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Trends and projections in cervical cancer incidence in northern Tunisia (1994–2040)



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Abstract

Background Cervical cancer (CC) is a major public health problem; it is the fourth leading cause of cancer in women worldwide. The present study aimed to analyze trends and projections in incidence of CC in northern Tunisia during the period 1994–2040.

Methods Crude and Age standardized CC incidence were calculated. Joinpoint software was used to dress trends in incidence. Projections were assessed using the age period cohort model.

Results This study revealed 3092 cases of CC during the period 1994–2018 in northern Tunisia, representing an annual number of 129. The mean age at diagnostic was of 56 ± 12.9 years with extremes ranging from 19 to 88 years old. The crude and standardized incidence rates were respectively of 4.9/100,000 and 5.2 /100,000 women year in 2018. A downward trend in the age standardized incidence rate of CC was confirmed in northern Tunisia from 6.6 in 1994 to 4.7 in 2018 with an Annual Percentage Change (APC) of -1.8%, Confidence interval (CI) at 95% of [-2.9; -0.6]; ($p = 10^{-3}$). Trends analysis have also described three periods: the first one from 1994 to 1998 with a stable trend. The second period was from 1998 to 2006 with a significant decreasing trend with an APC of -7.2%, CI at 95% of [-13.0; -1.0]; (p = 0.02) and the third period was from 2006 to 2014 with a non-significant APC. According to projections, the number of new cases would be of 2017 in 2040 with an age standardized rate between 3.8 and 5.8/100,000 women year.

Conclusion Results of this study underscore the need for the application of CC control program in Tunisia, with efforts focused on improving access to and participation in screening programs, HPV vaccination for females and ensuring timely access to effective treatment services.

Keywords Uterine cervical neoplasms, Incidence, Epidemiology, Tunisia

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Introduction

Cervical cancer (CC) constitutes the fourth leading cause of morbidity and mortality in women worldwide [1]. According to the World health organization (WHO) the burden of CC is considerable in low-and middle-income countries in 2022 [2]. CC presents a disparity between incidence and mortality rates in different regions in the world [3]. Indeed, there is a socio-economic gradient where incidence and mortality rates decrease with the increase of the Human Development Index (HDI). According to the Global Cancer Observatory (GLO-BOCAN) 2022 estimates, a general decline in incidence was observed in most countries worldwide, with a stabilized incidence rate at relatively low levels in several high-income countries. In contrast, the incidence of CC increased in countries in East Africa and Eastern Europe [1, 4].

Countries around the world are working to accelerate the elimination of CC as recommended by the global strategy to eliminate CC by attending an incidence rate below 4/100,000 women year [5]. The World Health Organization (WHO) elimination strategy highlighted the need for a continuous and improved surveillance and monitoring of CC as a fundamental step towards action [6, 7, 8].

According to the latest report of the Northern Tunisia Cancer Registry (NTCR), the age standardized incidence rate (ASR) was 4.3/100,000 in 2014. The trend of the incidence was downward between 1994 and 2014, with an Average Annual Percentage Change (APC) of -2.3% (p<0.05) [9]. This cancer ranks 6th in women [9]. The estimated ASR would be of 3.9/100 000 in Tunisia in 2023 [10]. According to Globocan, CC mortality was of 2.4/100 000 in Tunsia in 2022 [1] (Tunisia lack of exhaustive data on mortality).

Tunisia like other countries adhered to the WHO initiative on CC elimination. This initiative aims to reduce the incidence below a threshold of 4 cases per 100,000 women-year in each country. The 90-70-90 target set by the initiative to be achieved by 2030 requires that 90% of girls are vaccinated by the age of 15, 70% of women are screened with a high-performance test at least twice by the age of 45 years, and 90% of women identified with cervical precancerous lesions or cancer are treated.

Currently CC prevention in Tunisia uses mainly cytology screening for women aged between 35 and 59 years every 5 years. This strategy has encountered many difficulties with a low coverage around 15%. In addition, a pilot project on the implementation of the PCR test proved its feasibility in Greater Tunis, so it was decided to replace cytological screening by HPV DNA Testing as recommended by the WHO. HPV vaccination would be also implemented in the national vaccination program in 2025. In Tunisia cancer surveillance is assured by three regional cancer registries in northern, central and southern Tunisia [11]. NTCR encompasses around the half of the Tunisian population [12]. Cancer surveillance constitutes a fundamental component to track and stay aligned with WHO targets on CC elimination [7]. The last data on CC incidence are back to 2014. In this context, the present study aimed to analyze trends in incidence of CC in northern Tunisia during the period 1994–2018 and to dress projections till 2040.

Methods

This was a descriptive retrospective and exhaustive study about CC cases of the northern Tunisia region during the period 1994–2018.

Study design and population

CC cases were extracted from the NCRT database for the period 1994–2018. The NTCR covers around the half of the Tunisian population including habitants of Greater Tunis, northeastern and northwestern Tunisia.This region encompasses 5,233,700 inhabitants: 2,636,160 males and 2,597,540 females according to the National Institute of Statistics (NIS) of Tunisia [13].

NTCR process

The NTCR was established since 1997 and uses the active method to collect data. Trained cancer registrars visited retrospectively and collected data of cancer patient's records in all health care departments of both public and private sectors in the northern Tunisia region. These data concerned patient demographic data (age, gender, origin...), and characteristics of the tumor (site, histological type, grade, extension, evolution...).

The codification of tumors followed the first International Classification of Diseases for Oncology (ICD-O) between 1994 and 2003 then the third ICD-O was used since 2004 [14]. CC codes correspond to 180 according to the ICDO-1 and to C53 in the ICDO-3.

Concerning data check of the registry database, research for duplicates was carried out systematically upon entry and periodically, messing data of the mandatory variables were verified, check for inconsistencies regarding gender and site, age and site and finally site and morphology were carried out by the registry teem. Data collection, coding and check followed the international recommendations of the International Agency for Research on Cancer (IARC). All measures to respect confidentiality have been taken.

Data quality of NTCR

We explored data exhaustiveness through two parameters: the average number of notification sources which was of 1.1 and the percentage of cases verified histologically which was of 95.0% for males and of 95.6% for females. To assess the validity of data, the rate of missing cases for the mandatory variables was calculated: the variable sex was specified for all patients, the percentage of unknown age was of 5.5%, the rate of unknown primary was of 3.6% and the percentage of cases with unknown place of residence was close to 4%.

Statistical analysis

Stata and excel software were used to analyse data. Joinpoint software was used to dress trends.

Calculation of the crude and standardized incidence rate

We calculated crude incidence rate (CIR) using cases by gender and age group collected by the NTCR corresponding to the period 1994–2018 in the numerator. The number of Tunisian population by gender, age group and region were extracted from the NIS during the period 1994–2018 and corresponded to the denominator [13]. The CIR was calculated as follow:

$$CIR = \frac{Number \ of \ cases}{Number \ of \ population \ per \ time \ periode}$$

We used the direct method of standardization to calculate the age standardized rate (ASR) as fellow [15]:

$$ASR = \sum_{i=1}^{n} \mathbb{R} (ti * proportion of$$

age class i in the reference population)

Where n represents the number of total age classes and ti the specific incidence rate by age class, these age groups consisted of 5-year intervals as recommended to achieve standardization [15, 16]. When the effective was very small for example in ages under 40 and below 65 years we aggregated the corresponding age groups.

The ASR was calculated using the WHO standard population as a reference (as showed in the previous formula) [16]. The (WHO) standard population is based on the mean world population age structure which removes the difference between population age composition over the world and to allow comparison of incidence rates between countries [17].

$$ti = \frac{number \, of \, observed \, new \, cases \, in \, the \, class \, i}{Total \, population \, of \, the \, class \, i} * 100 \, 000$$

Trend analysis

We used Joinpoint software to analyze trends in incidence. Joinpoint is a statistical software package recommended by the IARC to analyzes patterns [18]. This software tests whether an apparent change in trend is statistically significant or not and fits selected trend data (e.g., cancer rates) to the simplest model that the data allow. It assesses the significance level of any statistically upward or downward trends. This analysis facilitated the calculation of the annual percentage change (APC) with its 95% confidence interval. The significance level was set at 5%. Concerning trends in the specific incidence rate by age group, as the number of cases was very small in some age categories, we aggregated some of them such as age groups less than 40 years old and over than 65 years. We also used the joinpoint software to assess trends in the proportional distribution of CC extension (local, regional and metatstatic), histological grade (grade 1, grade 2 and grade 3) and histological type (essentially epidermiod carcinomas and adenocarcinomas).

Projection analysis

Projections were assessed using the age period cohort (APC) model [19]. The APC constitute one of the most common modeling approaches for projecting cancer rates. The APC model provide useful and important information about cancer evolution over time that could be attributable to three main metrics: age, period and cohort [20]. Age refers to the chronological time since birth, Period signifies the date of diagnosis (in this study the event is cervical cancer) and Cohort refers to the date of birth. Usually, the relationship between these variables is correlated as: cohort = period-age [21].

Ethical considerations

The confidentiality of personal information's was respected during the collection and the data analysis. It is also useful to mention that cancer registries in Tunisia are governed by Decree No. 2008 – 846 of March 24, 2008; on the other hand, the NTCR received authorization from the National Authority for the Protection of Personal Data on April 27, 2017.

Results

Incidence of CC in northern Tunisia (1994–2018)

During the period 1994–2018, 3092 cases of CC were identified, representing an average annual number of 129. The crude and standardized incidence rates were respectively of 4.9/100,000 and 5.2/100,000 women year (Table 1). The mean age at diagnostic was of 56 ± 12.9 years with extremes ranging from 19 to 88 years old and the age specific incidence rate (ASIR) increased regularly with age. During the period 1994–2018, regional extension represented more the half of cases with 53.6%, followed by local (37.9%) and metastatic extension (7.9%). CC in situ represented 0.5% of CC cases.

Table 1Incidence rate of cervical cancer in Northern Tunisia1994–2018

Age group (Year)	Number	Pourcentage	Standardised incidence rate/100,000 habitants
0-4	0	0.0	0.0
5–9	0	0.0	0.0
10-14	0	0.0	0.0
15–19	1	0.0	0.0
20-24	8	0.3	0.1
25–29	29	0.9	0.5
30–34	74	2.4	1.4
35–39	168	5.4	3.6
40-44	316	10.2	7.6
45–49	418	13.5	11.7
50-54	421	13.6	13.6
55-59	419	13.6	16.3
60–64	360	11.6	17.3
65–69	280	9.1	18.0
70–74	220	7.1	18.1
75–79	159	5.1	19.9
≥80 years	122	3.9	15.5
Missing	97	96.9	
Total	3092	100.0	
CIR			4.9
ASR			5.2

CIR: Crude incidence rate

ASR: Age standardized incidence rate

 Table 2
 Trends in the age standardized incidence rate of cervical cancer in Northern Tunisia (1994–2018)

Period	ASR/100 000 person year	APC	CI 95%	р	
1994–2018	6.6–4.7	-1.8	[-2.9; -0.6]	10 - 3	
1994–1998	6.6–6.4	6.6	[-8,5; 24.1]	0.4	
1998-2006	6.3–4.0	-7.2	[-13.0;-1.0]	0.02	
2006-2018	4.0-4.7	1.5	[-1.3; 4.5]	0.2	
CC: cervical c	CC: cervical cancer				

ASR: Age standardized incidence rate

APC: Annual percentage change

CI: Confidence interval

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p=level of significance

Trends in incidence of CC in northern Tunisia (1994–2018)

The ASR decreased significantly from 6.6 in 1994 to 4.7 in 2018 with an APC of -1.8%, CI at 95% of [-2.9; -0.6]; $(p=10^{-3})$ (Table 2; Fig. 2). Trends analysis have also described three periods: the first one from 1994 to 1998 with a stable trend APC of 6.6%, CI at 95% of [-8.5; 24.1]; (p=0.4). The second period was from 1998 to 2006 with a significant decreasing trend with an APC of -7.2%, CI at 95% of [-13.0; -1.0]; (p=0.02) and the third period was from 2006 to 2014 with a non-significant APC of 1.5%, CI at 95% of [-1.3; 4.5]; (p=0.2) (Table 2; Fig. 1).

The trend of the ASIR was significantly decreasing for the age groups between 40 and 54 years; however it was stable under 40 years and over 55 years old (Table 3; Figs. 2 and 3).

Trend of the repartition of cervical cancer cases according to the extension stage, histological grade and type

Concerning local stage, proportional distribution of CC cases was significantly increasing from 20.0% in 1994 to 75.8% in 2018 with an APC of 7.9%; [5.9; 10.0]; $(p < 10^{-3})$. In the other hand, regional distribution has significantly decreased from 73.9% in 1994 to 15.2% in 2018 with an APC of -7.7%; [-9.2;-6.2]; $(p < 10^{-3})$. Proportional distribution of the metastatic stage was stable during 1994-2018 (APC: 1.1%; [-1.8; 4.4]; p=0.4) (Table 4; Fig. 4). Time trend of grade 1 has significantly decreased from 66.7% to 28.2% from 1994 to 2018 with an APC of -4.1%; [-4.7;-3.6]; $(p < 10^{-3})$. However, trends of the repartition of CC grade 2 and 3 were significantly increasing from 16.7% in 1994 to 48.1% and 24.0% respectively in 2018 (APC of 5.6%; [4.3;6.9]; $(p < 10^{-3})$ for grade 2 and APC of 4.4%; [1.5; 6.1]; (*p*=0.001) for grade 3) (Table 4; Fig. 5). While the trend of the repartition of squamous cell carcinoma CC was significantly decreasing (APC: -0.5%; IC at 95% [-0.7;-0.3]; $p < 10^{-3}$), the repartition of adenocarcinoma CC was significantly increasing (APC: 2.6%; IC at 95% [1.2;4,1]; *p* < 10⁻³) (Table 4; Fig. 6).

Projections of cervical cancer cases in northern Tunisia till 2040

According to projections, the number of new cases would be stable and will reach 217 cases in 2040 with an expected ASR between 3.8 and 5.8/100,000 (Table 5).

Discussion

CC constitutes a major public health problem ranking as the fourth most frequent cancer in women woldwide[22]. Analyzing trends in incidence of this cancer is an essential step to monitor progress towards WHO goals for CC elimination [23]. This study aimed to analyze trends in incidence of this cancer in northern Tunisia during the period 1994–2018 and to dress projections till 2040.

This study revealed a low level of incidence in CC in northern Tunisia. Trends analysis have also described two periods: the first one from 1994 to 1998 with a stable trend significant decreasing trend and the second period was from 2008 to 2018 with a non-significant APC. Projections in CC incidence were stable till 2040. Trends analysis have also described three periods: the first one from 1994 to 1998 with a stable trend. The second period was from 1998 to 2006 with a significant decreasing trend with an APC of -7.2%, CI at 95% of [-13.0; -1.0]; (p = 0.02) and the third period was from 2006 to 2014 with a non-significant APC.

The incidence rate in northern Tunisia reported by this study was low (4.7/100,000 person year in 2018). This

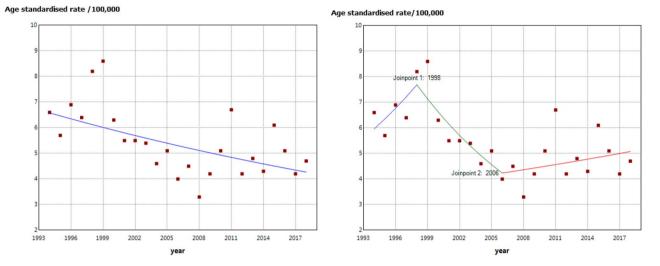


Fig. 1 Trends in the age standardized incidence rate of cervical cancer for the period 1994-2018

Table 3 Time trends of the age-specific incidence	e rates
(1994–2018)	

Age (years)	ASIR (per 100000 persons years)		APC	CI	p
	1994	2018			
<40	1.1	0.8	0.5	[-1.8;2.9]	0.6
40-44	17.5	8.4	-3.7	[-5.7;-1.6]	0.001
45–49	11.9	9.7	-4.0	[-6.1;-1.8]	< 0.001
50-54	16.1	10.0	-2.7	[-4.8;-0.5]	0.01
55-59	14.9	15.0	-0.3	[-2.7;2.1]	0.8
60-64	29.1	19.3	-0.5	[-3.0;2.2]	0.7
≥65	16.3	15.8	-1.4	[-3.2;0.4]	0.13

ASIR: age-specific incidence rates

APC: annual percentage change

CI: confidence interval

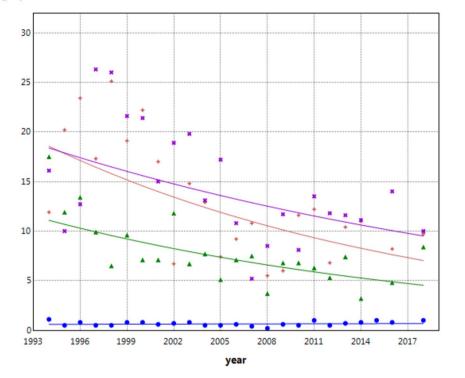
p = level of significance

level of incidence of CC in north Tunisia was similar to those in many Arab countries such as Jordan, Palestine, Egypt, Iran, Iraq and Yemen [24]. In addition, the trends in the incidence of CC decreased significantly in northern Tunisia from 6.6 in 1994 to 4.7 in 2018 with an APC of -1.8%, CI at 95% of [-2.9; -0.6]; $(p = 10^{-3})$. This trend is in line with global trend of this cancer in the world with a decreasing trend in most countries [1, 25]. In fact, a recent study on CC incidence trends during the period 1988-2017 based on data of GLOBOCAN 2020 reported a universal decline in CC incidence in most countries of the world; most important declines were observed in some Latin American (Brazil, Colombia and Costa Rica) and Asian countries (India, Thailand and Indonesia) [1, 23, 25]. This was essentially due to the implementation of CC screening programs [26, 27]. In contrast, increases were observed in the Baltic countries in eastern Europe and in eastern Africa which is due to the absence of effective population-based screening programs [28]. Poverty,

weak health systems and low levels of education are the main obstacles to prevention efforts [29].

It is difficult to associate the downward trend in CC incidence in Tunisia to the screening program as the coverage of CC screening in Tunisia was low, estimated to less than 17% among women aged 35 to 59 years [12]. This also could be approved by the very low percentage of carcinoma in situ in this study which represented only 0.5% of all cases. It could probably be attributed to the improvement of sociocultural characteristics among women related to factors associated with the decrease of HPV infections such as improvement of genital hygiene and sexual behavior [30, 31]. Male circumcision also plays a protective role in HPV transmission and is very widely practiced in Muslim-majority countries [32]. The improvement of socioeconomic status of the Tunisian population could also explain at least a part of the CC incidence decrease [33].

Moreover, the downward trend in incidence of CC in Tunisia should not reassure us as to the absence of risk of an increase in this incidence. Indeed, by analyzing sexuality among young Tunisians, we must fear an increase in the risk of sexually transmitted infections, including HPV infections [34]. According to a study conducted by Khemakhem et al. in 2015 [35] among 104 Tunisian adolescents of both genders, hetero-sexual activity was reported in 46.2% (n = 24) of adolescents and 44.2% teenagers. The average age of first sexual intercourse was 16.15 years for males and 15.83 for females [35]. No protection means has been used by the boys at the first sexual intercourse in 91.7% (n = 22) of cases and 26.1% of girls had a first act under protection [35]. The prevalence of HPV among Tunisian women was estimated at 7.8% [34]. However, in the absence of population-based studies, it is difficult to have non bias estimates of this prevalence. Consequently,



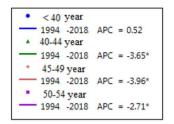


Fig. 2 Global trends in the age group less than 54 years specific incidence rate of cervical cancer cases for the period 1994-2018

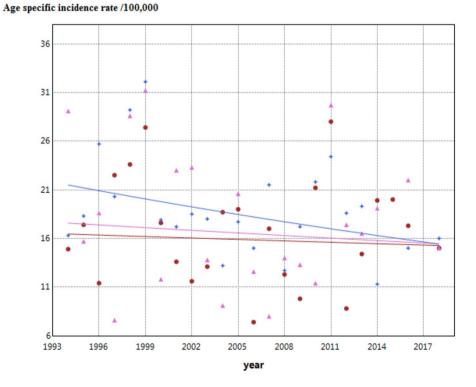




Fig. 3 Global trends in the age group over 55 years specific incidence rate of cervical cancer cases for the period 1994–2018

Table 4 Trends of the proportional repartition of cervical cancer cases according to the extension, histological type and grade ir	۱
Northern Tunisia (1994–2018)	

	Characteristic	Proportiona	al distribution (%)	APC	Cl at 95%	p
		1994	2018			
Extension	Local	20.0	75.8	7.9	[5.9; 10.0]	< 10 ⁻³
	Regional	73.9	15.2	-7.7	[-9.2;-6.2]	< 10 ⁻³
	metatstatic	5.0	7.0	1.1	[-1.8; 4.4]	0,4
Histological grade	grade 1	66.7	28.2	-4.1	[-4.7;-3.6]	< 10 ⁻³
	grade2	16.7	48.1	5.6	[4.3;6.9]	< 10 ⁻³
	grade3	16.7	24.0	3.8	[1.5;6.1]	0.001
Histological type	squamous cell carcinoma	87.5	79.7	-0.5	[-0.7;-0.3]	< 10 ⁻³
	adenocarcinoma	9.6	13.7	2.6	[1.2;4.1]	< 10 ⁻³
	Carcinoma in situ					

APC: annual percentage change

CI: confidence interval

p = level of significance

Percentage (%)

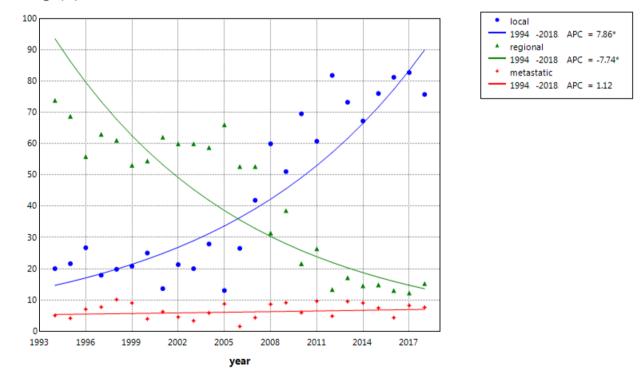


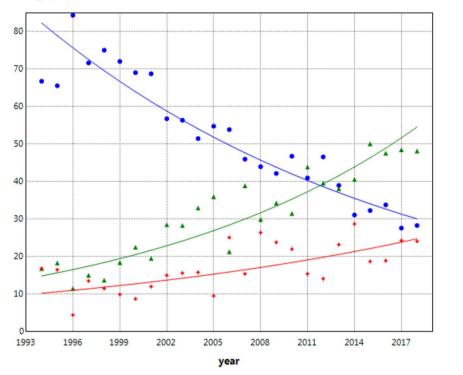
Fig. 4 Trends of the proportional repartition of cervical cancer cases according to the extension in northern Tunisia (1994–2018)

the adhesion to the WHO initiative on CC elimination is justified.

According to the period, the present study has shown a significant decrease in CC incidence between 1998 and 2006 which could reflect the effect of CC screening; however, since 2006, the present study reported a stable trend. This result has been observed, in Oceania (Australia and New Zealand), north America (Canada and the United States), and Western Europe since the mid-2000s where trends in incidence were stabilized [1, 25, 36, 37] but also in Saudi Arabia [38]. The stagnant incidence in Tunisia reported in this study highlights the need to adhere to the Cervical Cancer Elimination Initiative which has set national 90–70–90 targets for CC elimination by 2030 [6, 39]. The targets require that 90% of girls are vaccinated with HPV vaccine before the age of 15 years, 70% of women are screened with a highperformance test at between 35 and 45 years, and 90% of women well treated [40]. Screening strategy in Tunisia has encountered many limitations such as the problems of interpretation, late results and a low coverage which has never exceeded 17% among Tunisian women aged 35



Percentage (%)



• grade	1		
- 1994	-2018	APC	= -4.12*
 grade 	2		
- 1994	-2018	APC	= 5.60*
• grade	:3		4
- 1994	-2018	APC	= 3.78*

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adenocarcinoma

1994 -2018 APC = 2.65* epidermoid carcinoma

1994 -2018 APC = -0.50*

Fig. 5 Trends of the proportional repartition of cervical cancer cases according to the histological grade in northern Tunisia (1994–2018)

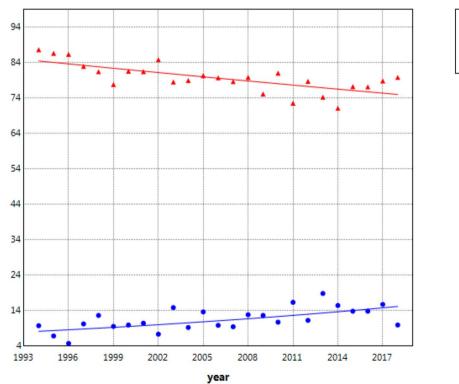


Fig. 6 Trends of the proportional repartition of cervical cancer cases by histological type in northern Tunisia (1994–2018)

Table 5Projections of cervical cancer cases in Northern Tunisia2020–2040

year	Number of cases	CIR/ 100 000	CI at 95%	ASR	Cl at 95%
	of cases	person			95%
2030	182	5.6	[4.7; 6.7]	4.2	[3.5;
					5.1]
2035	201	6.0	[5.0; 7.2]	4.5	[3.7-;
2000	201	0.0	[3:077.12]	11.5	5.3]
					-
2040	217	6.4	[5.2; 7.9]	4.7	[3.8;
					5.8]

CIR: Crude incidence rate

ASR: Age standardized incidence rate

CI: confidence interval at 95%

to 59. So, it has become imperative to replace cytology screening by DNA test recommended by the WHO (50). This transition would allow screenings to be spaced every 10 years, i.e. at ages 35 and 45. In 2022, a pilot project was carried out to study the feasibility of the implementation of high-risk HPV testing as a primary screening test for CC in the district of Tunis [41]. Results of this project have proven the feasibility of this strategy in the Tunisian context and a decision has been taken to gradually extend this project to centerSouthern Tunisia and gradually to the entire country. This would allow increasing the coverage of screening in Tunisia in order to further reduce the incidence of CC which has been stabilized for a while. In addition to screening, Cervical Cancer Elimination Initiative recommends the introduction of HPV vaccine which would bear fruit in the medium and long term. However, some experiences have demonstrated a low coverage due to vaccine hesitancy. This highlights the need to study the willingness of the general Tunisian population for HPV vaccination before its introduction.

Trend in the proportional distribution of CC local stage cases was significantly increasing, however; regional distribution has significantly decreased while metastatic stage was stable during 1994–2018. It's difficult to relate the increasing trend of the proportional distribution of local stage to the implementation CC screening strategy in Tunisia, because the coverage of the program was low. In addition, the trend of SCC CC between 1994 and 2018 was significantly decreasing, that of adenocarcinoma was significantly increasing which was reported in the literature [42] and explained by the insufficient screening strategy to detect adenocarcinoma precursor lesions [43].

A key strength of this study is the use of high-quality population-based cancer registry data from the NTCR, which follows standardized international guidelines for case ascertainment and coding [16, 44, 45]. The methodology used for cancer registration in NTCR complies with IARC recommendations [45]. The use of the active method for data collection ensured satisfactory completeness; this one ensured the exclusion of selection bias. Similarly, elimination of duplicates and correction of incompatibility errors (sex/topography, topography/ histology, age/topography/histology) ensured data quality [46]. Strengths related to the quality of the NTCR concerned essentially the exhaustiveness: in deed, the sex variable was specified for all patients, the age distribution did not show an excess of cases with age ending in 0 or 5 and only 3.6% of unknown primary site.

The main limitation of this study was the absence of a unique identifier for each citizen which constitutes a problem for efficient duplicate search. Moreover, the unique identifier could help to perform correspondence with medical deaths certificates and include CC deaths in the registry. Also, the quality of data records for some items, especially for the TNM stadium, governorate was poor and was the cause of the missing data. Concerning the quality of the NTCR there was essentially a problem of domiciliation with a percentage of unknown place of residence close to 4%. The delay between actual data and cancer registry publication in Tunisia as well as other low and middle income countries is essentially due to insufficient material and human resources, lack of medical information system and a problem of governance [12, 47].

Conclusion

Despite the downward evolution of CC incidence in northern Tunisia, it's difficult to relate this decline to the implementation CC screening strategy in Tunisia, because the coverage of the program was low. The Tunisian CC strategy needs to be improved by adhering to the WHO CC initiative to eliminate this cancer, with efforts focused on improving access to and participation in screening programs, the implementation of HPV vaccination in females and ensuring timely access to effective treatment services, particularly for women residing in underserved regions. Targeted interventions addressing regional disparities and barriers to screening and preventive care will be key to achieving this goal in Tunisia and other countries with similar epidemiological patterns. The evaluation of the response to these interventions should be monitored and evaluated through surveillance which emphasis the need to improve cancer registries in Tunisia by providing the necessary material and human resources and facilitating access to data.

Abbreviations

/ woor c via cions	
APC	Annual percentage change
ASR	Age standardized incidence rate
ASIR	Age specific incidence rate
CC	Cervical cancer
CI	Confidence interval
CIR	Crude incidence rate
GLOBOCAN	Global cancer observatory
ICD	O-International Classification of Diseases for Oncology
IARC	International Agency for Research on Cancer
NIS	National Institute of Statistics of Tunisia
NTCR	Northern Tunisia cancer registry

Р	Level of significance
WHO	World Health Organization

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Author contributions

H.K. and M.H: Conceptualization, methodology and validation H.K, M.H. and Y.A: Data analysis H.K. and N.M: Writing W.A, A.C. and H.M: validation. All authors have read and agreed to the published version of the manuscript.

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Data availability

The datasets generated and/or analysed during the current study are not publicly available due to data confidentiality but are available from the corresponding author on reasonable request.

Declarations

Ethical approval

This study was approved by the ethical comity of Jendouba Hospital of Tunisia.

Consent to participate

Not Applicable.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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References

- Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74:229–63.
- Stelzle D, Tanaka LF, Lee KK, Ibrahim Khalil A, Baussano I, Shah ASV, et al. Estimates of the global burden of cervical cancer associated with HIV. Lancet Glob Health. 2021;9:e161–9.
- Soerjomataram I, Bray F. Planning for tomorrow: global cancer incidence and the role of prevention 2020–2070. Nat Rev Clin Oncol. 2021;18:663–72.
- Guida F, Kidman R, Ferlay J, Schüz J, Soerjomataram I, Kithaka B, et al. Global and regional estimates of orphans attributed to maternal cancer mortality in 2020. Nat Med. 2022;28:2563–72.
- 5. WHO (World Health Organ.). Cancer fact sheet 2020. Geneva: WHO.
- 6. Global strategy to. Accelerate the elimination of cervical cancer as a public health problem. Geneva: World Health Organization.
- Brotherton JML, Wheeler C, Clifford GM, Elfström M, Saville M, Kaldor J, et al. Surveillance systems for monitoring cervical cancer elimination efforts: focus on HPV infection, cervical dysplasia, cervical screening and treatment. Prev Med. 2021;144:106293.
- Jena S, Epari V, Chandra Sahoo K. Integration of National cancer registry program with Ayushman Bharat digital mission in India: A necessity or an option. Public Health Pract. 2022;3:100263.
- Hsairi Mohamed K, Hyem M, Rym. Cherif Ines. Registre du cancer de la région du Nord de la tunisie 2010–2014 [Internet]. 2021. Disponible sur: https://ww w.institutsalahazaiez.com/medias/bulletin%202010_2014_final%20(1).pdf
- Khiari H, Arfaoui E, Mahjoub N, Henchiri S, Sliti A, Hsairi M. Estimated Cancer incidence in Northern Tunisia in 2023: Northern Tunisia Cancer registry. Asian Pac J Cancer Prev. 2024;25:4359–69.
- Khiari H, Ben Ayoub HW, Ben Khadhra H, Hsairi M. Colorectal Cancer incidence trend and projections in Tunisia (1994–2024). Asian Pac J Cancer Prev [Internet]. 2017 [cité 18 juin 2024];18. Disponible sur: https://doi.org/10.22034 /APJCP.2017.18.10.2733

- 12. Khiari H, Mallekh R, Hsairi M. Strategies of the Maghreb countries in the fight against cancer. Tunis Med. 2021;99:148–57.
- Institut National de la Statistique [Internet]. S CEDEX– 265 BP Cham-Ech Rue 7; Disponible sur: tn.ins.www.
- World Health Organization. International classification of diseases for oncology (ICD-O). 2013.
- Morris JK, Tan J, Fryers P, Bestwick J. Evaluation of stability of directly standardized rates for sparse data using simulation methods. Popul Health Metr. 2018;16:19.
- Boyle P. and D.M. Parkin. Statistical methods for registries. International Agency for Research on Cancer 150 cours Albert Thomas, 69372 Lyon Cidex 08, France.
- Ahmad OB, Boschi-Pinto C, Lopez AD, Murray CJL, Lozano R, Inoue M. Age standardization of rates: A new WHO standard. GPE Discussion Paper Series-EIP/GPE/EBD. No.31. 2001.
- Kim H, Chen H, Byrne J, Wheeler B, Feuer EJ. Twenty years since joinpoint 1.0: two major enhancements, their justification, and impact. Stat Med. 2022;41:3102–30.
- Yang Y, Land KC. Age-period-cohort analysis: new models, methods, and empirical applications. Taylor & Francis; 2013.
- Murphy CC, Yang YC. Use of Age-Period-Cohort analysis in Cancer epidemiology research. Curr Epidemiol Rep. 2018;5:418–31.
- Bell A, Jones K. Age, period and cohort processes in longitudinal and life course analysis: A multilevel perspective. Life Course Perspect Health Trajectories Transit. 2015;197–213.
- 22. Pimple S, Mishra G. Cancer cervix: epidemiology and disease burden. Cytojournal. 2022;19:21.
- Arbyn M, Weiderpass E, Bruni L, De Sanjosé S, Saraiya M, Ferlay J, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. Lancet Glob Health. 2020;8:e191–203.
- 24. Sharkas G, Arqoub K, Khader Y, Nimri O, Shroukh W, Jadallah H, et al. Trends in the incidence of cervical Cancer in Jordan, 2000–2013. J Oncol. 2017;2017:1–4.
- Singh D, Vignat J, Lorenzoni V, Eslahi M, Ginsburg O, Lauby-Secretan B, et al. Global estimates of incidence and mortality of cervical cancer in 2020: a baseline analysis of the WHO global cervical Cancer elimination initiative. Lancet Glob Health. 2023;11:e197–206.
- Piñeros M, Laversanne M, Barrios E, Cancela MDC, De Vries E, Pardo C, et al. An updated profile of the cancer burden, patterns and trends in Latin America and the Caribbean. Lancet Reg Health - Am. 2022;13:100294.
- Rajappa S, Singh M, Uehara R, Schachterle SE, Setia S. Cancer incidence and mortality trends in Asia based on regions and human development index levels: an analyses from GLOBOCAN 2020. Curr Med Res Opin. 2023;39:1127–37.
- Vaccarella S, Franceschi S, Zaridze D, Poljak M, Veerus P, Plummer M, et al. Preventable fractions of cervical cancer via effective screening in six Baltic, central, and Eastern European countries 2017–40: a population-based study. Lancet Oncol. 2016;17:1445–52.
- Singh G. Global Inequalities in Cervical Cancer Incidence and Mortality are Linked to Deprivation, Low Socioeconomic Status, and Human Development. Int J MCH AIDS IJMA [Internet]. 2012 [cité 18 juin 2024];1. Disponible sur: https://mchandaids.org/global-inequalities-in-cervical-cancer-incidenc e-and-mortality-are-linked-to-deprivation-low-socioeconomic-status-and-hu man-development/
- Choi S, Ismail A, Pappas-Gogos G, Boussios S. HPV and cervical cancer: A review of epidemiology and screening uptake in the UK. Pathogens. 2023;12:298.
- Shi R, Devarakonda S, Liu L, Taylor H, Mills G. Factors associated with genital human papillomavirus infection among adult females in the united States, NHANES 2007–2010. BMC Res Notes. 2014;7:544.
- International Agency for Research on Cancer (IARC). IARC Handbooks of Cancer Prevention. Volume 10. Cervix Cancer Screening. IARC Press. 2005. Accessed November 23, 2020. [Internet]. Disponible sur: http://www.iarc.fr/e n/publications/pdfs-online/prev/handbook10/ HANDBOOK10.pdf.
- Fidler MM, Soerjomataram I, Bray F. A global view on cancer incidence and National levels of the human development index. Int J Cancer. 2016;139:2436–46.
- Ardhaoui M, Letaief H, Ennaifer E, Bougatef S, Lassili T, Bel Haj Rhouma R, et al. The prevalence, genotype distribution and risk factors of human papillomavirus in Tunisia: A National-Based study. Viruses. 2022;14:2175.
- 35. Khemakhem R, Homri W, Bram N, Romdhane IB, Labbane R. Sexualité des adolescents Tunisiens. Sexologies. 2017;26:74–8.

- Rayner M, Welp A, Stoler MH, Cantrell LA. Cervical Cancer screening recommendations: now and for the future. Healthc Basel Switz. 2023;11:2273.
- Bruni L, Diaz M, Castellsagué X, Ferrer E, Bosch FX, De Sanjosé S. Cervical human papillomavirus prevalence in 5 continents: Meta-Analysis of 1 million women with normal cytological findings. J Infect Dis. 2010;202:1789–99.
- C Allemani. Cervical cancer in Saudi Arabia: trends and regional disparities in incidence and survival. Cerv. Cancer Saudi Arab. Trends Reg. Disparities Incid. Surviv; 2021.
- WHO. Global strategy to accelerate the elimination of cervical Cancer as a public health problem. [01/02/22]. [Internet] [https://www.who.int/publicatio ns-detail-redirect/9789240014107]
- Simms KT, Steinberg J, Caruana M, Smith MA, Lew J-B, Soerjomataram I, et al. Impact of scaled up human papillomavirus vaccination and cervical screening and the potential for global elimination of cervical cancer in 181 countries, 2020–99: a modelling study. Lancet Oncol. 2019;20:394–407.
- Ardhaoui M, Rhouma RB, Guettiti HT, Fehri E, Ouerhani K, Jemia ZB, et al. Distribution of high-risk human papillomavirus in women with ASC-US or LSIL in Tunisian women: place of HPV testing for women triage in Tunisia. Diagn Microbiol Infect Dis. 2023;105:115859.
- Smith HO, Tiffany MF, Qualls CR, Key CR. The rising incidence of adenocarcinoma relative to squamous cell carcinoma of the uterine cervix in the united States—A 24-Year Population-Based study. Gynecol Oncol. 2000;78:97–105.

- 43. Wang M, Huang K, Wong MCS, Huang J, Jin Y, Zheng Z-J. Global cervical Cancer incidence by histological subtype and implications for screening methods. J Epidemiol Glob Health. 2024;14:94–101.
- World Health Organization. National cancer control programmes: policies and managerial guidelines [Internet]. World Health Organization.; 2002. Disponible sur. https://iris.who.int/handle/10665/42494.
- 45. International Agency for Research on Cancer [Internet]. Disponible sur: http://www.iacr.com.fr/
- Giusti F, Martos C, Negrão Carvalho R, Van Eycken L, Visser O, Bettio M. Quality indicators: completeness, validity and timeliness of cancer registry data contributing to the European Cancer information system. Front Oncol. 2023;13:1219128.
- Pramesh CS, Badwe RA, Bhoo-Pathy N, Booth CM, Chinnaswamy G, Dare AJ, et al. Priorities for cancer research in low- and middle-income countries: a global perspective. Nat Med. 2022;28:649–57.

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