RESEARCH ARTICLE

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The Trend and Prediction of Cervical Cancer Incidence in Delhi, India: An Age-Period-Cohort Analysis

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Abstract

Objective: The objective of the study is to assess the trend of age-standardised incidence rate (ASIRs) of cervical cancer, standardised median age at diagnosis, and projection of cervical cancer incidence rate and the number of new cases up to 2030. The projections help in making strategies for resource allocation to circumvent the future burden. **Methods:** The data were extracted from the Delhi population-based cancer registry from 1990 to 2014. Joinpoint regression analysis was applied to ASIRs to assess the trend. The natural cubic splines age-period-cohort (APC) model was fitted to project the incidence rate and incidence cases. The trend of standardised median age at diagnosis and percentage of cervical cancer to total women cancer was also assessed using regression analysis. Projections of new cases are decomposed into three components aging, the structure of the population, and age-specific incidence rate. **Results:** The age-standardised incidence rate of cervical cancer decreased with an annual decline at a rate of 2.98% (95% CI -3.48 to -2.47) from 1990 to 2014. The standardised median age at diagnosis showed an upward trend with an average annual increase of 0.167 per year and the median age increased by 4.18 years during 25-years period, this change was due to the shifting of the peak from 40-44 in 1990 to 60-64 in 2014. The APC model revealed ASIRs would decline by 43.8% in 2030 compared to average ASIRs 2010-2014, albeit a net 12% increase in the incidence cases. An increase in incidence cases is primarily attributed to the aging of the population and population growth by 38.87% and 33.84% respectively. The trend analysis of cervical cancer ASIRs in pre (< 50 years) and post menopause (≥ 50 years) showed a decreasing trend. However, the ratio of cervical to total women increased over time from 1:1 in 1990 to 2:3 in 2014. **Conclusion:** The declining trend in ASIRs was observed in Delhi and will continue to decrease up to 2030. The burden of the number of new cases of cervical cancer showed an upward trend primarily due to the aging of the population and shifting of population structure. To counter this big challenge a cost-effective vaccination for vulnerable populations, community-based screening programs, and awareness about cervical cancer prevention might help in eliminating this preventable cancer.

Keywords: Age-period-cohort model- cervical cancer- projection- cubic splines

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Introduction

Cervical cancer ranked the fourth most common cancer among women worldwide for incidence as well as for mortality after breast, colorectal, and lung cancer (WHO, 2020). The burden of cervical cancer was estimated with 604127 new cases and 341831 deaths worldwide in 2020 with a ratio of mortality to the incidence of 57% (WHO, 2020). The new cases contributed to 6.95% of total women's cancer and cervical cancer mortality attributed to 7.5% of total women's cancer deaths. Age standardised incidence rate (ASIR) of cervical cancer was 13.3 per 100,000 women and the cumulative risk of developing cervical cancer was 1.39% in 2020 (WHO, 2020). Both China and India together contributed nearly 35% of the new cases burden of cervical cancer and mortality worldwide. The distribution of cervical cancer incidence varies geographically; the Asian population has a lower incidence than the African population but higher than the European and American populations. The ASIR of the Asian population was 12.7 per 100,000 while in the African population it was 24.6 per 100, 000 (WHO,2020). A downtrend in cervical cancer ASIRs has been observed globally over the past decades with an estimated annual percentage change (EAPC) of nearly -0.38%(95% CI: -0.41 to -0.34 (Zhang et al., 2021), albeit, there is an increase in incidence cases from 1990 to 2019 was 68.5%. East Asia and Southern sub-Saharan Africa observed a rising trend in the ASIRs from 1990 to 2019 with EAPC 1.33% and 0.28% respectively (Zhang et al., 2021).

In India, the incidence of cervical cancer also varies due to geographical or cultural diversity but an

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overall decreasing trend is observed for cervical cancer across India. According to a recent report based on 28 PBCRs, the proportion of new cervical cancer to total women cancer varies from 5.5% to 26.5%. Delhi ranked 11th among these PBCRs with a proportion of 10% and second-leading women's cancer site after breast cancer. The Age-standardised Incidence rate (ASIR) of Delhi was observed at 14.0 per 100,000 based on the 2012-2014 data. The Highest ASIR were reported in West Arunachal Papumpare district with 27.7 per 100,000 and the lowest was 4.8 per 100,000 in Dibrugarh district respectively(Report of National Cancer Registry Program, 2020).

The median age at onset of disease varies worldwide. The median age at diagnosis for cervical cancer reported in Asian countries including India is higher than in Western countries. The change in median age at the onset of the disease may be due to demographical changes like population aging and growth, improvement in risk factors, and the health care system. No study has assessed the trend of standardised median age at diagnosis of cervical cancer in India.

Effective control of cancer planning needs accurate statistics, as well as high-quality data and a health monitoring system. The trend helps in evaluating the past behaviours of data and projections are needed for making strategies for resource allocation for early diagnosis, therapeutic management, and palliative services for future patients and cancer survivors. In addition to these, it provides a baseline from which the success of future interventions can be assessed (Bray and Moller, 2006). The Age-Period-Cohort (APC) model worldwide is used to study the time trend and projection of future burden of cancer incidence (Poirier et al., 2019; Smittenaar et al., 2016). There are few studies published in India using the APC model for assessing the temporal trend of various cancer sites (Sathishkumar et al., 2021; Malhotra et al., 2018), and one study used the APC model for projection (Malhotra et al., 2019). No study was found from India that projected cervical cancer using APC models and reports the net change according to decomposition analysis.

The objectives of the present study were to (1) update the temporal trend of cervical cancer using the natural cubic splines age-period-cohort model, (2) Evaluate the trend of standardised median age at diagnosis and percentage of cervical cancer to total women cancers over the 25-years period, (3) Forecast the cervical cancer incidence in Delhi up to the year 2030, (4) Decomposition of net change into three major components - population aging, population growth, and age-specific incidence. The past data trend, projection, and the number of new cases were further stratified to less than 50 years, 50 years and above.

Materials and Methods

Incidence Data

The data for present study was extracted from the Delhi population-based cancer registry (PBCR), one of the longstanding cancer registries of India established in 1986. The cervical cancer cases diagnosed between 1990 and 2014 were obtained from this registry. This registry fulfilled the IARC data quality standards and the data published in Cancer Incidence in Five Continents Volumes IX and volume X (Forman et al., 2014).

Region

Delhi is the capital of India carrying an area of the 1113.63 km2. According to the 2011 census, the total population of Delhi was 1, 67, 53,235(males and females) with 97.5% of people living in urban areas.

Population Data

The difference distribution method was performed on 1991, 2001, 2011 census data to get the risk population for calculating the age-wise incidence rate per 100,000 each year from 1990 to 2011 (Census of India, 2011; Takiar and Shobana, 2009). For future population projection (2016 to 2030) and for between 2011 to 2015 difference distribution method was applied to the recently published population projection report of the census of India that provides the age-wise projection of 2016, 2021, 2026, and 2031 (Census of India, 2020).

Statistical analysis

Age-specific incidence rates were calculated for sixteen age groups (0-4, 5-9, ...75+) and twenty-five calendar periods from 1990 to 2014 (1-year intervals). Age-standardised incidence rates per 100,000 (ASIRs) were calculated by the direct standardisation method using WHO World standard population distribution (Ahmad et al., 2019) as reference. We evaluated the incidence trend in the < 50 age group and >=50 age group as well as for total. The temporal trend in cervical cancer incidence from 1990 to 2014 was examined using JoinPoint regression software (United State national Cancer Institute; http://surveillance.cancer.gov/joinpoint). The standardised incidence of cervical cases was fitted to a log-linear model and applied Monte Carlo permutation test with 4999 permuted data sets to detect significant changes in the incidence rate trends (Joinpoint Regression Program, 2020; Kim et al., 2000). We applied a maximum number of 4 Joinpoints to <50 years, >=50 years, and for total, allowing up to the maximum five distinct segments. The estimated annual percentage change (EAPC) was calculated and considered as significant if the respective 95% confidence interval is not included in zero. A rising trend was observed when EAPC was greater than zero and a significant decline trend was observed when EAPC was less than zero and significant.

The APC regression was performed to investigate the independent effect of age, calendar, and birth cohort on the incidence of cervical cancer. The risk of cancer increases with age and depicts the risk associated across the multiple age groups. Moreover, period effects reflect the factor that influences all the age-group simultaneously, such as screening programming assuming it is implemented to all-age groups, not to a specific group. Cohort effects are historical exposure like war, pandemic, external exposure, and lifestyle changes. The four classic age-period-cohort plots are used to explain the incidence of cervical cancer (1) Incidence by age for different periods;

(2) Incidence by period for different age-groups; (3) Incidence by cohort for different age groups; (4) Incidence by age for different cohorts

The median age at diagnosis of each year was calculated using the group method. The direct method of standardisation was used to calculate the age-standardised median age at diagnosis using WHO World standard population distribution. The linear and polynomial regression was applied to assess the trend of median age of diagnosis and percentage of change in the proportion of cervical cancer to total female cancer over a 25-year period. Method used for determination of age-standardised percentage for a required year is : First calculate the expected number of incidences cases in standard population for ith age-group = $\frac{I_i \times S_i}{Y_i}$; where I_i= Incidence cases in the ith age-group; S_i = WHO standard population values in ith age-group having sum of all the age-group as 100,000; Y_i =population at risk in the it age-group of respective year; i = 1, . . ,. A (maximum A=16). Then age-standardised percentage in the ith age-group is calculating using this formula

$$\frac{(I_i \times S_i)/Y_i \ \times 100}{\sum_{i=1}^{A} (I_i \times S_i)/Y_i}$$

Method of projection

The cervical cancer projection for all age groups combined, as well as for two age groups <50 years and >=50 years were performed with the age-period-cohort method described by Carstensen (2007). Poisson, Negative binomial, and power of 5 function applied using STATA apcspline command, with counts as a dependent variable and corresponding log of the population as an offset. All the three variables age, period, and cohort treated as continuous and using natural cubic splines to model non-linear patterns. Smoothing method used age, period, and cohort terms as varying continuously and provides a better fitting model than the commonly used practice APC model that takes these terms as a factor (Mistry et al., 2011). The model fit was assessed using the lowest Akaike Information Criteria (AIC)-. The comparison was done for selecting among the three as well as for the selection of appropriate knots.

This method used the existing cohort effects for the future and allowed the drift to continue but attenuated on the assumption that the past trend will not continue indefinitely. A damping rate of 8% each year chosen and this attenuated drifts effects reduction by nearly 50% over 8-years on the linear trend (Moller et al., 2003).

To get reliable estimates the age 20-75+ were included in the model because cervical cancer rarely occurred in less than 20 years females. We also report observed and projected numbers of incidence under four age-groups 40-49, 50-59,60-69, and 70+ years.

Decomposition

Further, using average 2010-2014 incidence cases as the reference year, we decompose the drivers of the increase in the number of cervical cancers in Delhi from 2015 to 2030 in three components: population growth, population aging, and changes in age-specific incidence rate. The change in age-incidence rate represents epidemiology changes, including the changes in new cases that cannot be explained by aging and population growth, like the prevalence of HPV, screening availability, awareness about cervical cancer, lifestyle changes, etc. The net change is equal to the sum of these three components and the decomposition was performed using the validated algorithm (Bashir and Esteve, 2000).

The STATA(Version 12.0, Stata Corporation, College Station, TX) statistical software (Sasieni , 2012) and Epi package available in R-software(EPI,2013) were applied for analysis and making graphs.

Ethics Approval

No ethical approval and patient consent were needed because our study used existing tabulated data from Delhi PBCR.

Results

Between 1990 to 2014 a total of 20,505 females were diagnosed with cervical cancer contributing 14.6% of total female cancers. Out of these below 50 years were 9095 and >=50 years were 1410 cases with the ratio of 1:1.25. The percentage of women diagnosed in >=50 was 49% in 1990-94 and this percentage was increased to 61% in 2010-2014. The unstandardised and standardised median age at diagnosis of cervical cancer was (47.1 to 53.8) years and (51.0 to 56.7) years from 1990 to 2014 and 51.3 years and 56.2 years respectively in combined 25-year period.

JoinPoint analysis

The age-standardised incidence rate of cervical cancer declined by 56.6% from 32.7 in 1990 to 14.19, per 100,000 in 2014. The average crude and age standardised average incidence rate of cervical cancer was 13.89 and 20.02 per 100,000 respectively during the 25-years. The overall decline trend of ASIRs was observed in cervical cancer with EAPC= -2.98(95% CI: -3.48 to -2.47). Similar decline trend reflected in 50+ years women with EAPC = -2.42(95% CI: -2.98 to -1.86). Whereas less than 50 years women a rapid decline trend was observed until the year-2000 with EAPC=-7.26(95% CI: -9.98 to -4.45) and thereafter APC of decline trend closer to the EAPC of total and 50+ years women (Figure 1).

Temporal trend of median age of diagnosis and age-standardised percentage change

The trend of standardised median age at diagnosis showed an upward movement with a linear significant slope of 0.167 per year on an average (Figure 2A) and the total increase during 25-years will be 4.18 (0.167±25) years. However, the actual standardised median age at diagnosis was 51.01 in 1990 which increased to 56.67 years in 2014. The percentage of cervical cancer to total female cancer decreased significantly from 21.86% in1990 to 9.63% in 2014, with a linear trend of -0.474% per year on an average (Figure 2B). Figure 2C depicts the comparison of age-standardised percentages at diagnosis for cervical cancers between 1990 and 2014. The main

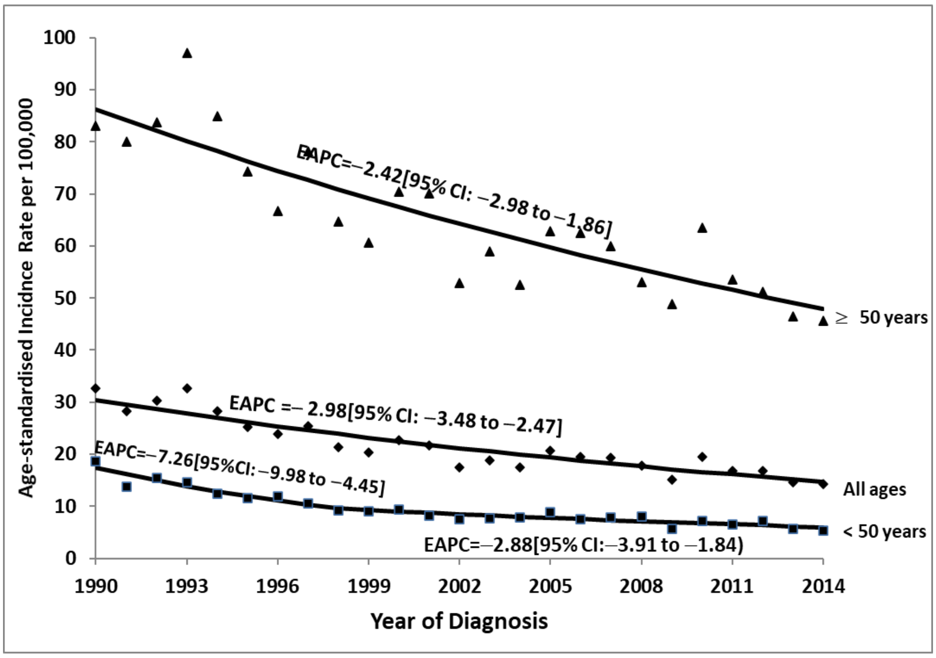

Figure 1. Age-Standardised Incidence Rate for Cervical Cancer <50 years, ≥50 years, and Total from 1990-2014. EAPC, Estimated Annual Percentage Change

peak and secondary peak appeared during 1990 in age-group 40-44 years and 45-49 years, while in 2014 these peaks moved to 60-64 years and 50-54 respectively (Figure 2C). These two-year percentages were comparable because these percentages were standardised according to the World WHO population 2000. Furthermore, figure 2D represents the change in women population distribution from 1990 to 2014. The figure clearly showed in 1990, Delhi population skewed towards the younger population and usually had a cone-shaped population pyramid while in 2014 distribution had less skewed and the peak shifted from 0-4 years to 20-24 years, and the distribution of females after 29 years higher percentage in 2014 compared to the year 1990.

Age-period-cohort analysis

Figure 3 (AP), the classic age period cohort diagram, reveals that the incidence rate increases exponentially with age, and the peak reaches nearly 63 years in all the 5-year periods. There is clearly a non-linear age effect of cervical cancers in all five periods. However, the most recent period had the lowest incidence rate while the oldest period had the highest incidence rate in almost all the age groups. A sharp decrease was observed in the

Table 1. Estimated Age-Specific and Total Incidence Cases of Cervical Cancer from 2015 to 2030

Year	Incidence cases of age-specific and total cervical cancer*											Total
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+	
2015	2	9	29	66	110	140	136	133	136	98	55	51	965
2016	2	9	28	64	110	141	139	135	132	103	58	54	974
2017	2	8	27	62	108	140	139	136	132	102	60	56	972
2018	1	8	26	61	106	139	140	138	132	101	62	59	972
2019	1	8	25	60	105	138	141	139	132	101	64	61	975
2020	1	7	24	59	104	138	142	142	133	100	66	64	981
2021	1	7	23	58	103	138	144	144	135	100	68	67	989
2022	1	7	23	57	102	138	144	146	138	101	68	70	996
2023	1	7	23	56	102	138	145	149	141	102	68	73	1005
2024	1	6	23	55	102	138	147	152	144	103	68	76	1016
2025	1	6	23	55	102	139	148	155	148	105	69	79	1029
2026	1	6	23	54	102	139	150	159	152	107	69	82	1044
2027	1	6	22	55	102	140	151	161	156	110	70	84	1057
2028	1	6	22	55	101	140	152	163	160	113	72	86	1072
2029	1	6	22	55	101	142	154	166	165	117	73	88	1089
2030	1	5	22	56	101	143	155	169	169	121	75	91	1108

Table 2. Contribution of Changes due Population Aging, Population Growth, and Risk Factors to a Net Change of Incidence Cases of Cervical Cancer in Delhi from 2015 to 2030, using average(993) of (2010-2014) as the reference year

Year	Change in cervical cancer cases due to population aging	% Change due to population aging	Change in cervical cancer cases due to population	% Change due to population growth	Change in cervical cancer cases due to age-specific incidence rate	% Change due to age-specific incidence rate	New Change	% Change from an average of 2010-2104
2015	53	5.34	62	6.24	-143	-14.40	-27	-2.72
2016	76	7.65	88	8.86	-188	-18.93	-19	-191
2018	120	12.08	121	12.19	-262	-26.38	-21	-2.11
2020	164	16.52	157	15.81	-333	-33.53	-12	-1.21
2021	186	18.73	175	17.62	-365	-36.75	-4	0.40
2022	209	21.04	191	19.23	-397	-39.98	3	0.30
2023	230	23.16	208	20.95	-426	-42.90	12	1.21
2024	253	25.48	226	22.76	-455	-45.82	23	2.32
2025	276	27.79	244	24.57	-483	-48.64	36	3.63
2026	298	30.01	263	26.49	-510	-51.36	51	5.14
2027	320	32.23	279	28.10	-535	-53.88	64	6.44
2028	341	34.34	298	30.10	-560	-56.39	79	7.96
2029	363	36.56	316	31.82	-584	-58.81	96	9.67
2030	386	38.87	336	33.84	-606	-61.03	115	11.58

younger age group(<50 years) till the year 2000 and in 50+ age-group had consistent decrease in incidence rate. Nearly all the age groups showed a downfall except 60 to 69 years which showed a flat trend (Figure 3, PA). However, both AP and PA curves are parallel providing evidence of a period effect. The older birth cohort had

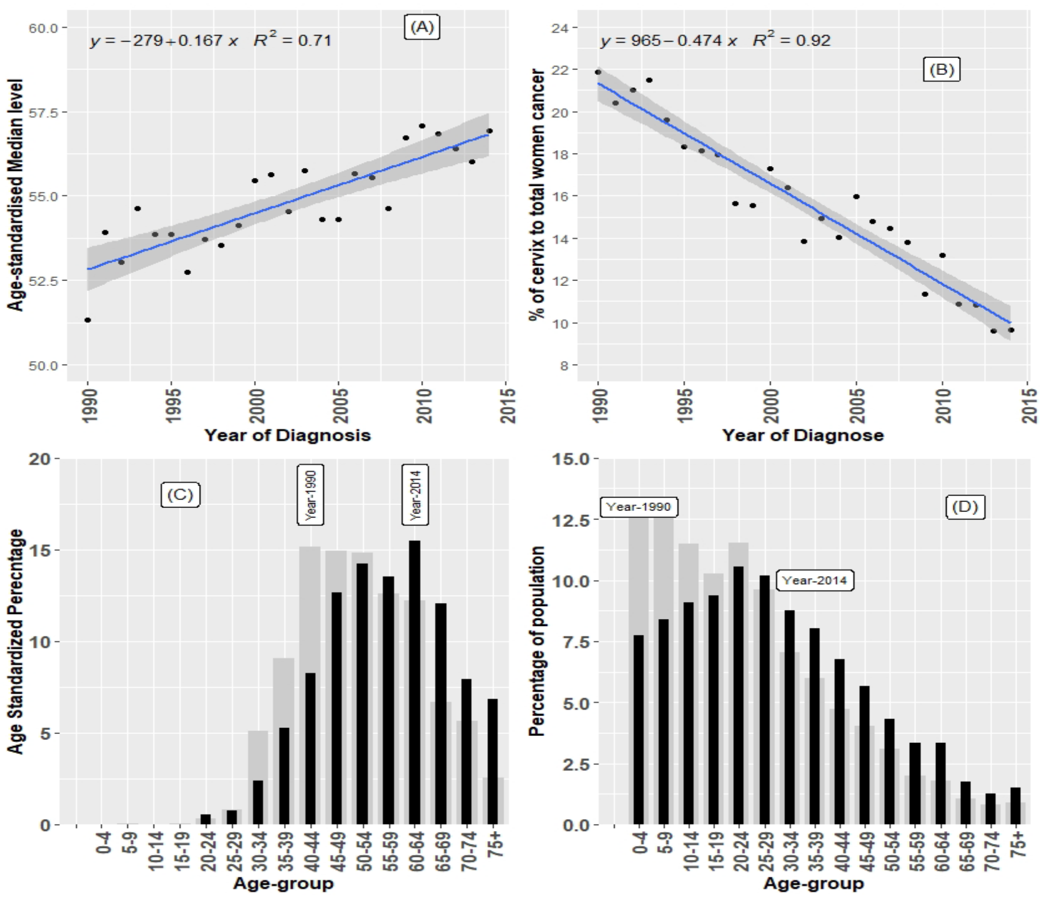

Figure 2. (A) Trend of standardised median age at diagnosis (B) Percentage change in cervix cancer to total women cancers (C) Age-standardised percentage change in 1990 and 2014 by 5-year age groups(D) Distribution of Indian population in 1990 and 2014 by 5-year age groups

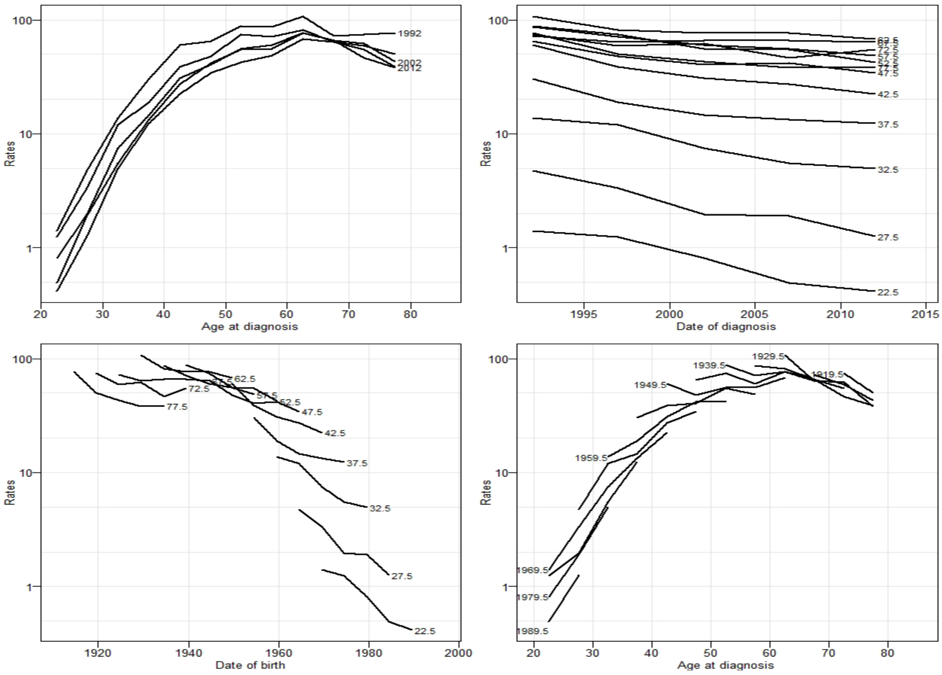

Figure 3. Incidence Rates of Cervical Cancer in Women per 100,000 PY by Age, Period, Cohort. (AP) age by period; (PA) period by age, (CA) Birth cohort by age (AC) age by birth cohort. In AP plot 1992, ... ,2012 lines represents the period 1990-1994, ... 2010-2014 respectively, Age-group are labelled at the middle point of the age-interval like 37.5=35-39 and Birth cohort are results of period-age

less decrease in incidence as compared to the younger birth cohort. (Figure 3 CA). The cohort effect suggested a non-linear effect because the younger cohort was somewhat parallel to the older cohort.

Projections

Power-5 function link APC model with seven internal knots for age, five knots for the period, and four knots for the cohort were chosen based on lower AIC. The projected cervical cancer ASIR in all age-group in 2030 will be 8.91 cases per 100,000. While in lower than 50 years women ASIR will be 3.25 cases per 100,000 and will be 29.22 cases per 100,000 in 50+ women in the year 2030 (Figure 4). The projected incidence cases of cervical cancer will be reached to 328, 780, and 1108 for <50 years, >=50 years, and for total respectively. The age-specific projection of cancer cases from 2015 to 2030 is presented in Table 1. Figure 5 represents the observed and predicted age-standardised incidence rates according to the four major age groups.

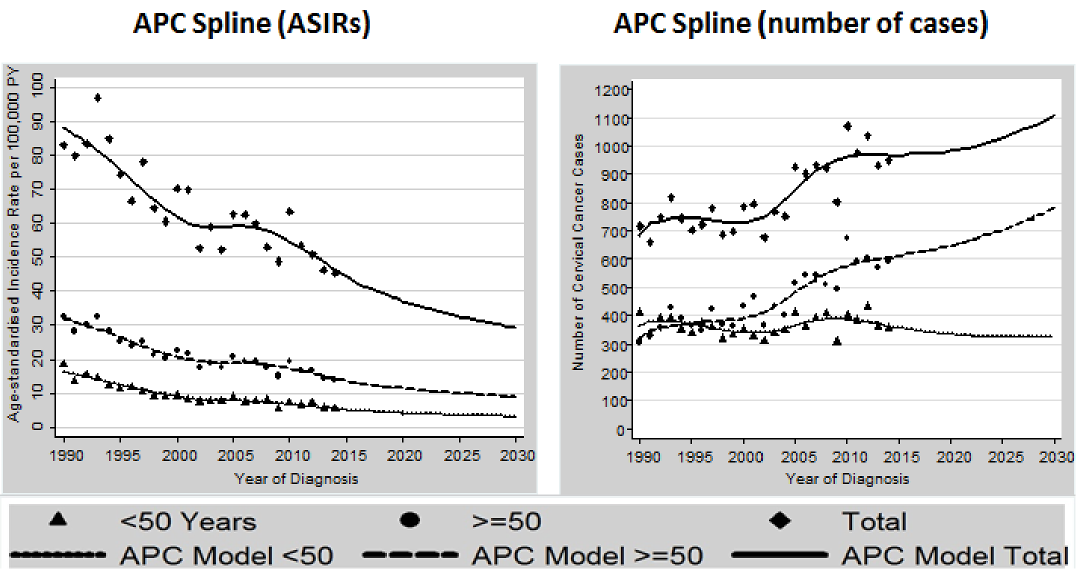

Figure 4. Observed (Filled Circle) and Projected (Lines) of Age-Standardized Incidence Rate and the Number of Cases of Cervical Cancer

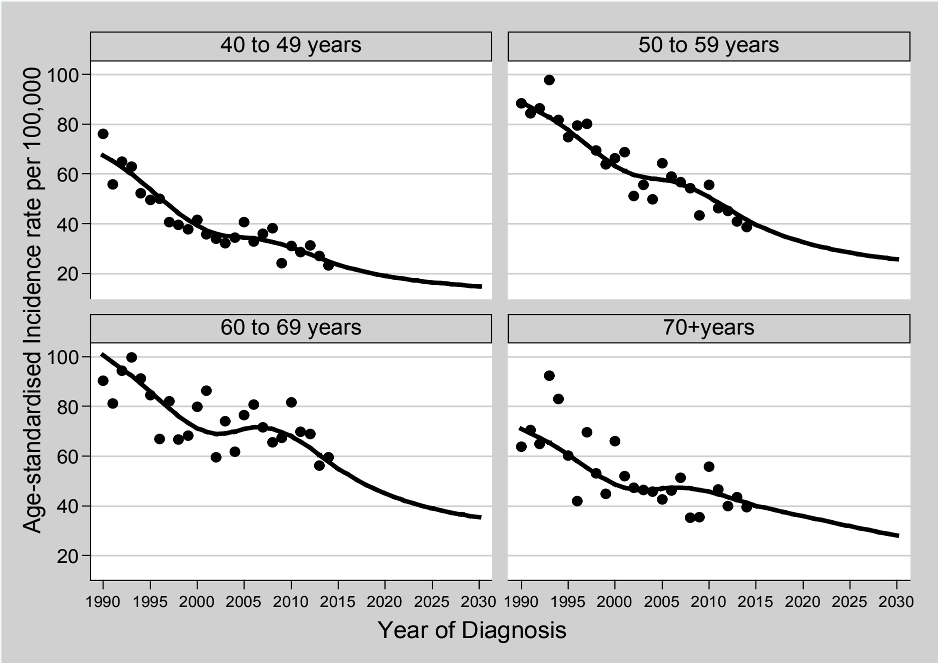

Figure 5. Age-Standardised Incidence Rate Observed (Filled Circle) and Projected (Lines) in Four Major Age-Group for Cervical Cancer in Delhi

Decomposition analysis

The demographical decomposition analysis was conducted to find the potential epidemiology factors of incidence cases of cervical cancer from 2015 to 2030. Our finding suggests that population growth and population aging play a vital role in increasing the incidence of cervical cancer in Delhi.

There was an increase of 11.58% in cervical cancer cases in 2030 compared to the average incidence cases of 2010-2014 and the decline in ASIR was 43.8%. The factors for increasing the new cervical cancer cases were population aging (38.87%) and population growth (33.84%) whereas age-specific rates showed a decline of 61.03% (Table 2).

Discussion

The key findings of the present study are --(1) A decline in ASIR cervical cancer in Delhi from 1990 to 2014; (2) Decreasing trend in the percentage of cervical cancer to total women cancers over the same period ; (3) Shifting the peak of age-standardised percentage from 40-44 years in 1990 to 60-64 years in 2014; (4) A significant increase in median age at diagnosis by average of 4.18 years from 1990 to 2014; (5) Net increase of cervical cancer case would be by 12% in 2030 compared to an average of 2010-2014, despite a decrease in ASIRs by 43.8%. The main factors for new cervical cancer cases rising were aging and population growth.

Our study revealed that on an average every seventh women's cancer was attributable to cervical cancer for 25-years period. However, a significant decline trend was observed in cervical cancer percentage to total women cancer with an annual decline of -0.474 that showing the contribution of cervical cancer reduced to one in every 10th women cancer in 2014 and corroborate with other Indian PBCRs such as Pune and Kolkata based on 2012-2016 data (Report of National Cancer Registry, 2020). The contribution of less than 50 years and 50+years was nearly equal during 1990-94 (1:1) and this change to 2:3 in 2010-2014 indicated the number of cases is reducing in younger women (<50 years) than 50+ that confirming the shifting of cervical cancer incidence from pre-menopause to post-menopause women in Delhi. In addition, our Cohort-age graphs also revealed that younger women has a greater decline than older.

The unstandardised median age at diagnosis was 53.8 in the year 2014, which is almost identical to the global median age at diagnosis of cervical cancer (53 years) while higher than Vanuatu (44 years) and lower than Singapore (68 years) (Arbyn et al., 2020). An increasing trend in standardised median at diagnosis was primarily due to a shifting in the age-standardised percentage from 40-44 years in 1990 to 60-64 years in 2014. Parallel period curves with a peak nearly at the same age reflect the less likely period effect on the median age trend. Changes may be due to cohort effects like education enhancement, and changes in social culture factors. However, in China, a negative trend of standardised average age at diagnosis over a period was observed (Li et al., 2017). The decreasing trend of median age was also observed in a US study from 53 years in 1974-78 to 47 in 1990-2003 (Hayat et al., 2007).

Globally, the cervical cancer ASIR declined, albeit some countries like East Asia and Southern sub-Saharan Africa showed an upward trend (Zhang et al., 2019)). Our study revealed a declining trend with EAPC -3.0% which was marginally higher than EAPC reported in Khon Kaen Thailand (-2.8.%; 1990-2014) (Saenrueang et al., 2019). The decline of cervical cancer is primarily a result of the change in preventive measures such as behaviours of social culture factors, improvement in health care services, enhancement in the literacy rate, delay in marriage age, and family planning behaviours (Vu et al., 2018). During this period, Delhi observed a decrease in total fertility rate, an increase in the average age of marriage, improvement in health care facilities, literacy rate, and good hygienic practices (Park, 2015; National Family Health Survey (NFHS-4), 2015-2016), and women empowerment. Other factors, such as HPV vaccination for girls aged 12 years and a hospital-based cervical cancer screening program that started in Delhi 2016. The effect of these two programs would reflect after 20 and 30 years.

However, some cervical cancer risk factors showed an upward trend like smoking in women (Mishra et al., 2016), and promiscuous sexual behaviours among the young population.

Countries having effective screening programs for a long time observed a decrease in cohort-led effect while other countries either increase or stable effect in cervical cancer ASIR was observed (Vaccarella et al., 2013). In India, still, cervical cancer screening program is in the preliminary stage, and in 2016 Indian Government recommended visual inspection with acetic acid every 5-year for women aged 30-65 years, but still, this screening program is limited to hospitals only(Sankaranarayanan et al., 2019). A community-screening program for cervical cancer is still lacking. In 2030 the cervical cases will be increased by 12% compared to an average of 2010-2014 whereas a Western Study reported the change closer to 0% in 2030 compared to 2007 (Mistry et al., 2011). Aging and change in population structure are two main reasons for the increase in cervical cancer cases. Some of the cancer registries in China have reported an increase in cervical cancer after a steep decline primarily due to altering sexual behaviour in the younger population (Krishnamoorthy et al., 2021). The change in sexual behaviour leads to an increase in the likelihood of infection with human papillomavirus (HPV) which is a well-known cause of cervical cancer. However, Indian major PBCRs showed a consistent downtrend in cervical cancer (Sathishkumar et al., 2021).

Strength and Limitation

The data was ascertained from Delhi PBCR which is a well-established registry that has complete coverage and has been collecting high-quality data. On an average 85% of cervical cancer diagnosed were microscopically verified. The estimated population has been taken from the Indian census report to calculate future ASIRs and incidence cases, which incorporated immigration and fertility in the projection of the population. Thus, projected ASIRs and incidence cases will be robust.

However, the caveat is that the latest incidence data available in Delhi PBCR is until 2014. Moreover, due to cervical cancer diversity within India, our findings cannot be generalised to whole of the country.

In conclusion, the present study concludes the gap of ratios between pre and post-menopause women increased during 25-years period and will continue to increase further. The standardised median age at onset of disease increased to confirm this statement. The age-standardised incidence rate of cervical cancer was declining in both pre and post-menopausal women as well as in total. However, new cases of cervical cancer are increasing due to aging and shifting in population structure. To counter this big challenge a cost-effective vaccination, community-based screening program, and enhancement of awareness of these two programs might substantially help in potentially eliminating cervical cancer.

Author Contribution Statement

RKM, NM, SVS Deo contributed in conceptualizing of the study. RKM, NM extracts the data, analyse these data. All three authors contributed in interpret the results, writing, editing and finalising the manuscript.

Acknowledgments

This study does not require any ethical and patient consent because study data are already available in the public domains via websites and individual year monographs

Availability of data

The majority of data are available in website (http://ncdirindia.org/ncrp/Annual_reports.aspx). However, some of data are available in hardcopy and in the custody of Delhi cancer registry in the form of monographs.

Conflict of Interest

There is no conflict of interest among the authors

References

Ahmad OB, Boschi-Pinto C, Lopez AD, et al (2019). Age standardization of rates: A new WHO standard. World Health Organization; 2001. available from: http://www.who.int/healthinfo/paper31.pdf, accessed November 9, 2021

Arbyn M, Weiderpass E, Bruni L, et al (2020). Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *Lancet Glob Health*, **8**, 191-203.

Bashir S, Estève J (2000). Analysing the difference due to risk and demographic factors for incidence or mortality. *Int J Epidemiol*, **29**, 878-84.

Bray F, Moller B (2006). Predicting the future burden of cancer. *Nat Rev Cancer*, **6**, 63 – 74.

Carstensen B (2007). Age-period-cohort models for the Lexis diagram. *Stat Med*, **26**, 3018-45.

Census of India (2020). Report of the technical group on population projection for India and states 2011-2036. Available from Population Projection Report 2011-2036 - upload_compressed_0.pdf (mohfw.gov.in), accessed December 10, 2021.

Census of India, Registrar General of India(2014). C-13 tables single-year age data.. Available from: https://www.censusindia.gov.in/2011 census/population_enumeration.html, accessed November 24, 2021.

Epi (2013). A package for statistical Analysis in Epidemiology [Homepage on the Internet]: R package version 1.1.49;c2013. Available from: Http://CRAN.R-project.org/package=EPI.

Forman D, Bray F, Brewster DH, et al. editors. Cancer Incidence in five continents Vol. X International Agency for Research on Cancer scientific publication no. 164, IARC Lyon, France, pp 550.

Hayat MJ, Howlader N, Reichman ME, Edwards BK (2007). Cancer statistics, trends, and multiple primary cancer analysis from surveillance epidemiology, and end results (SEER) program. *Oncologist*, **12**, 20-37.

Joinpoint Regression Program, Version 4.8.0.1 - April 2020; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute.

Kim HJ, Fay MP, Feuer EJ, Midthune DN (2000). Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med*, **19**, 335-51.

Krishnamoorthy Y, Rajaa S, Giriyappa DK (2021). Global pattern and trend of cervical cancer incidence from 1993 to 2012: Joinpoint regression and age-period-cohort analysis. *Indian J Cancer*, **10**, 4103/ijc.IJC_1043_19.

Li X, Zheng R, Li X, et al (2017). Trends of incidence rate and age at diagnosis for cervical cancer in China, from 2000 to 2014. *Chin J Cancer Res*, **29**, 477-86.

Malhotra RK, Manoharan N, Nair O, Deo SVS, Rath GK (2018). Trends in Lung cancer incidence in Delhi, India 1998-2012: Age-period-cohort model and joinpoint analyses. *Asian Pac J Cancer Prev*, **19**, 1647-54.

Malhotra RK, Manoharan N, Nair O, Deo SVS, Rath GK (2019). Trends and future burden of Tobacco-related cancers incidence in Delhi urban areas: 1998-2001. *Indian J Public Health*, **63**, 33-8.

Mishra S, Joseph RA, Gupta PC, et al (2016). Trends in bidi and cigarette smoking in India from 1998 to 2015, by age, gender and education. *BMJ Glob Health*, **1**, e000005

Mistry M, Parkin DM, Ahmad AS, Sasieni P (2011). Cancer incidence in the United Kingdom: projections to the year 2030. *Br J Cancer*, **105**, 1795-803.

Møller B, Fekjaer H, Hakulinen T, et al (2003). Prediction of cancer incidence in the Nordic countries: empirical comparison of different approaches. *Stat Med*, **22**, 2751-66. doi: 10.1002/sim.1481.

National Family Health Survey (NFHS-4), 2015-2016: India. Mumbai, India: international Institute for Population Sciences, Available from:2017http://rchiips.org/nfhs/NFHS-4Reports/India.pdf.(Accessed 16 March 2022).

Park K(2015). Demography and family planning. In: Park's Textbook of Social & Preventive Medicine. BanarsidasBhanot; Jabalpur 23rd edition, pp 470-519.

Poirier AE, Ruan Y, Walter SD, et al (2019). The future burden of cancer in Canada: Long-term cancer incidence projections 2013-2042. *Cancer Epidemiol*, **59**, 199-207.

Report of National Cancer Registry Programme. National Centre for Disease Infromatics and Research, Bengaluru, India. 2020. Available from: https://www.ncdirindia.org/All_Reports/Report_2020/default.aspx, Accessed November10, 2021.

Saenrueang T, Promthet S, Kamsa-Ard S, Pengsaa P (2019). Cervical Cancer in KhonKaen, Thailand: Analysis of 1990-2014 Incidence Data and Prediction of Future Trends. *Asian Pac J Cancer Prev*, **20**, 369-75.

Sankaranarayanan R, Basu P, Kaur P, et al (2019) Current status of human papillomavirus vaccination in India's cervical cancer prevention efforts. *Lancet Oncol*, **20**, 637-44.

Sasieni PD (2012). Age–Period–Cohort Models in Stata. *Stata J*, **12**, 45-60.

Sathishkumar K, Vinodh N, Badwe RA, et al (2021). Trends in breast and cervical cancer in India under National Cancer Registry Programme: An Age-Period-Cohort analysis. *Cancer Epidemiol*, **74**, 101982.

Smittenaar CR, Petersen KA, Stewart K, MoittN (2016). Cancer incidence and mortality projections in the UK until 2035. *Br J Cancer*, **115**, 1147-55.

Takiar R, Shobana B (2009). Cancer Incidence rates and the problem of denominators - A new approach in Indian cancer registries. *Asian Pac J Cancer Prev*, **10**, 123-6.

Vaccarella S, Lortet-Tieulent J, Plummer M, Franceschi S, Bray F(2013). Worldwide trends in cervical cancer incidence: Impact of screening against in disease risk factors. *Eur J Cancer*, **49**, 3262-73.

Vu M, Yu J, Awolude OA, Chuang L (2018). Cervical cancer worldwide. *Curr Probl Cancer*, **42**, 457-65.

World Health Organisation (2020). CANCER TODAY International agency for research on cancer. Available from: https://gco.iarc.fr/today/online-analysis-table, accessed November 20, 2021.

Zhang X, Zeng Q, Cai W, Ruan W (2021). Trends of cervical cancer at global, regional, and national level: data from the Global Burden of Disease study 2019. *BMC Public Health*, **21**, 894.