RESEARCH ARTICLE

Editorial Process: Submission:11/14/2024 Acceptance:04/14/2025

Incidence and Survival Trends of Cervical Cancer in Khon Kaen, Thailand

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Abstract

Objective: To evaluate and report the incidence and survival trends of cervical cancer in Khon Kaen, Thailand, during 1991-2020. **Methods:** A retrospective study was conducted by using the electronic cancer registry database of Khon Kaen province population. Joinpoint regression model was used to analyze the Age-Standardized Incidence Rate (ASR) and the incidence trend graph was built. Overall Observed Survival (OS) was analyzed by Kaplan Meier method and the survival trend graph was built similarly. **Result:** During 1991-2020, 3,071 cervical cancer patients were found in Khon Kaen. Their mean age was 51.7 year-old. The ASR had decreased from 13.51 (95%CI: 10.67-16.35) per 100,000 women-year in 1991 to 7.63 (95%CI: 5.93-9.33) per 100,000 women-year in 2020. This trend was consistent with the country's and international trends. The highest incidence was found in 1993, which was 17.73 (95%CI: 14.65-20.81), and the lowest incidence was found in 2016, which was 5.7 (95%CI: 4.30-7.10) per 100,000 women-year. However, the 5-year OS was 48.37% (95%CI: 46.49-50.22), which was a constant trend. At the beginning in 1991-1995, the OS was 40.31% (95%CI: 35.43-45.12), and at the end in 2016-2020, the OS was 40.46% (95%CI: 34.59-46.23). These were very similar. **Conclusion:** In Khon Kaen, Thailand, during 1991-2020, the cervical cancer incidence (ASR) trend was decreasing, while the cervical cancer survival (OS) trend was constant. WHO elimination of cervical cancer initiative target should be reached by 2030.

Keywords: Cervical cancer- incidence- survival- trend- Khon Kaen

Asian Pac J Cancer Prev, **26 (4)**, 1393-1400

Introduction

In 2020, cervical cancer was the fourth most common cancer globally and also ranked fourth in terms of mortality rates among women. Additionally, it was among the most frequently diagnosed cancers in 23 countries worldwide and a leading cause of death in 36 countries, including in Asia and the Southeast Asian region [1]. In Thailand, during the period from 1998 to 2000, cervical cancer was the most prevalent cancer among women, with a notably high number of cases (an age-standardized incidence rate, or ASR, of 24.7 per 100,000 women per year) [2]. However, between 2010 and 2012, the incidence of cervical cancer decreased [3], making it the second most common cancer following breast cancer, with a reduced number of cases (ASR decreased to 11.1 per 100,000 women per year) in 2016-2018 [4].

Cervical cancer screening is recognized as an effective preventive measure for cervical cancer and has proven efficacy in reducing both the incidence and mortality rates [5,6]. Consequently, the Thai Ministry of Public Health initiated a cervical cancer screening policy in 2002 for women aged 35-60 in the first 5 years [7], which was later expanded to include women aged 30-60 [8]. Initially in 2002, the Universal Coverage scheme only included Pap smear and VIA (Visual Inspection with Acetic Acid) screening methods. Subsequently, in 2017, the cervical cancer vaccine was incorporated into the basic vaccination program for Thai girls [9], and later, primary HPV testing became the main screening method [10].

Khon Kaen is the sixth largest province in the northeastern region of Thailand, covering an area of 10,866 square kilometers. It has the third-largest population in the region, approximately 1.7 million people [2-4]. Statistical data reveal that the age-standardized incidence rate (ASR) for cervical cancer in Khon Kaen was notably high at 8.2 per 100,000 women per year in 2014, with a projected continuous decrease to 5.0 per 100,000 women per year by 2024-2029 [11]. Universal health coverage in Khon Kaen began to include cervical cancer screening primarily via Pap smear in 2005 [10] and introduced primary HPV testing in 2022 [12].

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Under the World Health Organization's (WHO) cervical cancer elimination initiative, each country is required to reduce the age-standardized incidence rate (ASR) of cervical cancer to below 4 per 100,000 females per year. Achieving this goal involves three strategic processes: (1) Vaccinating young females with the human papillomavirus (HPV) vaccine to achieve a coverage of 90% before the age of 15. (2) Conducting high-performance screening tests for female at the age of 35 and again at 45, aiming to reach a coverage of 70%. (3) Ensuring effective management and treatment for female with pre-cancerous lesions or invasive cancer, aiming to cover 90% of all such cases. The WHO expects that countries should be able to implement these measures by the year 2030 to successfully move towards eliminating cervical cancer [13].

Given the World Health Organization's initiative to eliminate cervical cancer by reducing the age-standardized incidence rate (ASR) to below 4 per 100,000 females per year, there remains a notable absence of research on the trends in incidence and survival rates for cervical cancer patients in Khon Kaen Province. To address this gap, this research was conducted to report the actual incidence rates and survival rates of cervical cancer, not merely estimates or forecasts, among patients in Khon Kaen from 1991 to 2020. This study also aims to compare these actual rates with the projections reported in 2019 by Saenrueang et al. [11], using data from the provincial cancer registry maintained by the Cancer Registry Unit at Srinagarind Hospital. This registry consolidates patient data from Khon Kaen University Hospital, Srinagarind Hospital, and 23 community hospitals within the province. This research was crucial and aimed for assessing the real progress in eliminating cervical cancer in Khon Kaen and aligning local data with global health objectives.

Materials and Methods

Study design and samples

This study is a descriptive analysis conducted using an electronic database of cervical cancer patients in Khon Kaen Province. The inclusion criteria encompass all cervical cancer patients recorded in the provincial population cancer registry. Data were collected from Khon Kaen University Hospital, Srinagarind Hospital, and 23 community hospitals in the province, with diagnoses made by physicians from January 1, 1991, to December 31, 2020.

The exclusion criteria for this study are as follows: (1) patients diagnosed with multiple primary cancers, (2) patients who were lost to follow-up, applicable specifically in the analysis of survival rates, (3) patients with unknown disease staging, (4) patients who were alive but had the date of diagnosis the same as the date of death, and (5) patients lacking essential data for incidence rate analysis, such as age, the year of cancer diagnosis, and year of birth. This methodology ensures a focused and detailed study of cervical cancer trends within the specified region and timeframe.

Sample size and sampling

This research is a study utilizing the cancer registry database covering the entire population of Khon Kaen Province, which consists of approximately 2 million people. Due to the comprehensive nature of this database, no sampling was necessary. The province consistently records more than 100 new cases of cervical cancer annually. The 95% confidence interval (95% CI) for the incidence rates obtained is accurate within ±10%, which is considered sufficiently precise for drawing annual conclusions from the data.

The data for new cervical cancer patients in Khon Kaen Province are sourced from the provincial population cancer registry, where diagnoses are confirmed by physicians according to the International Classification of Diseases for Oncology, Third Edition (ICD-O-3). The specific codes used to identify the locations of the cervical cancer include C53.0 for the endocervix, C53.1 for the exocervix, C53.8 for overlapping lesions of the cervix, and C53.9 for the cervix uteri. Additionally, all patients included in this registry must have their domicile registered in Khon Kaen Province.

Data collection process

The use of an electronic cancer registry database in Khon Kaen Province necessitates a structured procedure for data collection and analysis. This process begins with obtaining authorization from the director of Srinagarind Hospital and the head of the Cancer Registry Unit. This permission enables access to the cancer registry data for the population of Khon Kaen Province. Once access is granted, the data are extracted and recorded in a standardized data collection form. The collected data are then meticulously reviewed to ensure completeness and accuracy of the variables intended for analysis. This step is crucial to guarantee the reliability of the study findings.

Statistical analyses

Descriptive statistics are used to analyze the general characteristics of the sample. Count data is presented as counts, percentages, and for continuous data that follows a normal distribution, means along with standard deviations are provided. For continuous data that does not follow a normal distribution, median and interquartile range values are used instead. The Crude Incidence Rate (CR) and the Age-Standardized Incidence Rate (ASR) were calculated and standardized using the Segi world standard population estimates [14]. Incidence rates were presented in cases per 100,000 by decades of diagnosis and age at diagnosis. These statistics are accompanied by the reporting of 95% Confidence Intervals (95%CI) to ensure the reliability and accuracy of the estimates.

To analyze trends and identify turning points (joinpoints) in the Age-Standardized Incidence Rate (ASR) between 1991 and 2020, the Joinpoint Regression Model is used. This model captures changes in trend over specific periods by calculating the Annual Percent Change (APC) for each interval and the Average Annual Percent Change (AAPC) for the overall period. The incidence rate trends are visualized using trend graphs, and changes in these trends are statistically tested using permutation tests

at a significance level of 0.05.

In Thailand, it has been mandatory to declare death within 24 hours to a designated government officer. Therefore, survival was determined by calculating the follow-up time from diagnosis to each patient's last known vital status. The status was obtained by linking records between the Mortality Registry of Thailand (through the National Health Security Office) and the National Statistical Office, updated to dd-mm-yyyy. To calculate the overall observed survival (OS) rate, the Kaplan-Meier method is used. This method presents the median survival time, the survival rate along with the 95% confidence interval (95%CI), and creates a survival trend graph. Additionally, an analysis of the survival trends and identification of turning points (joinpoints) in the OS are conducted using the same method. Three statistical software were used; (1) STATA version 18, or (2) SPSS for general data analysis of the study sample, (3) Joinpoint Regression Program (version 5.0.2, May, 2023) to calculate ASR, create incidence trend graphs, create survival rate trend graphs, and analyze whether APC and AAPC significantly differ from 0 at the 0.05 significance level.

Ethics approval

This research project has been reviewed and approved by the Center for Ethics in Human Research of Khon Kaen University according to the announcement from Khon Kaen University, No. 7/2566, under project number HE661024, dated January 24, 2023.

Results

General information of the samples

During the period from 1991 to 2020, there were 3,071 cases of cervical cancer in Khon Kaen Province. The average age at diagnosis was 51.7 years (SD = 12.27), with the most common age group at diagnosis being 45-49 years, comprising 485 cases or 15.79% of the total. The primary diagnostic method was predominantly histopathology of the primary tumor tissue. The most frequently diagnosed stage in this population was Stage 3, with 1,037 cases accounting for 33.8% of the total. The most common histopathological type was squamous cell carcinoma, found in 2,297 cases or 74.8% of the total, as shown in Table 1.

Incidence analysis

The Age-Standardized Incidence Rate (ASR) for cervical cancer among all patients from 1991 to 2020 was 10.13. It was observed that the ASR varied annually, with the highest rate occurring in 1993, which was 17.73 per 100,000 female population per year. The lowest rate was recorded in 2016, at 5.7 (95%CI: 4.30-7.10) per 100,000 female population per year, and in 2020, the ASR was 7.63 (95%CI: 5.93-9.33) per 100,000 female population per year (Table 2).

Survival rate analysis

The overall 5-year survival rate for cervical cancer is 48.37% (95%CI: 46.49-50.22). When considering the period of diagnosis, the highest 5-year survival rate was observed during the years 2006-2010, at 55.56% (95%CI: 51.61-59.31), and the lowest was during the years 1991-1995, at 40.31% (95%CI: 35.43-45.12). Ultimately, the survival rate returned to a similar low level in the years 2016-2020, at 40.46% (95%CI: 34.59-46.23) (Table 3).

Trend analysis

The trend in the incidence of cervical cancer in Khon Kaen Province between 1991 and 2020 shows an Annual Percent Change (APC) in the age-standardized incidence rate decreasing by 2.33% per year (95% CI: -3.21 to -1.45, p-value = 0.000002), as illustrated in Figure 1. Additionally, the trend in 5-year survival rates has remained stable; during the period from 1991-1995, the Overall Observed Survival (OS) was 40.31% (95% CI: 35.43-45.12) and from 2016-2020, it was 40.46% (95% CI: 34.59-46.23). Analysis using the Joinpoint Regression Program revealed p-values for 1-year OS = 0.06, 3-year OS = 0.08, and 5-year OS = 0.14, as shown in Figure 2.

Discussion

This study analyzes the incidence of cervical cancer in Khon Kaen Province from 1991 to 2020 and compares it with national and international levels. Data were sourced from the Khon Kaen Provincial Population Cancer Registry. The study population consisted of all new cervical cancer patients diagnosed between January 1, 1991, and December 31, 2020. Exclusion criteria included patients diagnosed with cancer at other sites, those lost to follow-up, those with unknown disease staging, and patients who were alive but had a diagnosis date the same as their date of death. The statistical analysis focused on estimating the Age-Standardized Incidence Rate (ASR) using the Joinpoint Regression Program (version 5.0.2, May, 2023).

The study successfully achieved its primary objective by determining the real Age-Standardized Incidence Rate (ASR) of cervical cancer in Khon Kaen Province from 1991 to 2020. The incidence trend fluctuated, initially increasing and then showing a general decline. Several factors could contribute to this pattern, such as the shift from opportunistic screening before 2004 to more organized screening programs starting in 2005, leading to increased detection of pre-cancerous stages and asymptomatic cancer cases. This systematic screening likely contributed to earlier and more appropriate treatment for patients before the disease progressed to cancer or advanced stages, clearly reflected by a subsequent decrease in incidence rates.

The highest 5-year survival rate during this period was observed between 2006 and 2010 at 55.56%, aligning with increased detection and early treatment. Later, this increase was subsided as the dormant cases decreased but the high-risk cases (late diagnosed and staged) were still constantly found. Similar initial increases in incidence following the introduction of organized screening were previously observed in Roi Et Province by Chumworathayi et al. [15], although subsequent decreases in incidence or changes in survival rates were not reported, unlike in this study.

Table 1. Characteristics of Study Participants

Characteristics	1991-1995		1996-2000		2001-2005		2006-2010		2011-2015		2016-2020	
	n	%	n	%	n	%	n	%	n	%	n	%
Age at diagnosis												
20-24	5	1	0	0	1	0.2	2	0.3	2	0.4	5	1.2
25-29	7	1.4	5	1	5	1	5	0.8	9	1.9	11	2.6
30-34	28	5.6	22	4.5	25	4.8	24	3.7	25	5.2	20	4.7
35-39	44	8.7	45	9.2	64	12.2	67	10.4	36	7.5	36	8.4
40-44	79	15.7	78	16	86	16.4	99	15.4	62	12.8	39	9.1
45-49	84	16.7	69	14.1	84	16	120	18.6	62	12.8	66	15.4
40-54	81	16.1	81	16.6	75	14.3	85	13.2	71	14.7	80	18.6
55-59	63	12.5	72	14.8	66	12.6	72	11.2	64	13.3	39	9.1
60-64	59	11.7	46	9.4	42	8	62	9.6	47	9.7	44	10.3
65-69	28	5.6	33	6.8	35	6.7	46	7.1	37	7.7	43	10
70-74	19	3.8	19	3.9	25	4.8	23	3.6	34	7	24	5.6
75-79	6	1.2	9	1.8	12	2.3	28	4.3	21	4.3	13	3
80-84	0	0	7	1.4	3	0.6	8	1.2	9	1.9	8	1.9
85+	0	0	2	0.4	1	0.2	3	0.5	4	0.8	1	0.2
Mean = 51.7	50.1	11.2	51.7	11.7	50.7	11.8	51.8	12.2	53.4	13.3	52.6	13.1
SD = 12.3	11.2		11.7		11.8		12.2		13.3		13.1	
Median = 51	50	16	51	16.5	49	17	50	17	53	20	52	18
IQR = 17	16		16.5		17		17		20		18	
Basis of Diagnosis												
Cytology or Hematology	5	1	6	1.2	2	0.4	3	0.5	0	0	1	0.2
Endoscopy & Radiology	5	1	5	1	3	0.6	2	0.3	3	0.6	13	3
Histology of Metastasis	0	0	3	0.6	2	0.4	6	0.9	0	0	0	0
Histology of Primary	459	91.3	446	91.4	504	96.2	625	97	465	96.3	404	94.2
History & Physical examination	33	6.6	21	4.3	13	2.5	8	1.2	12	2.5	9	2.1
Surgery & Autopsy (no histology)	1	0.2	7	1.4	0	0	0	0	3	0.6	2	0.5
Stage at diagnosis												
Stage I	119	23.7	97	19.9	133	25.4	215	33.4	171	35.4	93	21.7
Stage II	138	27.4	162	33.2	166	31.7	160	24.8	138	28.6	148	34.5
Stage III	191	38	187	38.3	175	33.4	210	32.6	140	29	134	31.2
Stage IV	55	10.9	42	8.6	50	9.5	59	9.2	34	7	54	12.6
Histological type												
Squamous cell carcinoma	385	76.5	380	77.9	386	73.7	503	78.1	355	73.5	288	67.1
Adenocarcinoma	61	12.1	57	11.7	98	18.7	114	17.7	90	18.6	98	22.8
Adenosquamous carcinoma	11	2.2	14	2.9	16	3.1	5	0.8	7	1.4	7	1.6
Unspecified carcinoma	4	0.8	1	0.2	3	0.6	6	0.9	3	0.6	4	0.9
Sarcoma	0	0	0	0	1	0.2	2	0.3	0	0	0	0
Unspecified malignant neoplasm	42	8.3	36	7.4	20	3.8	14	2.2	28	5.8	32	7.5

With continuously organized screening program, cervical preinvasive and invasive cancers would be captured and managed earlier thus impacting for the better overall 5-year survival rates.

The incidence trend of cervical cancer in Khon Kaen Province has shown a continuous decline since 1991, starting with an Age-Standardized Incidence Rate (ASR) of 13.51 per 100,000 female population per year, decreasing to 7.63 in 2020. This was consistent with the projection done by Sanrueang et al of 8.2 in 2014 to 5.0 in 2024 [11]. This trend is consistent with the incidence trends observed in Thailand and across Asia, which have also seen continuous declines. For Thailand, the ASR was 24.7 per 100,000 female population in 2000 [2], decreasing to 11.1 by 2018 [4]. Similarly, in Asia, the ASR decreased continuously from 1998 to 2012 [16]. These trends likely share a common cause, which is the implementation of organized screening programs, contributing to the systematic detection.

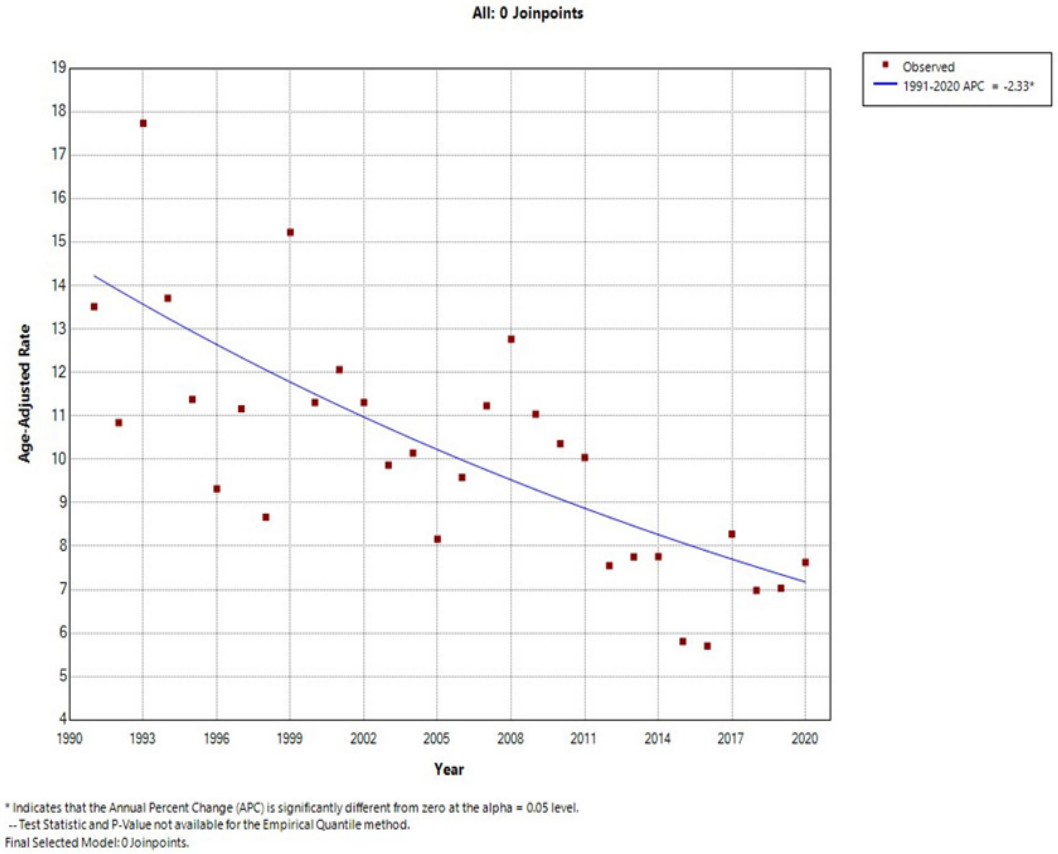

Figure 1. Relationship between ASR and Year of Diagnosis

Limitations

This study may have some limitations. Specifically, the cervical cancer screening systems before and after 2004 differed significantly. Before 2004, the screening was opportunistic, while after 2004, it became an organized system. The exact start date of the organized screening is not clearly known, which makes the incidence trends before 2004 less reliable and makes it challenging to

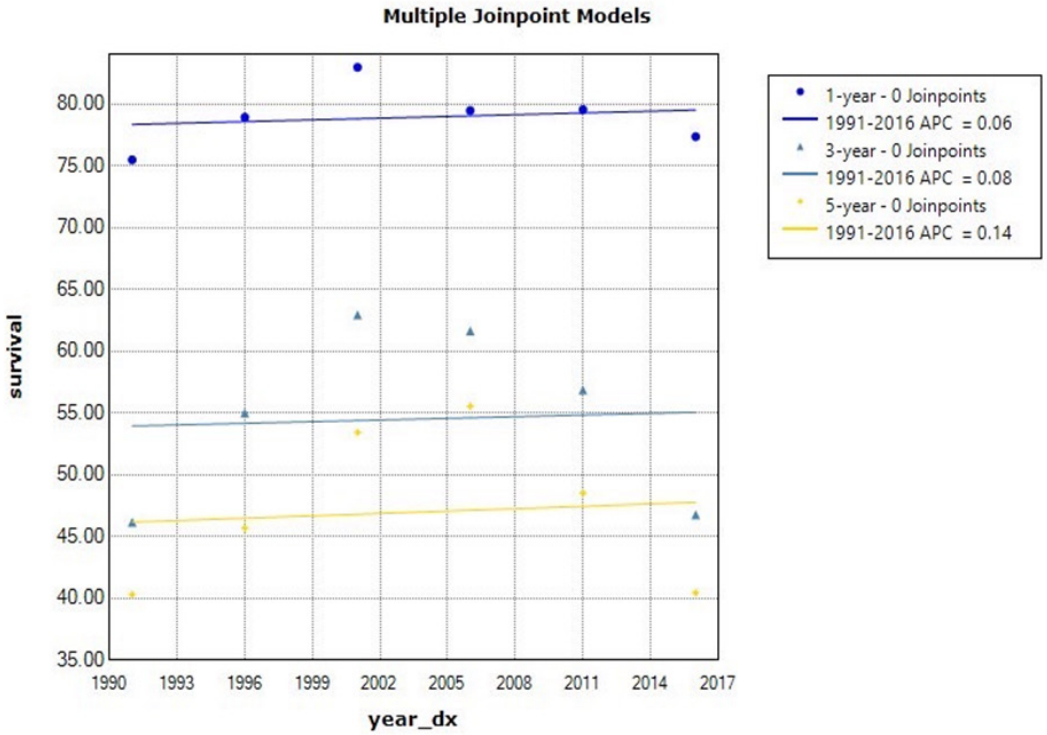

Figure 2. Relationship between OS and Year of Diagnosis.

Table 2. Incidence by Time Period and All Ages in Khon Kaen Province between 1991-2020.

Year of diagnosis	n	CR	ASR	95%CI
1991	91	11.13	13.51	10.67, 16.35
1992	81	9.85	10.84	8.42, 13.26
1993	133	16.09	17.73	14.65, 20.81
1994	106	12.74	13.7	11.04, 16.36
1995	92	10.99	11.38	9.01, 13.75
1996	77	9.13	9.32	7.19, 11.45
1997	94	11.07	11.16	8.88, 13.44
1998	78	9.11	8.67	6.72, 10.62
1999	135	15.65	15.22	12.61, 17.83
2000	104	11.95	11.31	9.10, 13.52
2001	117	13.46	12.06	9.85, 14.27
2002	110	12.67	11.31	9.18, 13.44
2003	100	11.52	9.87	7.92, 11.82
2004	108	12.43	10.15	8.22, 12.08
2005	89	10.23	8.16	6.45, 9.87
2006	106	12.15	9.59	7.76, 11.42
2007	131	14.96	11.23	9.30, 13.16
2008	146	16.61	12.76	10.67, 14.85
2009	134	15.16	11.04	9.16, 12.92
2010	127	14.29	10.36	8.54, 12.18
2011	125	14.04	10.04	8.25, 11.83
2012	94	10.55	7.55	6.01, 9.09
2013	95	10.65	7.76	6.15, 9.37
2014	93	10.42	7.76	6.09, 9.43
2015	76	8.51	5.8	4.43, 7.17
2016	70	7.84	5.7	4.30, 7.10
2017	96	10.76	8.28	6.50, 10.06
2018	91	10.22	6.98	5.46, 8.50
2019	81	9.11	7.03	5.38, 8.68
2020	91	10.27	7.63	5.93, 9.33

Table 3. Overall Observed Survival (OS) of Cervical Cancer for Each Age-Group in Khon Kaen Province between 1991-2020.

Survival time	% OS (95% CI)					
	5-year period at diagnosis and % OS (95% CI)					
	1991-1995	1996-2000	2001-2005	2006-2010	2011-2015	2016-2020
1-year	79.17 (77.64, 80.62)	75.51 (70.94, 79.47)	78.95 (74.72, 82.55)	83 (79.38, 86.03)	79.5 (76.16, 82.43)	79.58 (75.69, 82.92)	77.39 73.13, 81.06)
3-year	55.96 (54.10, 57.77)	46.17 (41.17, 51.02)	55.02 (50.12, 59.65)	62.96 (58.53, 67.04)	61.66 (57.77, 65.30)	56.88 (52.32, 61.17)	46.77 (41.48, 51.88)
5-year	48.37 (46.49, 50.22)	40.31 (35.43, 45.12)	45.69 (40.86, 50.39)	53.44 (48.94, 57.73)	55.56 (51.61, 59.31)	48.54 (44.00, 52.93)	40.46 (34.59, 46.23)

pinpoint factors influencing the trends during that period. Additionally, the exclusion criteria defined in this study may also lead to some discrepancies between the reported incidence and survival rates and the actual figures.

Strengths

This research involves retrospective data collection for the period 1991-2020, which represents the most recent data on the incidence and survival rates of cervical cancer in Khon Kaen Province. Additionally, this study utilized a population cancer registry database, which is expected to closely represent the entire population of Khon Kaen. The results are presented using the Age-Standardized Incidence Rate (ASR), a method aligned with international standards. This approach allows the findings to be comparable at an international level, providing a global context to the local data observed.

Recommendations for practice implementation

In any local setting where a cancer registry is

established, it is crucial to define clear inclusion and exclusion criteria for patients with cervical cancer. This ensures the accuracy and reliability of the data collected. Additionally, rigorous screening of raw data to align perfectly with the established criteria is necessary to ensure the highest accuracy. This data can then be used for statistical analysis to yield results that are both accurate and reflective of reality, allowing for comparisons at the international level.

Recommendations for future research

The data obtained from this study can be leveraged to further investigate the various factors that influence changes in the incidence and survival rates of cervical cancer. Additionally, it can be used to predict future incidence rates. Future research could also explore survival rates according to the stage at diagnosis or histological type, which would provide insights into the prognostic outcomes of different treatment approaches. Continuously organized screening program is still needed and must be monitored. Furthermore, the data from this study could be compared with other gynecological cancers or different types of cancers to understand how their trends and outcomes may differ.

In conclusion, this research found that the Age-Standardized Incidence Rate (ASR) of cervical cancer in Khon Kaen Province, diagnosed between 1991 and 2020, has shown a decreasing trend, aligning with national and international trends. This significant decline is largely due to the more extensive coverage of systematic cervical cancer screening. However, the overall survival rate (OS) for cervical cancer patients in Khon Kaen has remained stable. Considering the WHO's cervical cancer elimination initiative, which aims to reduce the cervical cancer incidence rate to below 4 per 100,000 women per year, it appears that Khon Kaen could achieve this target before 2030.

Nevertheless, to further reduce the incidence and potentially increase the survival rate of cervical cancer, it is recommended to enhance the effectiveness of cervical cancer screening. This can be achieved by adopting primary HPV testing and by campaigning to increase the screening coverage beyond 70%. It is also important to promote timely and appropriate treatment for those with abnormal screening results, aiming for a treatment rate exceeding 90%. Additionally, vaccinating over 90% of young girls can also contribute significantly to reducing the incidence of cervical cancer and improving survival outcomes.

Author Contribution Statement

JP drafted articles for important knowledge content. KS and KK planned and monitored the study. NS and CS participated in the article's structure design, manuscript drafting and data analysis. BC was responsible for research question, design, and made the critical revisions to the manuscript. All authors read and agree with final version of the manuscript.

Acknowledgements

General

The research team would like to extend our gratitude to the Cancer Registry Unit (CRU) at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, for their generous provision of data on cervical cancer patients in Khon Kaen Province. Their support has been instrumental in achieving the objectives of this study.

Approval

This research was a medical student's thesis of the Department of Community Medicine, Khon Kaen University, approved by the department's academic committee.

Ethical Declaration

This research protocol had been reviewed and approved by the Center for Ethics in Human Research of Khon Kaen University according to the announcement from Khon Kaen University, No. 7/2566, under project number HE661024, dated January 24, 2023.

Data Availability

All data and materials included in this study are available upon request by contact with the corresponding author.

Conflict of Interest

Authors declare no conflict of interest.

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