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REVIEW

Milestones along the road of infection prevention in Egypt

H. A. El-Mahallawy[1] · **L. M. Mohsen**[2] · **M. Wassef**[2]

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Abstract Sequela of infectious diseases include not only morbidity and mortality, but are also associated with chronic illnesses that has long constituted public health problems and huge economic burdens. This review gives a brief idea about important infectious diseases (ID) in Egypt, the main lines taken to combat them, the challenges still existing, and the possible barriers keeping IDs still forming threats to the community. Egypt has the highest prevalence rates of HCV infection worldwide. Significant evidence points towards that the HCV epidemic was initiated and propagated by the anti-schistosomal mass campaigns during the last century. Though the rates of HCV infection are declining, still the decline has not yet met the full expectations. Therefore, infection control programs are gaining more ground all over the country, especially with the growing problem of antimicrobial resistance complicating healthcare-associated infections (HAI) worldwide. Also, mass immnunization of childhood, mycobacterial tuberculosis infections, and avian influenza will be discussed.

Schistosomiasis: a monster from the past with a trail on the present

More than 50 years ago, schistosomiasis constituted a major public health problem in Egypt's rural areas. The Egyptian Ministry of Health together with the civil medical society cooperated through large scale campaigns to combat this highly prevalent infection with major consequences on the economy of the country [1]. The main line of treatment was parenteral anti-schistosomal therapy (PAT) of antimony potassium tartrate which was given to millions of Egyptians utilizing reusable glass syringes [2]. The PAT strategy, in combination with a campaign addressing the need for behavioural changes, were the initial steps that lowered the large numbers of infected citizens of rural areas [3]; still it appeared to have been causal in furthering the high rates of hepatitis virus infections that was recorded in the years following PAT. This was due to lack of significant infection control practices at that time with deficient sterilization of glass syringes as a major predisposing factor. Later on, with the development of a single dose oral medication, schistosomiasis was successfully controlled in Egypt [4]. However, in the 1990s, HCV continued to rank as the primary cause of liver disease in Egypt, replacing schistosomiasis as the country's major infectious disease [5].

The major public health problem nowadays in Egypt is HCV infection with its complications including chronicity and associated hepatocellular carcinoma. Egypt has the highest prevalence of HCV infection worldwide with an estimation of 14.7 % in the 15–59 years age group, with an RNA prevalence of 9.8 % as recorded by the Egyptian Demographic Health Survey (EDHS) in 2008 [6] and with an increase in rates among higher age groups and among rural more than urban areas [7, 8]. The burden of HCV infected citizens is illustrated in Table 1. In a systematic review conducted on 150 studies concerned with HCV prevalence and incidence in Egypt, HCV among blood donors ranged between 5 and 25 %, among other general population groups between 5 and 15 % and among multi-transfused patients between 10 and 55 % clearly substantiating the added risk of receiving a transfusion [9]. As previously mentioned, one of

✉ H. A. El-Mahallawy
hadir38@hotmail.com

[1] National Cancer Institute, Cairo University, Kasr el-Eini, Kornish el-Nil, Fom el-Khalig, Cairo 11796, Egypt

[2] Kasr Al-Aini School of Medicine, Cairo University, Cairo, Egypt

Table 1 Total numbers of HCV positive cases in different age groups in 2008 as compared to previous total numbers in 1996 (El-Zanaty and Way 2009)

Age group (years)	1996 HCV positive cases	2008 HCV positive cases	Chronic HCV 1996	Chronic HCV 2008
15–19	722,443	359,423	469,588	269,568
20–24	669,146	310,692	434,945	233,019
25–29	1,038,067	339,416	674,744	254,562
30–34	1,395,238	582,980	906,904	437,235
35–39	1,505,101	660,825	978,316	495,619
40–44	1,284,800	908,550	835,120	681,412
45–49	1,087,426	985,458	706,827	739,093
50–54	914,678	959,275	594,541	719,457
55–59	627,704	732,483	408,008	549,363
Total	9,244,604	5,839,102	6,008,993	4,379,326

the main causes of this high prevalence is postulated to be iatrogenic transmission during the early years of parenteral anti-schistosomal therapy extensive treatment campaigns [10, 11]. In favour of this postulation is a reported 28 % prevalence of HCV infection among patients previously treated with PAT, as compared to a prevalence of 13 % among patients who received oral therapy [6]. A recent review discussing the geographical distribution of the predominant type of HCV in Egypt, namely, the HCV 4 genotype, concluded that the Egyptian HCV epidemic was initiated and propagated by the anti-schistosomal mass campaigns during the 1930s and on to the early 1980s [12]. Still, there is an ongoing HCV transmission in Egypt especially in rural areas, with an estimated incidence based on analysing cohort data of 150,000 new infections annually [13].

Understanding the exact contribution of different modes of transmission is of utmost importance to set nationwide preventive policies. Intravenous drug injection is known to be the predominant mode of transmission of infection in many areas of the world [14], yet this represents a rare risk factor in Egypt and likely accounts for less than 1 % of infections in Egypt [5]. Medical exposure is believed to constitute the main mode of transmission of infection even after the implementation of more strict infection control policies in the nationwide medical setting and changing the more selective strategies of recruitment of blood donors towards more safe blood products. This could be partly explained by a number of risk factors related to social and cultural rituals such as circumcision, deliveries, and tattooing performed in rural areas by traditional, non-health care providers that possibly spread the infection [12]. Still, there is evident transmission in those who lack any known risk factors with intra-familial transmission through household exposure being the only explanation [15]. At this stage, the lack of mass estimation of the exact load of the disease in different governorates hinders preventive efforts.

In Egypt, there is a pool of 5 to 7 million people infected with HCV of a total population approaching 90 million. In the last two decades the Egyptian Ministry of Health has directed its efforts mainly at offering therapy to infected patients, previously by interferon, ribavirin combination therapy and more recently by treatment using sofosbuvir. This strategy has also included infection prevention as it was clear that treatment alone is not enough to reduce the numbers of infected citizens. Owing to the increased burden of infections acquired in health care settings coinciding with a rapidly evolving demands on services directed to high risk patients involving an increase in invasive procedures, a program promoting infection control has been mandatory in Egypt. Blood-borne pathogen transmission related to poor adherence to infection prevention practices has been among the most prompting factors for initiation of implementation of an infection control program in health care facilities in 2001 [16]. Steps undertaken in the evolution of an infection control program in Egypt are summarized in Table 2. The difficulties encountered during the

Table 2 History of evolution of an infection control program in Egypt (Talaat et al. 2006)

Year	Action taken
1999	Infection control working group established
2001	Baseline assessment Infection control advisory group initiated the plan
2002	National Infection control guidelines were developed
2003	Applied training for infection control in a phased approach, with the goal to train and promote four hospitals within each governorate to develop them as centres of excellence
2003	Monitoring and supervision
2003	Ensure availability of supplies and equipment in settings with limited resources
2003	Promotion of occupational safety and health
2005	Establishment of a surveillance system for hospital acquired infections piloted in a network of 12 large hospitals in six Egyptian governorates

implementation of the program were the limited resources, the lack of trained health care professionals, and factors related to the structure of health care services. Monitoring the health-care workers' compliance to the infection control program generated some improvements in reducing rates of infection. The annual incidence of HCV infection among dialysis units in 60 facilities was reported to drop from 28 to 6 % in previously uninfected patients undergoing dialysis after implementation of the program [16]. After a decade of beginning the program, the services have improved, and currently stepping towards an accreditation process is expected to further reduce the burden of health care associated infections.

Nowadays, and through the National Committee of Hepatitis Viruses established in 2006, in cooperation with more than 30 international institutions including the WHO, the aim was to improve the care and prevention of HCV infection as the decline in HCV incidence had not yet met the full expectations [17]. A national network of 23 viral hepatitis study centres located throughout Egypt was established allowing better access to care and treatment [18]. Besides, with the assistance of WHO, CDC and Institute Pasteur, an advisory group was formed. The group advised on the implementation of a comprehensive viral hepatitis control program including the expansion of the current infection control program beyond governmental facilities, raising community awareness and education, enhancing access to hepatitis B vaccination and establishing a surveillance system with proper mapping of distribution of infection. In 2011, it was concluded that the Egyptian infection control guidelines had achieved a decrease in iatrogenic transmission of HCV, but not yet eliminating it, after an assessment was done by an International Health Regulations team as shown in Table 1 [6, 17]. Thus, many challenges still exist in the ultimate goal of control of HCV infection including the densely populated areas around the River Nile (as shown in Fig. 1) [19] that hinders the efforts to prevent the spread of infection, and the high costs of the newer HCV therapies complicating the supply of medication to the millions of patients with chronic HCV infection.

The role of a national immunization program in the control of infectious diseases

Routine, active immunization is the most effective method for decreasing the burden of vaccine-preventable (childhood) diseases. Egypt's child immunization program recommends that children in the first year of life should receive a BCG vaccination against tuberculosis, three doses of the DPT vaccine to prevent diphtheria, pertussis and tetanus, four doses of polio vaccine, and the required three doses of the hepatitis B vaccine. The latest compulsory vaccine added to the program has been the three doses of Hib vaccine to protect from *Haemophilus influenzae* pneumonia, which was added in

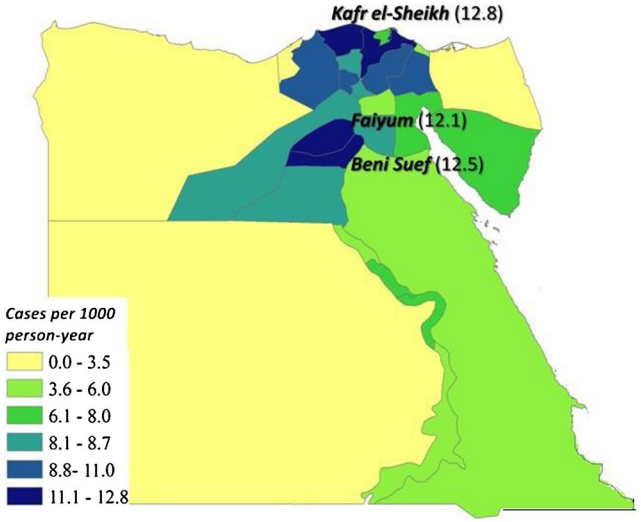

Fig. 1 Map of Egypt demonstrating the heavily dense population surrounding the River Nile with high prevalence of HCV rates of infection in these areas (Cuadros et al. 2014)

January 2014. Two doses of measles-mumps-rubella (MMR) vaccine are recommended for prevention of these three diseases in countries with universal mass vaccination. However, neither a compulsory Rota virus nor pneumocoocal vaccination are yet implemented in Egypt [20].

A significant decline in the morbidity of neonatal tetanus was recorded. This decline was found to be unrelated to the increase in the maternal immunization coverage, but was significantly correlated with the increase in childhood immunization via DPT, the increase in the public awareness and the improvement of sanitary measures. Egypt demonstrated a significant positive trend in DPT immunization coverage rate during the period from 1995 to 2005. This was significantly correlated with the reduction in the number of recorded cases, and since 2003 there were no recorded cases in Egypt as reported by The Ministry of Health [21]. The Egyptian National Plan of Action for Polio Eradication was adopted in February 1990 [22]. The strategy involved the recording of cases, routine immunization, implementation of Supplementary Immunization Activities (SIAs) targeting all children under 5 years, as well as establishment of an efficiently performing surveillance system to detect and investigate all cases of acute flaccid paralysis. As a result of these extensive efforts, substantial progress was achieved nationwide with the last confirmed paralytic polio case reported in May 2004 in the Assiut governorate [22].

All Egyptian children aged 18–29 months have received the majority of the recommended vaccinations. Coverage levels for BCG are nearly universal. Ninety-seven percent of the children have received the recommended three doses of the DPT and polio vaccine. Coverage levels are also high for the hepatitis B vaccine, and has significantly increased from 91 % in 1996 to 97 % by 2005. Overall, 92 % of children aged 18–29 months are considered immunized against all major

preventable childhood diseases. There has been a significant increase during the period from 1995 to 2000 in the vaccination coverage rate of measles for children under 5 years in Egypt leading to a 97.3 % coverage in 2005 which declined to 94.8 % in 2014 [23]. Overall, the morbidity rates of vaccine preventable childhood diseases have significantly decreased. The political turbulence that occurred in the country from January 2011 has probably caused some disturbances in the response to the national compulsory immunization program. This necessitates more integrated cooperation from the civil society with the government to overcome this threat.

The long fight against mycobacteria tuberculosis

The WHO declared TB as a global public health emergency in 1997. Tuberculosis used to be one of the important public health problems in Egypt. The Eastern Mediterranean region (EMR), including Egypt covered 6–7 % of the global TB burden as estimated by WHO [24]. The Ministry of Health has addressed this problem in cooperation with the university hospitals through establishing the National Tuberculosis Control Programme (NTP) in order to reduce the prevalence of TB in the community. Implementation of the NTP strategy primarily ensures that TB patients all over the country receive care according to international standards in cooperation with the WHO, together with new case notification and registration of response to therapy [25]. Tuberculosis control activities were integrated through the primary health care system distributed among 111 chest centres and 39 chest disease hospitals. The program has achieved its targets after decades of national and international collaboration including NGOs and the private health sector. Investigation for TB is carried out by the National Reference Laboratory (NRL), which was selected as a supra-national reference laboratory in the WHO Eastern Mediterranean region. It acts as a central laboratory for 18 intermediate TB laboratories distributed in different governorates. The NRLs provide culture services, surveillance of antituberculous drug resistance and the help to ensure quality control [26].

These efforts changed the prevalence rates of TB in Egypt with a reported decline of annual risk of infection from 3.5 % in 1952 to 0.24 % in 2006 [27]. The prevalence of tuberculosis in Egypt was recently reported as 27 per 100,000 of the population in 2013, with a total number of 22,000 infected individuals [24]. Still, there are more challenges facing the authorities adopting strategies aiming for further progress in TB control. Thus, the STOP TB Strategy was adopted to cover such challenges including improving TB detection, to identify and characterize multidrug resistant-TB, health system strengthening and co-infection of TB and human immunodeficiency virus. Egypt is one of the countries that has adopted the expanded STOP TB Strategy with achieving progress in its implementation. The STOP program aims for a TB-free region by 2050 by implementing the global strategy after tailoring it to the country context [28]. Thus, the aim of this collaborative integrated working plan in Egypt is to prevent, care and control TB toward the targets of the global plan to stop TB.

Emerging viral infections

Recently, an emerging infectious disease has become a fearful threat as it causes high rates of morbidity and mortality, in addition to its impact on the economy. In 2008, avian influenza A virus (H5N1) has shifted into an enzootic form among poultry in Egypt [29]. It is postulated that it might have emerged as a result of vaccine use in commercial farms [30]. During influenza activity in poultry, human H5N1 infections occur during contact with sick or dead chicken. This is reported to occur in a seasonal pattern peaking during February and March. Upon large scale surveillance, it has been found that avian influenza A virus (H5N1) is really widespread among poultry in Egypt, especially in the Delta region indicating that sectors dealing with chicken industry and domestic breeding are at risk of these severe life-threatening infections [31]. The authorities are dealing with these risks through follow up, and surveillance of population at risk together with early intervention by getting rid of sick birds whenever cases are discovered. However, the help of the social sector of the community is needed to cause behavioural changes among citizens dealing with poultry.

Healthcare-associated infections and antimicrobial resistance

Antimicrobial resistance is a growing problem complicating healthcare-associated infections (HAI) worldwide. In Egypt, studies investigating antimicrobial resistance in HAIs in high risk areas of general hospitals showed high levels of resistant pathogens. In a large study undertaken at five major teaching hospitals in Cairo, a high degree of antimicrobial resistance was reported among the different isolates studied [32]. Among the *Staphylococcus aureus* blood stream infections, 70 % of isolates were methicillin resistant. In another study investigating HAI in intensive care settings, *Staphylococcus aureus* constituted 30 % of infections, 65 % of these isolates were methicillin resistant, and of 30 % gram negative (GN) organisms, *Klebsiella pneumoniae* were the most common [33]. Within the gram negative pathogens, several studies pointed to the high prevalence of extended spectrum B-lactamase (ESBL) producers among GN organisms isolated from hospitalized patients varying from 38 to 65 % among isolates from HAIs [32, 33]. Mortality was significantly associated with

resistant pathogens, as MRSA and ESBLs [33]. In a study investigating the molecular types of ESBL in a specialized hospital, an ESBL phenotype was recognized in 66 % of the GNR isolates and all isolates belonged to the CTX-M group 1. Sequencing of the amplicons in the former study demonstrated the prevalence of CTX-M-15 [34, 35].

With the advent of the global problem of rapid increase of multidrug resistant gram negatives, especially Carbapenemase producing Enterobacteriacae (CRE), different hospitals in Egypt are experiencing a steady increase in infections caused by these pathogens [36]. Within Acinetobacter species, isolates causing HAI from different cancer hospitals >70 % carbapenem resistance was encountered. On attempting to study the epidemiological relatedness of carbapenem resistant Acinetobacter strains, a large diversity was encountered with eight different blaOXA-51, and 28 % similar patterns by pulsed-field gel electrophoresis [37]. Among *Pseudomonas aeruginosa* isolates causing HAIs in Cairo University hospitals, 39 % were carbapenem resistant, and 27 % were metallo-β- lactamases, with bla_{VIM-2}, bla_{OXA-10} being the most commonly encountered genotypes in 58 and 42 % of isolates, respectively [38].

Among the important emerging types of antibiotic resistance are the New Delhi metallo-beta-Lactamases (NDM-β-Lactamases), which are spreading all over the world due to globalization and the fact that they are easily transmitted from one bacterium to another [39]. The NDM-β-Lactamases have been sporadically isolated from different GN bacteria in Egypt, including *Acinetobacter baumanii* and *Pseudomonas aeruginosa*c, but not incriminated in outbreaks, nor reaching endemic levels [37, 38]. Still, the data are scarce regarding the epidemiology and molecular types of carbapenem resistance among Enterobacteriacae. The problems associated with antimicrobial resistance recording in Egypt include lack of routine standardized phenotypic detection in many areas of the country, so the exact prevalence rates are unrecognized. In addition, there is no system connecting surveillance in hospitals performing proper detection, so data reported are not used to build on to prevent further dissemination of such bacteria. Thus, a national plan to face the problem of antimicrobial resistance is needed. Though the increase in antimicrobial resistance is a grave threat for modern healthcare service not only in Egypt but also in the whole world as it leaves minimal options for treating infected patients in high-risk settings, yet multi-disciplined corrective efforts are needed in Egypt to focus on this threat.

Many challenges still exist in the fight against infectious diseases in Egypt. Some of these challenges include administrative, motivational and behavioural difficulties. More efforts to create high level of awareness among people living in rural areas who score higher rates of infections are required to target behavioural changes. Other more important difficulties include limited financial supply and the need to extend the infection prevention campaigns to cover the 27 governorates of the country, together with the great need of establishment of a registration system for HAIs connecting all territories of the country. The process of developing a web-based network concerned with IDs data may serve as a breakthrough for early intervention and more effective preventive measures with the early appearance of clusters of cases. Of utmost importance among the priorities of infection control is a program including a nationwide plan aiming for prevention of infections caused by antimicrobial resistant pathogens.

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