ANALYSIS OF NATIONAL LIVER DISEASE STATE OF THE ART IN NORTH AFRICAN COUNTRY (EGYPT):
IDENTIFYING GAPS AND PRIORITY NEEDS TO RESHAPE LIVER DISEASE PROBLEM AND PROMOTE EURO-MIDETERREANEAN CO-OPERATION


Theodor Bilharz Research Institute, Egypt,
10-12 Academy of scientific Research &Technology, Egypt,
13-16 University of Pisa, Italy.

Corresponding Author: Amr Radwan

Abstract
Viral hepatitis comprises the major part of liver disease problem worldwide. Egypt possesses the highest burden of hepatitis C virus (HCV) coupled with socioeconomic implications representing a real challenge for development. Analysis of the national liver disease problem (mainly viral hepatitis) was conducted to identify research/management gaps and assign priorities compatible with the national socioeconomic needs. This analysis may help create links for further coordination with other Euro-Mediterranean countries targeting liver disease. The state of the art analysed the Egyptian national strategies, related research conducted over the period 2005-2010, and the potential of the Theodor Bilharz Research Institute (TBRI). The analysis pinpointed gaps and priority needs revolving around six main pillars: governance, finance, networking, education/training, policy and technical/research. The most salient priority needs recognized involved: the need for an oversight body to coordinate health service providers, enhancement of networking, strategies to increase awareness about modes of disease transmission, expansion of infection control and training programs for supportive staff. Operational research to scale up case detection, mathematical modelling for estimating future viral hepatitis burden, metadata analysis studies for best ranking prognostic and diagnostic biomarkers, new makeover e.g. home-made, more cost-effective shorter course treatments and paediatric antiviral preparations.

Keywords: liver disease, viral hepatitis, gaps, priority needs, Egypt

INTRODUCTION
The global liver diseases burden worldwide is estimated to be at 1.6%. The World Health Organization (WHO) deaths estimates for 2008 by cause revealed that liver disease is second to cardiovascular diseases as a common cause of death in Egypt. Moreover, liver cirrhosis is the third top cause of Disability-Adjusted Life Years (DALYs) after ischemic heart disease, cerebrovascular stroke in the country (GBD, 2010; WHO, 2011).

Over the past few decades the major liver problem in Egypt has been shifted from schistosomiasis to HCV (Frank et al., 2000). Egypt possesses the far highest burden of HCV infection in the world, with a prevalence of 14.7% of the population carrying the infection compared to a worldwide 3% prevalence (WHO, 2012). Moreover, ten percent of the Egyptian population is estimated to have an active infection (El-Zanaty & Way, 2008). A study focusing on the ongoing transmission of HCV in Egypt clarified an expected high cumulative prevalence within the coming years (Miller & Abu-Raddad, 2010). Another study on the future impact of HCV in Egypt by Lehman & Wilson, 2009 using Markov simulation model expected 127,821 deaths from chronic liver disease and 117,556 deaths from hepatocellular carcinoma over the next two decades.

Given the high burden of viral hepatitis in Egypt, the Ministry of Health and Population (MoHP) in 2006, established the National Committee for Control of Viral Hepatitis (NCCVH). By April 2008, this committee had developed a National Control Strategy (NCS) for Viral Hepatitis. The recommendations of the NCS were structured under four priority areas; namely, “Surveillance and monitoring” or Priority area 1, Priority area 2 or “Prevention” to reduce the incidence of hepatitis B virus (HBV) and HCV infection, “Patient management” Priority area 3 for scaling-up case detection efforts and expanding access to care and treatment for those with chronic infection and finally “Research” which represents Priority area 4 (NCCVH, 2008).

Several institutes and centres in Egypt are involved in the field of liver research and management; namely, the National Hepatology and Tropical Medicine Research Institute (NHTMRI), National Liver Institute (NLI), National Research Centre (NRC), also hepatology/tropical medicine departments in different universities e.g. Cairo, Ain Shams, Alexandria, Mansoura, Tanta universities and others, in addition to TBRI. Since its foundation in 1979, TBRI has been a pioneer in schistosomiasis related basic and clinical research. With the emergence of viral hepatitis as a banging national health problem, TBRI research focus targeted the related aspect of...
control, diagnosis and treatment of prevalent endemic diseases with viral hepatitis heading the list. TBRI coordinated and fostered THEBERA project «Theodor Bilharz into the European Research Area» which is an Seventh Framework Program of European Union (FP7) ERA-WIDE project. A systematic review on the analysis of the national state of the art regarding the liver disease problem was sponsored as an integral part of THEBERA.

The ultimate goal for improving health status through tackling liver disease problem and its overwhelming socioeconomic burden is directly linked to the Egyptian Millennium Development Goals (MDGs). For the MDGs sixth goal, Human Immunodeficiency Virus (HIV) and most of infectious diseases are not a major threat; however, viral hepatitis is the most serious problem through consequent liver cirrhosis and HCC (MoED and UNDP, 2010). Lessons learned from the MDGs progress in its diverse disciplines linking health, poverty, and hunger revealed multiple shortfall mainly related to a set of policy and operational failures that implicate many stakeholders (Sachs, 2012).

Limited research has been conducted till date to visualize the full picture of liver disease problem at a national level as a challenge for development. This analysis contributes to identify gaps to fill, capacities to leverage or build and needs to prioritize. The aim of this review is to provide a framework for the current situation with respect to policies, programs, cooperation patterns and relevant actors in liver disease at a national level. Accordingly, this analysis should be an initiative to create links for communication, interaction and coordination at the level of liver research actors, stakeholders and policy makers especially at the Euro-Mediterranean level.

**METHODS AND PROCEDURES**

The main approach of this systematic review on the analysis of the state of art regarding liver disease problem revolved around two sectors: First; analysis of the available Egyptian national policies and programs. The only available was the NCS on viral hepatitis which focused on some key priority areas including surveillance and monitoring, HBV vaccination, infection control, blood and injection safety and patient management. Analysis of the key priority areas in the NCS of viral hepatitis was performed guided by the health policy analysis checklist of Johns Hopkins School of Public Health with respect to objectives, evidence based and action take (THEBERA, 2012). The second sector comprised analysis of the research conducted to tackle the problem of liver disease in Egypt through the analysis of the international and national publications of national institutes involved in liver disease research and management during the period from 2005 to 2010; as well as TBRI projects and publications during the period from 2000 to 2010. Analysis of collected data was performed using Statistical Package for the Social Sciences (SPSS) 18 Windows Package.

As for the international publications, search was performed after filtering the irrelevant publications in Scopus database for liver diseases and resulted in a total of 592 publications to be included in the analysis. While for the national publications, search was done for the same topics and keywords using Oracle database where 1239 relevant publications were extracted. Collected data was sorted according to subjects: Diagnostic/Prognostic, Therapeutic / Management, Epidemiology/Prevention, and Drug studies. The frequency of publication/year, the impact factor, the different organization or research institutions participating in the activity, and relevance to the NCS priority areas (Surveillance and monitoring, Prevention, Patient management and Research) were basically considered. Out of total 592 national publications, further analysis of organizations involved in liver disease research resulted in a total sum of 1904 due to co-work done between different organizations in the same publication. In accordance, more than one disease subject involved within the same publication made a total sum of 2137 in analysis of studied liver diseases. Data analysis of national and international projects implemented by TBRI was conducted in relation to the different multi-sectorial research programs adopted by TBRI research programs (Control, Morbidity, Diagnosis and Therapy) and the NCS priority areas.

**RESULTS**

The NCS was found the only exclusive document in place that addresses liver disease in Egypt. The strategy focuses only on HCV and HBV infections and clearly defined its goals and outlined the necessary methods and interventions to achieve its targets (NCCVH, 2008).

A total sample of international publications on liver disease in Egypt examined included 592 publications over the period of 2005 to 2010. The research production was the deliverable of 333 international and 93 national institutions. A gradual increase in number of international publications was observed over the period 2005-2010, meanwhile the national publications showed a decreasing trend except for an overshooting increase in 2006 publications (Figure 1).

![Figure 1: Volume of international and national research publications on liver research over the period 2005–2010.](image-url)
The national universities and institutes showing the highest international scientific publications on liver disease were Cairo University, Mansoura University, NRC, Ain Shams University, TBRI, NLI and Alexandria University (14%, 7.9%, 7.5%, 7.5%, 4.5%, 4.1% & 3.7% respectively). The international production of the top seven national institutes compared to that of international institutes expressed in terms of percentage encountered was 49.4% versus 23.4%, while for other national institutes encountered the percentage was 27.2%.

With respect to national liver disease publications in national journals, Cairo University showed also the highest volume followed by Ain Shams University, TBRI, NLI, Al-Azhar University, Tanta University and Mansoura University (11.14%, 6.38%, 6.21%, 5.5%, 4.44%, 3.55% and 3.39% respectively).

Regarding the targeted field of research in international and national publications (Figure 2), most of the studies were within the scope of diagnostic/prognostic research (37.2% and 52.5% respectively). In respect of international publications, the fields of therapeutics/management, drug studies and epidemiology/prevention came next (26.2%, 18.2% and 16.2% respectively). As per national publications, epidemiology / prevention, therapeutic/management and drug studies research topics followed the diagnostic/prognostic research topic respectively (27.4%, 11% and 6.2%).

**Figure 2**: Volume of national and international publications on liver disease according to fields of research over the period 2005-2010.

Concerning the targeted disease (Figures 3 A&B), an estimated 39.1% of the international publications on liver disease dealt with HCV research followed by hepatocellular carcinoma (HCC), chronic liver disease (CLD) and HBV (19.3%, 9.7%, and 9.5% respectively). The national publications mainly involved the research conducted on HCV, Schistosomiasis, HCC and CLD (29.22%, 25.75%, 14.69% & 10.38% respectively).

Analysis of the quality of published articles showed that most publications (91.1%) had an impact factor between 0-2 while the rest (8.9%) had an impact factor between 4 and 10.

**Figure 3**: Volume of international (A) and national (B) publications according to studied liver disease over the period 2005-2010.

**DISCUSSION**

In the present study, mapping the landscape of the national liver disease state of the art is targeted to bring up and look thoroughly into urgent liver disease problem in order to intensify the interaction between policy makers and stakeholders. It also clarifies the current status providing policy makers with essential information about cooperation patterns, funding needs/offers, and relevant liver research actors to forecast a liver disease problem management plan foreseeable to disease climax in the near future. This responds more favourably to practical problems facing the not only the Egyptian health system but also socioeconomic development.

The situation analysis of the NCS showed a limited scope dealing with prevalence and disease burden focused solely on HCV and HBV as the main causes of viral hepatitis with no attention paid to other viral/parasitic co-infections, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH) and other liver diseases which may also play a major role influencing the outcome of viral liver disease. Criticism of the respective NCS key priority areas revealed essential points to consider. With respect to surveillance, the need for a reliable immunoglobulin M (IgM) assay for acute HCV is a mandate. An integrated information management system should be established to tackle the under-reporting problem and to include results of private facilities, also the need to strengthen the capacities of
laboratories by providing up to date technology to monitor annual disease incidence by surveillance of sentinel groups (NCCVH, 2008).

As regards patient management and treatment of viral hepatitis infected patients, 23 national treatment centres for HCV (from 2008-2012), under governmental control, covered the treatment of 12,089 patients in 2008, which increased to 190,000 patients in 2012 (El Sayed et al., 2012). Still, it is difficult to judge whether the number of patients to be treated is still far from ideal in absence of an annual recording of disease incidence prevalence. There is an urgent need not only for establishing more treatment centres but also for improving capacities of healthcare providers outside liver treatment centres on liver care. Additionally, treatment facilities and diagnostic tools should be expanded to the underserved remote rural areas where the highest prevalence of HCV exists. More coverage of subsidized antiviral therapy under the umbrella of Health Insurance Organization (HIO) is obviously needed. Attempts should be made for further lowering of the cost of treatment in private sectors through persuading pharmaceutical companies to reduce the cost of treatment and encouragement of local production of antiviral drugs. Implementation of a rehabilitating social program should be applied to stigmatized patients for their HCV status, pre and postoperative liver transplantation patients in order to improve their quality of life in addition to considering a program for training of paramedical staff. In view of the large proportion of the infected population having already advanced liver cirrhosis denoting the increased future need for liver transplantation, the call for more transplant centres with creation of the necessary regulations and allocating guidelines for post-mortem transplantation is important.

Concerning infection prevention, the MoHP implemented the infection control program in 2001 and expanded the implementation to almost cover all governmental hospitals yet proper infection control or no infection entails inclusion of infection control programs in private sector, medical and paramedical settings, in addition to full coverage of childhood HBV vaccination and high risk groups, the adoption of systematic sustainable plan for adult population hepatitis B prevention and control with creation of national guidelines for HBV treatment, facilitation of the availability of paediatric Ribavirin and an extensive public awareness campaign to tackle the significant proportion of HCV and especially HBV infection which are community acquired. As regards infection control, more dedicated effort should be given to nosocomial risk factors and blood safety measures involving all urban and rural areas.

The analysis of international publications addressing liver disease over the period 2005-2010, showed that 1904 national and international organizations were encountered, where the international organizations collaborating in liver research comprised only 23.4% clarifying the need for further enhancement of international cooperation. Promising trends could be concluded with respect to research production where some of the research institutions concerned with liver disease showed a comparable or close research production to the highest production recorded for the major universities in Egypt «Cairo and Ain Shams» that encompass several faculties and possess more human capital. Also, leading scientists in international publications affiliated to Egyptian universities and institutes comprised 88%, yet we need to encourage research excellence and publications in high impact Journals. Most of research published was in international journals with impact factor ranging from 0-2. Most of the international publications issued by different organizations were either relevant or indirectly relevant to NCS, targeting the NCS patient management sub-priority area «optimal clinical management» and the diagnostic and prognostic aspects of liver disease pointing to a well-developed human capital contrary to research production on epidemiology, prevention, infection control and social studies which needs to be fortified. Meta data analysis studies seem unsatisfactory to define the highest ranking biomarkers for the diagnosis/prognosis of liver disease, and to estimate future burden of the disease through mathematical modelling. International publications on liver transplantation were poorly represented. Care should be given to financial and technical constraints and striving efforts to develop the regulatory law on post-mortem transplantation.

As for the Theodor Bilharz Research Institute’s potential, excellence in basic and clinical research related to one of the neglected tropical diseases “schistosomiasis” specifically research targeting the control and therapy programs was clearly evident. The institute systematically updates its research plan in view of merging endemic diseases. This was clear where research production focusing on schistosomiasis was shown to decline over time when good control over the disease was exerted with more interest in the emerging viral hepatitis. With respect to priorities realized from the analysis of national liver disease state of the art, they may be classified under several pillars of governance, finance, policy, networking, technical/ research and education/training. The detailed priority needs could be found in the full detailed analysis of National Liver Disease State of the Art (THEBERA, 2012).

Last but not least, out of the ongoing debate on post MDGs agenda, the recently introduced Sustainable Development Goals (SDGs) approach is gaining much ground. In accordance with this directive, Euro-Mediterranean cooperation in research for addressing liver disease will contribute to real progress embracing the triple bottom line approach to sustainable development including economic development, social inclusion, and environmental sustainability (Sachs, 2012).
CONCLUSION
The salient priorities realized and retrieved out of this study could be summarized as a pressing need for assessment of the prevalence rate of viral hepatitis on an annual basis (patients with active infection, age of infected patients, prediction of chronic infection rates and consequent complications), an overarching institutional in sight to coordinate between health organizational structure responsible for patient treatment, an integrated information management system for proper disease surveillance, budget allowances, control over budget, as there is inequity in budget allocation between rural and urban areas, accessibility to innovation and technology as cross cutting contextual factors and priorities for development. In settings with limited resources, modification of existing research and development (R&D) tools as well as new makeovers should be considered. This could be ultimately fortified through higher international cooperative activities and investment in R&D within the Euro-Mediterranean region.

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ABBREVIATIONS

REFERENCES


