RESEARCH COMMUNICATION

Burden of Hepatocellular Carcinoma in Iran; Bayesian Projection and Trend Analysis

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Abstract

Background: Hepatocellular carcinoma (HCC) is the sixth most prevalent cancer worldwide. Iran is located in a low risk area but, while the true prevalence of HCC in Iran is unknown, it is not an uncommon malignancy. The aim of this study was to provide quantitative estimations of the burden of death due to HCC cancer in Iran and its trend during over recent decades for the Iranian population. Methods: National death statistics reported by the Ministry of Health and Medical Education (MOH&ME) from 1999 to 2004, stratified by age group, sex, and cause of death (ICD-9) were used to generate HCC mortality (ICD-9; 20) expressed as the mortality rate per 100,000 people. The Bayesian approach to correct for misclassification was employed and a time series model was applied to predict mortality. The burden of HCC, including years of life lost (YLL), was calculated using Iranian life expectancy. Results: The rate of HCC mortality and YLL moderately increased from 1999 to 2004 but according to our prediction it seems that these rates are going to level off. Also HCC mortality and YLL was higher for older age, and was considerably greater in men than in women. Conclusion: Burden of HCC is low in Iran because most of cases are due to HBV and this infection is less common in Iran than Southeast Asia and Africa and there is nomajor increase projected for the future. However, up to 40% of its death statistics are underreported. Screening can be advised for early HCC detection in chronic HCV and HBV carriers.

Keywords: Hepatocellular carcinoma - mortality - years of life lost

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Introduction

Hepatocellular carcinoma (HCC) represents approximately the sixth most prevalent cancer worldwide and due to the poor prognosis it is also the fourth cause of death related to cancer (Parkin et al., 2005). HCC is the third most frequent cause of cancer deaths among men worldwide (Parkin et al., 2005). The incidence ranges from <10 cases per 100,000 population in North America and Western Europe to 50-150 cases per 100,000 population in parts of Africa and Asia where HCC is responsible for a large proportion of cancer deaths (Taylor-Robinson et al., 1997; Deuffic et al., 1998; El Serag and Mason, 1999; Law et al., 2000). Males are affected more than females usually and it is most common between the age of 30 to 50 (Kumar et al., 2003) Hepatocellular carcinoma causes 662,000 deaths worldwide per year (World Health Organization, 2006).

Iran is located in low risk areas with an annual incidence much less than 5 per 100,000 populations (Gomaa et al., 2008).The most important risk factor for HCC is cirrhosis. So, HCV and HBV are the major etiological agents that lead to the development of HCC (Colombo et al., 1989).

Although the true prevalence of HCC in Iran is unknown, it is not an uncommon malignancy; 80% of HCC cases in Iran are positive for at least one of the markers of Hepatitis B virus and this virus appears to be the most common cause of HCC in Iran (Shamszad and Farzadgan, 1982; Merat et al., 2000).

Measures of mortality of diseases are clearly important for public health policy makers. With regards to cancer mortality, data are important to monitor the effects of screening program, earlier diagnosis, demographic data and other prognostic factors (Burnet et al., 2005).

In order to facilitate the quantification of diseases in the case of mortality, a new health status the years of life lost' (YLL), was developed (Gardner and Sanborn, 1990; Mariotti et al., 2003; Burnet et al., 2005). YLL is the number of years which would be saved in the absence of the disease. Because mortality does not directly reflect the issue of premature death, YLL provides a more accurate depiction of premature death by weighting deaths occurring at younger ages more heavily than those occurring in older populations, and therefore function as an additional tool for quantifying the burden of disease.

Determining of YLL is not exactly the same as the analysis of mortality and survival for HCC. Even if the

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mortality and survival analysis are more familiar and easier to understand, the analysis of YLL which provides more information on burden due to premature death.

The aim of the this study was to provide quantitative estimations of the burden of death due to HCC cancer in Iran and its trend during this recent decades for Iranian population in order to guide priorities in public health intervention program planning for future.

Materials and Methods

National death Statistic Reported by the Ministry of Health and Medical Education (MOH&ME) from 1999 to 2004 included in this analysis. The Ministry of Health published all reported death statistics annually and these data extracted and stratified by age group, sex, and cause of death (coded according to the 9th revision of the International Classification of Diseases [ICD-9]) (Naghavi, 2004). HCC mortality [ICD-9; 20] expressed as the mortality rate for each 100,000 people.

The populations of Iran in 1999-2004 were estimated by age group and sex using the census from 1996 conducted by Statistics Centre of Iran and its estimation according to population growth rate for years before and after national census. Since Iran has incomplete mortality information (Khosravi et al., 2007) and up to 20% death statistics were recorded in undefined categories, we employed a Bayesian approach in which subjective prior information on at least some subset of the parameters used to estimate misclassified parameter and then re-estimate death statistic (Pourhoseingholi et al, 2009; 2010). A time series model (autoregressive) was used to predict the mortality with original mortality data and their corresponding Bayesian estimation. Finally the burden of HCC including YLL was calculated.

Results

We considered data consisting of all deaths due to HCC from 1999 to 2004, (up to 7076 records). The prior probability to correct misclassification which proposed here was based on Iranian death registration which introduced up to 20% misclassified records in total deaths. So a beta prior assumed to re-estimate death statistic of HCC. The rate of HCC mortality and its prediction according to an autoregressive model appeared in Table 1 and Figure 1. According to the Bayesian re-estimation there were between 30 to 40 percent underreported mortality records in death due to HCC from 1999-2004. YLL due to HCC and the Bayesian adjustment for age and sex group showed in Table 2. The rate of HCC mortality and YLL moderately increased from 1999 to 2004 (Figures 1 to 4) but according to our prediction it seems that these rates are going to be leveled off.

Also HCC mortality and YLL was higher for older age (Table 1 and Table 2). Besides mortality rate and YLL due to HCC for men were high comparing to women considerably (Figure 2 and 4).

Table 1. Mortality Rate of HCC Adjusted for Sex and Age Groups

		<5 Years		5-14 Years		15-49 Years		>=50 Years		All ages		Total
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	
1999	FR	0	0.44	0	0	0.89	0.28	21.05	14.25	3.13	1.96	2.56
	BR	0.45	0.89	0.13	0.14	1.3	0.42	31.15	21.07	6.34	4.42	3.85
2000	FR	0.13	0	0.21	0	1.01	0.87	23.14	18.79	3.41	2.66	3.04
	BR	0.27	0.14	0.34	0.04	1.47	1.26	33.8	27.52	4.99	3.91	4.46
2001	FR	0.25	0.19	0.2	0.14	1.1	0.89	22.4	16.32	3.80	2.84	3.33
	BR	0.37	0.32	0.31	0.21	1.64	1.33	33.38	24.32	5.66	4.23	4.96
2002	FR	0	0.07	0.11	0.19	1	0.99	30.31	20.7	4.43	3.30	3.88
	BR	0.07	0.14	0.17	0.31	1.46	1.45	44.72	30.55	6.54	4.89	5.74
2003	FR	0	0.12	0.21	0.24	1.1	0.88	27.8	20.58	4.28	3.22	3.76
	BR	0.06	0.18	0.33	0.36	1.7	1.36	42.98	31.82	6.62	4.98	5.82
2004	FR	0.43	0.27	0.23	0.16	1.27	0.96	27.35	17.13	4.26	2.77	3.53
	BR	0.69	0.41	0.37	0.26	1.87	1.41	34.8	25.26	5.60	4.09	4.86

FR: Frequentist Rate, BR: Bayesian Rate

Table 2. YLLs per 100,000 Due to HCC Adjusted for Sex and Age Groups

		<5 Years		5-14 Years		15-49 Years		>=50 Years		All ages		Total
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	
1999	FR	0	15.08	0	0	23.6	7.65	189.42	139.5	36.32	22.65	29.62
	BR	15.39	30.17	4.87	5.23	34.41	11.4	280.34	206.58	56.03	35.65	46.04
2000	FR	4.51	0	7.88	0	26.7	23.29	208.24	184.21	41.67	33.74	37.78
	BR	9.02	4.69	12.65	1.69	38.84	34.01	304.16	269.67	61.31	50.23	55.88
2001	FR	8.38	6.53	7.54	5.32	29.21	23.98	201.63	159.92	46.41	37.31	41.96
	BR	12.57	10.88	11.74	7.95	44.07	35.7	300.4	238.33	69.57	55.68	62.78
2002	FR	0	2.32	4.04	7.27	26.44	26.62	272.77	202.82	50.33	43.31	46.93
	BR	2.22	4.64	6.48	11.8	38.82	39.28	402.46	299.37	74.45	64.26	69.51
2003	FR	0	4.18	7.86	25.3	29.12	23.23	250.18	201.7	50.78	45.46	48.18
	BR	2.01	6.27	12.44	13.62	44.94	35.96	386.82	311.86	78.68	64.27	71.64
2004	FR	14.72	9.25	8.62	6.11	33.64	25.7	246.15	167.82	53.17	37.87	45.68
	BR	23.55	13.88	13.81	9.77	49.61	37.84	313.21	247.58	72.51	56.01	64.43

FR: Frequentist Rate, BR: Bayesian Rate

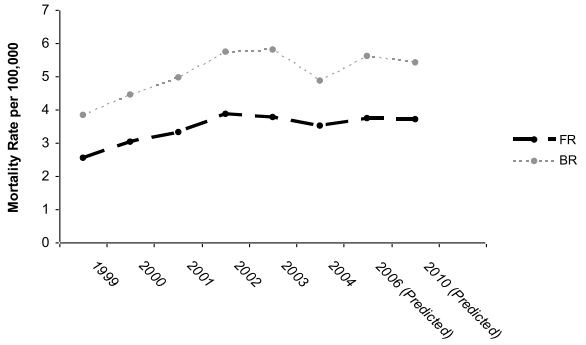

Figure 1. Mortality Rate Due to HCC Through the Years FR: Frequentist Rate, BR: Bayesian Rate

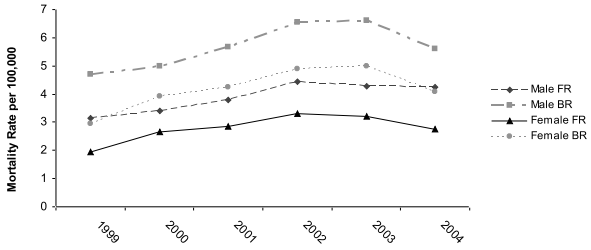

Figure 2. Mortality Rate Due to HCC Adjusted for Sex Groups FR: Frequentist Rate, BR: Bayesian Rate

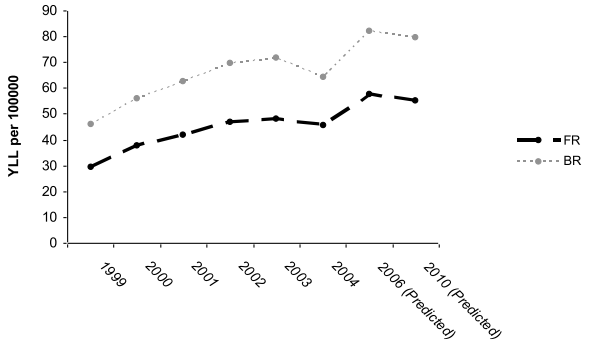

Figure 3. Years of Life Lost Due to HCC Through the Years FR: Frequentist Rate, BR: Bayesian Rate

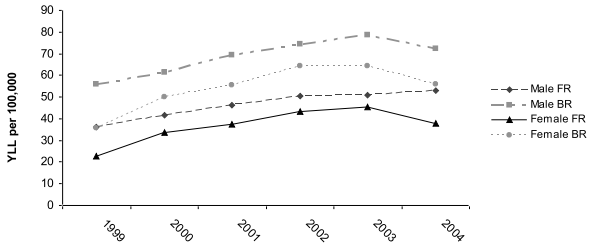

Figure 4. Years of Life Lost Due to HCC Adjusted for Sex Groups FR: Frequentist Rate, BR: Bayesian Rate

Discussion

Our results indicated low YLL due to HCC in Iran but with a constant increase during these recent years.

Iran is located in Middle East, a region where majority of HCC cases presents with intermediate or advanced stages of the disease (Siddique et al., 2004). The high relative frequency of liver carcinoma in Middle East is related to endemicity of hepatitis B infection (Koriech and Al-Kuhaymi, 1994). A recent study in southern Iran indicated that the predominant cause for HCC was hepatitis B (Hajiani et al., 2005). Although alcohol is one of the potent risk factors of HCC (McGlynn and London, 2005), A study conducted in the south of Iran suggested less than three percents of HCC patients was associated with alcohol consumption and Hepatitis B was the most common risk factor for HCC (Hajiani et al., 2005). Another Iranian study revealed that in contrast to Western countries which alcoholism remains the most common cause, HBV and HCV chronic infections are the most common causes of HCC (Fani et al., 2007).

Current available data about epidemiology of hepatitis C in Iran revealed the prevalence of less than 1% in general population (Alavian et al., 2005). The prevalence of chronic hepatitis B among Iranian population is around 3% (Mousavi et al., 2007). The reports of transfusion organization showed that the prevalence of Hbs antigen among blood donors were around 6 per 10,000 samples (Hajjarizadeh, 2008).

Moreover it is estimated that about 1.5 million people in Iran are living with HBV and 15% to 40% of them are at risk of developing cirrhosis and/or hepatocellular carcinoma (HCC) without intervention (Alavian et al., 2008) and a progressive increase in HCC was observed as age increased (Somi, 2005).

Since hepatitis B or C is one of the main causes of hepatocellular carcinoma, prevention of this infection is the key to prevent hepatocellular carcinoma and treating them can reduce the burden of HCC, but its effectiveness is not known (Somi, 2005). Mass vaccination has been shown to be a safe and highly effective way in order to control and prevention of HBV and protective efficacy following complete vaccination exceeds 95% (Tong, 1985; Ghendon, 1990). Although in Iran, the mass vaccination program started in 1993 and reached 94% coverage in 2005 (Alavian et al., 2007), its impact on decreasing the burden of HCC is suppose to be in future decades. In addition to this, because the age at which HBV infection occurs influences the long-term outcome, giving vaccines to infants of HBeAg-positive mothers as soon as possible after birth is reasonable (Alavian, 2006). Periodic surveillance of patients at risk for HCC remains contentious (Larcos et al., 1998) and the efficacy of screening for HCC in patients who are chronic HBV carriers has generally been disappointing (Kanematsu, 1997). In the case of patients with cirrhosis, alcohol consumption is to be avoided. Also, screening for hemochromatosis may be beneficial for some patients (Kao and Chen, 2005).

According to this study, mortality and YLL are high in men comparing to women and increases as age increases. Men are at higher risk for HCC than women (Nagasue, 1985) also some prospective studies conducted in Asia and Europe noted a mean age at presentation between 50 and 60 years (Tsukuma et al., 1993; Velazquez et al., 2003).

In conclusion, burden of HCC is low in Iran because most of cases are due to HBV and some cases due to HCV. Fortunately HCV infection is low in Iran (Alavian et al., 2009) and it is predicted that about 2.14% of Iranian are HBV infected (Alavian et al., 2008). HBV is less common in Iran than that in Southeast Asia and Africa (Chen et al., 1997; Dyer et al., 2005; Bosch et al., 2004). Furthermore, after national vaccination of infants against HBV in Iran,

the epidemiology is changing and decreasing significantly (Alavian et al., 2007). Early screening for HCC can be useful for HCC detection in HCV and HBV chronic carriers (Fani et al., 2007).

In conclusion, although the mortality rate of HCC seems to be low, up to 40% of its death statistics are underreported. It does not appear that any major change other than gradual decrease will occur in the future.

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