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Retrospective Study

Decrease in liver cancer incidence rates in Bamako-Mali over 28 years of population-based cancer registration (1987-2015)

Amadou A *et al*. Decrease in liver cancer incidence rates in Mali between 1987-2015

Abstract

BACKGROUND

Primary liver cancer is common in West Africa due to endemic risk factors. However, epidemiological studies of the global burden and trends of liver cancer are limited. We report changes in trends of incidence of liver cancer over a period of 28 years using the population-based cancer registry of Bamako, Mali.

AIM

To assess the trends and patterns of liver cancer by gender and age-groups by analysing cancer registration data accumulated over 28 years (1987-2015) of activity of the population-based registry of Bamako district.

METHODS

Data obtained since the inception of the registry in 1987 to 2015 were stratified in three periods (1987-1996, 1997-2006, and 2007-2015). Age standardized rates were estimated by direct standardisation, using the world population. Incidence rates ratios (IRR) and the corresponding 95% confidence intervals (CI) were estimated using the early period as reference (1987-1996). Joinpoint regression models were used to assess the Annual Percentage Change (APC) and highlight trends over the entire period (from 1987 to 2015).

RESULTS

Among men, the age standardized incidence rates significantly decreased from 19.41 to 13.12 and 8.15 per 10^5 person-years (p-years), respectively over the three periods considered. The IRR over 28 years was 0.42 (95%CI: 0.34-0.50) and the APC was -4.59 [95%CI: (-6.4)-(-2.7)]. Among women, rates dropped continuously from 7.02 (1987-1996) to 2.57 (2007-2015) per 10^5 p-years, with an IRR = 0.37 (95%CI: 0.28-0.45), and an APC = -5.63 [95%CI: (-8.9)-(-2.3)].

CONCLUSION

Population-based registration shows that the incidence of primary liver cancer has steadily decreased in the Bamako district over 28 years. This trend does not appear to result from biases or changes in registration practices. This is the first report of such a decrease in an area or high incidence of liver cancer in Africa. This decrease may be explained by the changes and diversity of diet that could reduce exposure to aflatoxins through dietary contamination in this population.

Key Words: Hepatocellular carcinoma; Hepatitis B infection; Aflatoxin; West Africa; Cancer registration; Annual percentage change

Amadou A, Sighoko D, Coulibaly B, Traoré C, Kamaté B, Mallé BS, de Seze M, Kemayou Yoghoum FN, Biyogo Bi Eyang S, Bourgeois D, Curado MP, Bayo S, Gormally E, Hainaut P. Decrease in liver cancer incidence rates in Bamako-Mali over 28 years of population-based cancer registration (1987-2015). *World J Hepatol* 2022; In press

Core Tip: Epidemiology of liver cancer is limited in West Africa. This study investigated incidence trends of liver cancer over 28 years of the population-based cancer registry of Bamako-Mali. Findings show a significant decrease in liver incidence rates in both men and women. This is the first study, reporting a decrease in the incidence rates of liver cancer in an urban population in West Africa. Evidence points to a reduction of exposure to aflatoxin caused by changing lifestyles and dietary patterns in this population. The magnitude of this effect suggests that reduction for aflatoxin exposure may achieve major protective effects in West Africa.

INTRODUCTION

Evidence shows that global trends of incidence for primary liver cancer are undergoing contrasting changes in different parts of the world[1-7]. Primary liver cancer includes hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (ICC) and several rare forms of mesenchymal or lymphoid origin. Globally, HCC is by far the most common diagnosed liver cancer, representing 80%-90% of the cases in most regions, with the exception of defined regions of South-East Asia where ICC is predominant owing to infections by endemic liver flukes. Analysis of cancer registration data collected in Cancer Incidence in Five Continents (International Agency for Research on Cancer, IARC, CI5V-XI and CI5plus) and the NORDCAN database reveals that incidences of liver cancer between 1978 and 2012 in high-risk countries, mostly in Eastern and South-Eastern Asia remain high but are decreasing for the most recent period. In contrast, in low risk countries such as India and some countries in Europe, America and Oceania incidence rates are rising[5].

A projection of the future burden of liver cancer to 2030 in 30 countries predicts an increase in the incidence rates in most countries, with the exception of some Asian countries (China, Japan, Singapore) and European countries (Estonia, Czech Republic, and Slovakia), where declines in rates are foreseen[4,6]. Liver incidence rates in Sub-Saharan Africa are high though data are scarce (Figure 1). Africans are more likely to develop liver cancer at a younger age and to be diagnosed at an advanced stage, resulting in poorer outcomes than in patients from countries with high development index[8-11]. Worldwide, primary liver cancers are mostly HCC (> 90%)[3] and in West Africa it is the most fatal malignancy in men and the third most fatal malignancy in women[12]. The main risk factor is the synergistic effect of chronic infection by hepatitis B virus (HBV) which is endemic in these populations, and dietary exposure to the carcinogenic mycotoxin aflatoxin, a widespread contaminant of traditional diet[6,11,13-17]. In 2020, in West Africa, age standardized rates (ASR) for liver cancer were estimated to range between 21.8 (Guinea) and 4.9 (Togo) ASR p-100000 persons[18,19] (Figure 1; https://gco.iarc.fr/). Recent changes in dietary patterns and lifestyles, in awareness and prevention of the main risk factors and the introduction of neonatal and infant vaccination against HBV are raising expectations that the incidence of chronic liver diseases and liver cancer may significantly decrease in the coming years[11]. However, until now, the only two studies on trends of liver cancer in Sub-Saharan Africa, in

Uganda (Kyadondo) and in the Gambia have observed a relative stability or only a limited decrease in incidence rates among men, whereas among women, a significant increase was observed[20,21]. Understanding the reasons for these variations is crucial for the correct interpretation of ongoing changes in the prevalence and population impact of the main risk factors for liver cancer in this region.

Population-based cancer registration is limited in Africa. Maintaining a registry in a low-resource context is complex from an operational viewpoint. Furthermore, variations in clinical procedures, in patterns of patient referral and in diagnostic practices are often insufficiently documented, making it difficult to distinguish between biological effects and cancer registration biases when analyzing observed variations in incidence. Mali (Bamako district, also covering the city of Kati) and the Gambia (National cancer registry) are among the rare countries of the sub-region of West Africa to have operational population-based cancer registries. In this study, we have used cancer registration data accumulated over 28 years of activity of the population-based registry of Bamako district to assess the trends and patterns of liver cancer by genders and age-groups.

MATERIALS AND METHODS

Study population

Cancer data from 1987 to 2015 of the cancer registry of Bamako district, Mali were used. Mali (surface area 1246238 km^2) had an estimated population of 18343000 in 2016, with life expectancy of 60 years for women and 59 years for men[22]. Bamako district, the capital city, had a population estimated at 2529328 in 2019[23]. Mali is one of the poorest countries in the world. It has few resources for health care, and child and infant mortality rates are among the highest in the world. Education services are poorly developed, particularly at the primary level, and in rural areas. The expected years of schooling in 2019 was 7.5 years. Despite improvements in medical care, Mali is still challenged by a lack of personnel, facilities, resources, and supplies. However, over the past 20 years, Mali has defined several policies that have served as a reference framework for all social and health development programs, in order to strengthen the health system, to provide equitable access to health care and to prevent, detect, and respond effectively to epidemics and public health emergencies[24,25].

The health care system in Mali comprises local community health centers delivering primary health care, secondary referral centers, six of which are located in Bamako district and which provide specialized care in, among others, gynecology and obstetrics, general surgery, pediatrics, stomatology and oto-rhino-laryngology, and tertiary referral centers represented by the three university hospitals of Mali, namely the hospitals of Point G and Gabriel Touré (both localized in Bamako city) and of Kati (15 km south-east of Bamako).

The cancer registry for Bamako district was created in 1987. This registry records information on cancer cases from all possible sources within the district of Bamako. Initially located at the National Institute of Research in Public Health, the registry moved to the department of pathology of the university hospital of Point G in Bamako in May 2010. The cancer registry is managed by pathology interns. Every month, they perform an active collection of all cases diagnosed in all medical services (public or private) in Bamako district. Information is collected through pathology files, patient clinical files, hospital-based registries (such as chemotherapy, endoscopy and surgery registries), and through death certificates managed by a non-governmental Malian organization, the Center for Information, Counselling, Care and Support for People Living with HIV/AIDS. After collection, all data are computerized using the software CanReg 4[26]. Tumors are coded according to the ICD-O third edition.

Patients who were resident from locations outside of the Bamako district were excluded from the incidence data analyses. Bamako residents are defined as being in residence for the previous 3 mo in the district[27]. Demographic data for Bamako district in person-years (p-years) from 1987 to 2015 were obtained by the interpolation of data extracted from the national censuses of 1976, 1998 and 2009.

Statistical analysis and data modelling

ASR were estimated by direct standardization, with rates adjusted to the world population by 5-year age group. Incidence data were calculated for three arbitrarily defined periods: 1987-1996, 1997-2006 and 2007-2015. The incidence rates ratios (IRR) and the corresponding 95% confidence intervals (CI) were calculated using the early period as reference (1987-1996), using STATA software version 14 (College Station, Texas, United States). Temporal trends over the whole period of 28 years, were assessed using Joinpoint regression analyses [program version 3.3 (https://www.cancer.gov/joinpoint)]. Data for the year 2005 were excluded because of an apparent unexplained registration bias.

Liver cancer cases diagnosed by endoscopy were further excluded to avoid potential overestimation of liver cancer cases, since endoscopy is not one of the standard methods of liver cancer diagnosis. As for most parts of Africa, Mali and Bamako district have a population structure characterized by a strong representation of younger age groups, with only 2.5% of the population aged 65 years and over. This distribution causes a bias when evaluating incidence rates in the older age groups because of the small population denominators. Therefore, instead of expressing the age-specific rates per 100000, we modelled the expected number of cases in a standard population in which the age-specific rate is adjusted to the world standard population[28]. This approach minimizes the tendency to overestimate cancer incidence in older age groups and thus provides a more accurate picture of the distribution of common cancers across the different age groups. For sake of comparison with liver cancer, we additionally analyzed the most frequent cancers (breast, bladder, stomach, prostate, cervix uteri). All statistical tests were two-sided and P values < 0.05 were considered statistically significant.

RESULTS

Characteristics of the cancer cases and liver diagnostic criteria

Table 1 shows the characteristics of the study subjects, for all cancers and according to the three periods of diagnosis. From 1987 to 2015, the cancer registry of Bamako-Mali registered 19553 cancer cases including 8553 (44%) in men and 10950 (56%) in women. The median age of the study subjects at the time of cancer diagnosis was 49 years. Overall, diagnosis of all cancers was based on histopathology for 58.16% of the cases in men and 70.16% in women, with an increase in this trend over the years.

There were 634 primary liver cancer cases (11.17% of the total cases), after exclusion of those diagnosed by endoscopy. The diagnosis of primary liver cancer mainly relied on the biopsy/cytology (26.3%), the classical triad of clinical signs (hepatomegaly, icterus and ascites) (25.8%) and ultrasonography (25.6%). Diagnosis based on biopsy/cytology increased from 5.7% in the earlier period (1987-1996) to 55.6% in the late period (2007-2015), whereas diagnosis based only on clinical signs decreased from 45.9% in the earlier period (1987-1996) to 8.4% in the late period (2007-2015). A review of clinical bases of diagnoses at the two tertiary referral centres of Bamako city (Hospital Gabriel Touré; Department of Gastroenterology and Point G Hospital; Department of Internal Medicine) indicated that the most common clinical signs were hepatomegaly, icterus and presence of ascites, and the main symptoms were pain, nausea, vomiting and weight loss. Alpha-fetoprotein levels were ≥ 400 ng/mL in 45% of the cases.

Incidence rates and trends of liver cancer

Table 2 compares the incidence of the four most common cancers among men and women over the three periods. These cancers are liver, stomach, bladder and prostate in men; and liver, stomach, cervix uteri and breast in women. In men, a total of 426 cases of liver cancers were diagnosed during the early period 1987-1996, representing 21.93% of all cancers, compared to 378 cases in the period 1997-2006 (17.69%) and 405 cases in the period 2007-2015 (8.95%). In women, the total number of liver cases diagnosed in the early period 1987-1996 was 151 (7.96% of all cancers), compared to 144 (5.66%) in the period 1997-2006 and 129 cases (1.98%) in the period 2007-2015. ASR for liver cancer significantly decreased over the 3 periods in both genders. In men rates dropped from 19.41 per 10^5 p-years for the period 1987-1996 to 13.12 for the period 1997-2006 [33%

decrease; IRR: 0.67 (95%CI: 0.59-0.76)], and 8.15 for the period 2007-2015 [58% decrease over period 1987-1996; IRR: 0.42 (95%CI: 0.34-0.50)]. Among women, rates decreased from 7.02 per 10^5 p-years for the period 1987-1996 to 5.15 in the period 1997-2006 [27% decrease; IRR: 0.73 (95%CI: 0.56-0.91)], and 2.57 for the most recent period [2007-2015, representing a decrease of 63% compared to period 1987-1996; IRR: 0.37 (95%CI: 0.28-0.45)] (Table 2).

It is noteworthy that variations in incidence were also observed for several other common cancers in men and women over the entire registration period (Table 2). Namely, a significant increase was observed for prostate, breast and cervical cancers. When comparing earlier (1987-1996) and later (2007-2015) periods, incidence rates of prostate and breast cancers increased by 2.57 and 2.99-fold, respectively. In contrast, rates of bladder cancer remained stable in men whereas rates of stomach cancer showed a decrease of 33% and 38% in men and women, respectively.

Trend analyses of liver cancers covering the 28 years of registration (encompassing the three periods) showed that incidence rates steadily and progressively declined in both genders. The Annual Percentage Change (APC) was -4.59 [95%CI: (-6.4)-(-2.7)] in men (Figure 2) and -5.63 [95%CI: (-8.9)-(-2.3)] in women (Figure 1). When analyzing age specific curves, we observed that for the three periods and for both genders, curves were similar and showed peaks in approximately the same age group (Supplementary Figures 1 and 2).

DISCUSSION

In this study, we have analyzed data from the population-based cancer registry covering the district of Bamako over 28 years of registration (1987-2015) to assess trends in incidence of liver cancer, one of the most common forms of cancer in the West African populations. We have compared incidence rates over three defined periods, 1987-1996, 1997-2006 and 2007-2015. Over these periods, liver cancer showed a remarkable and progressive decrease in the ASR in both genders and in all age groups, with a significant APC of -4.59 among men and of -5.63 among women. Such a large reduction in incidence rate was not observed for other common cancers in the adult population of the district of Bamako. Notably, over the entire registration period, incidence rates for breast and prostate cancers significantly increased, a trend also observed in other West African countries[28,29] as well as globally in low-resource countries[30]. Factors such as westernized diet, urbanization, increasing awareness and improved registration and diagnosis have been implicated, although their precise specific contributions are yet to be fully established. In Mali, the fact that only liver cancer shows a strong and systematic decrease in incidence rate suggests that the decrease is not a bias caused by changes or discontinuity in cancer diagnosis or registration practices. A review of clinical practices indicated that clinical diagnosis and main symptoms for liver cancer have remained stable over the entire study period (28 years). Of note, the proportion of patients who received confirmation based on biopsy/cytology analysis substantially increased from 5.7% in 1987-1996 to 55.6% in 2007-2015. However, there is no evidence that absence of biopsy/cytology analysis has been used as a criteria to exclude patients from registration. In this respect, it should be noted that registration for other cancers (stomach, prostate, bladder, cervix, and breast) did not show such an important decrease despite increased usage of biopsy/cytology analysis in diagnosis. Therefore, we suggest that increased usage of microscopy as a diagnostic tool cannot be considered as the main explanation for the observed decrease in liver cancer incidence.

Trends in liver cancer incidence rates show contrasting patterns across the world. In an analysis of the data collected between 1978 and 2012 from 42 countries worldwide (registry data from CI5 volumes V-XI, CIplus and NORDOCAN database), Petrick *et al*[5] (2020) found that incidence rates significantly increased in India, across the Americas, in Oceania and in most European countries. On the other hand, incidence rates remained the highest in Eastern and South Eastern Asian countries though the rates in those countries have been decreasing in recent years. In the area of Qidong city, Eastern China, a dramatic reduction of liver cancer incidence has been seen in young adults over a period of 28 years (1980-2008)[31]. Qidong city is known as an area of very high liver cancer incidence associated with endemic HBV and high dietary exposure to aflatoxin. Overall, a 45% reduction in liver cancer incidence and mortality rates occurred among the Qidonese. Compared with 1980-1983, the age-specific liver cancer incidence rates in 2005-2008 significantly decreased 14-fold for ages 20-24, 9-fold for ages 25-29, 4-fold for ages 30-34, 1.5-fold for ages 35-39, 1.2-fold for ages 40-44 and 1.4-fold for ages 45-49, but increased at older ages[31]. Etiological interventions aimed at reducing risk factors for HBV have been developed in this area of China since the early eighties, namely universal neonatal HB vaccination (from 1980) and expanded access to commercial rice (controlled for low aflatoxin levels) instead of contaminated maize as the staple food (beginning in 1988). Retrospective studies on the distribution of aflatoxin-albumin adducts in randomly selected subsets of serum collected during screening surveys between 1982 and 2009 revealed that median levels declined from 19.3 pg/mg albumin in 1989 to 3.6 in 1995, 2.3 in 1999, 1.4 in 2003, and undetectable (< 0.5 pg/mg) in 2009[32]. These results suggest that the dramatic decrease in incidence in this population is most likely due to reduction in aflatoxin exposure, whereas neonatal HB vaccination may have only limited impact since the vast majority of the subjects developing liver cancer during the period under consideration (1983-2008) were born before the start of universal HB vaccination programs[31,32].

Available data on population-based cancer registries in Africa that have assessed liver cancer trends over a comparable period of time show a very different pattern to the one observed in Bamako, Mali. In the Gambia, a study on liver cancer trends from 1988 to 2006 has shown a small decrease among men during the period 1988-2006 (from 38.36 for the period 1988-1997 to 32.84 per 10^5 p-years in the period 1998-2006), while it clearly increased among women (from 11.71 for the period 1988-1997 to 14.9 p-years in the period 1998-2006) [APC: +3.01 (95%CI: 0.3-5.8)][21]. In the district of Kampala (Uganda), registration was initiated in 1960 but was interrupted between 1980 and 1991 due to the political context. The comparison between the periods before 1980 and after 1991 shows stability in the rate of liver cancer among men and an increase of more than 50% among women[20]. A reduction in the rate of liver cancer has been documented in a group of gold miners originating from Mozambique and working in South Africa. In this group, liver cancer incidence decreased from 80.4 per 10^5 p-years in 1964-1971 to 40.8 in 1972-1979 and 29.9 per 10^5 p-years in 1981[33,34]. However, in this later cohort, data were not population-based. To our knowledge, our observation of a dramatic decrease in the incidence of liver cancer in Bamako, Mali is not matched in any other African context.

Our observations based on the cancer registry of Bamako district require cautious interpretation because of multiple possible bias that may affect cancer registration in low-resource contexts. A recent review of trends in the global epidemiology of liver cancer has highlighted the lack of data of sufficient quality in most parts of sub-Saharan Africa[5]. As underlined in our study, increased usage of biopsy/cytology confirmation has taken place over the study period and may have led to under-registration of cases for which this confirmation was not available. With all due caution, however, we consider that our observations on liver cancer in Bamako district deserve to be documented in the literature. Of note, stomach cancer, that shares demographic and clinical signs that overlap with liver cancer (age-related incidence rates, signs and symptoms, gender distribution) showed only small changes in incidence in Bamako district during the study period[28]. Patients with stomach cancer are often diagnosed in the same medical services as those with liver cancer and it could be expected that biases may equally affect the registration of both cancers.

In Qidong city, the liver cancer decrease was mainly due to a reduction in aflatoxin exposure[32]. In Mali, there is only limited information available on temporal variations in the prevalence of the main documented risk factors for HCC namely chronic infection by HBV and exposure to dietary aflatoxins. A study of HBV chronic carriers in Bamako indicates that the incidence rate of chronic carriage is 18.8%[17]. There is no evidence that this rate has recently decreased. Universal infant HB vaccination has been introduced in Mali in 2002 and is unlikely to have a significant effect on the circulation of HBV and on population rates of chronic carriage in the target age groups for liver cancer before at least one decade. Presence of aflatoxin in peanuts (groundnuts) and their derived products at several points of the food supply chain from cultivation to marketing have been documented in several small surveys carried out in different parts of the peanuts production area (Southern Mali)[35-37]. A survey conducted in public markets of Kita, Kolokani and Kayes collected peanuts and peanut pastes over 7 mo between 2010 and 2011 from 30 different small retailers in each location. In these samples, contamination with aflatoxin was found to be above the permissible range (> 20 μg/kg) and ranged between 105 and 530.2 μg/kg. The level of aflatoxin was higher in peanut pastes and increased with the length of storage at the level of the small retailers, indicating that post-harvest contamination increased during storage[38]. Despite the continuous presence of aflatoxin as food contaminant, it is possible that actual levels of individual exposure in Bamako district have decreased over the past years. Several reasons could potentially explain the decrease in the incidence of liver cancer in the population of Bamako. First, changes in lifestyle and diversification of diet may have led to a decrease of the proportion of locally produced aflatoxin-contaminated products in the daily food intake. Indeed, a study exploring the association between the food variety score, dietary diversity score and nutritional status of children, or socioeconomic status level of the household, has shown that children from urban area in Mali have more dietary diversity than children from rural areas[39]. This study also reported that the food variety and dietary diversity in urban households with the lowest socioeconomic status were higher than the one found among rural households with the highest socioeconomic status[39]. Secondly, the systematic implementation of effective measures for reducing aflatoxin levels in crops in villages across the peanuts production area has led to a measurable reduction in aflatoxin levels documented in several local surveys[36-38]. These measures include pre- and post-harvest management options such as selection of host plant resistance, soil amendments, timely harvesting and postharvest drying methods, use of antagonistic biocontrol agents, and awareness campaigns, as well as training courses to disseminate technology to the end-users[38]. A study conducted in Bamako in chronic HBV carriers suggests that overall these carriers are exposed to aflatoxin to a lesser extent than HBV carriers from rural

Gambia[17]. In this study, the mutant R249S of the *TP53* gene, a mutation specific to aflatoxin exposure was used as a surrogate to measure levels of exposure to aflatoxin. In Bamako, HBV carriers had an average plasma concentration of R249S of 311 copies/mL while in rural Gambia the concentration varied between 480 to 5690 copies/mL. These data corroborate the idea that aflatoxin levels have reduced in the staple diet of people living in Bamako. Whether a decrease in exposure to aflatoxin is the cause of the decrease in incidence of liver cancer is a tantalizing hypothesis that may have a profound impact for promoting further efforts to reduce population exposure. Further assessment of a possible effect of decreased aflatoxin intake will require detailed studies on biomarkers of exposure as well as comparison between the urban area of Bamako and rural areas of Mali and other West African countries where contaminated peanuts may still represent a major part of the diet. The data presented here warrant further studies to uncover the sociocultural and biological changes that have occurred over the study period and might explain the decrease in liver cancer reported in this article.

CONCLUSION

In conclusion, this study reports a dramatic decrease in the registration of primary liver cancer over 28 years in an urban population of West Africa. This decrease cannot be accounted for by universal childhood HB vaccination, which was introduced only recently (2002). There is evidence that reduction of exposure to aflatoxin has occurred over the study period, caused by changing lifestyles and dietary patterns in this population. This suggests that controlled reduction of aflatoxin may achieve rapid and important protective effects against liver cancer in West Africa. However, our observations require cautious interpretation because of possible bias that might affect liver cancer registration in this low-resource context.

ARTICLE HIGHLIGHTS

Research background

There is evidence that trends in incidence of liver cancer in different parts of the world are undergoing contrasting changes.

Research motivation

There is very little data on liver cancer incidence trends in Sub-Saharian Africa.

Research objectives

Using the cancer registry of Bamako district (Mali), we have studied incidence trends of liver cancer over 28 years (from 1987 to 2015) by gender.

Research methods

Age standardized rates were estimated using a direct standardization method, by considering the world population. The incidence rate ratio and corresponding 95% confidence intervals were estimated using the early period as reference (1987-1996). The average annual percent change of the trends was evaluated from Joinpoint regression models.

Research results

Overall, the age standardized incidence of liver cancer varied substantially across the three periods of the study. There was a significant decrease of liver cancer incidence over the study period, in men and women.

Research conclusions

This study shows a decrease in the registration of primary liver cancer in an urban population of West Africa between 1987 and 2015. Lifestyle changes and diversification of diet may have led to a decrease in exposure to aflatoxin-contaminated products.

Research perspectives

Future studies are warranted to explore the potential reasons for this decrease, in order to better understand the specific etiological factors of liver cancer in West Africa.

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