Burden of Gastrointestinal and Liver Diseases in Middle East and North Africa: Results of Global Burden of Diseases Study from 1990 to 2010

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ABSTRACT

BACKGROUND

Gastrointestinal and liver diseases (GILDs) are major causes of death and disability in Middle East and North Africa (MENA). However, they have different patterns in countries with various geographical, cultural, and socioeconomic status. We aimed to compare the burden of GILDs in Iran with its neighboring countries using the results of the Global Burden of Disease (GBD) Study in 2010.

METHODS

Classic metrics of GBD have been used including: age-standardized rates (ASRs) of death, years of life lost due to premature death (YLL), years of life lost due to disability (YLD), and disability adjusted life years (DALY). All countries neighboring Iran have been selected. In addition, all other countries classified in the MENA region were included. Five major groups of gastrointestinal and hepatic diseases were studied including: infections of gastrointestinal tract, gastrointestinal and pancreatobilliary cancers, acute hepatitis, cirrhosis, and other digestive diseases.

RESULTS

The overall burden of GILDs is highest in Afghanistan, Pakistan, and Egypt. Diarrheal diseases have been replaced by gastrointestinal cancers and cirrhosis in most countries in the region. However, in a number of countries including Afghanistan, Pakistan, Turkmenistan, Egypt, and Yemen, communicable GILDs are still among top causes of mortality and morbidity in addition to non-communicable GILDs and cancers. These countries are experiencing the double burden. In Iran, burden caused by cancers of stomach and esophagus are considerably higher than other countries. There is an overall overestimation of liver cancer and underestimation of other gastrointestinal and pancreatobilliary cancers. The diseases that are mainly diagnosed in outpatient settings have not been captured by GBD.

CONCLUSION

Improving the infrastructure of health care system including cancer registries and electronic recoding of outpatient care is a necessity for better surveillance of GILDs in MENA. In contrast to expensive treatment, prevention of most GILDs is feasible and inexpensive. The health care systems in the region can be strengthened for prevention and control.

KEYWORDS
Gastrointestinal disease; Liver disease; Mortality; Disability; Burden; Middle East and North Africa

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INTRODUCTION

The epidemiological transition can be observed in almost all countries worldwide.[1] As neighboring countries may share geographical, political, and cultural characteristics, the pattern of transition may be somehow similar. However, heterogeneity in health indicators may also be observed due to heterogeneous socio-economic determinants and health system governance and infrastructure. It may be important for policy makers at national level to be aware of the health status in their country compared with their neighbors and other countries with similar socio-economic and cultural determinants. Policy makers can learn lessons from experiences of their neighboring countries in health care promotion.

Countries in Middle East and North Africa (MENA) share very important determinants including religion, socio-economic status, and partly ethnicity. However, significant differences in health indicators may also be observed between these countries. Gastrointestinal and liver diseases (GILDs) are among diseases that show variability in the pattern of their prevalence, incidence, mortality and the final burden they impose on societies. While some countries such as Afghanistan and Pakistan are still facing challenges regarding the control of gastrointestinal infectious diseases, other countries with better economy in the region have experienced the obvious transition from communicable to non-communicable GILDs.

In the current article, following the previous two articles regarding the burden of GILD in 2010 and its trend since 1990 in Iran, we are presenting the burden and its trend in Iran in comparison with the neighboring countries and other countries in MENA, which have been estimated in Global Burden of Disease (GBD) study 2010.[2,3] We have taken the advantage of the unique metrics developed by GBD that make it possible to compare the health status of countries within the past two decades.

MATERIALS AND METHODS

The methodology of GBD study 2010 has been explained elsewhere in details.[4] The concepts of death, years of life lost due to premature death (YLLs), years of life lost due to disability (YLDs), and the disability adjusted life years (DALYs) are the same as previous reports.[5-9]

In the estimates presented here, all countries neighboring Iran have been selected. These countries include: Pakistan, Afghanistan, Turkmenistan, Azerbaijan, Armenia, Turkey, and Iraq. In addition, all other countries classified in the MENA region were included as well. This group of countries consisted of: Algeria, Bahrain, Egypt, Jordan, Kuwait, Lebanon, Libya, Morocco, Palestine, Oman, Qatar, Saudi Arabia, Syria, Tunisia, United Arab Emirates, and Yemen. Five major groups of gastrointestinal and hepatic diseases were studied. These major groups included: infections of gastrointestinal tract, gastrointestinal and hepatobiliary cancers, acute hepatitis, cirrhosis, and other digestive diseases. The age-standardized rates (ASRs) were compared between countries in 2010. Countries were ranked in terms of total deaths and DALYs caused by overall gastrointestinal and hepatic diseases. Furthermore, trend of death and DALYs rates from 1990 to 2010 were also illustrated for all countries.

RESULTS

Figure 1 shows the ASRs of deaths, DALYs, YLLs, and YLDs per 100,000 for all digestive diseases in MENA region in 2010. Afghanistan, Egypt, Pakistan, Turkmenistan, and Yemen are the top five countries in terms of ASRs of deaths, DALYs, YLLs, and YLDs due to all digestive diseases in 2010. Syria, Lebanon, Kuwait, and Saudi Arabia are among the top five countries with the least ASRs of death, DALYs, and YLLs. Iraq is ranked among top five countries with least YLD rates that has replaced Kuwait. Also in 2010, Iran ranked 13th, 15th, 15th, and 12th in terms of ASR for deaths, DALYs, YLLs, and YLDs respectively caused by overall gastrointestinal diseases.

Figures 2 to 7 show the ASR for deaths and DALYs in Middle East countries for diarrheal diseases, acute hepatitis, cirrhosis, stomach cancer, esophageal cancer, and colorectal cancer. Rates for diarrheal diseases are highest in Pakistan, Afghani-

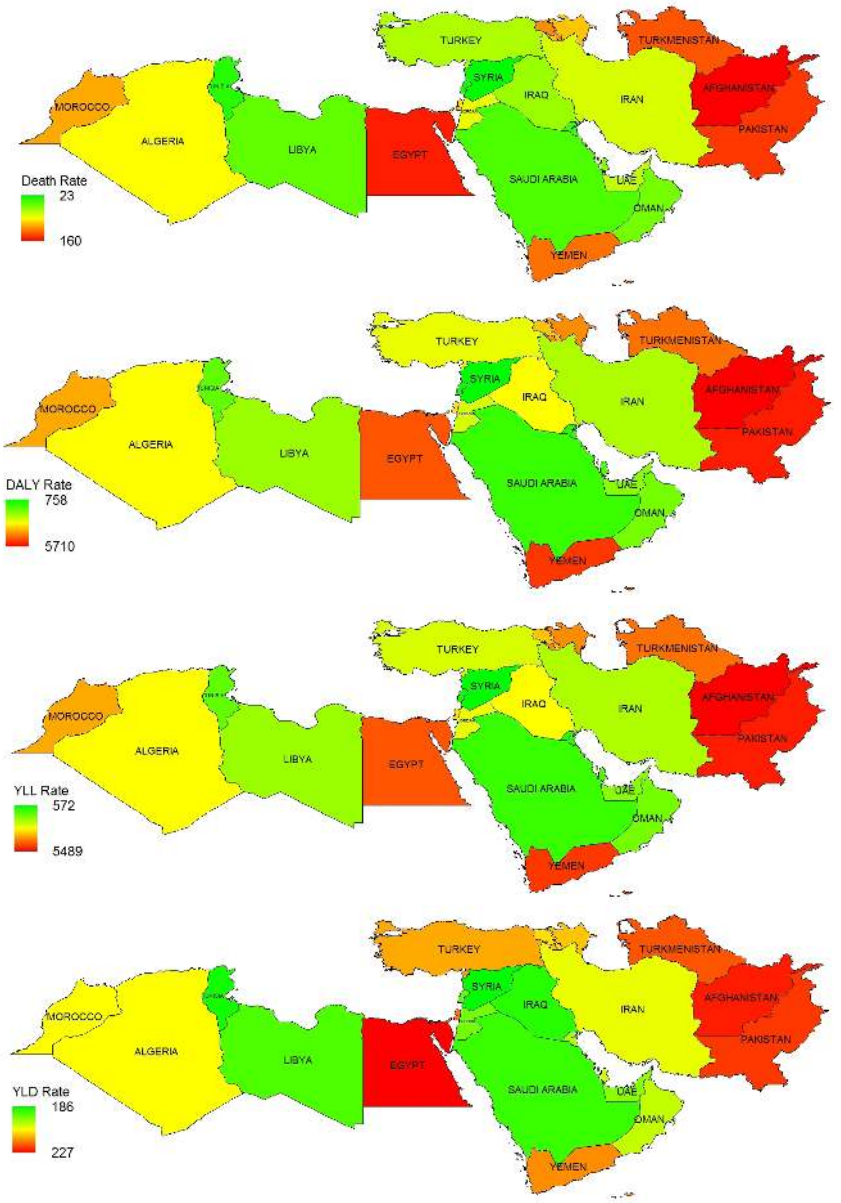

Fig. 1: The age standardized rates (ASRs) of death, DALYs, YLLs, and YLDs for all digestive diseases per 100,000 in countries neighboring Iran and other countries in Middle East and North Africa in 2010

stan, Yemen, Turkmenistan, and Egypt and lowest in Kuwait, Qatar, and Syria. The rates of hepatitis and cirrhosis are highest in Egypt, Pakistan, and Afghanistan and lowest in Syria and Turkey. Rates for stomach cancer are highest in Afghanistan, Iran, and Turkmenistan. The highest rates for esophageal cancer are observed in Turkmenistan, Iran, Pakistan, Afghanistan, and Azerbaijan. Finally, the burden of colorectal cancer is highest in Turkey, Palestine, Armenia, Jordan, and Lebanon.

Figures 8 and 9 show the ranking of main gastrointestinal diseases in 24 countries in 2010 by ASRs of death and DALY rates per 100,000 respectively. All data are reported for both sexes. Diarrhea is the first cause for both death rates and DALY rates in the entire region. It is among the top four causes of

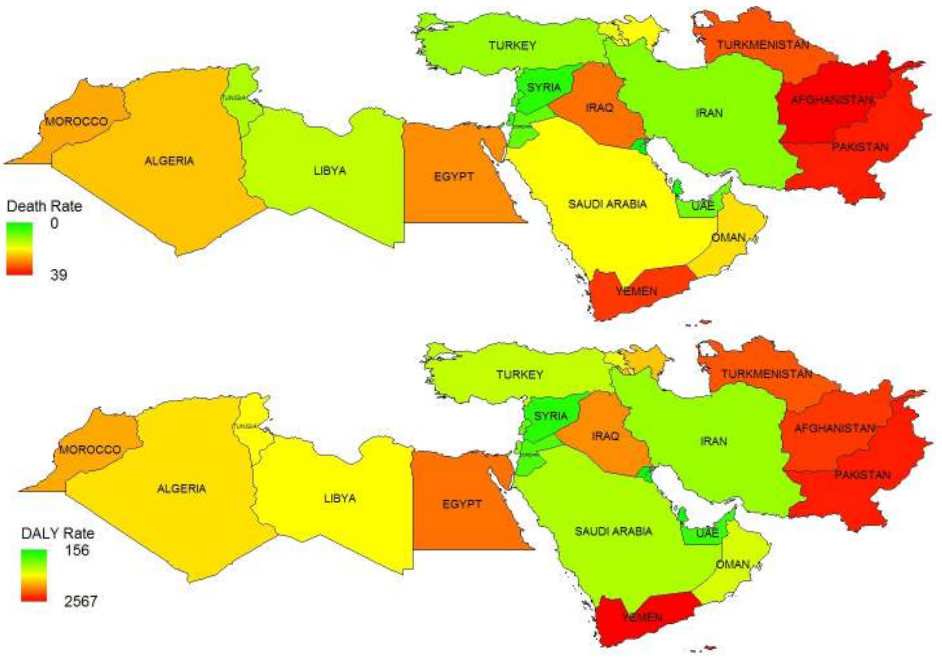

Fig. 2: The age standardized rates of deaths and DALYs per 100,000 caused by diarrheal diseases in Middle East and North Africa
DALYs: the disability adjusted life years

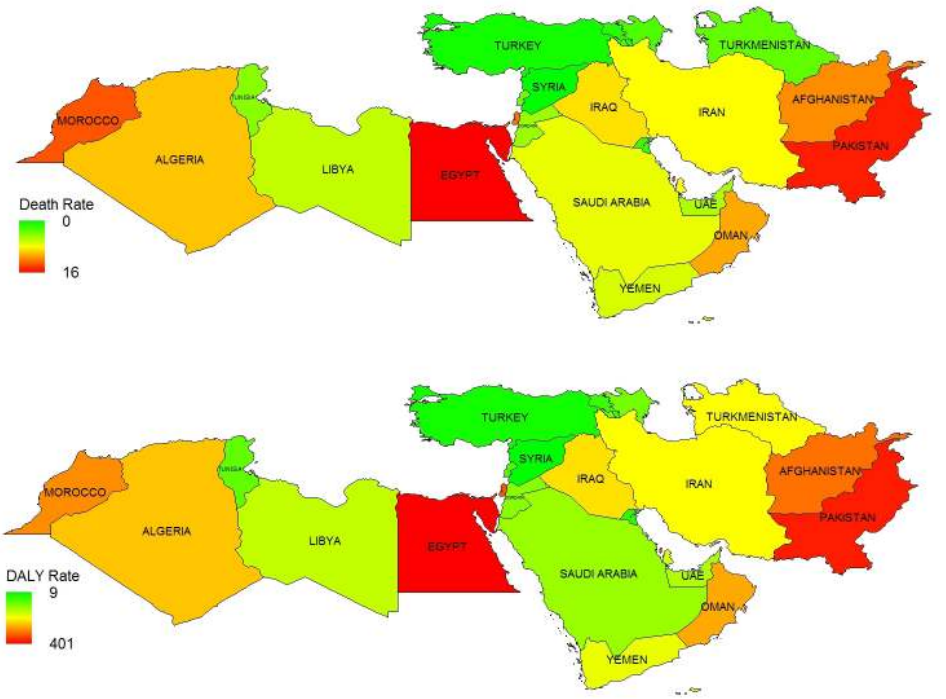

Fig. 3: The age standardized rates of deaths and DALYs per 100,000 caused by all types of acute hepatitis in Middle East and North Africa
DALYs: the disability adjusted life years

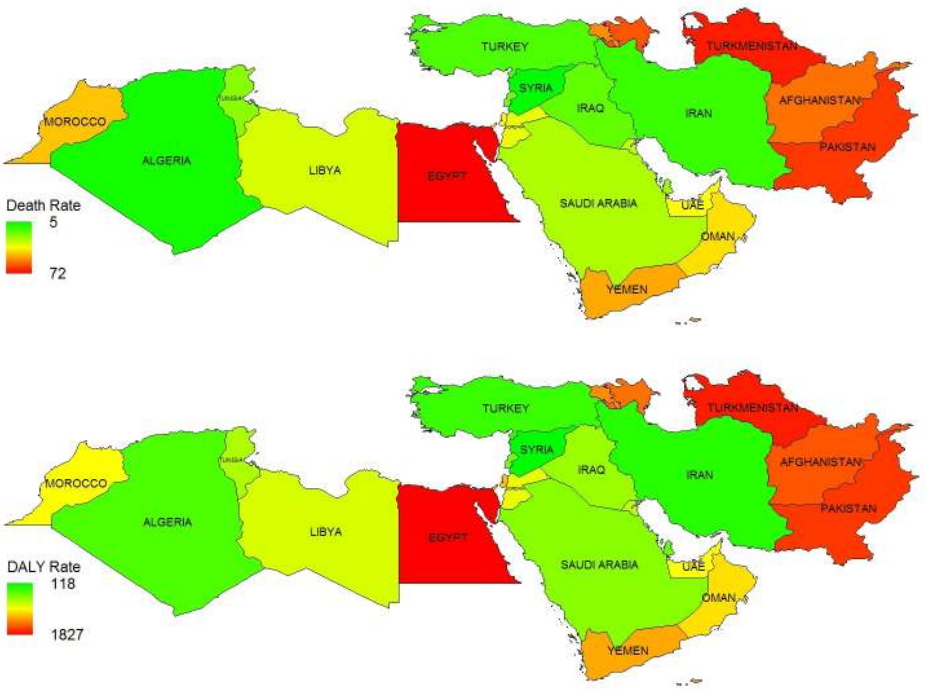

Fig. 4: **The age standardized rates of deaths and DALYs per 100,000 caused by cirrhosis secondary to all risk factors in Middle East and North Africa**
DALYs: the disability adjusted life years

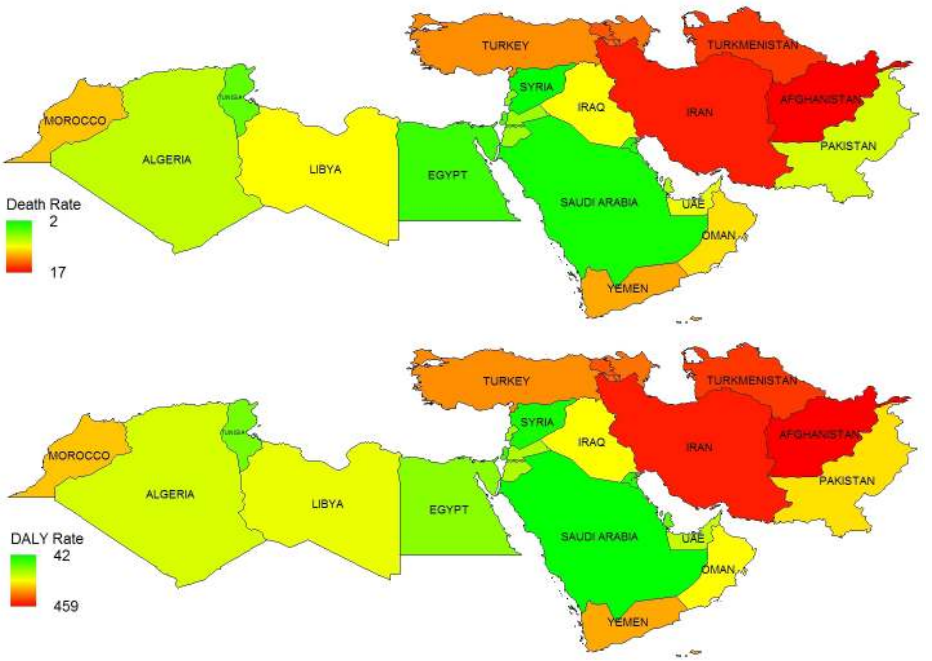

Fig. 5: **The age standardized rates of deaths and DALYs per 100,000 caused by stomach cancer in Middle East and North Africa**
DALYs: the disability adjusted life years

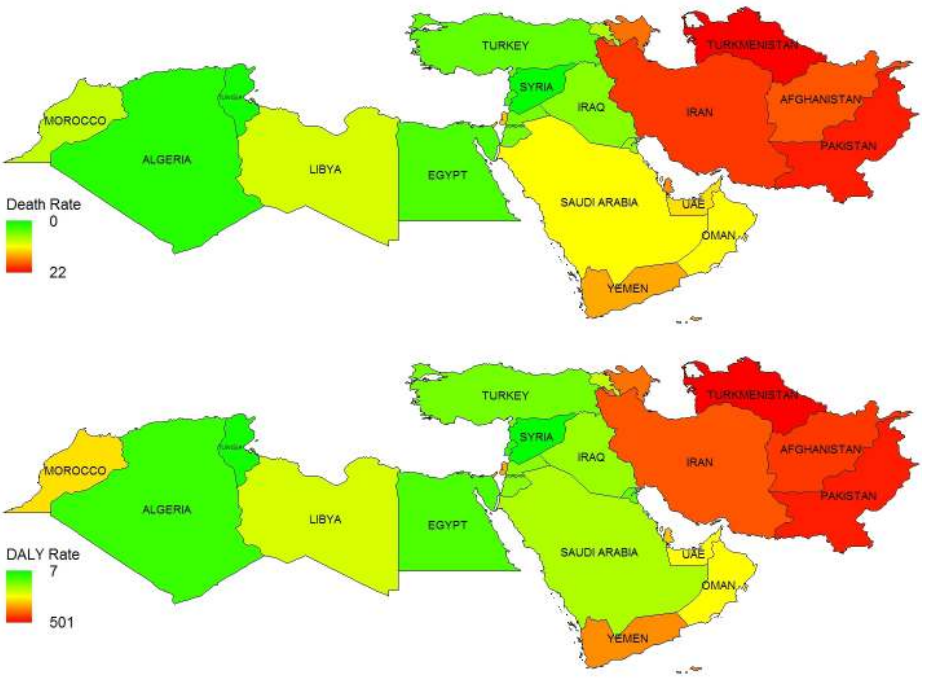

Fig. 6: The age standardized rates of deaths and DALYs per 100,000 caused by esophageal cancer in Middle East and North Africa
DALYs: the disability adjusted life years

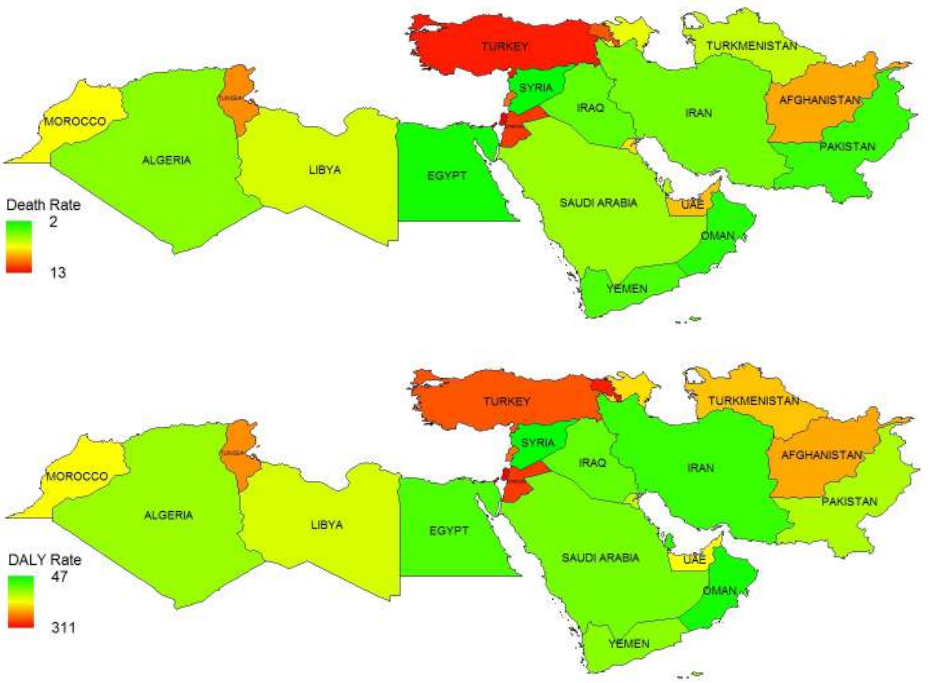

Fig. 7: The age standardized rates of deaths and DALYs per 100,000 caused by colorectal cancer in Middle East and North Africa
DALYs: the disability adjusted life years

	Diarrhea	Cirrhosis	Stomach cancer	Liver cancer	hepatitis	Colorectal Cancer	Peptic Ulcer
MENA	1	2	3	4	5	6	7
Iraq	1	2	3	4	9	5	7
Algeria	1	2	3	4	7	5	9
Oman	4	1	2	3	6	5	10
Yemen	1	2	3	5	9	6	4
Afghanistan	1	2	4	5	9	7	3
Turkmenistan	3	1	4	5	10	6	8
Tunisia	4	2	3	7	10	1	6
Pakistan	1	2	7	8	4	9	3
Saudi Arabia	4	1	6	2	9	3	7
Egypt	4	1	6	2	3	5	9
Libya	5	1	3	4	10	2	8
Morocco	5	1	2	3	6	4	7
Iran	6	3	1	4	8	5	10
Azerbaijan	6	1	2	4	10	3	8
Jordan	7	1	3	4	10	2	9
Armenia	7	1	2	3	10	4	6
Turkey	7	3	1	4	11	2	6
Lebanon	6	2	3	5	9	1	10
Syria	7	1	5	2	13	4	10
Palestine	8	1	6	3	5	2	9
United Arab Emirates	8	1	5	3	7	2	10
Bahrain	8	5	6	1	3	2	11
Qatar	10	2	5	1	8	4	11
Kuwait	11	1	6	2	10	3	9

MENA: Middle East and North Africa

Fig. 8: Ranking of main gastrointestinal diseases by death rate in 25 countries in Middle East and neighboring Iran in 2010

	Diarrhea	Cirrhosis	Typhoid	hepatitis	Stomach cancer	Liver cancer	Peptic Ulcer
MENA	1	2	3	4	5	6	7
Pakistan	1	2	3	4	7	8	5
Algeria	1	2	3	7	4	6	9
Iraq	1	3	2	6	5	4	8
Jordan	1	2	4	8	6	5	10
Libya	1	2	3	7	5	6	9
Saudi Arabia	1	2	3	6	8	4	7
Syria	1	3	2	9	6	4	11
United Arab Emirates	2	1	4	8	6	5	9
Kuwait	2	1	4	8	7	5	10
Palestine	1	2	5	6	8	4	9
Morocco	1	2	6	7	3	4	8
Afghanistan	1	2	7	9	4	6	3
Yemen	1	2	5	9	4	6	3
Tunisia	1	3	5	9	4	6	8
Qatar	1	3	5	9	8	2	11
Egypt	2	1	5	4	7	3	9
Oman	2	1	5	7	3	4	8
Lebanon	2	3	5	8	4	7	10
Iran	2	3	6	8	1	5	9
Turkey	2	4	8	11	1	5	6
Azerbaijan	2	1	13	9	3	5	8
Turkmenistan	2	1	13	9	4	5	7
Bahrain	1	5	7	2	8	3	11
Armenia	5	1	13	10	2	4	7

MENA: Middle East and North Africa

Fig. 9: Ranking of main gastrointestinal diseases by DALY rate in 25 countries in Middle East and neighboring Iran in 2010

death in 10 countries and is the first or the second cause of DALY in all countries except for Armenia. Diarrhea ranks 10th and 11th cause of death in Qatar and Kuwait, which is quite different from other countries.

Cirrhosis is the second cause of both death and DALY in the region. It is among the top three causes of death and DALY in all countries except for Bahrain. Typhoid and hepatitis are the 3rd and 4th causes of DALYs in the region but they are replaced by stomach cancer and liver cancer as 3rd and 4th causes of death. Stomach cancer is among the top four causes of death in 15 countries and among the top four causes of DALY in 12 countries. The respective figures for liver cancer are 19 and 11 countries. Hepatitis has high rank in Pakistan, Egypt, and Bahrain in terms of both death and DALY rates. Peptic ulcer is the 7th cause of both death and DALY in the region. Colorectal cancer is the 6th cause of death and 8th cause of DALY in the region. Esophageal cancer, pancreatic cancer, gall bladder and billiary cancer, appendicitis, and gastritis and duodenitis are the five diseases causing least deaths and DALYs in the region. The rankings of the first four causes of deaths and DALYs and the last five causes in most countries are almost compatible with the rankings in the entire region. Esophageal cancer has a specifically high rank in Iran and Turkmenistan in terms of both death and DALY. Pancreatic cancer has a specifically high death rate in Lebanon, Palestine, Bahrain, Qatar, and Kuwait.

In Iran, diarrhea is the 6th cause of death. The first cause of death is stomach cancer, followed by esophageal cancer, cirrhosis, liver cancer, and colorectal cancer. Stomach cancer is the first cause of DALY in Iran as well followed by diarrhea, cirrhosis, and esophageal cancer.

Figures 10 and 11 show the trend of ASRs and number of deaths and DALYs in all ages in 24 countries from 1990 to 2010 for all gastrointestinal and hepatobiliary causes. Figure 12 shows the trend of ASRs and numbers of deaths caused by diarrhea from 1990 to 2010 and figure 13 shows similar estimates for the entire gastrointestinal and pancreatobilliary cancers.

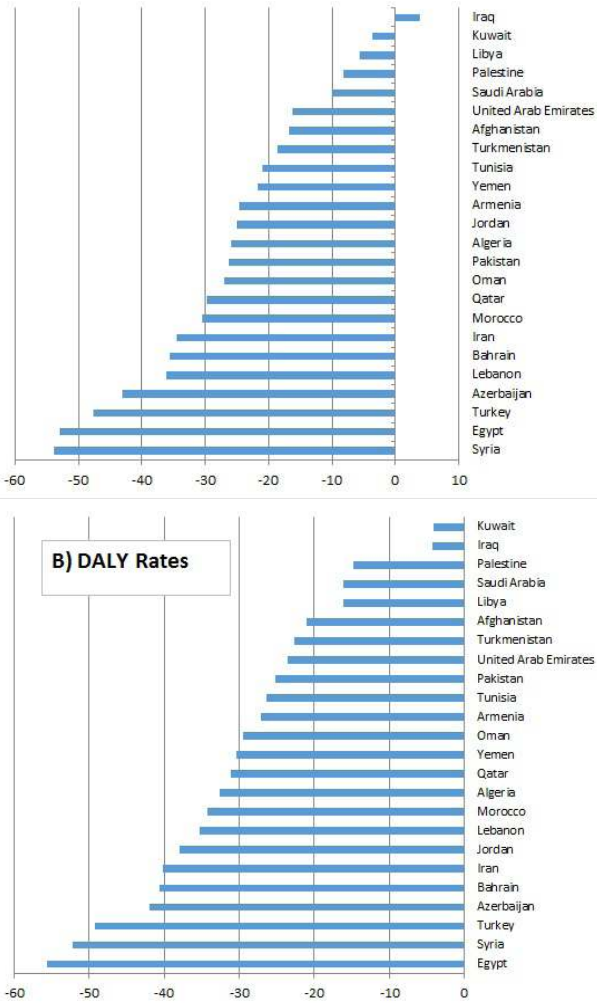

Fig. 10: Trend of the rate of deaths and DALYs for all gastrointestinal diseases in 24 countries from 1990 to 2010

DISCUSSION

The results of GBD study in MENA show that GILDs impose considerable burden on countries in this region. While the ASRs of deaths and DALYs have decreased in almost all countries in the region, the number of deaths and DALYs due to total GILDs shows rises in some countries such as Qatar, United Arab Emirates, Bahrain, Kuwait, and Palestine. These findings show that the increase in numbers may be due to ageing of the population in spite of decreasing ASRs.

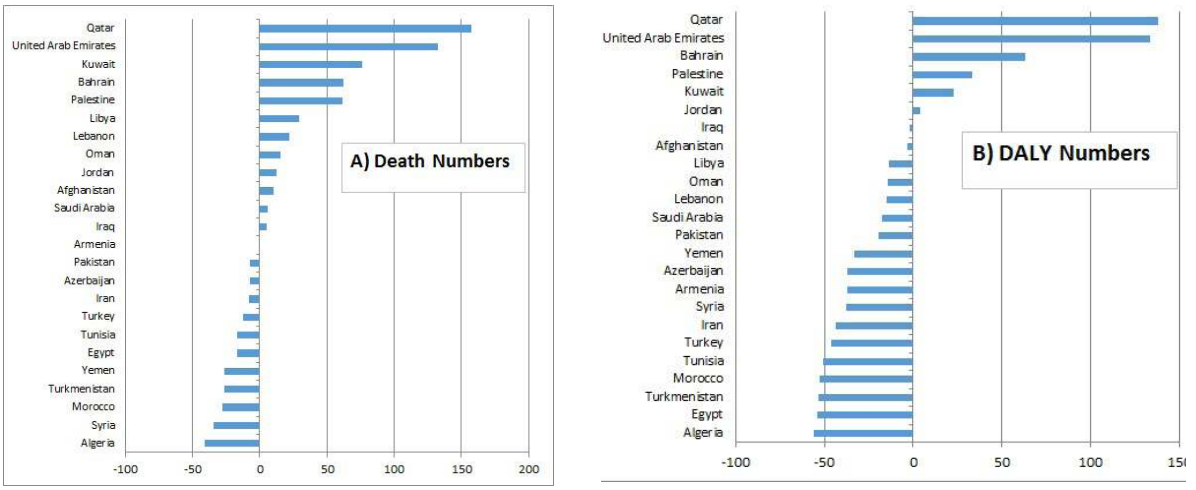

Fig. 11: Trend of the number of deaths and DALYs for all gastrointestinal diseases in 24 countries from 1990 to 2010

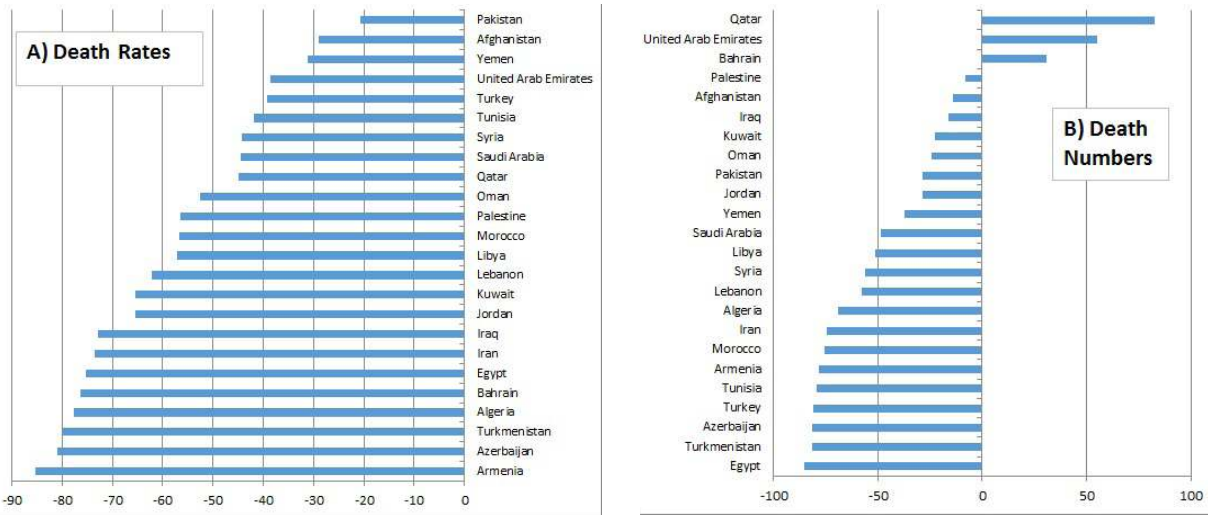

Fig. 12: Trends in number and rates of deaths due to diarrhea in 24 countries from 1990 to 2010

The rates and numbers of deaths due to diarrhea have decreased in most countries. For gastrointestinal and hepatobiliary cancers, although the rates of death decreased, the numbers of deaths have increased in all countries. In several countries such as Iran, Turkey, Syria, Kuwait, Lebanon, and Qatar, diarrheal diseases and acute hepatitis have been replaced by gastrointestinal and hepatobiliary malignancies. However, while malignancies impose increasing burden in some countries including Afghanistan, Pakistan, Turkmenistan, Egypt, and Yemen, the burden due to diarrheal diseases and hepatitis is still significant and these countries are suffering from double burden of both communicable and non-communicable GILDs.

Existing evidence shows that diarrheal diseases are still quite common in Afghanistan,[10,11] Pakistan,[12,13] Yemen[14] and Egypt.[15] The estimates are specifically made for deaths due to diarrheal diseases among children under 5 years old.[13,16-19] There is compelling evidence on effectiveness of improving hygiene including hand washing and sanitation facilities that significantly reduce the incidence and recurrence of diarrheal diseases.[20-23] Mothers' education has a substantial role in the home management of diarrhea in children,[24,25] and their health

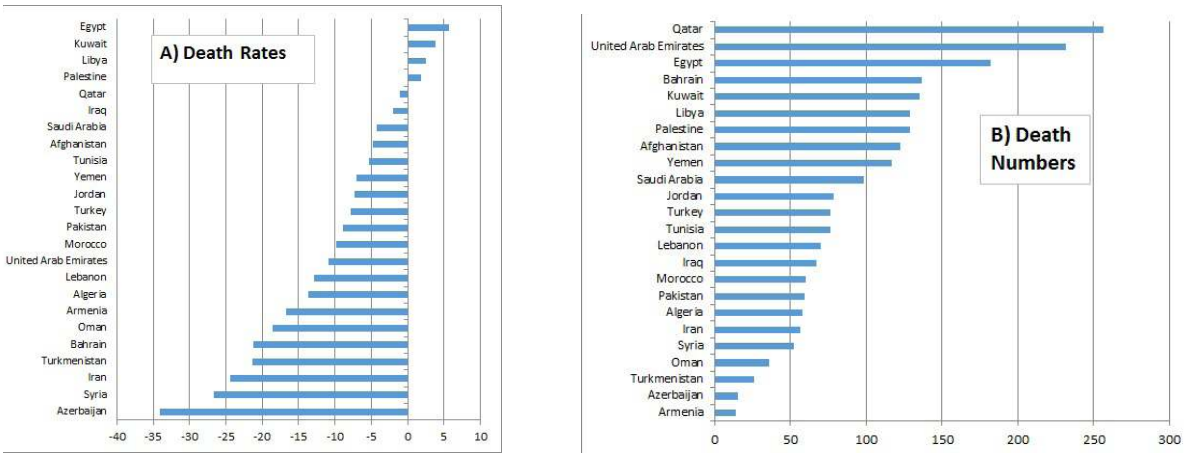

Fig. 13: **Trends in number and rates of deaths due to GI and pancreatobilliary cancers in 24 countries from 1990 to 2010**

seeking behavior for childhood illnesses.[26] Service packages specifically devised for management of diarrhea are demonstrated to be effective in Pakistan, Egypt, and Yemen.[14,23,27]

There is evidence on high prevalence of hepatitis C (>3.5%) and hepatitis B in MENA region.[28,29] However reports about the Maghreb region in Middle East including Algeria, Tunisia, Libya, and Morocco show that the prevalence of hepatitis B and C is low and comparable to developed countries.[30] The prevalence of hepatitis C in Maghreb is also low and comparable to developed countries. In contrast, there is abundant evidence on high prevalence of acute hepatitis of all kinds in Egypt and their subsequent progression to cirrhosis and hepatocellular carcinoma. Hepatitis B and C virus infections are major public health concerns in Egypt.[31,32] The prevalence of hepatitis C virus in Egypt is the highest in the world. About 14.7% of the population are antibody positive. It has become a massive epidemic in national level.[33,34] Transmission mainly occurs through sexual contact and intravenous drug use.[35] Evidence shows that Afghanistan is also facing a high prevalence of hepatitis B and C infection.[36,37] Intravenous drug use, unsafe sex, unsafe blood transfusion, and vertical transmission are the main routes of transmission.[38-44] Hepatitis B and C infections are prevalent in Pakistan as well and are higher than its neighboring countries such as India and Nepal.[45,46] Unlike hepatitis B, as there is no vaccine available to prevent hepatitis C, the primary prevention should be focused on safe blood transfusion, safe sex, and safe injection of drugs.[28,47]

Chronic hepatitis B and C are the main causes of liver cirrhosis and progression to hepatocellular carcinoma. The results of GBD 2010 show that cirrhosis is among the top four causes of death in all countries in MENA except for Bahrain. The death rate caused by cirrhosis in Egypt is by far the highest in the world, followed by Pakistan, Afghanistan, Yemen, and Morocco.48 Pakistan is specifically experiencing an epidemic of cirrhosis.[49] It is estimated that globally, 30% of cirrhosis is attributable to HBV and another 27% is attributable to HCV.[50] It is also estimated that mortality due to liver cirrhosis imposes substantial burden worldwide each year, causing more than one million deaths in 2010.[48] Its treatment is expensive and unavailable in most parts of the world. Additionally, treatment of cirrhosis does not significantly increase the survival in decompensated forms.[51] However, preventive measures such as safe blood transfusion, hygienic health facilities, vaccination for HBV, screening, and general education are inexpensive and cost-effective.[47,52-55] Preventive measures are highly recommended at national levels especially in low-income countries to tackle this growing public health concern.

Hepatocellular carcinoma is another complication of chronic hepatitis. It is estimated that 78% of

all cases are attributable to either chronic HBV or HCV infections.[50] In another report, 55% of global hepatocellular carcinoma is attributed to chronic HBV infection.[56] This figure is 89% in endemic regions.[56] Pakistan is specifically experiencing a significant rise in hepatocellular carcinoma secondary to HBV and HCV infections.[57]

Although it may seem that the burden of hepatitis B and C infections may be higher in long-term, the burden of acute hepatitis A and E should not be forgotten either.[58-62] Vertical transmission of hepatitis E is not uncommon in Egypt, Afghanistan, and Pakistan.[63]

Results of GBD 2010 show that 28% of all deaths and 16% of all DALYs due to GILDs are caused by gastrointestinal and hepatobiliary cancers in MENA. Stomach cancer ranks 3rd as a cause of death and 5th as a cause of DALY in the region. It is among top four causes of death in 15 countries and among top four causes of DALY in 12 countries. The rates of stomach cancer are highest in Afghanistan, Iran, and Turkmenistan. Cancer of stomach is followed by liver cancer, colorectal cancer, esophageal cancer, pancreatic cancer, and gall bladder and hepatobiliary cancer in the entire region. Liver cancer is among the top four causes of death in 18 countries and among the top four causes of DALY in 10 countries. Colorectal cancer has the highest rate of death and DALY in Turkey, Tunisia, Lebanon, and Jordan. The lowest rates are seen in Pakistan. Esophageal cancer is among the top four causes of death and DALY only in Turkmenistan and Iran. The results are compatible with global cancer data (GLOBOCAN) in 2012 in which stomach cancer, liver cancer, colorectal cancer, and esophageal cancer accounted for 8.4%, 8.1%, 7.8%, and 4.6% of all incidental cases respectively in less developed countries.[64] Globally, all gastrointestinal and hepatobiliary cancers accounted for almost 30% of all incidental cases and 37% of all cancer deaths in 2012 based on GLOBOCAN results.[64] Generally speaking, the rates of deaths and DALYs caused by gastrointestinal and hepatobiliary cancers in North African countries are lower than Middle Eastern countries.[64-68] In contrast, specifically in countries located in the Caspian Littoral, esophageal and gastric cancers are higher due to genetic and certain life style exposures.[69-71] Evidence shows that while esophageal cancer in this area is declining,[72] there is a general rise in stomach cancer.[73] A large prospective cohort study, the Golestan Cohort Study (GCS) in Golestan province, north east of Iran, has been conducted on over 50,000 Iranians, mostly of Turkmen ethnicity, to investigate the epidemiology and determinants of upper gastrointestinal malignancies in the Caspian Littoral. This study is the largest cohort study in Middle East.[74,75] The results of this study have shown that low consumption of fruit and vegetable, very hot tea drinking, life style and other aspects of diet, opium and tobacco use, and poor oral health, along with low socio-economic status are the most likely causes of high rate of esophageal cancer reported from this region.[76-79]

Cancer registries are the best existing sources for estimating the prevalence and incidence of major cancers. However, cancer registries in general have two defects: incompleteness and misclassification. Since the first results of national cancer registries were released in 1975, stomach cancer, cancer of the colon and rectum, and esophageal cancer have retained their ranks in the hierarchy of cancers, but there is a steep rise in the prevalence of liver cancer[80-83] in MENA and specifically in Egypt.[84,85] Yet, in effect, the cancers of stomach, colon and rectum, and esophagus are underestimated while the liver cancer is overestimated as metastatic cancers of other sites may be misclassified as liver cancer. Expansion and accuracy of population-based cancer registries is a necessity especially in developing countries for more precise estimations of the burden of cancers.[86]

The unique metrics developed and the novel statistical methods used in GBD have made it possible to make estimations for times and places where data is sparse or is of low quality. GBD has used novel methods to overcome these challenges among which, the scarcity and low quality of hospital data and data in outpatient settings are very bold.

There is compelling evidence on increasing trend of GILDs that are regularly diagnosed in outpatient setting and have not been captured by GBD. These include but are not restricted to gastroesophageal reflux disease (GERD),[87] inflammatory bowel diseases (IBD),[88,89] irritable bowel syndrome (IBS),[90,91] non-alcoholic fatty liver disease (NAFLD), and non-alcoholic steatohepatitis (NASH).[92]

DALYs reported in GBD 2010 show regional heterogeneity in the causes of premature death and disability, which highlights the importance of regular epidemiological assessments for every country in the MENA. To further improve precision of the estimated DALYs, qualitative studies should be done in every region to determine how people define quality of life. Collecting high quality evidence is a necessity for policy makers in developing countries in order to effectively allocate the limited resources for prevention and control.

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CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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