RESEARCH ARTICLE

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Spatio-Temporal Analysis of Cholangiocarcinoma in a High Prevalence Area of Northeastern Thailand: A 10-Year Large Scale Screening Program

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Abstract

Background: Cholangiocarcinoma (CCA) is experiencing a global increase, particularly in Northeast Thailand, which has the highest global incidence rates. However, there is a paucity of studies on CCA screening, especially in high-risk populations. This study aimed to investigate the distribution and spatial patterns of CCA in Northeast Thailand over a ten-year screening period. **Methods:** The study included CCA patients from the Cholangiocarcinoma Screening and Care Program (CASCAP) between 2013 and 2022, which encompasses 20 provinces and 282 districts in Northeast of Thailand. CCA data were based on pathological diagnosis to determine the distribution and spatial patterns. **Results:** Of the 2,515 CCA patients, approximately two-thirds were males (63.98%), and the majority were aged over 55 years (72.72%), with a mean age of 61.12 ± 9.13 years. The highest percentage of CCA cases occurred in 2014 at 19.01% of all patients, followed by 2018 at 15.23%. The overall CCA incidence rate in Northeast Thailand over ten years was 32 per 100,000 population. Hotspot statistical analysis identified high-scoring geographic clusters in the upper and middle regions, showing a tendency to expand from hotspot areas into nearby areas. **Conclusion:** The distribution of CCA in Northeast Thailand has continued to rise over the past decade, particularly in the upper and middle regions. Targeted screening in high-risk areas and increased awareness of CCA risks are crucial to mitigate its impact.

Keywords: Cholangiocarcinoma- Incidence- Northeast Thailand- Screening- Spatial analysis

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Introduction

Cholangiocarcinoma (CCA) is a matter of great concern worldwide [1]. This highly fatal cancer can arise anywhere in the biliary tract and is anatomically subclassified into intrahepatic CCA (ICC) or extrahepatic CCA (ECC), which can be further divided into perihilar and distal CCA based on the tumor location [2, 3]. Previous studies have reported an increasing incidence of CCA in western countries [4-6], and in Europe, the mortality rate was approximately 2 per 100,000 males between 2000 and 2004, which rose to about 3 per 100,000 population during 2010 to 2014 [7]. In Southeast Asia, particularly in Thailand, CCA remains a significant public health issue, with the country having the highest CCA incidence globally [8]. A study in 2017 highlighted the substantial burden of CCA in Thailand, with an incidence rate of 14.6 per 100,000 population per year of ICC patients and a high mortality rate of 14% [9]. Notably, the Northeast of Thailand reported the highest incidence rate, with 85 cases per 100,000 populations in 2016 [10]. Furthermore, a report in 2021 indicated that although the incidence rate of CCA in Thailand has decreased, patient survival remains poor [11]. These pieces of evidence underscore the highly lethal nature of CCA, emphasizing the need for further scientific and clinical insights to improve patient outcomes [12].

Risk factors associated with CCA that have been reported in the past include male gender, older age, non-alcoholic fatty liver disease, obesity, diabetes mellitus, repeated use of praziquantel treatment, and history of *Opisthorchis viverrini* infection, which is considered the

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main risk factor for developing CCA [13-16]. A previous study in 2020 reported an increased incidence rate of CCA in the majority of countries worldwide over the 20-year period examined (1993 to 2012), attributed to metabolic and infectious etiologic factors [17]. Recent research from the United States in 2022 revealed that CCA incidence continued to rise from 2001 to 2017, with the most significant increase observed among younger patients aged 18 to 44 years [18]. In Thailand, a study investigating trends in CCA incidence by reviewing cancer registry data between 1989 and 2018 projected that the age-standardized rates for males and females in 2028, 44.3 per 100,000 among males and 17.6 per 100,000 among females in 2018 world decrease to 7.6 per 100,000 and 3.6 per 100,000, respectively [11].

Furthermore, several studies have explored the geographic and spatial distribution of CCA. A study from the United States in 2015 reported that demographic patterns and geographical variation were closely related to CCA [19]. In Northeast Thailand, which has the world's highest incidence of CCA, a significant high-risk area cluster of CCA was identified in provinces adjacent to the main river basin [20]. Another study conducted in Thailand in 2020 focused on CCA screening and found a clear geographic association between CCA diagnosis and incidence of risk factors for CCA, including biliary tract abnormalities such as periductal fibrosis, dilated bile duct, and liver mass, as well as liver fluke infection [21].

Despite previous reports on CCA and associated risk factors, there remains a lack of comprehensive studies on trends in prevalence or incidence, including spatial analysis to identify high-risk areas. In an effort to address this issue and identify CCA cases at early stages, the Cholangiocarcinoma Screening and Care Program (CASCAP) in Northeastern Thailand has been actively screening high-risk groups since 2013, aiming to facilitate timely treatment for identified patients [22]. Now, as we approach the 10-year mark since the initiation of CASCAP, our study seeks to assess the 10-year CCA situation among at-risk individuals by estimating the time-trends in diagnosis, and the spatial distribution of CCA patients in Northeast Thailand who participated in the project. By shedding light on the distribution of CCA and spatial patterns in the at-risk population, our study aims to provide valuable insights that can support a more effective and targeted approach to CCA screening in high-risk populations, ultimately improving early detection and treatment outcomes. This knowledge has the potential to make significant strides in addressing the public health challenges posed by CCA.

Materials and Methods

Study area and participants

Our study gathered data from the CASCAP in Northeast Thailand, a region also known as Isaan. This region is situated in the northeastern part of Thailand, sharing its northern and eastern borders with Laos and its southern border with Cambodia. For the purpose of our study, we focused on the entire Isaan region, which encompasses 20 provinces and 282 districts (Figure 1) and an estimated total population of 10,882,305 individuals. The population of interest for CCA screening in this study are those aged 40 years and over. In the study area this comprises 5,199,617 males and 5,682,688 females.

CASCAP is an innovative initiative, the first of its kind, aimed at conducting large scale CCA screening among the high-risk population in northeastern Thailand [22]. The program's comprehensive approach seeks to reach all residents in the region, employing various methods and settings, including tertiary-care hospitals, district-level hospitals, and mobile screening sessions at the sub-district level. For our study, we included all CCA patients who underwent CCA diagnosis based on pathological methods and were enrolled in the CASCAP database between 2013 and 2022 (n = 2,515). These study participants were recruited through two primary pathways. The first approach involved inviting patients attending the participating institutions for any reason, who showed no symptoms of CCA, to join the program

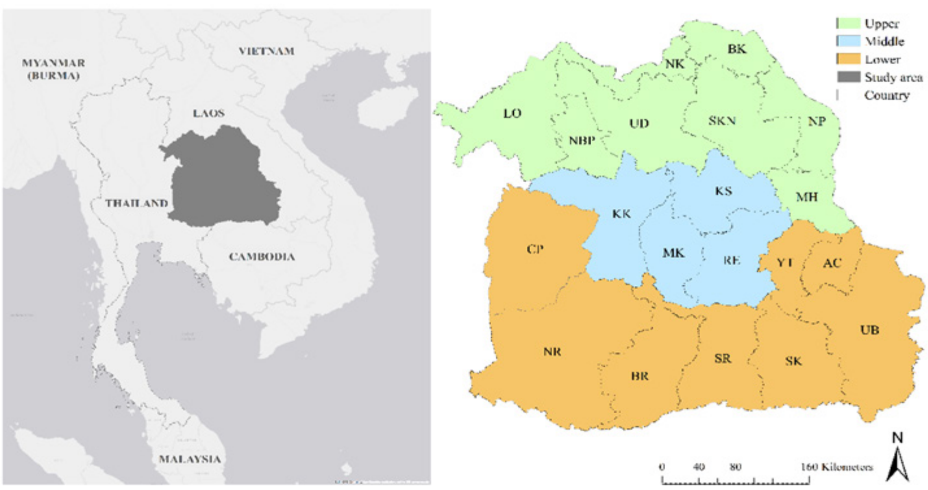

Figure 1. Map of Study Area. Provinces: AC Amnat Charoen, BK Bueng Kan, BR Buriram, CP Chaiyaphum, KS Kalasin, KK Khon Kaen, LO Loei, MH Mukdahan, MK Maha Sarakham, NP Nakhon Phanom, NR Nakhon Ratchasima, NBP Nong Bua Lamphu, NK Nong Khai, RE Roi Et, SKN Sakon Nakhon, SK Sisaket, SR Surin, UB Ubon Ratchathani, UD Udon Thani, YT Yasothon.

and undergo initial screening. This group is referred to as the 'screening' group, where participants suspected of having CCA from ultrasonography (US) will be sent for confirmation with CT/MRI. Then, if found to have CCA in the following this examination, this group will be forwarded for pathological diagnosis to further confirm the results of CCA. The second pathway, known as the 'walk-in' group, comprised individuals who presented at the hospital with symptoms suggesting the possibility of CCA and sought medical attention accordingly [23]. This group will be asked to participate in a CCA screening project. If participants do not have US or CT/MRI results, they will be asked undergo a screening test to confirm that they suspect CCA. It will then be forwarded for further confirmation of pathological results. Therefore, both the screening and the walk-in groups were the CCA screening participants in CASCAP.

Variable measurements

The primary study outcome was CCA positive determined through pathological examination based on biopsy. The study considered several independent variables, including gender (male/female), age at enrollment in years, educational levels, occupation, history of praziquantel (PZQ) treatment, history of *O. viverrini* infection, having relatives diagnosed with CCA, history of smoking cigarettes, history of alcohol consumption, year of screening, and geographic locations such as districts and provinces. These data were collected using registered forms from the CASCAP. To provide a population context for the districts in northeastern Thailand during the study period (2013 to 2022), district-level populations were obtained from the Official Statistics Registration Systems of Thailand website (https://stat.bora.dopa.go.th/new_stat/webPage/statByYear.php).

Statistical analyses

Participant characteristics were expressed as number and percentages for categorical data, while continuous data were presented with mean, standard deviation (SD), median, minimum, and maximum values. To determine the distribution of CCA, the number of CCA cases for each category of socio-economic and health related factors was used as the numerator, and the total number of CCA patients served as the denominator, presented as percentage. The incidence rate per 100,000 population was calculated by dividing the number of CCA cases by the population count for each year, and then multiplying it by 100,000. To obtain the overall incidence rate for the entire ten-year period (2013 to 2022), the annual incidence rates were combined and multiplied by 100,000. All statistical analyses were conducted using STATA version 18 (StataCorp, College Station, TX, USA) for this step.

The analysis covered 282 districts in Northeast Thailand, and spatial datasets, along with the incidence rate of CCA, were imported and analyzed using ArcGIS Pro software version 3.2 (ERSI, Redlands, CA). The incidence rate of CCA was computed by dividing the number of recorded CCA cases over the ten-year study period (2013 to 2022) by the total population during the same period, which was obtained from the website of the Official Statistics Registration Systems of Thailand. To visually differentiate the incidence rates across districts on the map, a Graduated color symbology will be utilized, with each range of incidence rates assigned a distinct color, allowing for easier interpretation of the spatial distribution of CCA within the region.

Hotspot analysis

We assessed the existence and characteristics of spatial autocorrelation, indicating the clustering of CCA incidence based on the notification location, by applying the Getis-Ord statistic (Gi*). The Gi* is a local spatial autocorrelation statistic utilized for spatial correlation analysis, specifically to identify high-value areas or hot spots, as well as low-value areas or cold spots [24, 25], of CCA incidence within each district which was classified by district code in the provinces of Northeastern Thailand from 2013 to 2022. The geographic location of each case was determined according to the district of their residence. By taking into account the current addresses of the study participants, which were reported in the initial CASCAP registration form. The Gi* statistic assesses the local incidence of CCA (i.e., the occurrence of CCA for a given location and its neighbors) in comparison to the global CCA incidence (the rates observed across all municipalities). Specifically, the Gi* statistic compares the z-score and p-value for each municipality with the mean global CCA incidence. The interpretation of the Gi* statistic provides a z-score for each feature in the dataset. For statistically significant positive z-scores (+1.96 at a confidence level of 95%), a larger z-score indicates a more intense clustering of high incidence values, indicating a hot spot of CCA incidence. On the other hand, for statistically significant negative z-scores (-1.96 at a confidence level of 95%), a smaller z-score suggests a more intense clustering of low incidence values, signifying a cold spot of CCA incidence [26]. By employing the Gi* statistic, our analysis aims to highlight and distinguish areas with significant spatial patterns of CCA incidence in Northeastern Thailand, providing valuable insights into the distribution and concentration of the disease within the region over the ten-year study period. Hotspot analysis and map creation were conducted using ArcGIS Pro software version 3.2 (ESRI, Redlands, CA).

Results

Baseline characteristics of cholangiocarcinoma patients

Of 839,286 participate the CASCAP between 2013 and 2022, 99.05% were no pathological confirm due to not suspected CCA or suspected CCA but did not come to confirm a diagnosis and 0.95% were undergo pathological diagnosis. A total of 2,515 CCA patients were diagnosed through pathology diagnosis, the mean age was 61.12 years (SD = 9.13). Approximately two-thirds of the patients were male (63.98%), and the majority were aged greater than 55 years (72.72%). In terms of educational level, a significant proportion had attained primary education or lower (80.76%), and worked as farmers (64.93%). More than one-third of CCA patients had used PZQ (36.22%), around one-fifth reported having been infected with *O. viverrini* (20.6%) and reported having relatives diagnosed with CCA (20.2%) (Table 1).

Based on the year of screening, the highest number and percentage of CCA cases was observed in 2014, accounting for 19.01% (478/2,515), closely followed by 2018 at 15.23% (383/2,515). In contrast, the lowest number and percentage was recorded in 2013, with only 0.48% (12/2,515) of all CCA cases. Further analysis by gender and age groups revealed that in 2014, the highest number of CCA cases was observed in males, with 303 cases, and in participants aged greater than 60 years, with 225 cases. Moreover, Figure 2 depicts the trend of overall CCA incidence, highlighting its peak in the year 2014. The elevated CCA incidence among males and individuals over 60 years old remained consistent throughout each 10-year screening period.

Spatial distribution of cumulative cholangiocarcinoma incidence

Over the course of a ten-year period, the overall incidence rate of CCA was 32 individuals per 100,000 population. The districts with the highest incidence rates were Pho Chai District, Roi Et Province (135.14 per 100,000 population), and Sri Boon Ruang District, Nong Bua Lamphu Province (122.59 per 100,000 population). Regarding the cumulative incidence of CCA, our findings revealed a higher incidence in the upper and middle parts of the Northeast region (Figure 3).

Hotspot analysis of cumulative cholangiocarcinoma incidence

Figure 4 depicts the results of the hot-spot analysis, revealing a clustering of high-scoring geographic features in the upper and middle parts of the studied area. The analysis indicated a tendency for incidence to increase and extend its boundaries into neighboring areas. Specifically, the incidence of CCA showed significant increases in provinces situated in the upper and middle parts of Northeast Thailand. Notably, this included parts of Mahasarakham and Roi Et provinces, and certain districts in the upper part of Chaiyaphum Province (Kaset Sombun, Phu Khieo, Ban Thaen, and Khon San districts), which are adjacent to the Phrom River originating from the Chulabhorn Dam. In addition, certain districts in the lower part of Kalasin Province (Mueang Kalasin and Tha Khantho districts) bordering the Lam Pao Reservoir, along with Kamalasai, Yang Talat, Huai Mek, and Khong Chai districts, which are adjacent to the Lam Phan and Lam Pao River from the Lam Pao Reservoir, also experienced an increase in CCA incidence. Similarly, districts in the lower part of Sakon Nakhon Province (Mueang Sakon Nakhon, Kusuman, Phanna Nikhom, Waritchaphum, Akat Amnuai, Sawang Daen Din, Khok Si Suphan, and Phon Na Kaeo districts) situated close to a branch of the Nam Un Dam and Nong Han Reservoir displayed higher incidence rates. Moreover, some districts in the lower part of Nakhon Phanom Province (That Phanom, Renu Nakhon, Na Kae, and Wang Yang districts), the middle part of Udon Thani

Figure 2. Incidence Rate of Cholangiocarcinoma Per Month for Overall (A), separated by gender (B), and separated by age groups (C), according to year of screening.

Table 1. Socio-Economic and Health Related Factors of Cholangiocarcinoma Diagnoses according to Year of Screening.

Characteristics	Number of CCA cases (%)										
		Year									
	All	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Overall	2,515	12	478	326	363	327	383	293	193	97	43
Gender											
Male	1,609 (63.98)	7	303	215	235	218	228	194	120	58	31
Female	906 (36.02)	5	175	111	128	109	155	99	73	39	12
Age groups (years)											
≤ 45	148 (5.88)	0	43	34	12	19	16	11	8	3	2
46-50	182 (7.24)	1	37	26	20	25	30	17	17	6	3
51-55	356 (14.16)	0	76	47	43	42	51	48	29	13	7
56-60	463 (18.41)	3	97	58	68	62	67	64	25	10	9
> 60	1,366 (54.31)	8	225	161	220	179	219	153	114	65	22
Educational levels											
Primary and lower	2031 (80.76)	10	410	260	284	270	297	237	148	76	39
Secondary	261 (10.38)	2	33	36	44	32	47	35	23	5	4
Certificate	47 (1.87)	0	8	8	6	8	7	3	4	3	0
Bachelor and higher	176 (7)	0	27	22	29	17	32	18	18	13	0
Occupation											
Unemployed	147 (5.84)	0	6	10	22	30	29	24	18	7	1
Farmer	1,633 (64.93)	7	309	229	248	214	238	200	113	53	22
Labor	134 (5.33)	1	21	12	14	25	24	21	8	6	2
Gov.official/State ent.	68 (2.7)	0	6	7	6	9	19	6	11	4	0
Own business	133 (5.29)	0	33	18	32	11	18	13	5	3	0
Others	400 (15.9)	4	103	50	41	38	55	29	38	24	18
Praziquantel treatment											
No	1,604 (63.78)	7	269	181	209	208	286	197	132	75	40
Yes	911 (36.22)	5	209	145	154	119	97	96	61	22	3
O. viverrini infection											
No	1,997 (79.4)	8	392	239	280	250	323	225	156	85	39
Yes	518 (20.6)	4	86	87	83	77	60	68	37	12	4
Relatives diagnosed with CCA											
No	2,007 (79.8)	10	351	250	278	270	317	253	163	76	39
Yes	508 (20.2)	2	127	76	85	57	66	40	30	21	4
Smoking cigarettes											
No	1,289 (51.25)	7	257	153	194	141	209	152	97	49	30
Yes	1,226 (48.75)	5	221	173	169	186	174	141	96	48	13
Drinking alcohol											
No	859 (34.16)	5	182	93	129	92	137	91	69	34	27
Yes	1,656 (65.84)	7	296	233	234	235	246	102	124	63	16

CCA, Cholangiocarcinoma

Province (Mueang Udon Thani, Kumphawapi, Nong Han, Thung Fon, and Phen districts), and the middle part of Nong Bua Lamphu Province (Mueang Nong Bua Lam Phu, Na Wang, and Na Klang districts) exhibited elevated CCA incidence. Lastly, certain districts in Khon Kaen Province, notably Mueang Khon Kaen and Chonnabot districts, were also identified as areas with a high incidence of CCA. Overall, the hot-spot analysis provided valuable insights into the geographic distribution of CCA incidence in the studied region, highlighting specific areas with higher rates of occurrence.

Discussion

Our study utilized data from the CASCAP project to investigate the distribution and assess the spatial patterns

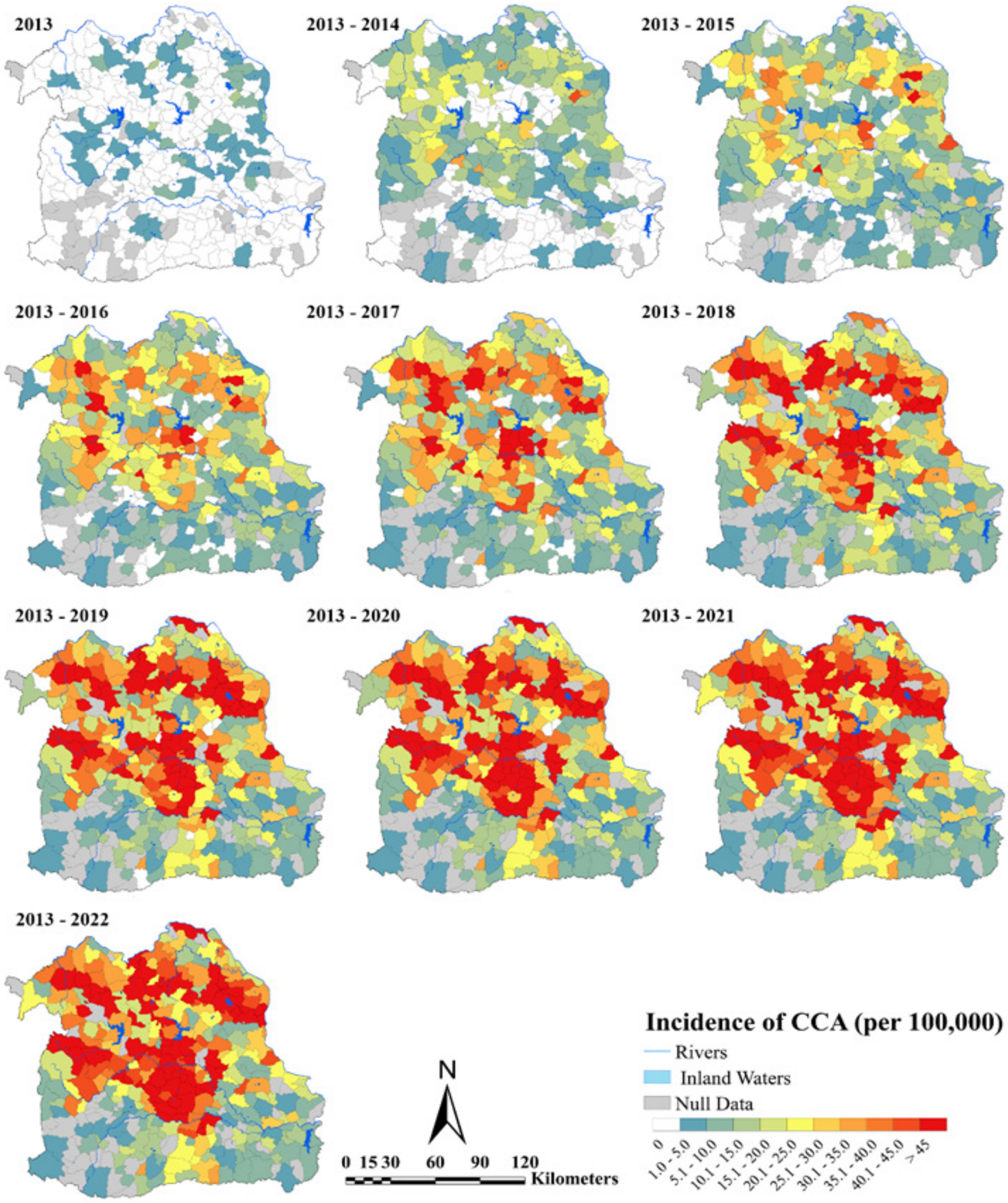

Figure 3. Spatial Distribution of Cumulative Cholangiocarcinoma Incidence from 2013 to 2022, District Level.

of CCA in the Northeast of Thailand. The CASCAP project, which has been conducted for 10 years from 2013 to 2022, focuses on CCA screening among at-risk groups in Thailand [22], and all relevant data from this project were included in our study. Approximately two-thirds of the patients were male, and the majority were aged greater than 50 years.

Our study revealed a total of 2,515 CCA positive cases identified over a ten-year period, with the incidence rate was 32 patients per 100,000 population. Interestingly, this distribution was higher than that reported in a previous study conducted in Thailand in 2019, which documented an incidence rate of 28.1 per 100,000 from 1989 to 2013 [27]. Upon classifying the data based on the factors studied, our research indicated a higher distribution of CCA among patients aged greater than 50 years, followed by those with lower than secondary education. These findings are consistent with previous studies from Thailand in 2017, which also reported an increased likelihood of CCA among older individuals compared to younger age groups [28]. Additionally, a study from Thailand in 2022 found higher CCA incidence rates in older age groups [29]. Our findings revealed a higher distribution of CCA in males compared to females (63.98% vs. 36.02%, respectively). This aligns with findings from a previous study in Thailand conducted in 2019, which similarly reported that males were more susceptible to developing CCA than females [20]. Taken together, our study's results align with and reinforce previous research findings regarding the factors influencing CCA incidence, including age, and gender.

Based on the years of CCA screening, the overall distribution was not notably high in 2013, which marked the beginning of the screening program [22]. However, the percentage distribution of CCA increased in the subsequent years, particularly between 2014 and 2015. The highest number of CCA cases was recorded in 2014, followed by a gradual decrease and increase in the number of cases observed from 2014 until the end of our study in 2022.

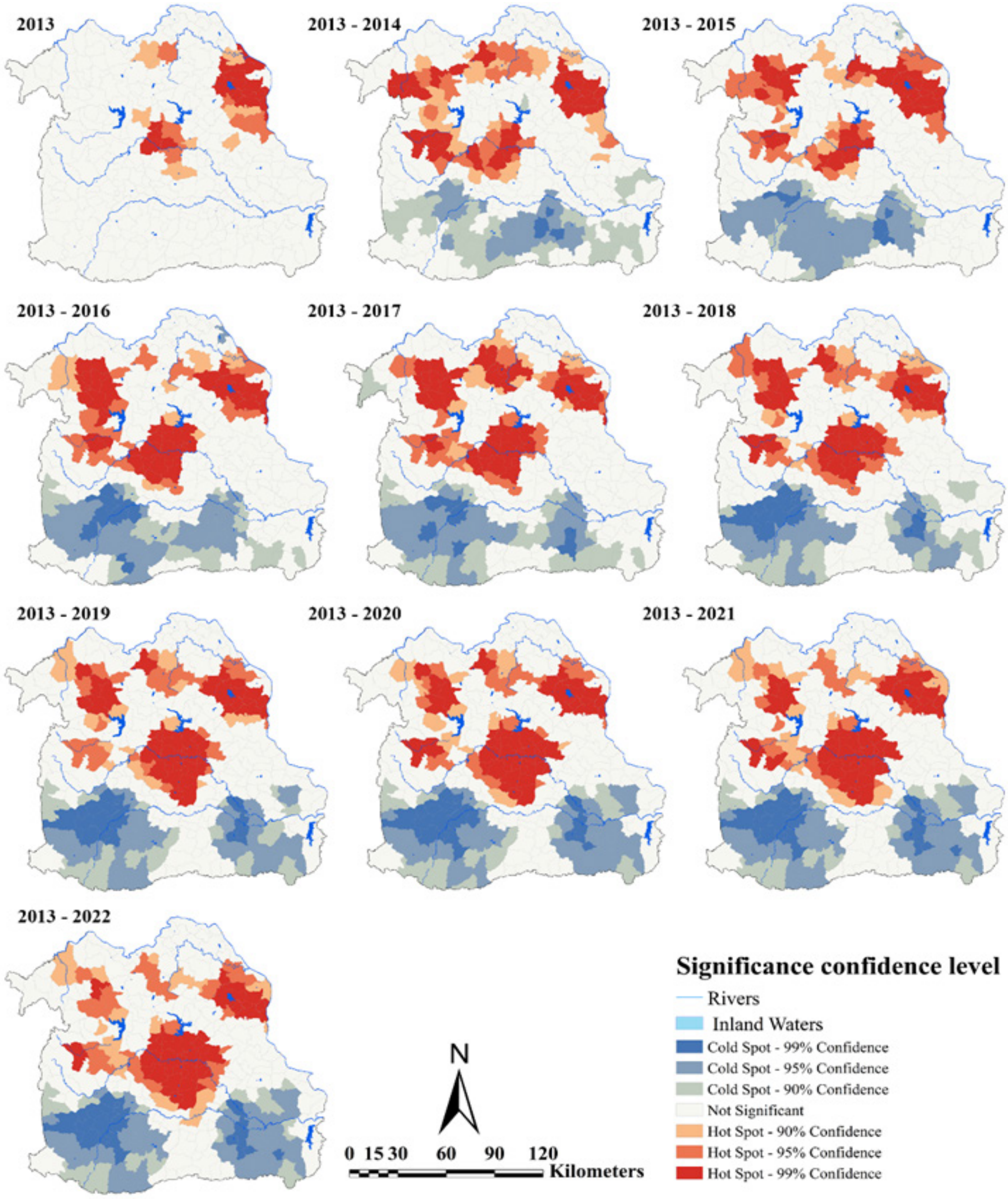

Figure 4. Hotspot Analysis of Cumulative Cholangiocarcinoma Incidence from 2013 to 2022, District Level

These findings align with previous studies from Thailand in 2019, which also reported a decrease in CCA incidence rates from 2002 through 2013, the end of their study period [27]. Additionally, a study from 2021 projected that the incidence rate of CCA would continue to decline until 2028 [11]. In our study, we observed a significant decrease in CCA cases in 2020, likely influenced by the decrease in the number of people coming for screening during the COVID-19 outbreak [30]. However, it's worth noting that the screening program continued despite the challenges posed by the pandemic. Furthermore, we found a higher number of CCA cases among males than females and in individuals over 60 years of age throughout each 10-year study period. These results are consistent with previous studies from Thailand, which have consistently shown that CCA incidence is higher in males than females, with the majority of cases occurring in individuals over 60 years old [31, 27, 20]. Furthermore, earlier studies conducted in Thailand in 2021 and 2023 also reported an association between higher rates of CCA and male gender and the age group over 60 years [32, 16]. This association has been reported in various studies conducted in different years, emphasizing the importance of monitoring these specific risk factors in CCA incidence. Overall, our study's findings corroborate and strengthen the existing body of evidence regarding the association between CCA incidence, gender, and age, in line with several prior studies from Thailand.

Our study focused on a district-level spatial analysis of 20 provinces in the northeastern region of Thailand. Our findings revealed a concentration of CCA distribution in the upper and middle parts of the region, with a tendency for its incidence to increase and expand into neighboring areas. This pattern of high CCA incidence is linked to dietary habits involving the consumption of raw or semi-raw freshwater fish, leading to liver fluke infection, which is a major factor contributing to the development of CCA. These dietary habits are commonly shared in neighboring territories, further explaining the clustering of cases in specific regions [33, 34, 16]. Additionally, our study identified a higher incidence of CCA in areas near main water sources, where a significant portion of the population is engaged in agricultural activities, such as farming or fishing. This observation aligns with a previous study from Thailand in 2019, which identified high-risk areas for CCA in provinces situated in the Chi, Mun, and Mekong River Basins [20]. The proximity to water bodies and the agricultural practices in these areas likely contribute to the higher incidence of CCA cases. Moreover, a previous study in 2020 further supported our findings by reporting a high rate of *O. viverrini* infection, which is the primary cause of CCA, among individuals living along the Mekong River in five Mekong sub-region countries, including Cambodia, Laos, Myanmar, Thailand, and Vietnam [35]. The close association between liver fluke infection and the incidence of CCA underscores the importance of addressing this parasitic infection to mitigate the burden of CCA cases in the region. Overall, our study provides valuable insights into the spatial distribution of CCA, highlighting the role of dietary practices, agricultural activities, and water sources in the incidence of this disease in the northeastern region of Thailand. These findings have implications for targeted interventions and preventive measures in high-risk areas.

One limitation of our study is that we focused solely on the CCA screening program, which may have excluded individuals diagnosed with CCA in hospitals but who chose not to participate in the CASCAP. This could potentially lead to an underestimation of the distribution of CCA in our study. Furthermore, our research was geographically limited to the northeastern region of Thailand, which may not fully represent the incidence and distribution of CCA across the entire country. We chose contiguous study areas within each region for the purpose of spatial analysis, which might introduce some regional bias and limit the generalizability of our findings to other areas in Thailand. Nevertheless, the distribution of CCA patients might be lower in certain areas due to the lack of necessary diagnostic tools or specialized medical professionals for accurate the disease diagnosis.

The strength of our study lies in the substantial sample size, which allowed us to have a representative population of individuals at risk for CCA. Additionally, by incorporating data spanning a 10-year period, covering the entire duration of the CCA screening program, we were able to discern trends in the number of CCA cases each year. This comprehensive approach enables us to gain insights into the incidence and distribution of CCA over time and helps inform future screening strategies for subsequent years.

In conclusion, our study highlights a concerning trend of increasing CCA distribution in the northeastern region of Thailand over the past ten years, particularly in the upper and middle areas. This upsurge can be attributed to various factors, including the high incidence of *O. viverrini* infection in this region. To effectively reduce the incidence of CCA, targeted screening efforts should focus on high-risk areas, accompanied by enhanced awareness campaigns aimed at educating both the public and healthcare providers about the risks associated with CCA. By fostering collaboration among different stakeholders, such as healthcare providers, public health officials, and community leaders, we can work together to combat the rising incidence of CCA in the northeastern region. There is a clear need for further research to gain a deeper understanding of the contributing factors driving the high incidence of CCA in this area. Such investigations can inform more effective preventive measures and treatment strategies. The findings of our study hold the potential to bring about positive change, leading to improved prevention and treatment approaches for CCA in the northeast of Thailand.

Author Contribution Statement

NA, KT, and ATS initiated the idea, and provided constructive criticism and edited of the drafts of the manuscripts. AT, WL, and MK edit the drafts of the manuscripts. NA, KT, and ATS performed data management and data quality assurance, data analysis, and wrote all statistical methods and the results sections of the manuscript. NA, KT, ATS, AT, WL, and MK initiated the idea, provided feedback and edited the drafts of the manuscript. All authors have seen and approved the final version of the manuscript.

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Approval

This paper is a part of the dissertation submitted in fulfillment of the requirements for the degree of Doctor of Public Health Program, Faculty of Public Health, Khon Kaen University, Thailand.

Competing interest

The authors declare that they have no competing interests.

Ethics considerations

The research protocol was approved by Khon Kaen University Ethics Committee for Human Research, reference number HE661289. The data were provided from the Cholangiocarcinoma Screening and Care Program (CASCAP). The CASCAP data collection was conducted according to the principles of Good Clinical Practice, the Declaration of Helsinki, and national laws and regulations about clinical studies. It was approved by the Khon Kaen University Ethics Committee for Human Research under the reference number HE551404. All subjects gave written, informed consent to participate in the study and for their anonymized data to be used for statistical analysis and dissemination.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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