Original Research Paper

Pathology

TIME TRENDS IN LEADING SITES OF CANCER AMONG FEMALES OF DIBRUGARH DISTRICT: 2004-2013

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ABSTRACT   Cancer figure among the leading causes of morbidity and mortality worldwide. The overall incidence of cancer is known to rise with increasing age The increase in population due to growth also contributes to the increase in the number of cancer cases. One measure of determining such an increase would be to examine the age adjusted incidence rates (AAR) over time which is achieved through time trend analysis of incidence rates. The study population, Dibrugarh District is predominantly a rural district where 80% of population are rural. Though the overall incidence of cancer cases increases gradually over the years ,the incidence among females has showed an higher increase than compared to the male incident cases in the district. The present study endeavors to analyze trends in incidence in five leading sites namely Breast, Oesophagus, Gall Bladder, Ovary and Cervix Uteri cancers among females of Dibrugarh District during the period 2004-2013.Incidence data from Population Based Cancer Registry of Dibrugarh district for the period of 2004-2013 were used. Incidence Crude and Age Adjusted Rates(AAR) were calculated. Time trends were obtained by using Jointpoint Regression Model. The time trend analysis suggested a statistically significant increasing trend in AARs of gall bladder with an annual percent change (APC) of 3.97%.over time. No statistically significant changes in AARs of Breast, Oesophagus, Ovary and Cervix Uteri were observed over the period.. It is concluded that though Breast was the leading site of cancer among females of Dibrugarh District, the incidence of Gall Bladder has increased alarmingly over the period.

INTRODUCTION :

Cancer figure among the leading causes of morbidity and mortality worldwide. The present cancer burden is quite alarming at 25 million globally and 2 to 2.5 million cancer patients in India with about 0.7 million new cases coming every year and nearly half die every year. The overall incidence of cancer is known to rise with increasing age. Control of communicable diseases, has increased life expectancy and therefore more of the population live longer resulting in a greater population in the older age groups. The increase in population due to growth also contributes to the increase in the number of cancer cases. The question is whether cancer is on the increase after accounting for the factor age and whether that rise is statistically significant.

One measure of determining such an increase would be to examine the age adjusted incidence rates (AAR) over time which is achieved through time trend analysis of incidence rates. Trend analysis is a technique that aims to identify a pattern of change, or trend in a series of observations. In cancer epidemiology, the series of observations are the incidence rates.

Monitoring cancer trends is one of the most important functions of cancer surveillance system. Change in occurrence for a particular cancer in a population often instigates research on potential reasons for the observed increase or decrease in cancer rates. Monitoring cancer trends is also important to evaluate the efficiency of cancer screening or detection methods, as well as to determine priorities in cancer control programs. Moreover, change in incidence of a specific cancer over a period of time would indicate changes in life-style and exposure to various factors of etiologic importance.

There has been a spike in cancer cases among women over recent years with breast cancer being of particular concern as it is found to be increasing in both developed and developing countries in the world. Cancers of the female breast and reproductive tract has a high incidence amongst Indian women. Around 50-60% of all cancers among women in India pertains to mainly four organs- breast, ovary, cervis uteri and corpus uteri.These cancers exercise an adverse influence on the productive role of women in the society.

It has been observed that there are marked variations in pattern and incidence rate of cancer between different countries, within the country, within the region as well due to customs, life-style, food habits, diverse ethnic groups etc. For that incidence of common cancers like Gallbladder, Oesophagus, Lung and Stomach among north eastern females are relatively vary high as compared to national figure. So it is important to see the pattern and incidence of cancer cases in a defined geographical area and to see whether certain types of cancers are on the rise in the area.

In Dibrugarh District, it has been observed that though the overall incidence of cancer cases increases gradually over the years; the ,the incidence among females has showed an higher increase than compared to the male incident cases in the district. It has also been observed that the trends of certain cancers particularly among female viz gallbladder, breast and ovary have been gradually rising and vice versa for cervix uteri over the years. Morever, oesophagus cancers has been the most common cancers overall.

The Registry and The Study Population : A Population Based Cancer Registry under the National Cancer Registry Programme (NCRP) of Indian Council of Medical Research (ICMR) has been functioning at Assam Medical Collage, Dibrugarh, Assam since 2003. The main objectives of the registry is to generate reliable data on the magnitude and patterns of cancer in the district and to undertake epidemiological studies based on results of registry data. Cancer is not a notifiable disease in India. Hence the registration of cancer cases is done by active method on a routine basis. Data on incident cancer cases have been collected by direct interview of the patient/attendant and /or from the medical records by visiting around 83 sources of registration in the district .Incident cases, who has been residing within the geographical area of Dibrugarh district for at least a year prior to the date of first diagnosis of cancer are included in the registry. Only invasive cancers are registered. The first 10 years data were very much crucial for a registry point of view that usually depicts the initial tread for the future. For that reason registry data from 2004 to 2013 has been analyzed for the study.

The study population Dibrugarh District covering an area of 3381 sq. km is situated on the south bank of the mighty river Brahmaputra in the eastern part of the state of Assam. Dibrugarh is predominantly a rural district where 81.6 % population are rural. Total population of the district is 13,26,335 out of which 6,76,434 are males and 6,49,901 are females. The male –female ratio is 961 females/1000 males. There are 7 towns in the district and 1348 villages which includes 160 tea gardens having workforce constituting 16.6% of the total population. This demographic figures are as per 2011 census report.

OBJECTIVES OF THE STUDY :
The main objectives of the study is to see whether there are an significant increases or decreases of cancer cases in specific sites among females of the district. So the study endeavors to analyze trends in cancer incidence among females of Dibrugarh district for the period between 2004 and 2013.Trends are presented for all sites as a whole and for five leading sites of cancers among females of the district viz breast, oesophagus, gallbladder, ovary and cervix uteri.

DATABASE AND METHODS :
Incidence data from Population Based Cancer Registry of Dibrugarh District for the period of 2004-2013 were used. For the estimation of the mid year population the Exponential Growth Rate Method was used and Difference Distribution Method was used to estimate the five yearly age group population. Incidence Crude (CR)and Age Adjusted rates(AAR) were calculated. In determining the significance of trends, the actual value of AAR for single year the Joinpoint Regression Program of the NCI of USA has been used.

Definations:
Incidence : Cancer incidence denotes new cases diagnosed in a defined population in a specific time period. For this study all registered cancer cases diagnosed from 1 January 2004 to 31 December 2013 in Dibrugarh District were included.

Rates : Rates for cancer are always expressed per 100,000 population.

Crude Incidence Rate (CR) : This refers to the rate obtained by division of the total number of cancer cases by the corresponding estimated population (mid-year) and multiplying by 100,000.

$$CR = \frac{\text{New cases of cancer of a particular year}}{\text{Estimated population of the same year}} \times 100,000$$

Age Adjusted Rate (AAR) : Age Adjusted or Age Standardized Rates are weighted average of age specific rates(ASpR), where the weights represents the age distribution of a standard population. Such adjustment eliminates difference in rates due to change in the age of a population over time, or due to difference in age distribution between population groups. The world standard population (by WHO)is used as a standard population to calculate AARs in cancer cases.

$$AAR = \frac{\sum (ASpR) \times (\text{No. of persons in Std. world population in 5 yr. age group})}{100,000}$$

Where,

$$ASpR = \frac{\text{New cases of cancer of a particular year in the given age group}}{\text{Estimated population of the same year for the given age group}} \times 100,000$$

Annual Percentage Change (APC) : The estimated annual percent change (APC) represents the average percent increase or decrease in cancer rates per year over a specified period of time. It is calculated by first fitting a linear regression to the natural logarithm of the annual age adjusted rates(AAR), using calendar year as the predictor variable $\ln(AAR) = \alpha + b(\text{year})$. From the slope of the regression line, the APC is calculated as $APC = 100*(e^b - 1)$.Testing the hypothesis that the APC is equal to zero is equivalent to testing the hypothesis that the slope of the line of regression (b) is equal to zero. Statistical significance was set at alpha( ) =0.05.

About Joinpoint Regression Program:
Joinpoint Regression Program, version 4.8.0.1 is a statistical software for the analysis of trends using Joinpoint models, that is, where several different regression lines are connected together at the "Joinpoints". The Joinpoint program uses an algorithm that tests whether a multi-segment line is a significantly better fit than a straight line or less segment line. The software takes trend data (e.g. cancer rates) and fits the simplest Joinpoint model that the data allow. The user supplies the minimum and maximum number of joinpoints. The program starts with the minimum number of Joinpoints (e.g. 0 Joinpoint, which is a straight line) and tests whether more Joinpoints are statistically significant and must be added to the model (upto that maximum number). This enables the user to test an apparent change in the trend is statistically significant. The tests of significance use a Monte Carlo Permutation method. The models may incorporate estimated variation for each point (e.g. when the responses are age adjusted rates) or use a Poisson model of variation. In addition, the model may also be linear on the log of the response (e.g. for calculating annual percentage rate change).The software also allows viewing one graph for each Joinpoint model, from the model with minimum number of Joinpoint to the maximum number of Joinpoints . In this study, one Jointpoint model wherever feasible has been fitted to the data.

RESULTS AND OBSERVATIONS:
Table 1: Estimated Population at Risk: Dibrugarh District: 2004-2013

Male	Female	Total
6600844	6324383	12925227

Table 2 : Number of Incidence cases, Relative Proportions (%),Crude Incidence Rates (CR) and Age Adjusted Rates (AAR) per 100,000 persons at risk.
Dibrugarh District: 2004-2013

	Male	Female

No. of Cases	4786	3656
%	56.7	43.3
CR	72.2	57.8
AAR	97.3	74.1

During the year 2004-2013,altogether 8439 incident cases of cancer have been registered at PBCR, Dibrugarh of which 4786 (56.7%) were males and 3656(43.3%) were females. Overall average annual CR and AAR for males were 72.2 and 97.3 respectively. For females average annual CR and AAR were 57.8 and 74.1 respectively.

Table 3 : Year wise Crude (CR) and Age Adjusted (AAR) incidence rates per 100,000 females at risk: Dibrugarh District: 2004-2013

Female

Year	CR	AAR
2004	52.1	70.2
2005	57.9	79.3
2006	55.9	75
2007	57.3	77.9
2008	53.2	70.8
2009	54.9	69.9
2010	51.4	63.5
2011	57.5	70.3
2012	64.5	77.9
2013	72.1	85.1

The burden of cancer among females of the district increases with an increased in Crude Incidence rates from 52.1 in 2004 to 72.1 in 2013.The Age Adjusted rates also increases from 70.2 in 2004 to 85.1 per 100,000 females in 2013

Table 4: Number of cases (#), relative proportions (%) ,CR and AARs of top five cancers among females of Dibrugarh district : 2004-2013

Common Cancers	#	%	CR	AAR
Breast	617	16.9	9.8	11.6
Oesophagus	401	11.0	6.3	9.0
Gallbladder	361	9.9	5.7	7.7
Ovary	298	8.1	4.7	5.5
Cervix Uteri	287	7.9	4.5	5.6

The above table shows that 53.8% of all cancers among females in the district pertains to mainly five leading sites viz Breast (16.9%) followed by Oesophagus(11.0%),Gallbladder (9.9%),Ovary(8.1%) and Cervix Uteri(7.9%)

Table 5. Average Annual Age-Adjusted Cancer Incidence rates and Annual percent change(APC) among females of Dibrugarh District : 2004-2013

Site	Average annual AAR	Joinpoint Analysis (2004-2013)		
		APC	95% CI	P value
All Sites	74.1	0.4	(-1.8 , 2.7)	0.7
Breast	11.6	1.52	(-3.4 , 6.7)	0.5
Oesophagus	9.0	- 4.12	(-9.3 ,1.3)	0.1
Gallbladder	7.7	3.97*	(0.8 , 7.3)	<0.0001
Ovary	5.5	2.40	(-1.4 , 6.4)	0.2
Cervix Uteri	5.6	- 3.06	(-6.7 , 0.8)	0.1

*APC is significantly different from zero at alpha = 0.05

The AARs of cancer cases (all sites) among females of Dibrugarh District were remained unchanged over time; increased sharply for 2010 through 2013 which was not significant. (Table 6.1).

The year-wise AARs of breast cancer did not show any significant changes over time among females of the district,(Table 6.2).

A statistically not significant decreases in AARs of oesophagus cancer was seen with an annual percentage change(APC) of - 4.12 % (Table 6.3).

Gallbladder cancer among females of the district showed a statistically significant increase in AARs with an APC of 3.87 %.(Table 6.4). There was no statistically significant changes in the AARs over time for ovary cancer .(Table 6.5).

The time trend indicates a decline in AARs for Cervix uteri cancer among females of the district with an APC of - 3.46 % over the period, which was not statistically significant.(Table 6.6)
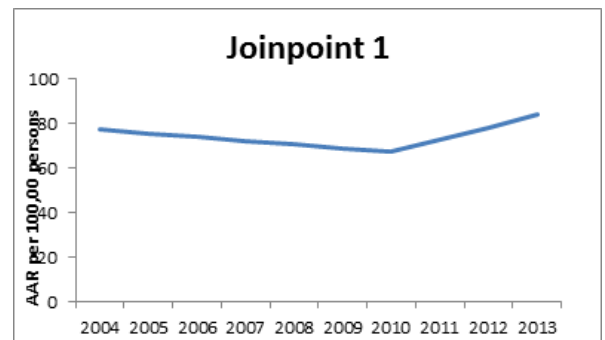
Table 6.1: All Sites Cancer –Female, Dibrugarh District: 2004-2013 Trends over time based on value of Joinpoint AARs with Annual Percent Change (APC)

Year	Observed AAR	Expected AAR
2004	70.2	77.34
2005	79.3	75.52
2006	75	73.73
2007	77.9	71.99
2008	70.8	70.29
2009	69.9	68.63
2010	63.5	**67.01**
2011	70.3	72.31
2012	77.9	78.03
2013	85.1	84.21
APCO		**0.4**
APC1		**-2.36**
APC2		**7.91**

Table 6.2: Breast Cancer –Female, Dibrugarh District: 2004-2013 Trends over time based on value of Joinpoint AARs with Annual Percent Change (APC)

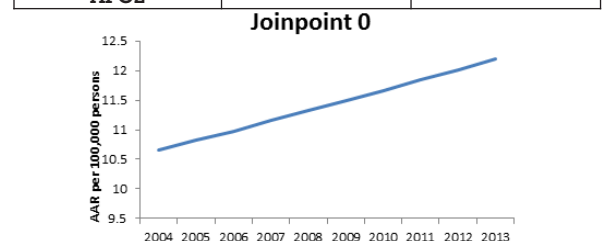| Year	Observed AAR	Expected AAR
2004	13	10.65
2005	10.6	10.82
2006	8.6	10.98
2007	14.2	11.15
2008	11.4	11.32
2009	10	11.49
2010	9.3	11.66
2011	10.7	11.84
2012	12.4	12.02
2013	15.7	12.2
APCO		**1.52**
APC1		
APC2		

Table 6.3: Oesophagus Cancer –Female, Dibrugarh District: 2004-2013 Trends over time based on value of Joinpoint AARs with Annual Percent Change (APC)

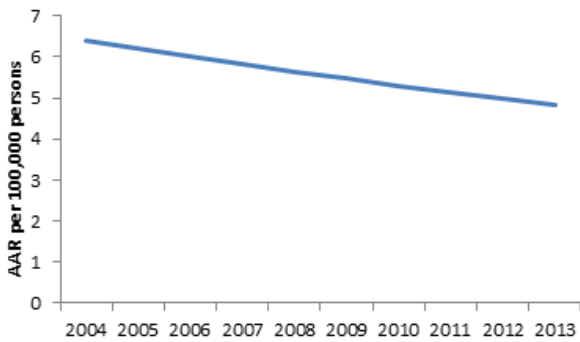| Year	Observed AAR	Expected AAR
2004	7.6	10.79
2005	12.6	10.34
2006	12	9.91
2007	10.9	9.51
2008	9.8	9.11
2009	9.4	8.74
2010	6.4	8.38
2011	6.3	8.03
2012	8.1	7.7
2013	8.5	7.38
APCO		-4.12
APC1		
APC2		

Joinpoint 0

Table 6.4: Gallbladder Cancer –Female, Dibrugarh District: 2004-2013 Trends over time based on value of Joinpoint AARs with Annual Percent Change (APC)

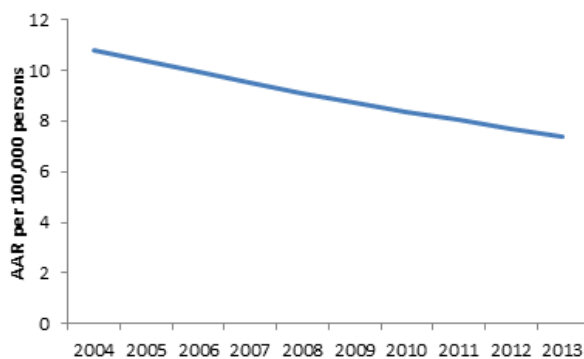| Year	Observed AAR	Expected AAR
2004	6.6	6.35
2005	6	6.6
2006	7.5	6.86
2007	7.3	7.14
2008	8.3	7.42
2009	6.5	7.71
2010	7.9	8.02
2011	7	8.34
2012	10.3	8.67
2013	9.2	9.01
APCO		3.97*
APC1		
APC2		

Joinpoint 0

Table 6.5: Ovary Cancer – Dibrugarh District: 2004-201 Trends over time based on value of Joinpoint AARs with Annual Percent Change (APC)

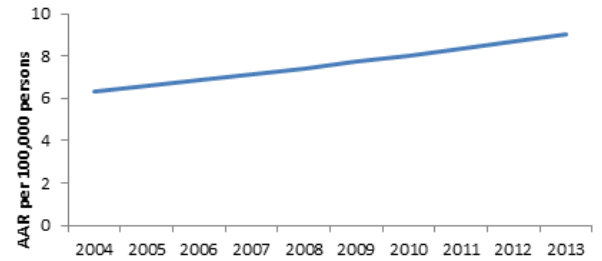| Year	Observed AAR	Expected AAR
2004	4.1	4.9
2005	6.8	5.02
2006	4.3	5.14
2007	5.8	5.26
2008	5.5	5.39
2009	5.5	5.52
2010	5.5	5.65
2011	5.3	5.78
2012	5.8	5.92
2013	6.5	6.06
APCO		2.40
APC1		
APC2		

Joinpoint 0

Table 6.6: Cervix Uteri Cancer – Dibrugarh District: 2004-2013 Trends over time based on value of Joinpoint AARs with Annual Percent Change (APC)

Year	Observed AAR	Expected AAR
2004	8.4	6.39
2005	5	6.2
2006	4.8	6.01
2007	6.4	5.82
2008	6	5.65
2009	5.4	5.47
2010	5.4	5.31
2011	5.1	5.14
2012	4.9	4.99
2013	5	4.83
APCO		-3.06
APC1		
APC2		

Joinpoint 0
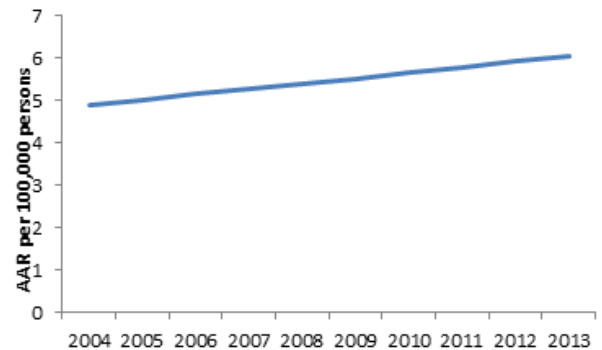
CONCLUSIONS :

The above analysis depicts that the burden of cancer among females of Dibrugarh district have been increasing for the period 2004 and 2013.The incidence rate of gallbladder cancer increases significantly whereas a statistically not significant decreases in AARs for oesophagus and cervix uteri

cancers among females of the district were observed over time . Again no significant trends were observed for breast and ovary cancer incidence rates.

So it is to be concluded that though breast is the leading site of cancer among females of Dibrugarh district, the incidence of gallbladder cancer increases alarmingly over the period of 2004-2013.Comparative analytical epidemiological studies are essential to provide leads for the risk factors of gallbladder cancers among females of the district.

REFERENCES :

1. Boyle,P. and Parkin, D.M. Statistical Methods for Registries- Ch. In Cancer Registration – Principles and Methods,Eds. Jensen, O.M., Parkin, D.M.,Maclennan,R.,Muir C.S. and Skeet R.G.,IARC Scientific Publications,No.95,Lyon 1991.
2. Esteve J., Benhamou E.,Raymond L. – Descriptive Epidemiology - Statistical Methods in Cancer Research, Volume IV,IARC Scientific Publications,No-128,Lyon 1994
3. Kim H.J.,Fay M.P. Feuer E.J.,Midthune D.N. – Permutation Tests for Joinpoint Regression with application to Cancer Rates. Stat Med 2000; 19:335-51(correction :2001;20:655)
4. Morris CR,Epstein J,Nassere K,Hofer BM,Rico J,Bates JH,Snipes KP – Trends in Cancer Incidence,Mortality,Risk Factors,and Health Behaviours in California.Sacramento,CA : California Department of Public Health,Cancer surveillance Section,January 2010 available at www.cdph.ca.gov
5. Yeole,BB – Time – Trend Studies with emphasis on Cancer,NCRP Newsletter,Cancer Registry abstract,Volume XII,2005
6. Mathew A,Vijayaprasad B – Epidemiology of female breast and reproductive tract cancers in India, NCRP Newsletter,Cancer Registry abstract,Volume XII,2005
7. Census of India- RegistrarGeneral of India,New Delhi [www.censusindia.net]
8. NCRP – Two year report of the Population Based Cancer Registry under North East Regional Cancer Registry,2005-2006,National Cancer Registry Programme,ICMR,Bangalore,2007
9. NCRP – Two year report of the Population Based Cancer Registry,2004-2005,National Cancer Registry Programme,ICMR,Bangalore,2008
10. NCDIR (NCRP)- Consolidated Three year Report of Population Based Cancer Registries 2009-2011,National Centre for Disease Informatics and Research (Indian Council of Medical Research),Bangalore,2013.
11. NCDIR (NCRP)- Time Trends in Cancer Incidence Rates 1982-2010, National Centre for Disease Informatics and Research (Indian Council of Medical Research),Bangalore,2013