



RESEARCH ARTICLE

MORTALITY AFTER VIRAL HEPATITIS IN CHINA: A SYSTEMATIC REVIEW AND AGGREGATED DATA STUDIES

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ABSTRACT

Background: The main purpose of this article is to focus on mortality rate among males and females in rural and urban areas of People's Republic of China (PRC) due to viral hepatitis. The age group of the reviewed population is between 0 and 87 years of age.

Study Design: Review of literatures relevant to the article.

Methods: The article uses the data from "3rd National Survey of Death Causes in China", which compare the mortality rate of viral hepatitis among the males and females in rural and urban areas in China. Additionally, overall mortality due to viral hepatitis all over China has been compared with regional mortality. Data are analyzed and graphically presented using Microsoft Excel, version 2007.

Results: In general, review of literatures and analysis of data reveals that mortality rate due to viral hepatitis is higher in the rural areas as compared to urban areas. Again, overall mortality due to viral hepatitis is higher among the males than the females. By sex and place of resident, mortality rate due to viral hepatitis is higher among the males than the females both in urban area rural areas Region-wise, overall mortality due to viral hepatitis is higher in Western part of China, closely followed by Middle part of China and least in Eastern part of China.

Conclusions: Susceptibility to viral hepatitis is general and mortality rate due to viral hepatitis is higher among the males than the females both in urban and rural areas in People's Republic of China (PRC).

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INTRODUCTION

Hepatitis B virus (HBV) infection is a major health problem and causes significant levels of morbidity and mortality worldwide. The World Health Organization (WHO) estimates that two billion people have at least one marker of HBV infection, and 350 million are chronically infected and at risk of developing chronic liver disease and hepatocellular carcinoma (HCC) (McQuillan *et al.*, 2004; Shepard *et al.*, 2006 and Hong Zhang *et al.*, 2011). The world can be broadly classified into regions of high, intermediate, and low HBV endemicity, and China is classified as having high endemicity for HBV infection (Andre *et al.*, 2000; Mahamat *et al.*, 2010 and Lin-Hong Ninga, 2012). In 1992, the Chinese national hepatitis seroepidemiological survey found that the prevalence of HBV surface antigen (HBsAg) for the population aged 1–59 years was 9.8% (Xia *et al.*, 1996).

Viral hepatitis has been a major human disease for at least 2,000 years (1), is a major public health problem in China and has a substantial impact on the health of people. According to investigations on hepatitis B virus (HBV) infection, China is a hyper epidemic area of HBV infection (An epidemiological study on viral hepatitis, 1986; Qu, 1986 and Chen, 2013). The prevalence of hepatitis B virus infection is as high as 60%, with a HBsAg carrier rate, among the general population. In view of the above, it is estimated that there are more than 120 million HBV carriers and 700 million HBV infections in China and that at least 20 million of them will die of HBV-induced liver diseases (Liu, 1991; Zhuanbo Luo *et al.*, 2011 and Chao, 2013). To intervene in the transmission of HBV and to prevent the subsequent occurrence of chronic liver disease, a stepwise HB vaccination program for all neonates has been implemented in China since January 1992 (Liu *et al.*, 1991; Zhuang Fangcheng, 2012 and Xiaofeng Lianga, 2009). It is essential to understand the nationwide distribution and major risk factors of HBV infection in the general Chinese population before large-scale vaccination. Hepatitis C virus (HCV) is the major causes

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of Non-A, Non-B post transfusion hepatitis and is also implicated as the cause in many of sporadic cases of Non-A, Non-B Hepatitis. Constant infection with HCV has also been linked to the development of hepatocellular carcinoma and chronic liver diseases (Plagemann, 1991). According to surveys in blood donors, injection drug users and other high risk population of HCV infection (Lok *et al.*, 1992; Jian Lu *et al.*, 2009; Lavanchy *et al.*, 2004; Merican *et al.*, 2004 and Xia *et al.*, 1992) prevalence of anti-HCV is 1-70% in different high risk Chinese population. The proportion of acute viral hepatitis C is about 10-15% in acute hepatitis cases in China (Xia *et al.*, 1992 and Xian Xia *et al.*, 2008). However, the distribution and risk factors of HCV infection is unknown in the general Chinese population. A nationwide cross-sectional sero-epidemiologic study of hepatitis A, B, C, D, and E virus infections in the general Chinese population was carried out in 1992. The purpose of that study was: (i) to understand the distribution and major risk factors of hepatitis A, B, C, D, and E virus infection in the general Chinese population; (ii) to provide a basis for developing and evaluating preventive procedures and public health practices on viral hepatitis control (Xia *et al.*, 1996 and Xia *et al.*, 1996).

Study Methods

The article uses the data from "3rd National Survey of Death Causes in China", which compare the mortality rate of viral hepatitis among the males and females in rural and urban areas in China. The Table 1 provides detailed description of age specific mortality for each sex in rural and urban areas in China due to viral hepatitis. The Table 2 and 3 demonstrates the age specific mortality for each sex as well as overall mortality in different regions (West, Middle and East) of China due to viral hepatitis. All these Tables are considered as data sets and utilized as available sources for measurement of death among the males and females in rural and urban areas due to viral hepatitis and evaluated the same with mortality in different regions of China to see the differences.

Table 1. Distribution of mortality rate due to viral hepatitis in China

Age	Mmrra	Fmrra	Mrrua	Fmrrua	B/c	D/e
0	0.75	0.86	0	1.03	0.872	0
2	0.38	0.2	0	0	0.052	0
7	0.09	0.13	0.15	0.24	0.069	0.62
12	0.16	0.11	0.11	0.06	0.68	0.54
17	0.19	0.18	0.05	0.05	0.94	1
22	0.7	0.28	0.47	0.28	0.4	0.59
27	1.39	0.27	1.12	0.19	0.194	0.16
32	2.45	0.68	1.4	0.53	0.277	0.37
37	4.57	1.02	2.96	0.86	0.22	0.29
42	6.43	1.75	5.28	0.94	0.27	0.17
47	9.17	2.36	6.2	2.01	0.25	0.32
52	13.46	4.22	10.88	3.05	0.31	0.28
57	17.16	7.9	12.84	3.43	0.46	0.26
62	17.37	9.97	12.74	6	0.57	0.47
67	22.94	12.18	14.17	8.49	0.53	0.59
72	26.42	16.44	16.71	9.89	0.62	0.59
77	34.62	18.49	23.43	13.38	0.53	0.57
82	37.2	25.81	30.98	11.16	0.69	0.36
87	35.71	25.4	29.99	21.06	0.71	0.7

The patients' information are not considered and not included in this article as the article is not related with any treatment or

management plans. Moreover, there is no any personal information of the patients who suffered from viral hepatitis. For the convenience of statistical analysis, all the data's are graphically presented with help of Microsoft excel, version 2007. A total of fourteen graphs are drawn by using the stated data sets. Figure-1 illustrates the comparison of mortality rate between male and females due to viral hepatitis in rural areas. Figure-2 illustrates the comparison of mortality rate between male and females due viral hepatitis in urban areas. Figure-3 illustrates the comparison of overall mortality rate between male and females due to viral hepatitis in urban and rural areas. Figure 4-5 illustrates the average mortality rates of viral hepatitis between male and females due to viral hepatitis in rural and urban areas. Figure-6 explains the comparison of mortality rates of males between rural and urban areas. Figure-7 illustrates the comparison of mortality rates of females between rural and urban areas. Figure - 8 explains overall birth rate of both sexes for past 12 years in China. Figure - 9 explains overall death rate of both sexes for past 12 years in China. Figure - 10, depicts the viral mortality rate of male and female in East, Middle and West part of China. Figure 11, presents the viral hepatitis mortality rate of male and female in East, Middle and West part of China. Figure 12 shows the viral hepatitis mortality of male and female in East part of China. Figure 13 shows the viral hepatitis mortality of male and female in Middle part of China. Figure 14, illustrates the viral hepatitis mortality of male and female in West part of China. The mortality data of viral hepatitis in China is provided in Table -1, the mortality of viral hepatitis in East, Middle and West part of China in Table 2, mortality of viral hepatitis of both sexes in rural and urban areas in East, Middle and West part of China in Table 3 and the birth and death rate from the year 2000 to 2012 is provided in Table 4.

Table 2. Distribution of mortality rate among the males and females due to viral hepatitis in East, Middle and West part of China

AGE	TMREC	TMRMC	TMRWC
0	0.87	0.85	0.42
2	0.05	0.1	0.47
7	0.03	0.13	0.23
12	0.07	0.08	0.24
17	0.1	0.16	0.18
22	0.23	0.52	0.65
27	0.55	0.74	1.09
32	0.7	1.24	2.42
37	1.84	2.58	3.36
42	2.66	3.93	5.49
47	4.37	5.1	6.78
52	5.95	8.26	11.88
57	7.87	12.04	14.21
62	8.27	12.38	17.26
67	10.05	16.49	21.85
72	11.26	22.05	25.49
77	18.17	28.22	24.88
82	18.56	32.05	34.17
87	19.85	40.23	28.17

Statistical Analysis

Inferential analysis has been done with the help of Microsoft Excel, version 2007 and graphs are generated in the following manner, a graph is drawn by using the data of : Male Mortality Rate in Rural Area(MMRRRA) and Female Mortality Rate in

Rural Area (FMRRA , Figure -1), and then a graph is drawn by using data of Male Mortality Rate in Urban Area (MMRUA) and Female Mortality Rate in Urban Area (FMRUA, Figure 2). Together with these, a graph is drawn by using MMRRA, FMRRA, MMRUA, FMRUA (Figure 3). Thereafter, the average of mortality rate of males and females in rural and urban areas are displayed in Figure 4 and 5. Explanation and interpretation of each figure were carried out to derive the final outcome of results and conclusion of mortality rates due to viral hepatitis in rural and urban areas as well as differences between birth and death rates over last 12 years in China.

observed among the males. The first rapid rise mortality is noticed between the age of 47 to 52 years and then gradually increased to up to age of 67 years.

The second sharp rise is seen between the age of 67 and 72. The third peak at the age range of 77-87 with declination from the age 87. On the hand, there are two sharp rise peak patterns is observed among the female mortality rate. The first one is observe between the age group of 62 and 67 years with a slow increase until it reaches up to the age of 77 years. The second is seen from the age of 77-87 years with a high risk of mortality rate and then decline.

Table 3. Distribution of mortality rate due to viral hepatitis among the males and females in urban and rural areas in Eastern, Middle and Western part of China

AGE	VHMRMEC	VHMRFEC	VHMRMMC	VHMRFMC	VHMRMWC	VHMRFWC
0	0.41	1.39	0.80	0.91	0.39	0.45
2	0.10	0.00	0.09	0.11	0.62	0.30
7	0.00	0.07	0.18	0.07	0.12	0.35
12	0.09	0.05	0.08	0.08	0.31	0.17
17	0.09	0.10	0.27	0.05	0.06	0.31
22	0.30	0.15	0.76	0.27	0.85	0.45
27	0.96	0.14	1.35	0.09	1.62	0.53
32	1.11	0.29	1.87	0.57	3.63	1.14
37	2.85	0.81	3.87	1.23	5.73	0.84
42	4.50	0.75	6.13	1.62	8.38	2.40
47	6.93	1.73	7.86	2.19	10.23	3.14
52	9.51	2.28	12.49	3.73	17.21	6.25
57	11.55	4.02	16.55	7.20	19.98	8.15
62	11.30	5.10	16.13	8.26	21.00	13.32
67	13.03	7.12	21.65	11.19	27.47	16.06
72	13.92	8.82	27.12	17.15	31.87	19.16
77	22.12	14.92	39.83	18.51	33.13	17.35
82	23.52	15.09	40.90	25.87	46.70	24.37
87	27.15	15.87	48.49	35.37	30.93	27.25

Table 4. Distribution of overall death rate of both sexes in China for the past 12 years

YEAR	BIRTH RATE	DEATH RATE
2000	16.12	6.73
2001	15.95	6.74
2002	15.85	6.77
2003	12.96	6.74
2004	12.98	6.92
2005	13.14	9.94
2006	13.25	6.97
2007	13.45	7.00
2008	13.71	7.03
2009	14.00	7.06
2010	12.17	6.89
2011	12.29	7.03
2012	12.31	7.17

RESULTS

In Figure: 1, it is observed that, the occurrence of mortality rates due to Viral Hepatitis is less than one or almost zero-bound until the age of 17 to 22 years. The occurrence slowly begins to rise from the age of 27 years among the males and 37 year among the females. The considerable rise of mortality rate is observed between age group of 27 and 32 years for male and 37 to 42 years for female. The chance of developing viral hepatitis is higher as the age progresses especially in males as compared to the females. The peak age of mortality due to viral hepatitis among male and female is observed between the age group of 82 and 87 years and then decline in both the cases. There are several rapid or sharp of rapid rise of mortality peaks

Figure: 2, illustrates the comparison of mortality rate between male and female in urban area. It is observed that the incidence of viral hepatitis mortality rate was not much reported until the age of 17-22 in male and the age of 37-42 in female due to life style changes and better livelihood compare to rural area. The considerable rise of mortality rate is seen between the age group of 27 and 32 years in male and 42 and 47 years in female. There are three patterns of sharp risen peak seen among the males. The first rapid rise of mortality is observed between the ages of 47 and 52 years, followed by second rapid rise between 72 and 77 years and last one between 77 and 82 years and then decline slowly. In case females, first rapid rise is noticed between the age of 72-82 years and second rise between 82 and 87 years.

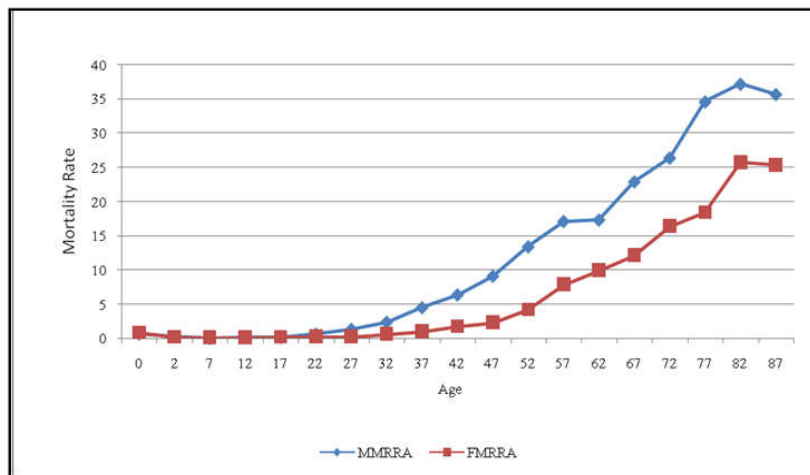


Fig. 1. Distribution of Male and Female Mortality Rate due to Viral Hepatitis in Rural area by ages

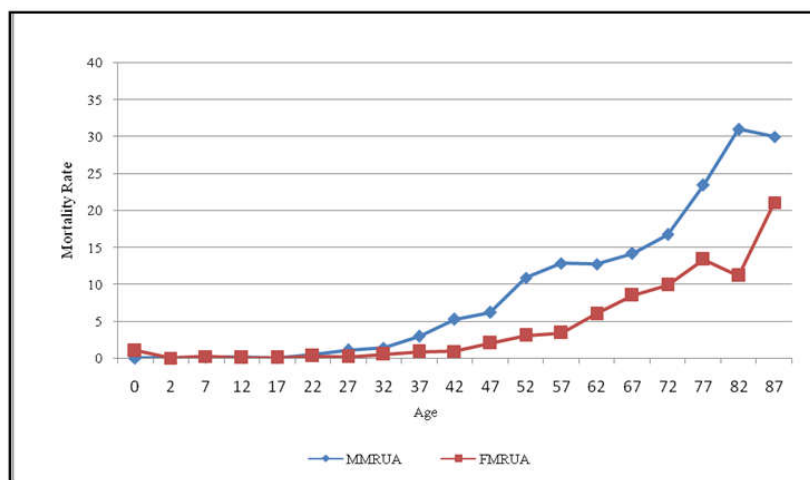


Fig. 2. Distribution of Male and Female Mortality Rate due to Viral Hepatitis in Urban area by ages

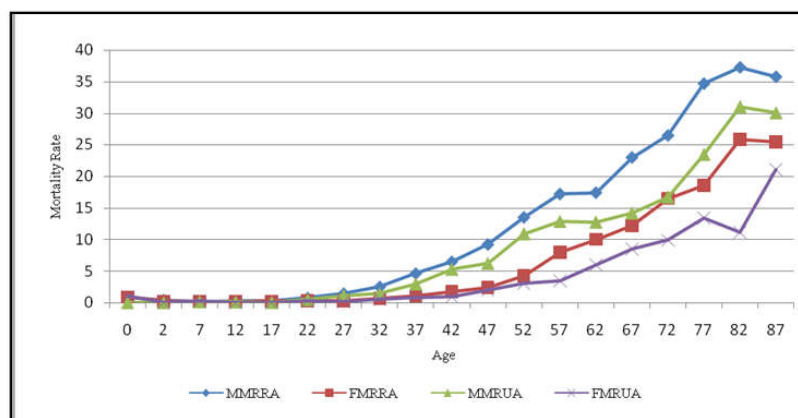


Fig. 3. Comparison of Male vs Female Mortality Rate due to Viral Hepatitis in Rural and Urban ares

Figure: 3, demonstrates the overall comparison of mortality rate of male and female in rural and urban area. It is noticed that overall mortality rate of viral hepatitis among males is higher in the rural area than their counterparts among females. Alike rural area, the mortality rate of male in urban area is higher than the mortality rate of female in rural area. The mortality rate of male and female in rural area is declined after the age ranges between 82 and 87 years.

In urban area, mortality of male is found to decline after age of 87 years. In contrast, mortality rate is increased in case females after the age of 87 years. In rural area mortality rate of female become steady rather than the mortality rate female in urban area .The mortality rate of female in rural area in Figure - 4 and 5, depicts the average mortality rate of viral hepatitis for both male and female summarized from Figure 1. Figure: 4, it is seen that, there are two peaks of mortality in the rural areas.

The peaks are observed between the age of 57 and 87 years. The low mortality rate is seen between the age of 0 and 27 years. The mortality rate is then gradually increased between the ages 32 and 37 years, which is rapidly increased after the age of 47 years. Figure: 5, it is seen that, there is one peak of mortality in the urban area. It is observed that the minimal mortality rate of both male and female in urban area is seen between the age of 52 and 74 years.

However, it declined at the age of 74 years. Then it rise up at the age between 72 and 82 years .The peak mortality rate is observed at the age between 82 and 87 years. Figure: 6, demonstrates the mortality rate of male in urban and rural area. From this figure it is observe that male mortality rate is higher in rural area than the urban area. In urban area mortality starts from the ages 27-32 years then it gradually increases and goes to peak at the age of 82 year.

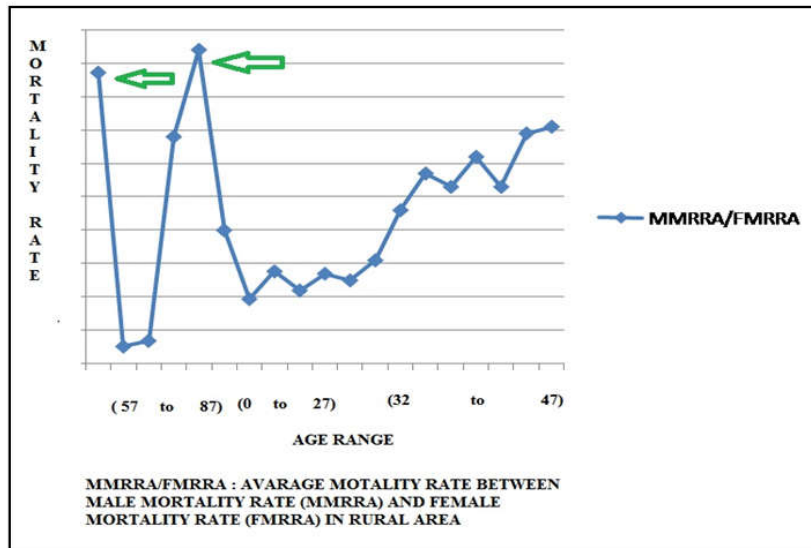


Fig. 4. Comparison of Male and Female Mortality Rate due to Viral Hepatitis in Rural Area

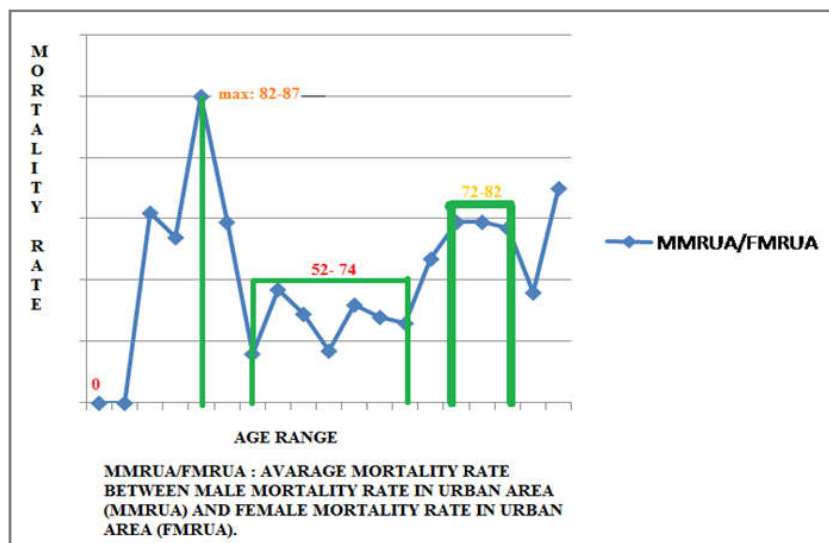


Fig. 5. Comparison of male and female mortality rate for viral hepatitis in urban area

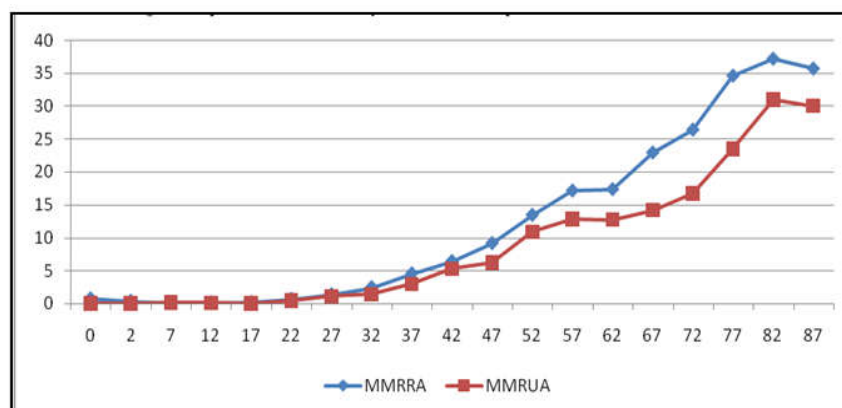


Fig. 6. Comparison of Male Mortality rate due to Viral Hepatitis in between Rural and Urban areas

On the other hand in rural are the mortality starts from ages 27 - 32 years. Then it increases to the age between 47 and 57 years. At the age of 62 it declines, then again it increases. Mortality rate rises to peak at age between 77 and 82 years. Figure: 7, demonstrates the mortality rate of female in urban and rural area. It is observed that female mortality rate is less in urban area than the rural area. In urban area mortality rate starts to a perceptible level from the age between 32-42 years. Then it increases and reaches to the peak at the age between 82 and 87 years.

In rural area mortality starts from the age of 37-42 years. Then it gradually increases. It goes to peak at the age of 82 years and then declines. Substantial. Figure: 8, explains overall birth rate of both sexes in China from 2000 to 2012, and shows that birth rate is gradually decreases from 16.12 to 12.31 per 1,000 populations. According to Figure 8, declination of birth rate was gradual up to 2003 and then fall rapidly 15.85 to 12.96 per 1,000 populations in 2004. After 2004, declination of birth rate was almost Plateau up to 2006 and then tends to rise from 12.98 to 14.00 per 1,000 populations until 2009.

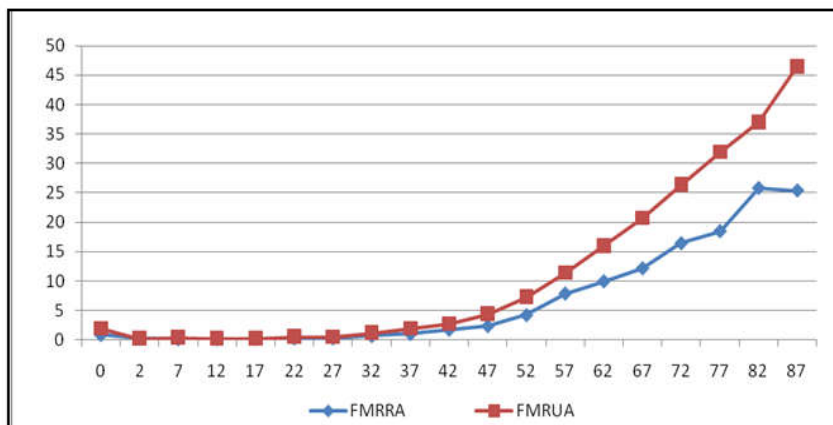


Fig. 7. Comparison of Female Mortality rate due to Viral Hepatitis in between Rural and Urban

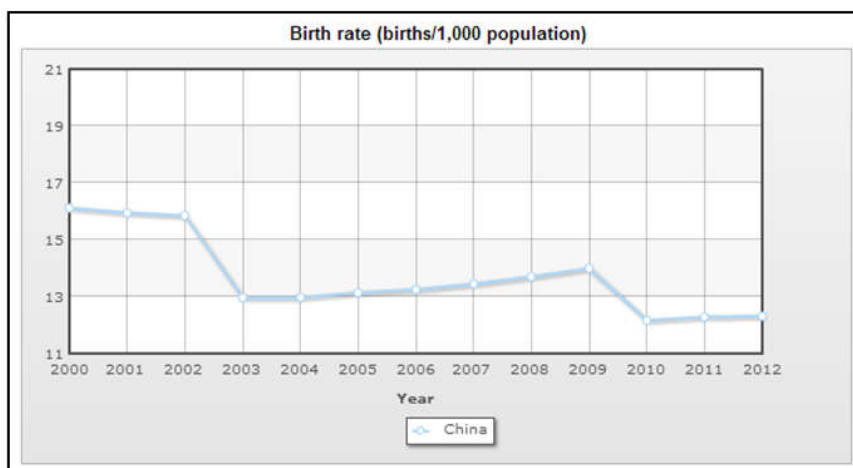


Fig. 8. Overall birth rate of both Sexes for last 12 years in China

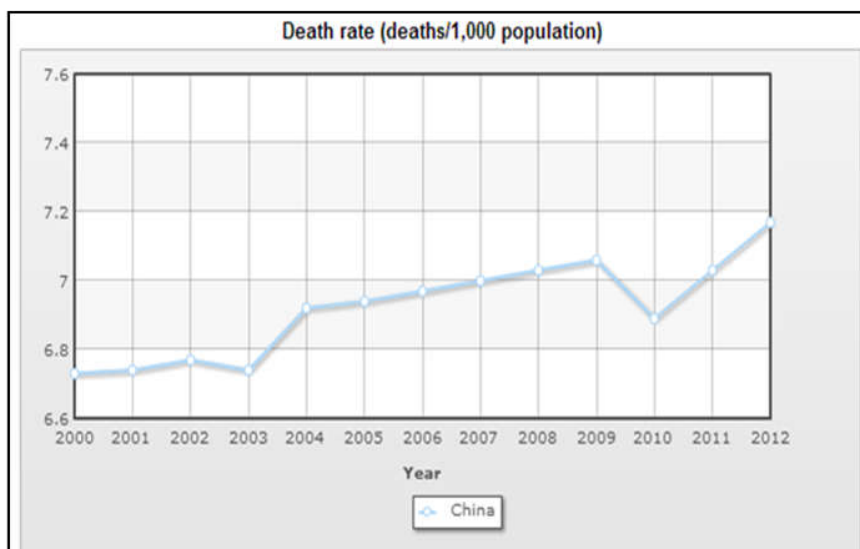


Fig 9. Overall death rate of both sexes for 12 years in China

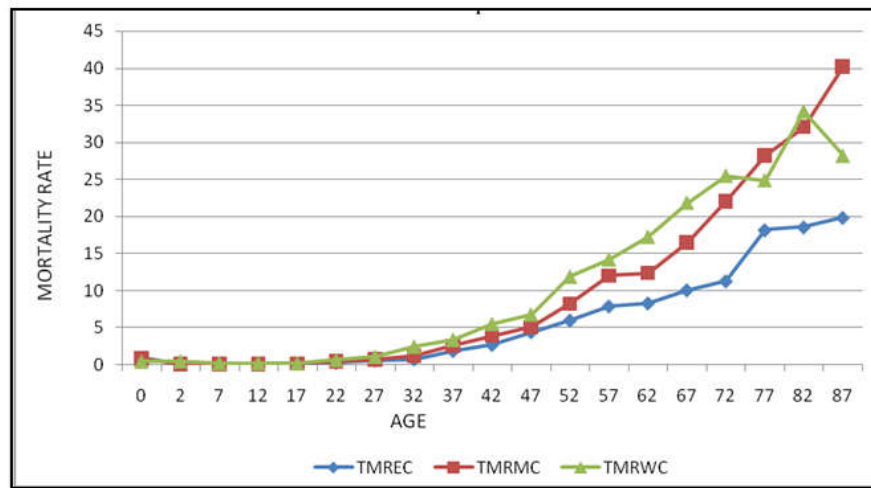


Fig. 10. Distribution of Mortality rate of Male and Female due to Viral Hepatitis in East, Middle and West part of China

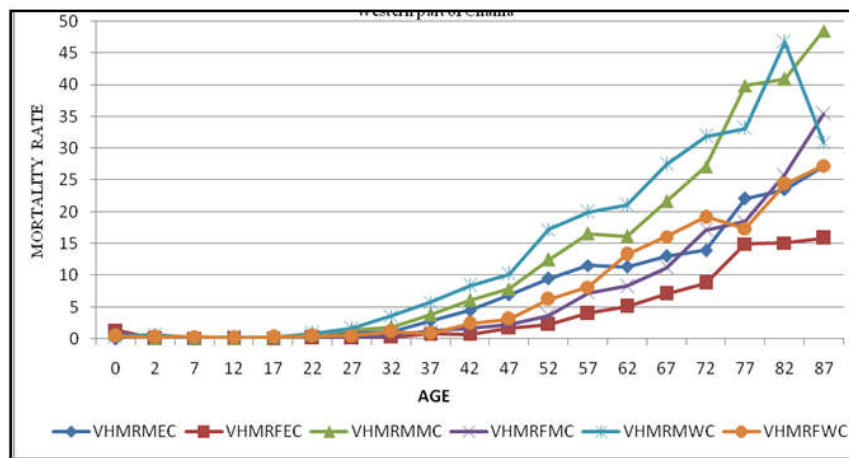


Fig. 11. Distribution of Viral Hepatitis Mortality rate Male and Female in East, Middle and Western part of China

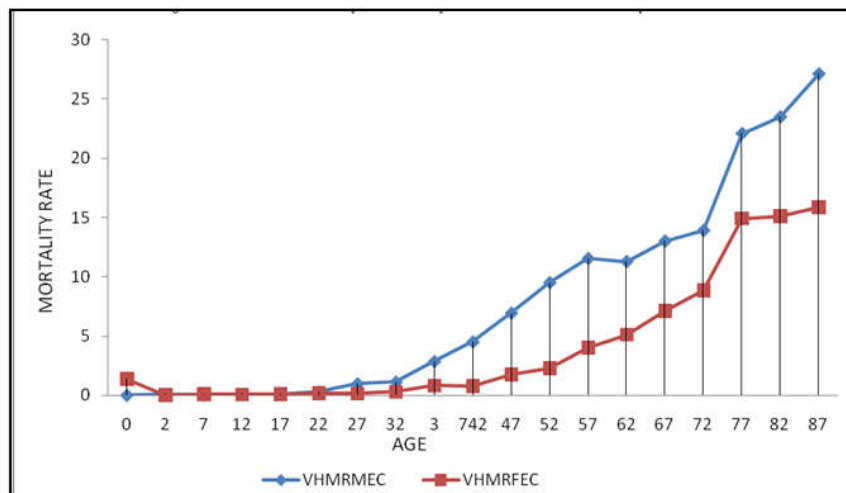


Fig. 12. Distribution of Viral Hepatitis Mortality rate of Male and Female in East part of China

Nevertheless, birth rate again decline and reach to 12.31 per thousand populations in 2012. Figure: 9, explains overall death rate of both sexes in china, and shows that in year 2000 to 2003 the death rate was less significant (6.7deaths/1000 population), in 2004 to 2009 the mortality gradually increased (7.03 deaths/1000 population) but in 2010 death rate decreased but was not less than the previous years, then increased again in

2011 to 2012 (7.17 deaths/1000 population). Figure: 10 shows distribution of mortality rate due to viral hepatitis together in East, Middle and West part of China regardless of sex. It demonstrates that in all the regions mortality rate is almost zero-bound up to the age of 27 years. The mortality rate starts to rise thereafter and rise of mortality is directly related with the rise of age of the population.

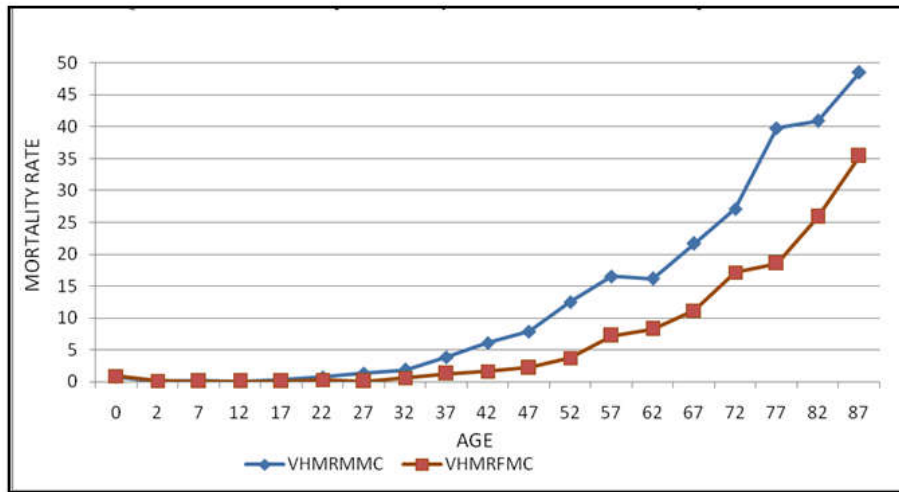


Fig. 13. Distribution of Viral Hepatitis Mortality rate of Male and Female in Middle part of China

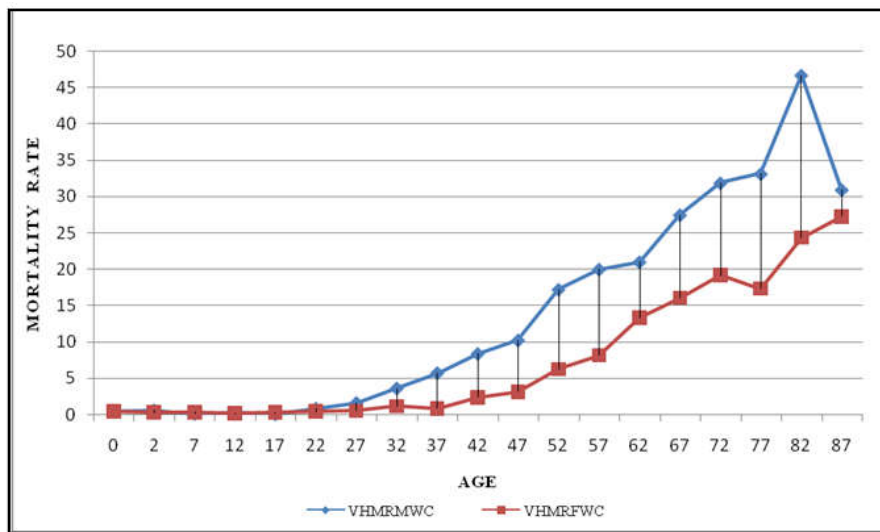


Fig. 14. Distribution of Viral Hepatitis Mortality rate of Male and Female in West part of China

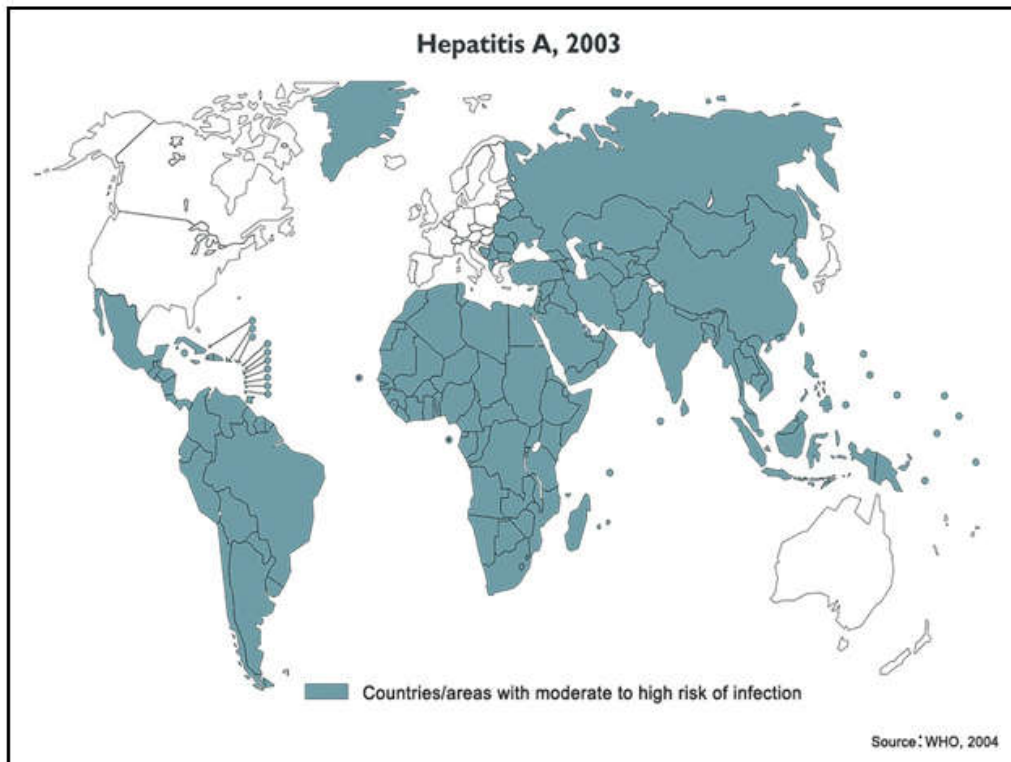


Fig. 15. Countries / areas with moderate to high risk of Hepatitis A infection (Source from WHO)

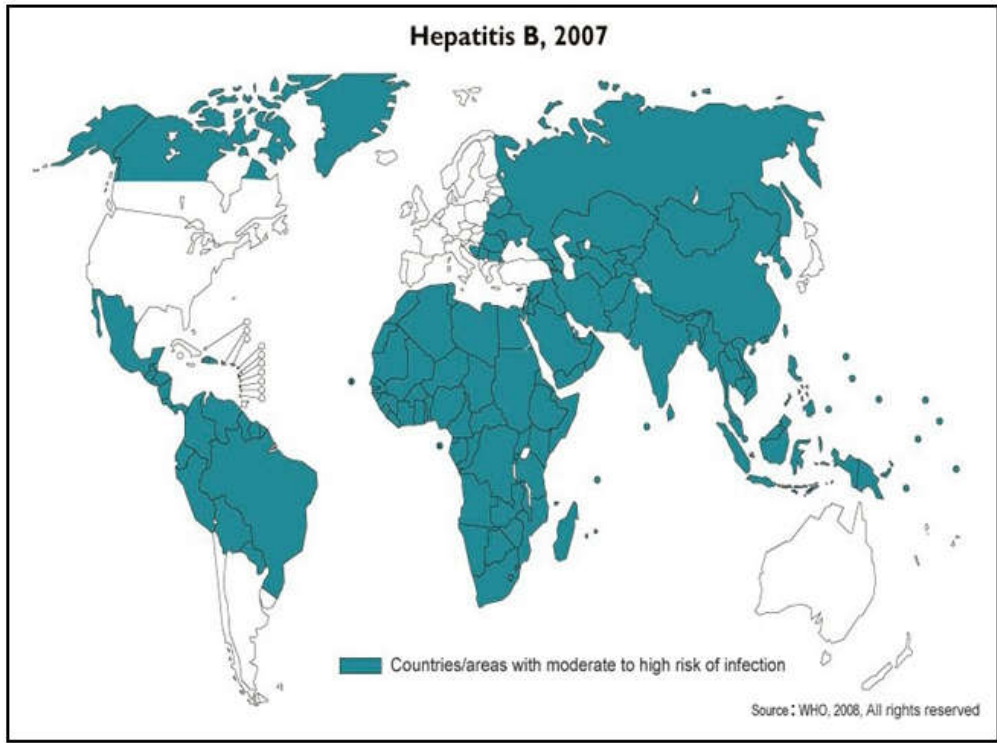


Fig. 16. Countries / areas with moderate to high risk of Hepatitis B infection (Source from WHO)

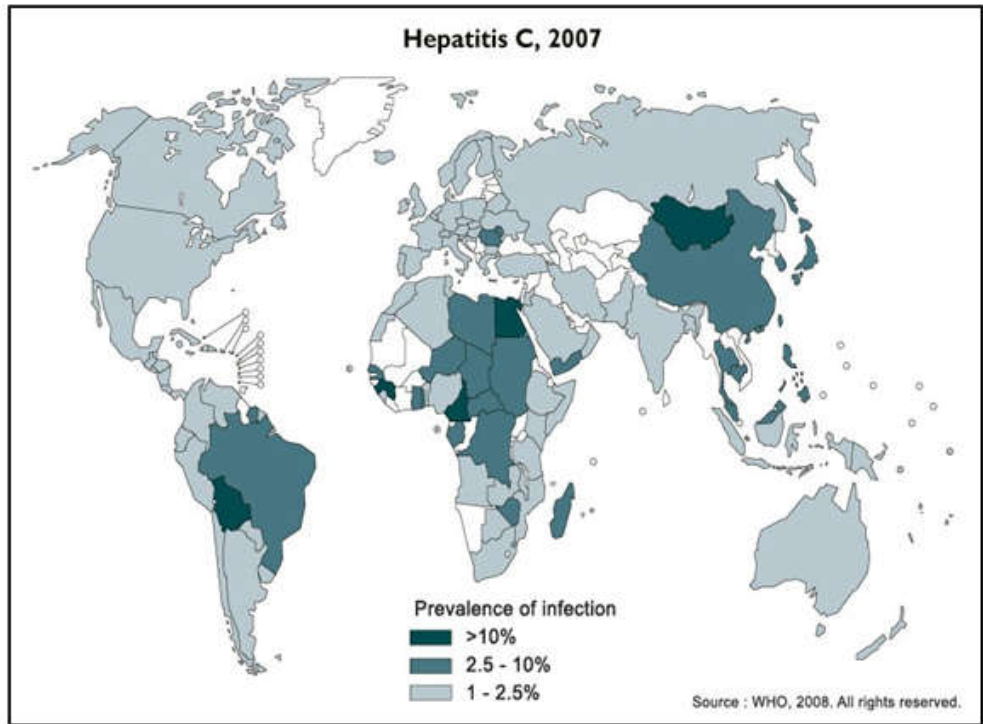


Fig. 17. Countries / areas with moderate to high risk of Hepatitis C infection (Source from WHO)

The Figure 10 further explains that mortality rate is highest in west part in most of the age groups except the age groups of 77-82 and 87-92 years, followed by Middle part and least in East part of China. Figure: 11, presents the distribution of mortality rate of male and female in East, Middle and west part of China. It illustrates that in all the parts of China, male mortality rate is higher than female mortality due to viral hepatitis and progressively increases with the age of the population.

Figures: 12, 13 and 14 demonstrates the mortality rate of male and female due to viral hepatitis, individually in three parts of China. A like Figure: 11, male mortality is higher than female in all the parts of China in all age groups.

DISCUSSION

Hepatitis B is among the most important infectious diseases in China. Viral hepatitis B infection accounts for well over 1

million deaths each year and represents the 10th leading global cause of death (Lavanchy, 2004). Viral hepatitis infection contributes for the vast majority of chronic liver disease in endemic areas of main land China (73%) (Merican *et al.*, 2000). China is one of the countries with the highest prevalence of HBV and HCV in the world, reported to be 9.75% in a 1996 nationwide cross-sectional study (Jian Lu *et al.*, 2007). This is a prevalence level confirmed repeatedly in further reports with some regional variations. The main form of transmission in China is vertical. Vertical transmission perpetuates itself due to the resultant tolerant phase, which could be decades long, with consequent high transmission rates to future generations (Lok *et al.*, 1992). Choric hepatitis infection accounts for 60% to 80% of primary liver cancer globally, which is one of the three major cause of death in Asia, Africa, Pacific rim and viral hepatitis has been a major human disease for at least 2000 years (Lavanchy, 2004). China is one of the countries with the highest prevalence of HBV in the world, reported to be 9.75% in a 1996 nationwide cross-sectional study (Xia, 1996). It is estimated that 15% or more than persons living in south East Asia and Japan are infected by hepatitis B. The high incidence of viral hepatitis infection is most likely the reason for liver cancer and liver Cirrhosis, which is the leading cause of death in china during this decade.

It is estimated that 30% of the world's population had contact with or carrier of viral hepatitis according to World Health Organization (WHO). An estimate 350 million of peoples are infected with hepatitis B virus (HBV) corresponding to 5.6% - 6% of the world total population and there are 130 - 170 million people infected with hepatitis C virus (HCV), corresponding to 2 - 2.5% of the world total population (22). Countries/areas with moderate to high risk of Hepatitis A, B and C infection (http://www.info.gov.hk/hepatitis/english/hep_a_set.htm), http://www.info.gov.hk/hepatitis/english/hep_c_set.htm), is shown in the figure 15, 16 and 17. The difference of mortality between in urban and rural areas is largely related to better educational status of the population and improved life style as well as implication of effective vaccination coverage in urban area. All these result a substantial fall in the incidence of hepatitis B in urban area and which remains an important cause of mortality. On the other hand, difference in age of incidence of viral hepatitis among the males and females may be a possible factor for higher rate mortality in males than the females.

The incidence of new infections has decreased in most developed countries, most likely due to the implementation of vaccination strategies (Rantala 2008). However, exact data is difficult to generate as many cases remain undetected due to the asymptomatic nature of many infections. Although the incidence of acute HBV infection has decreased in most countries due to the implementation of vaccination programs, HBV-related complications such as cancers and deaths have been on the increase (Gomaa 2008, Hatzakis 2011, Zhang 2013). Reasons might be the delay of vaccination effects, improved diagnosis, and better documentation of HBV cases. There is a wide range of HBV prevalence rate in different part of the world. Hepatitis B virus prevalence varies from 17% to 20%. High prevalence areas (10% - 20%) include South East Asia, China and Sub-Saharan Africa. Intermediate prevalence

(3% - 5%) are the Mediterranean countries, Japan, Central Asia, middle east, Latin America, south America. The low prevalence areas (0.1% - 2%) are in Western Europe, United States, Canada, Australia and Newzeland. Although the incidence of acute HBV infection has decreased in most countries due to the implementation of vaccination programs, HBV-related complications such as cancers and deaths have been on the increase (Gomaa 2008, Hatzakis 2011, Zhang 2013). Reasons might be the delay of vaccination effects, improved diagnosis, and better documentation of HBV cases. Although a drop in prevalence has been observed in many countries, estimates are difficult due to a continuously growing migration from high or medium prevalence areas to low prevalence areas (Belongia 2008).

The number of patients HCV RNA positive is estimated to be around 80 to 90% of all HCV antibody-positive persons. Certain groups are preferentially affected: the highest risk factor in most cases is injection drug use. But patients undergoing hemodialysis and persons who received blood transfusions before 1991 are at risk also. In Europe and the United States chronic hepatitis C is the most common chronic liver disease and the majority of liver transplants performed are for chronic HCV. It is difficult to determine the number of new HCV infections, as most acute cases are not noticed clinically. Fewer than 25% of acute cases of hepatitis C are clinically apparent (Vogel 2009). In addition, the age of infection upon diagnosis is not possible to determine in most cases. Nevertheless, it has to be assumed that the number of new infections has considerably decreased over the past decades. In the US it is estimated that the number of new cases of acute HCV infection has fallen from approximately 230,000 per year in the 1980s to about 20,000 cases per year currently (Wesley 2008). This decrease is primarily associated with reduce infections in injection drug users, a probable consequence of changes in injection practices motivated by education about human immunodeficiency virus (HIV) transmission. In case of hepatitis C in some countries e.g.: Egypt, Africa and China the prevalence rate is high as 22% (WHO, 2011), intermediate prevalence (10% - 15%) in North America and South America. The low prevalence (1% - 2%) in USA and Europe (15).

Conclusion

In conclusion, it is observed from this review that male mortality rate is higher than female mortality rate in both urban and rural areas. Peak age of male mortality rate are in both rural and urban area is 82-87 years and the peak age of female mortality rate in rural area is 82-87 years and urban is 87-92 years.

Ethical Issues

The authors declare no competing financial interest.

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