC multidisciplinary clinics. The aim is to early detect the development of hepatic focal

lesions and real-life document status for the incidence of HCC post DAA therapy. The program is expected to expand to include all patients who are at high risk for HCC. This includes HBV patients and all cases with liver cirrhosis irrespective of their etiologies.

### **3.2. Treatment failures and difficult to treat populations**

More recently, a particular protocol was launched for the management of relapsers and non-responders. Patients who failed response to interferon-based therapy, SOF based mono-DAA therapy with/without interferon or SOF-SIM, are re-treated using SOF-DCV-RBV for 24 weeks. Treatment experienced patients to SOF-DCV-RBV for 12 weeks, and are suffering from hepatic decompensation will be re-treated using sofosbuvir/velpatasvir/ribavirin (SOF-VEL-RBV) for 24 weeks. Otherwise, SOF combined with VEL and voxilaprevir (VOX), will be given to non-cirrhotic or well-compensated cirrhotic patients who previously failed treatment using SOF-DCV. SOF combined with ombitasvir-paritaprevir is another alternative in patients who failed SOF-DCV for 12 weeks.

### **3.3. Need to have a complimentary screening campaign with more emphasis on drop out cases from the**

Coming to the discovered HCV infected patients during the extensive nationwide screening program, positive results were referred to the nearest viral hepatitis treatment center where HCV PCR is performed to confirm HCV infection. Cases with positive viremia were scheduled to receive their treatment free of charge in the various treatment centers.

Toward the elimination of HCV in Egypt and the zero transmission of the disease, a possible second check through a complimentary screening program for those who were seropositive with HCV PCR negative results during the screening campaign. Also, dropouts from the previous screening campaign could be targeted and have them tested. Most of these dropouts are located in remote places and rural areas. Providing more mobile units to places away from health facilities is very important, encouraging more people to come for screening and more involvement of media and social networks. Encouraging those who live in rural areas and who are more prone to acquire infections from seeking medical advice from unqualified personnel [29]. Furthermore, during such complimentary screening campaigns, retesting of a selected sample from those with previously negative HCV antibodies to detect newly acquired HCV cases. Data on HCV transmission risk factors could be obtained by questionnaires that could be used at the time of screening. These questionnaires can include all sociodemographic characteristics, past risk exposures in the community (e.g., injection practices, sharing of toothbrushes and razors, shaving at the barber's shop), iatrogenic exposures (e.g., hospital admission, invasive and noninvasive procedure, blood transfusion and obstetric history) and occupational exposures (e.g., syringe/sharps injury, body fluids, and HBV vaccination).

### **3.4. Need to have a new demographic health survey in 2020 to evaluate the previous efforts**

In 2016, the World Health Assembly designed and agreed on the Global Health Sector Strategy on viral hepatitis, 2016–2021, for the elimination of viral hepatitis by 2030 through both prevention and treatment strategies. Their goal is to decrease the incidence of hepatitis infection in 2030 by 90%, although the prevention and treatment methods are widely distributed [30]. In Egypt, the percentage of population aged 15–59 with positive HCV Ab decreased from 14.2% in 2008 to 10% in 2015. Moreover, the percentage of the population in the same age group with positive HCV RNA decreased from 10% in 2008 to 7% in 2015 [29,31]. HCV transmission is still ongoing, and incidence rates have been estimated at 2.4 per 1000 person-years (close to 165 000 new infections annually) [32]. After screening 57 million citizens and treating 4 million patients, with very high rates of sustained virological response, there is a need to have a new demographic health survey in 2020 to evaluate previous efforts and design the plan whether on the field of prevention or the field of treatment.

### **3.5. Need to enforce prevention and control measures**

Prevention of infection is complicated among our population, especially in rural areas where members of the same family may share their instruments. Most probably, the development of new cases will not stop, and so elimination will not be adequately achieved. Global partners, as WHO and the Center for Disease Control and Prevention (CDC), set a strategy for HCV prevention with special consideration to infection control measures, blood safety measures, awareness, and education [7]. Egypt made many efforts to improve the infection control practices and measures over the past years, especially among dialysis patients with decreasing the incidence of new HCV infection among them from 28% to 6% in 2008 [33].

The implementation of the global injection safety program in Egypt in 2015, with the help of WHO, had a high impact. The knowledge of the health team (physicians, nurses, and even medical students) regarding the infection control measures and blood safety guidelines were updated. A nationwide media campaign dealing with problems facing patients was of great value [34].

A big challenge is facing Egypt nowadays after the successful screening and treatment programs performed during the last five years toward the chronic HCV problem, as they need to maintain this success by making more efforts toward prevention. Health education, awareness programs, disseminating the knowledge of different modes of transmission, especially in the family, awareness for patients who cured of HCV to prevent their reinfection, proper control, and supervision of blood banks and dialysis machines will pave the way to the complete elimination of HCV soon.

Proper training of hepatologists and physicians in the treatment centers not only on the treatment protocols and the management of side effects but also on the prevention

methods and awareness given to patients during or after their treatment were done. Explaining the possible modes of transmission and protection from reinfection to patients is the cornerstone of the success of the prevention strategy.

#### 4. Conclusion

Egypt succeeded in founding a successful program for HCV management. The enthusiastic objective of disease elimination from the country appears to be achievable, mainly after treating more than 4 million patients and screening about 57 million. Further steps are still required to achieve such a goal, including enforcing infection control measures and providing specific care for some special patient groups.

#### 5. Expert opinion

Egypt succeeded in establishing a successful model of care for HCV management in the country with the highest worldwide disease prevalence. The Egyptian ministry of health announced an optimistic goal of near disease elimination. The HCV model of care in Egypt prospered to a large extent in creating an excellent infrastructure and have achievements on the way to eliminate the diseases from the country. Egypt was able to treat more than 4 million HCV patients by using locally produced generic medications. The formulated infrastructure with the widely distributed specialized HCV treatment facilities was the backbone of such a model of care. These centers are responsible for providing integrated care for HCV patients starting from diagnosis, evaluation, treatment, and ending with providing the necessary post-treatment follow up. A dedicated internet network was launched to connect all these centers to the headquarter, which helped a lot in data collection and having accurate estimates of treatment results. The availability of highly effective, locally manufactured DAA drugs at a much lower cost could pave the way to target screening for everyone in Egypt through the '100 million Health' campaign. This sizable nationwide screening program was conducted over six months to screen all adults living in the country, with success in testing 57 million. Governmental support covered the whole program and the cost of the screening, which was provided for free. Despite this enormous work of the country during the past few years in the field of HCV controlling, there are still some required further steps to achieve total and rapid elimination of the disease. We recommend the adoption of a unique follow up program for cirrhotic patients who received DAAs treatment for the management of HCV, to early discover HCC cases and hence improving the patient chances of cure. Additionally, some HCV special population groups like previous treatment failure, and patients with renal impairment are creating an extra burden for the Egyptian HCV management system given their need for special care and medications. Specific plans targeting these groups are mandated with providing required medications for these groups. We also suggest a possible second check through a complimentary screening program for those who were seropositive in the massive nationwide campaign and tested HCV PCR negative results. Also, dropouts from the previous screening campaign could be selectively targeted and have them

tested. In our opinion, there is a current necessity to have a new demographic health survey to be able to evaluate previous management efforts and design the plan, whether on the field of prevention or the field of treatment. Prevention of infection is one of the challenging missions in the Egyptian fight to eliminate the disease, especially in rural areas where personal sharing instruments are still practiced. Intense health education programs, raising the awareness of the community, and legalizing infection control measures, especially in proper control and supervision of blood banks and dialysis machines, are among the prerequisites to control further propagation of infection within the community. Based on the Egyptian achievements on the way of eliminating HCV from the country, including the colossal treatment program and the nationwide screening initiative for all citizens, we are influenced that such a dream became reachable in the next few years. Few further steps are missing, which could create a needed difference to achieve this goal.

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