RESEARCH COMMUNICATION

Cervix Cancer in Khon Kaen, Northeast Thailand, 1985-1999

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Abstract

The incidence of cancer of the cervix uteri in Khon Kaen Province is moderately high (age-standardised rate 16.8 per 100 000 person-years), with about a two-fold variation in incidence between different districts. Stage at presentation is considerably more advanced than in the United States and Europe, and there has been little change in incidence over the last 15 years. Currently, control of cervix cancer is through early detection and treatment. Screening programmes have, to date, been opportunistic, but a new national plan anticipates that all women will be screened six times during their lifetime. The results from Khon Kaen provide a benchmark against which the success of this policy can be evaluated.

Key Words: Cervix cancer - incidence - trends - screening

Asian Pacific J Cancer Prev, **4**, 312-318

Introduction

Cancer of the cervix uteri is an important public health problem worldwide. It is the second most common cancer among women, with an estimated 468 000 new cases and 233 000 deaths in the year 2000. Almost 80% of the cases occur in developing countries, where, in many regions, it is the most common cancer of women; the highest incidence rates are observed in Latin America and the Caribbean, Sub-Saharan Africa, and South and Southeast Asia (Parkin et al., 2001). Screening by cytology (the Pap smear), through organised population screening programmes, is the established method for control of cervix cancer. The incidence in most of Europe, North America, and Australia/ New Zealand is generally low, but before the introduction of screening programmes in the 1960's and 70's, incidence was much as we see in developing countries today (Gustafsson et al., 1997).

In Thailand, as in most Asian countries, there has been no truly organised screening programme, involving identification of women at risk, ensuring their examination at regular, defined intervals, with appropriate follow-up and treatment of those found to have as abnormal finding on cytology. For the most part, opportunistic screening has been provided to women on demand, or when attending services such family planning, pregnancy counselling, ante and post-natal clinics, sexually transmitted diseases (STD) clinics and so on. Generally, however screening is even more haphazard than this, involving fee-for-service testing by doctors, with sporadic campaigns mounted by local health departments, or charitable foundations (Pengsaa et al., 1989, Himakoun et al., 1990, Swaddiwudhipong et al., 1999). In 2002, government policy has adopted the goal of screening the entire population of women in Thailand who are aged 35, 40, 45, 50, 55 and 60 in that year (Deerasamee et al., 2002). As a first step, measures to increase the capacity for obtaining and interpreting Pap smears have been put in place – e.g. training courses for nurses and cytologists - as well as for treating the abnormalities detected by screening, with cryotherapy and loop electrosurgical excision procedure (LEEP).

It will be very important to determine the success achieved by this programme. To do so, it is necessary to have secure information, before the programme is widely implemented, on incidence, stage distribution, screening history of the population, and the protection against invasive

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cancer provided by a screening test carried out locally (which implies all of the possible defects in the quality of the smear and its interpretation).

In this paper we present information on the descriptive epidemiology of cervix cancer in Khon Kaen Province, in the Northeast of Thailand, including trends in incidence and stage distribution of the disease, before the introduction of any organised screening programme. The results are compared with those from other centres in Asia, and worldwide.

Subjects and Methods

Cancer Data

Data on cases of cervix cancer recorded in the 15-year period 1985-1999 by the population-based cancer registry of Khon Kaen province have been used. Khon Kaen province is situated in the Northeast region of Thailand. It covers an area of 10 886 km^2 and has a population of 1.73 million people in the year 2000 (National Statistics Office, 2002). A hospital-based cancer registry was established in 1984 at Srinagarind Hospital, the teaching hospital of the Faculty of Medicine of Khon Kaen University. The registry became population-based in 1988, collecting data on all incident cases in Khon Kaen province, and began with a retrospective registration of incident cases of cancer diagnosed since 1 January 1985. Data for the periods 1988-1989, 1990-1992 and 1993-1997 have been published in successive volumes of "Cancer Incidence in Five Continents" (Parkin et al., 1992; 1997; 2002).

For the present study, the following variables were extracted from the registry database for each case of cervix cancer: age, area (district) of residence, date of birth, date of diagnosis, basis of diagnosis, morphology and stage of disease.

Population Denominators

The population denominators used for the calculation of incidence rates at province level were taken from the annual population projections produced in 1986 (Working Group on Population Projections, 1986) and in 1995 (Working Group on Population Projections, 1995). The person-years for calculating the incidence were estimated by summing the estimates for each age group for the individual years of the periods studied.

Population by age and sex for districts within the province were available from the 1990 and 2000 Population and Housing Census (National Statistics Office 1994, 2002). Incidence rates at district level were calculated for the period 1985-1999 (15 years), using person-years based on the mid-period (1992) population estimate, multiplied, within each age-sex group, by 15.

There were 20 districts in Khon Kaen province up to 1994. Recently, local government reorganization increased this to 25, but for the purposes of this study, the original 20 districts were retained.

Analytical Methods

Incidence rates for the province were calculated for 3 five-year periods (1985-1989; 1990-1994; 1995-1999), and for districts within the province for a fifteen-year period, 1985-1999. Age-standardised rates (ASRs) were calculated by the direct method, using the world standard population (Doll et al., 1966).

Results

A total of 1848 cases of invasive cervix cancer were registered in the 15 year period, 1985-1999. Cancer of the uterine cervix accounted for 14% of all cancers in women, in whom it was second in importance to liver cancer (26% of cancers).

For the period 1985-1999, the overall crude incidence rate (CR) for the province was 14.9 per 100 000 person-years, and the ASR 16.8 per 100 000 person-years. Table 1 shows the incidence rates in three time periods, 1985-1989, 1990-1994 and 1995-1999. The rates were relatively stable: the ASRs were 16.2, 17.7 and 16.2 per 100 000 person-years for each period respectively.

Age-specific incidence shows a pattern of early increase (starting before age 20), with a steep rise to about ages 45-50, followed by a plateau and a decline. There is little change in the shape of the age curve with time (Figure 1).

ASRs by district are shown in Figure 2. The highest incidence was observed in Muang district (ASR = 23.8). Figure 2 also shows those districts with rates significantly ($p<0.05$) above (+) or below (∞) the provincial average. In general, the distribution was relatively scattered, both high and low incidence areas were close to each other.

1414 cases (76.5%) had been microscopically confirmed, 18.2% were registered based upon a clinical diagnosis, and there were 3.5% death certificate only cases. Of the cases with a histological diagnosis, 84% were squamous cell carcinomas (SCC) and 15% adenocarcinomas (Adeno CA).

About 30% of cases were of unknown stage. Of the patients for when the stage was known, the disease was often

Table 1. Annual Incidence of Cervix Cancer in Khon Kaen, Northeast Thailand 1985-1999, in Three Time Periods

Year of diagnosis	Number	CR per 100 000	ASR per 100 000	95% Confidence Interval of ASR	Truncated Rate (35-64)
1985-1989	511	13.0	16.2	14.8-17.7	40.8
1990-1994	652	15.8	17.7	16.3-19.1	43.6
1995-1999	685	16.1	16.2	15.0-17.5	40.1

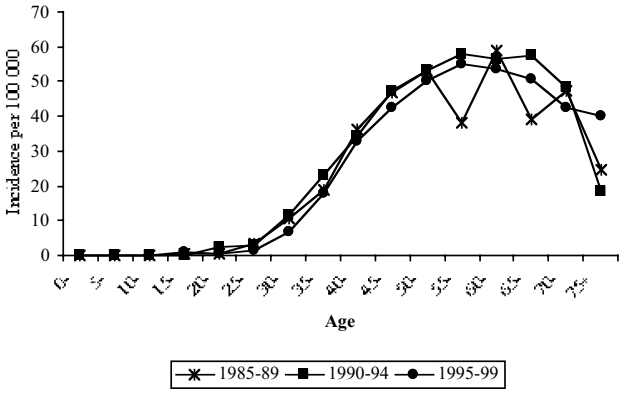

Figure 1. Age-specific Incidence of Cervix Cancer in Khon Kaen, Northeast Thailand, by Time Period.

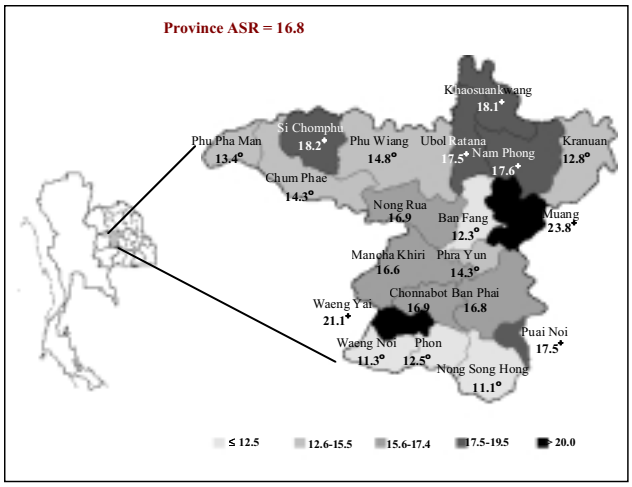

Figure 2. Age-standardised Annual Incidence Rates (per 100 000) of Cervix Cancer in Khon Kaen, Northeast Thailand, 1985-1999, by District, Showing Rates Significantly above (+) and below (∞) the Province Average (ASR 16.8 per 100 000).

advanced at diagnosis; 18–22% of patients presented themselves to the hospital at early stage (localised) during each 5-year period (1985-1989, 1990-1994, 1995-1999), about 70% were at regional stage, 7-9% presented with distant metastasis (Table 2).

Comparison with other registries

Figure 3 compares incidence rates in Khon Kaen province in 1993 to 1997, with those from other registries in Southeast Asia, China, and India for the same period (Parkin et al., 2002). The rates in Khon Kaen were in the middle range. The incidence in Chennai, India was double that in Khon Kaen. Among the Thai registries, Khon Kaen had the lowest incidence. Nevertheless, the rate in Khon Kaen was 3 times higher than that in Finland, and almost seven times higher than that observed in Tianjin, China.

The distribution of cases by histological type is also shown in Figure 3. In the Thai registries, some 15-20% of cases with histological verification were adenocarcinomas, and the majority of cases were squamous cell carcinoma (75-85%). The proportion of adenocarcinoma cases is lowest in the high incidence populations (<20%), and greatest in the low incidence populations (25-30%). Therefore, there was much less variation in the incidence than in the proportion of adenocarcinoma by area.

The age-specific incidence curve showed a similar pattern to that in other high-risk populations, such as Chiang

Table 2. Stage Distribution of Registered Cases of Cervix Cancer in Khon Kaen, Northeast Thailand 1985-1999, in Three Time Periods and Selected Other Cancer Registries

Registry	Localised		Regional involvement		Distant metastasis		Un-staged	Total
	No.	% staged	No.	% staged	No.	% staged	No.	No.
Khon Kaen 1985-1989	76	21.1	257	71.2	28	7.8	150	511
Khon Kaen 1990-1994	102	22.3	318	69.6	37	8.1	195	652
Khon Kaen 1995-1999	82	18.4	320	71.9	43	9.7	240	685
Chiang Mai (1992-1994)*	237	42.5	299	53.6	22	3.9	6	564
Songkhla (1992-1994)*	30	16.5	140	76.9	12	6.6	68	250
India : Bombay (1982-1986)*	804	36.0	1198	53.7	230	10.3	112	2354
USA : SEER,white (1992-1994)*	2704	58.1	1552	33.3	400	8.6	351	5007

*Source: Cancer survival in developing countries (Sankaranarayanan et al., 1998)

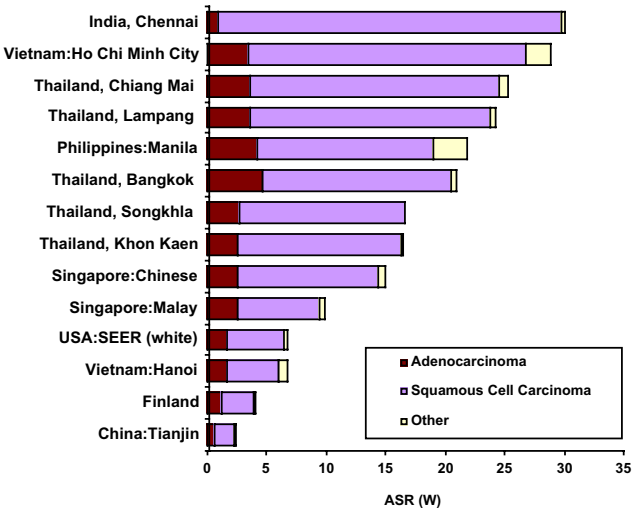

Figure 3. Incidence Rates of Cervix Cancer (ASR per 100 000) in Selected Registries 1993-1997, with Proportion by Histological Type (Source: CI5 volume VIII, Parkin *et al*., 2002)

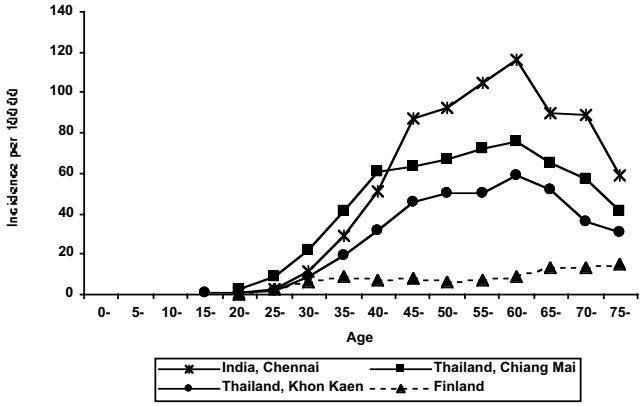

Figure 4. Comparison of Annual Incidence of Cervix Cancer by Age Group in Selected Registries 1993-1997 (Source: CI5 volume VIII, Parkin et al., 2002)

Mai, Thailand, and Chennai, India, with an early increase (starting before age 20), a steep rise to about ages 45-49, followed by a plateau, then decline (Figure 4). This is very different from age-specific incidence in Finland, where there is a much smaller increase in rates after the age of 35-39.

The proportion of cervix cancer cases in localised stage at diagnosis was lower in Khon Kaen when compared to other registries in Thailand, and much lower if compared with developed country such as the US (Table 2) (Deerasamee et al., 1999).

Figure 5 shows time trends in age-adjusted (world standard) incidence rates of cervix cancer in cancer registries in Asia, and in Finland, taken from the last 5 volumes of Cancer Incidence in Five Continents (Waterhouse et al., 1982; Muir et al., 1987; Parkin et al., 1992; Parkin et al., 1997; Parkin et al., 2002) and the incidence of cervix cancer in Khon Kaen, Thailand in the three different period (1985-1989, 1990-1994 and 1995-1999). For most registries in Asia (including Chiang Mai, in northern Thailand), there have

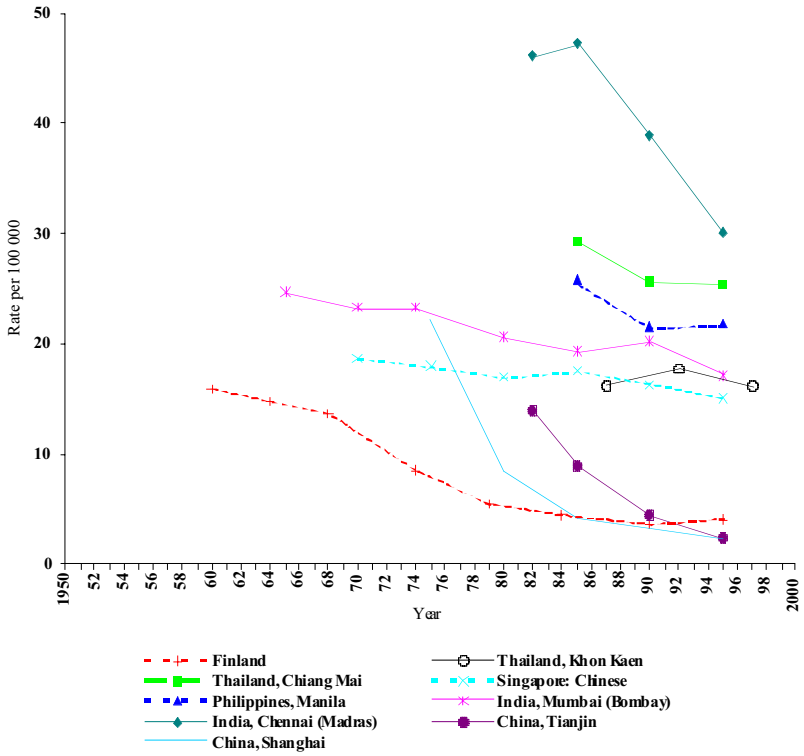

Figure 5. Trends of Cervix Cancer Incidence in Different Cancer Registries (Source: CI5 volume I - VIII)

been rather small declines in incidence. In India, the large decline observed in Chennai (Madras) since 1985 contrasts with the relative stability in Mumbai (Bombay). In China, both cancer registries (Shanghai and Tianjin) showed large falls in incidence, so that the incidence since 1990 has been the same as in Finland.

Discussion

Cancer of the uterine cervix is a common cancer of women in Khon Kaen, Northeast Thailand; it is second in frequency after liver cancer. In general, rates of this cancer are higher in economically developing societies. When compared with incidence rates from other registries in Asia, it is clear that the risk of cervix cancer is moderate; less than, for example, Chennai (India), Manila (Philippines), and Ho Chi Minh (south of Vietnam), but higher than in China (Shanghai) and the north of Vietnam (Hanoi). Compared with the results from the other registries in Thailand, the rates in Khon Kaen are lower than seen in the northern region (Chiang Mai and Lampang), or in the capital, Bangkok (central Thailand), but similar to those in Songkhla in the south.

Within Khon Kaen province itself, there is some variability by district, with the highest rates in the central district (Muang) where the city of Khon Kaen, with the major treatment facilities, is located. The lowest rates are seen in three districts in the extreme south of the province (Nong Song Hong, Waeng Noi and Phon) and one in the extreme north-east (Kranuan). It may be that some patients from these districts are missed by the registry, perhaps going for treatment in the adjacent provinces (Nakornratchasima, and Udonthani, respectively), both of which have cancer treatment facilities.

The proportion of histologically verified cases that are adenocarcinoma is about 15%, similar to that in other registries in Thailand. Where rates of cervix cancer are relatively low, as a result of screening, the proportion of adenocarcinoma is higher than 15%. This is because cytological screening differentially prevents squamous cell carcinoma, but is less effective in detecting and preventing adenocarcinomas (Sigurdsson, 1995: Nieminen et al.,1995). In fact, the incidence of adenocarcinoma is relatively constant internationally, and variation in the proportion is mainly due to differences in incidence of squamous cell cancer (Vizcaino et al., 1998).

Stage at diagnosis is advanced and this is similar to what is observed in other developing countries, for example in Chennai, India or Bangalore, India (Shanta et al., 1998; Nandakumar et al., 1998). It is clear that the stage is very advanced when compared with developed countries, such as reported in US whites (Sankaranarayanan et al., 1998). This presumably relates to lack of knowledge about cancer and its early symptoms among this rural population. Effective screening programmes result in detection and treatment of cervix cancer precursor lesions, and reduce the incidence of invasive disease, although the invasive cancers that do occur in a screened population are often advanced (occurring in non-attenders, or rapidly progressive tumours missed by screening) so that stage distribution and survival are less favourable than in unscreened populations (Dickman et al., 1999).

The incidence in Khon Kaen over the fifteen-year period appears to be relatively stable; in other regions of Asia, in which cancer registries have been established for some time, the declines in incidence have also been rather modest, although the dramatic decreases in incidence and mortality in China, is an exception (Yang et al., 2003). On the other hand, incidence rates have declined over time in western Europe, U.S.A, Canada, Australia, New Zealand, and Japan; this has been ascribed to a combination of a reduction in risk in older generations of women (improved genital hygiene, less parities, etc.), and the success of population screening programmes (Hakama et al., 1986; Coleman et al., 1993; Sigurdsson, 1999), although in some countries rates of invasive cancer have shown increases recently, particularly in young women, despite the continued operation of screening programmes (Antila et al., 1999, Nieminen et al., 1999).

In Thailand, although a national cancer control committee has recently been established, there is as yet no official provincial cancer control programme, to address the burden of cervix cancer. Primary prevention by vaccination against infection with oncogenic HPV offers the long-term prospect of preventing cervix cancer, but in the medium term other methods are available to alleviate disability and death from the disease in rural populations such as that of Khon Kaen province. An attempt should be made to diagnose women at an earlier stage of disease, for which prognosis is much better than in advanced (Stage III and IV) disease (Sriamporn et al., 1995; Martin et al., 1998). The review of cervix cancer cases treated in the main cancer hospital in Stockholm, Sweden, over 4 decades showed that, since early years of the 20th century, stage at presentation progressively improved (Ponten et al., 1995). This must have been due to better knowledge and awareness. The same can be achieved in a short period of time, by health education programmes, as was shown by Jayant et al., (1995) among rural populations in India, where a significant stage shift was observed in a population in regular contact with health workers making enquiry about cancer cases.

Current screening programmes in developing countries are not very effective. The quality of the smear taking, preparation, and reading in many programmes is not good (Lazcano-Ponce et al., 1998; Sankaranarayanan et al., 2001). Coverage of the population may be too low to be effective; a recent study in Nam Phong district, Khon Kaen province, found that there was a high proportion of women who had never been screened for cervix cancer during their life time (33%) (Kritpetcharat et al., 2003). This finding was based on self-report of Pap smears, which may not be entirely accurate; in the USA (Gordon et al., 1993) found that women in a medical care programme had a tendency to over report Pap tests, compared with the records of actual tests. In

addition to low coverage, it has been shown that the follow-up of women found to have a positive smear at screening is quite defective in Northeast Thailand (Thinkhamrop et al., 1998). The national programme aims to improve the quality of cytology, and increase the coverage of screening, by limiting examinations to women at exact ages of 35, 40, 45, 50, 55 and 60 (Deerasamee et al., 2002). Other methods of screening are being tested in Thailand. In Roi-Et province, near to Khon Kaen, an experimental project is evaluating the safety and efficacy a programme based on screening by visual inspection following acetic acid (VIA), followed by immediate treatment of observed lesions by cryotherapy ("see and treat") (Gaffikin et al., 2003). This approach has been suggested to be a more cost effective method of reducing death and disability in developing country populations than the conventional Pap smear programme (Goldie et al., 2001; Mandelblatt et al., 2002). Whatever method of screening is used, it is essential to monitor the overall results of the programme in terms of coverage and trends in incidence. Population-based cancer registries provide an effective and economical method of evaluating their impact at community level (Sankila et al, 2000).

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