Original paper

The epidemiology of hepatocellular cancer in Poland

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Abstract

Introduction: This article summarize the available data on hepatocellular carcinoma (HCC) epidemiology in Poland. Data regarding the HCC incidence rate are divergent. Statistical data presented by NFZ appear more credible in that matter than data published by the Polish Oncology Center (POC).

Material and methods: The analysis included data from the Polish Bibliography Database (GBL), the Polish National Health Fund Institution (NFZ), the scientific paper “Malignant neoplasms in Poland” issued by POC and the central liver transplant registry maintained by the Polish transplant coordinating center “Poltransplant” (2010-2015).

Results: Data regarding the HCC incidence rate are divergent. Statistical data presented by NFZ appear more credible in that matter than data published by POC.

Conclusions: The occurrence of HCC in Poland is at the average European level and is similarly rising. The incidence rate is underestimated. It is due to faulty epidemiology data collection techniques. The highest risk group comprises men over the age of 50 with concomitant liver cirrhosis. The most common HCC etiology is HCV infection.

Key words: liver transplantation, hepatocellular carcinoma, chronic liver disease.

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Introduction

Hepatocellular carcinoma (HCC) is prevalent globally, currently ranking 5th amongst malignant tumors and 3rd as their cause of death. It is prominently increased in the sub-Saharan region and in Asiatic countries, but some Western countries (e.g. USA, Europe, Australia) and Mediterranean regions are of no rare exception. Global HCC morbidity is constantly rising. Its main etiology is attributed to liver cirrhosis. Post-inflammatory HBV cirrhosis historically concerned Asiatic countries, while Western countries were dominated by post-alcoholic and HCV-related liver cirrhosis. It is presumed that over 50% of all HCC cases are diagnosed in China [1, 2]. Nowadays, wealthy countries such as Japan, South Korea and Taiwan represent a newer trend. Owing to the widely introduced hepatitis-B vaccination program, but leaning towards hepatitis-C morbidity increase (according to global tendencies), increase of alcohol intake and having a vast population with metabolic syndrome and diabetes, the proportions between etiological factors are shifting and resemble those of the Western countries [1-8].

According to the seemingly more reliable data from the USA, throughout the past 30 years HCC morbidity has significantly increased, doubling in the last 20 years [1]. The annual incidence rate increased and exceeded 18 000 cases at the end of the century [7]. Between 1999 and 2010 in the USA alone, the incidence rate increased by 3.7%.

According to WHO data, Poland, Western Europe, USA and Australia belong to a group with a low HCC
incidence rate, ranging from 2.5 to 4.9 per 100,000 [4, 5]. Those data are approximated and based on reporting of primary liver cancer classified as C22 (ICD 10), consisting of hepatocellular carcinoma and cholangiocellular carcinoma. In the majority of countries cholangiocellular carcinoma is responsible for 10% of primary liver cancer or less. Thailand is an exception to that rule, having higher rates of cholangiocarcinoma due to frequent schistosomiasis in that region [1, 2]. Mortality increases alongside HCC morbidity.

Different geographic regions present with a diverse HCC mortality. In Cameroon HCC mortality constitutes 1/3 of all oncology-related deaths, seemingly not exceeding 5% [1, 2] in Western Europe and USA. Mean survival time is expected to be one year [9]. Without effective treatment it decreases to 5 months; 1 and 3-year survival rates are 20.9% and 5.7% [1, 2]. In Poland, between 2000 and 2002, 1, 3, and 5-year survival rates were 23%, 10.9%, 7.9%, respectively, and were three times higher than in the general population with other malignant neoplasms [10]. Disheartening data from official registries do not always correspond with clinical sample data, hence new better therapies result in improved, over previously cited, outcomes [1, 4]. On the other hand, only a small fraction with diagnosed HCC is committed to potentially therapeutic treatment [1, 7, 8, 11]. Such low survivability is related to insignificant clinical symptoms in early phases, the aggressive nature of the disease and coexisting liver failure. Onset of clinical symptoms heralds deep clinical progression at the point when therapeutic options are already severely narrowed down [1, 11]. Moreover, in western countries peak morbidity falls at 75 years old and after. In Asia, a much younger population is involved due to high incidence of hepatitis B virus (HBV) infection in childhood [1, 2, 7, 8].

In an overwhelming majority of countries the primary liver cancer incidence rate is higher in men. The ratio between men and women ranges from 2 : 1 to 4 : 1 [1, 2, 7, 8, 12]. Likewise, male mortality attributed to HCC is higher. Major differences are seen in countries with highest HCC incidence rates [1]. It is believed to be due to a higher overall HCC cancer rate in men and higher exposure to risk factors in men. Men more often have B/C viral hepatitis, they consume alcohol, smoke and are in danger of metabolic syndrome [1, 13].

The HCC incidence rate varies not only among geographical locations but also among different populations inhabiting the same area. For example, in the USA, the incidence rate in Caucasian White is two times lower than in Latino and Afro-Americans. That seems to be related to altering viral hepatitis susceptibility in different ethnic groups [1, 14].

The aim of the study was to present Polish epidemiologic data regarding HCC and its dynamics based on the recent scientific literature.

# Material and methods

The annual HCC incidence rate and rate of liver transplant secondary to HCC in the total transplant group were assessed.

Analysis included data from the Polish Bibliography Database (GBL), the Polish National Health Fund Institution (NFZ), the scientific paper “Malignant neoplasms in Poland” issued by the Polish Oncology Center (POC) and the central liver transplant registry maintained by Polish transplant coordinating center “Poltransplant” (2010-2015).

References regarding HCC in Polish language are sparse. The results of the search “hepatocellular carcinoma” in the GBL database showed 237 titles published in 1991-2014 [15], mostly in English. In comparison, the same search run on PubMed showed over 75 thousand published papers. Publications in Polish were outweighed by book chapters, case reports and overview papers. Only a small minority were original publications reviewing the diagnosis and treatment of HCC, but not epidemiology. According to that, only the latter 3 sources of listed data were used. Although the process of publishing the above-mentioned data was slightly delayed, the information contained was found to be useful to illustrate the epidemiology and determine HCC etiology in Poland.

Epidemiology data acquired from NFZ pertain to 2008-2013 and consider new cases and their onset according to geographical region. The general crude incidence rate and rate for each county were calculated using Polish demographic data [16], regarding the years 2008, 2010, 2011, 2013 (Fig. 1).

Available epidemiologic data from POC were based on reports from 2006, 2008, 2009, 2013, 2015 and statistical data from 2002 to 2013 [10, 17-20]. It consisted of data concerning the incidence rate and mortality (including division according to geographic location, age, gender, crude and standardized incidence rates) (Figs. 2-4).

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Fig. 1. Data from Polish National Health Fund Institution (NFZ) and Central Statistical Office (Polish: Główny Urząd Statystyczny – GUS) – number of hepatocellular carcinoma cases in years 2008-2013 according to geographic region; incidence rate calculated for both genders (per 100 000 of general population). The data regarding number of cases originated from NFZ and the demographic data from GUS yearly statistical reports [23, 24]
Fig. 2. Data from Polish Oncology Center (POC) and Central Statistical Office (Polish: Główny Urząd Statystyczny – GUS) – hepatocellular carcinoma total number of cases and incidence rate according to geographic region in years 2006, 2010, 2011 and 2013. Data concerning number of cases derived from POC, demographic data from GUS yearly statistical reports [16, 17, 19, 20].
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Fig. 3. Data from Polish Oncology Center (POC) – hepatocellular carcinoma incidence among men and women; absolute case numbers, incidence rate crude and standardized, position on the neoplasm incidence list [17]

Fig. 4. Data from Polish Oncology Center (POC) – hepatocellular carcinoma mortality among men and women in 2006, 2010, 2013; absolute case numbers, incidence rate crude and standardized, position on the neoplasm incidence list [17]
Fig. 5. Data from Polish Oncology Center (POC) and Central Statistical Office (Polish: Główny Urząd Statystyczny – GUS) – hepatocellular carcinoma mortality, mortality rate according to geographic region, years 2006, 2010, 2011 and 2013. Data concerning number of cases derived from POC, demographic data from GUS [16, 17, 19, 20].
Fig. 6. Data from Polish Oncology Center (POC) – hepatocellular carcinoma incidence rate and mortality according to geographic region, years 2006, 2010, 2011 and 2013 [17, 19, 20]
Results

Comparison of hepatocellular carcinoma incidence rates in women, 2006 vs. 2013

There was a significant decrease in incidence rate in women aged 30-34 (Table 1). All comparisons between 2006 and 2013 groups performed using χ² Pearson test.
Comparison of hepatocellular carcinoma incidence rates in men, 2006 vs. 2013

There was a significant decrease in incidence rate in men aged 45-49. There was a significant increase in incidence rate in men aged 60-64 (Table 2). All comparisons between 2006 and 2013 groups performed using $\chi^2$ Pearson test.

Comparison of hepatocellular carcinoma incidence rates between genders, 2006 vs. 2013

The change in incidence rate in men and women in 2006 vs. 2013 was statistically significant (Table 3). All comparisons between 2006 and 2013 group performed using $\chi^2$ Pearson test.
Fig. 9. Poltransplant data regarding hepatocellular carcinoma (HCC) treatment with liver transplantation (LTx) in Poland concords with the tendencies noted by European Liver Registry (ELTR).
Comparison of hepatocellular carcinoma mortality between in women, 2006 vs. 2013

There was a significant decrease in mortality at age 45-49 and 75-79. There was a significant increase in mortality at age 60-64 and 85+ (Table 4). All comparisons between 2006 and 2013 group performed using $\chi^2$ Pearson test.

Comparison of hepatocellular carcinoma mortality between in men, 2006 vs. 2013

There was a significant decrease in mortality at age 45-49 and 70-74. There was a significant increase in mortality at age 60-64 and 85+ (Table 5). All comparisons between 2006 and 2013 group performed using $\chi^2$ Pearson test.

Comparison of hepatocellular carcinoma mortality between genders, 2006 vs. 2013

No statistically significant differences were found (Table 6). All comparisons between 2006 and 2013 group performed using $\chi^2$ Pearson test.

Treatment of hepatocellular carcinoma with liver transplantation

HCC treatment with liver transplantation (LTx) was associated with early recurrence at first. In spite of the above-mentioned reservation, nowadays LTx has become a standard method of treatment, presenting the best prognosis. It is strongly associated with the introduction of Milan criteria introduced in 1996 by Mazzaferro.

Poltransplant data regarding HCC treatment with LTx in Poland concords with the tendencies noted by European Liver Registry (ELTR).

In 2001, the percentage of liver transplantation in treatment of HCC was equal to 1.1, while in 2015 it exceeded 21% and was even 25.8% a year before. Although the number of liver transplants in the HCC group increased, the total number of transplants is still trifling. In 2013, transplanted patients with HCC constituted a group of only 3.2% of the new cases.

Discussion

Data regarding the HCC incidence rate are divergent. Statistics presented by POC showed even a slight
Table 1.

| Age group | Incidence rate 2006 | Incidence rate 2013 | χ² | p* |
|-----------|---------------------|---------------------|----|----|
|           |                     |                     |    |    |
| 0-4       | 4                   | 5                   | .82| .366|
| 5-9       | 0                   | 0                   | .82| .366|
| 10-14     | 2                   | 3                   | 1.00| .331|
| 15-19     | 1                   | 2                   | 1.00| .331|
| 20-24     | 1                   | 2                   | 0.20| .065|
| 25-29     | 0                   | 0                   | .50| .480|
| 30-34     | 0                   | 0                   | .25| .617|
| 35-39     | 0                   | 0                   | 0.04| .841|
| 40-44     | 0                   | 0                   | 0.03| .852|
| 45-49     | 0                   | 0                   | 0.03| .852|
| 50-54     | 0                   | 0                   | 0.03| .852|
| 55-59     | 0                   | 0                   | 0.03| .852|
| 60-64     | 0                   | 0                   | 0.03| .852|
| 65-69     | 0                   | 0                   | 0.03| .852|
| 70-74     | 0                   | 0                   | 0.03| .852|
| 75-79     | 0                   | 0                   | 0.03| .852|
| 80-84     | 0                   | 0                   | 0.03| .852|
| 85+       | 0                   | 0                   | 0.03| .852|
| Total     | 800                 | 668                 | 0.17| 0.680|

*Nonparametric χ² Pearson test.

Table 2.

| Age group | Incidence rate 2006 | Incidence rate 2013 | χ² | p* | OR** |
|-----------|---------------------|---------------------|----|----|------|
|           |                     |                     |    |    |      |
| 0-4       | 4                   | 7                   | 0.82| .366|
| 5-9       | 0                   | 0                   | .82| .366|
| 10-14     | 2                   | 3                   | 1.00| .331|
| 15-19     | 1                   | 3                   | 1.00| .331|
| 20-24     | 1                   | 2                   | 0.20| .065|
| 25-29     | 0                   | 0                   | .50| .480|
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| 45-49     | 0                   | 0                   | 0.03| .852|
| 50-54     | 0                   | 0                   | 0.03| .852|
| 55-59     | 0                   | 0                   | 0.03| .852|
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| 75-79     | 0                   | 0                   | 0.03| .852|
| 80-84     | 0                   | 0                   | 0.03| .852|
| 85+       | 0                   | 0                   | 0.03| .852|
| Total     | 800                 | 668                 | 0.17| 0.680|

*Nonparametric χ² Pearson test.

**Odds ratio (OR > 1 increase in risk, OR < 1 decrease in risk)

Table 3.

| Age group | Incidence rate 2006 | Incidence rate 2013 | χ² | p* | Φ-Yule |
|-----------|---------------------|---------------------|----|----|--------|
|           |                     |                     |    |    |        |
| 0-4       | 4                   | 5                   | 0.40| 0.5283| 0.019 |
| 5-9       | 0                   | 1                   | 0.82| .366|
| 10-14     | 1                   | 2                   | 1.00| .331|
| 15-19     | 1                   | 3                   | 1.00| .331|
| 20-24     | 1                   | 2                   | 0.20| .065|
| 25-29     | 1                   | 2                   | 0.50| .480|
| 30-34     | 0                   | 0                   | 0.25| .617|
| 35-39     | 0                   | 0                   | 0.04| .841|
| 40-44     | 0                   | 0                   | 0.03| .852|
| 45-49     | 0                   | 0                   | 0.03| .852|
| 50-54     | 0                   | 0                   | 0.03| .852|
| 55-59     | 0                   | 0                   | 0.03| .852|
| 60-64     | 0                   | 0                   | 0.03| .852|
| 65-69     | 0                   | 0                   | 0.03| .852|
| 70-74     | 0                   | 0                   | 0.03| .852|
| 75-79     | 0                   | 0                   | 0.03| .852|
| 80-84     | 0                   | 0                   | 0.03| .852|
| 85+       | 0                   | 0                   | 0.03| .852|
| Total     | 800                 | 668                 | 0.17| 0.680|

*Nonparametric χ² Pearson test.
Table 4.

| Age group | Deaths | χ² | p* | OR** |
|-----------|--------|----|----|------|
| 2006      | 2013   |    |    |      |
| 0-4       | 0      | 1  | –  | –    |
| 5-9       | 0      | 1  | –  | –    |
| 10-14     | 0      | 0  | –  | –    |
| 15-19     | 1      | 1  | –  | –    |
| 20-24     | 2      | 0  | –  | –    |
| 25-29     | 0      | 1  | –  | –    |
| 30-34     | 3      | 3  | –  | –    |
| 35-39     | 2      | 1  | –  | –    |
| 40-44     | 11     | 7  | 0.89 | 0.346 |
| 45-49     | 22     | 7  | 7.76 | 0.006 | 0.32 |
| 50-54     | 36     | 23 | 2.86 | 0.091 |
| 55-59     | 74     | 63 | 0.88 | 0.347 |
| 60-64     | 74     | 105| 5.37 | 0.021 | 1.42 |
| 65-69     | 104    | 89 | 1.17 | 0.280 |
| 70-74     | 148    | 126| 1.77 | 0.184 |
| 75-79     | 192    | 159| 13.70 | < 0.001 | 0.83 |
| 80-84     | 179    | 174| 0.07 | 0.790 |
| 85+       | 97     | 130| 4.80 | 0.029 | 1.34 |
| Total     | 945    | 891| 1.59 | 0.208 |

*Nonparametric χ²: Pearson test
**Odds ratio (OR > 1 increase in risk, OR < 1 decrease in risk)

Table 5.

| Age group | Deaths | χ² | p* | OR** |
|-----------|--------|----|----|------|
| 2006      | 2013   |    |    |      |
| 0-4       | 1      | 0  | –  | –    |
| 5-9       | 0      | 0  | –  | –    |
| 10-14     | 1      | 0  | –  | –    |
| 15-19     | 1      | 1  | –  | –    |
| 20-24     | 3      | 0  | –  | –    |
| 25-29     | 3      | 1  | –  | –    |
| 30-34     | 6      | 4  | 0.40 | 0.527 |
| 35-39     | 5      | 6  | 0.09 | 0.763 |
| 40-44     | 6      | 11 | 1.47 | 0.225 |
| 45-49     | 37     | 21 | 4.41 | 0.036 | 0.57 |
| 50-54     | 88     | 64 | 3.79 | 0.052 |
| 55-59     | 129    | 150| 1.58 | 0.209 |
| 60-64     | 92     | 163| 19.70 | < 0.001 | 1.77 |
| 65-69     | 143    | 168| 2.01 | 0.156 |
| 70-74     | 198    | 145| 8.19 | 0.004 | 0.73 |
| 75-79     | 175    | 153| 1.48 | 0.224 |
| 80-84     | 115    | 120| 0.11 | 0.744 |
| 85+       | 42     | 82 | 12.90 | < 0.001 | 1.95 |
| Total     | 1045   | 1089| 0.91 | 0.341 |

*Nonparametric χ²: Pearson test
**Odds ratio (OR > 1 increase in risk, OR < 1 decrease in risk)

Table 6.

| Age group | Deaths 2006 | Deaths 2013 | χ² | p* | Φ-Yule |
|-----------|-------------|-------------|----|----|--------|
| Men       | Women       | Men         | Women |
| 0-4       | 1           | 0           | 0   | 1  | –      | – |
| 5-9       | 0           | 0           | 0   | 0  | –      | – |
| 10-14     | 1           | 0           | 0   | 0  | –      | – |
| 15-19     | 1           | 1           | 1   | 1  | –      | – |
| 20-24     | 3           | 2           | 0   | 0  | –      | – |
| 25-29     | 3           | 0           | 1   | 1  | 1.88   | 0.1709 | 0.375 |
| 30-34     | 6           | 3           | 4   | 3  | 0.15   | 0.6963 | 0.010 |
| 35-39     | 5           | 2           | 6   | 1  | 0.42   | 0.5148 | 0.030 |
| 40-44     | 6           | 11          | 11  | 7  | 2.33   | 0.1267 | 0.067 |
| 45-49     | 37          | 22          | 21  | 7  | 1.29   | 0.2560 | 0.015 |
| 50-54     | 88          | 36          | 64  | 23 | 0.17   | 0.6792 | 0.001 |
| 55-59     | 129         | 74          | 150 | 63 | 2.22   | 0.1358 | 0.005 |
| 60-64     | 92          | 74          | 163 | 105| 1.23   | 0.2668 | 0.003 |
| 65-69     | 143         | 104         | 168 | 89 | 2.98   | 0.0844 | 0.006 |
| 70-74     | 198         | 148         | 145 | 126| 0.85   | 0.3560 | 0.001 |
| 75-79     | 175         | 192         | 153 | 159| 0.12   | 0.7248 | 0.000 |
| 80-84     | 115         | 179         | 120 | 174| 0.18   | 0.6738 | 0.000 |
| 85+       | 42          | 97          | 82  | 130| 2.63   | 0.1047 | 0.008 |
| Total     | 1045        | 945         | 1089| 891| 2.47   | 0.1160 | 0.001 |

*Nonparametric χ²: Pearson test
The occurrence of HCC in Poland is at the average European level and is similarly rising. The incidence rate is underestimated. It is due to faulty epidemiology data collection techniques. The highest risk group comprises men over the age of 50 with concomitant liver cirrhosis. The most common HCC etiology is HCV infection.

The percentage of liver transplantation secondary to HCC increases every year. When properly following the Milan criteria, this method offers the best possible HCC treatment modality.

Disclosure

Authors report no conflict of interest.

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