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Original Article

Trends in Gallbladder Cancer Incidence in the High- and Low-Risk Regions of India

Abstract

Background: Gallbladder cancer (GBC), a common cancer surrounding the Gangetic belt of India, accounts for 80%–90% of biliary tract cancers. GBC incidence shows striking geographical variation in India. **Materials and Methods:** We used the data from the National Cancer Registry Programme for the year 2001–2014 to study the time trends of GBC in the high- and low-risk geographical regions of India. Annual percentage change (APC) in age-adjusted incidence rates was computed by log-linear regression model. **Results:** Among females, a statistically significant increase in trend was observed in Cachar (APC: 7.0, $P = 0.02$), Delhi (APC: 4.0, $P = 0.04$), and Kamrup (APC: 4.3, $P = 0.02$) marked under high-risk region and in Bengaluru (APC: 5.7, $P = 0.04$) and Pune (APC: 3.4, $P = 0.04$) marked under low-risk region. Among males, increasing but statistically nonsignificant trends were observed in Cachar, Dibrugarh, Kamrup, Nagpur, and Sikkim, whereas decreasing trends were observed in Bengaluru, Barshi, Bhopal, and Kolkata. Aurangabad showed a statistically significant decrease in trend (APC: −14.5, $P < 0.001$) among males. **Conclusion:** The time trend and pattern of GBC have striking differences within the country as well as in state. Further large-scale region-wise studies are needed to find the risk factors of GBC.

Keywords: *Gallbladder cancer, incidence rate, India, trend*

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Introduction

Gallbladder cancer (GBC) is less common in developed countries while its incidence is highest in some parts of India, Chile, and Mexico.[1] Within India, the states such as Assam (rate ratio [RR] [95% confidence interval [CI]] – female: 7.18 [4.89–10.55] and male: 3.61 [2.44–5.36]) and Delhi (RR – female: 4.70 [3.93–5.61] and male: 2.04 [1.61–2.60]) showed highest rate compared to South India (RR – female: 0.39 [0.24–0.66] and male: 0.53 [0.33–0.85]).[2] To investigate secular trends in GBC over the past 14 years, we conducted this study to estimate the annual percentage change (APC) in the incidence rate within different regions of India and performed a comprehensive analysis to understand the time trends in different geographical regions of India.

Materials and Methods

Incidence data

We retrieved age-adjusted incidence rate (AAR) per 100,000 of GBC from the National Cancer Registry Programme (NCRP) database,[3] for the period of 14 years (2001–2004 to 2012–2014). The NCRP database includes 30 population-based cancer registries (PBCRs), namely, Ahmedabad, Aurangabad, Bengaluru, Barshi, Bhopal, Cachar, Chennai, Delhi, Dibrugarh, Kamrup, Kolkata, Kollam, Manipur, Meghalaya, Mizoram, Mumbai, Nagaland, Nagpur, Naharlagun, Pasighat, Patiala, Pune, Sikkim, Thiruvananthapuram, Tripura, Wardha, Sangrur, Mansa, Chandigarh, and SAS Nagar. However, for trend analysis, we considered only 18 registries having AAR available for at least three time periods.

Definition of high- and low-risk regions

We divided Indian states and territories into high- and low-risk regions using incidence rates extracted from the PBCRs. States were considered to be in the high-risk region if PBCR existing in the state observed average AARs of >5.0 per 100,000 persons.[2] Others were considered as low-risk regions. According to the definition, Cachar, Delhi, Kamrup, Dibrugarh, Kolkata, and Sikkim were in the high-risk region, and the rest of the registries were considered to be in the low-risk region. For comparison, average

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AARs of all registries from high- and low-risk regions were taken for four time periods (2001–2004 to 2012–2014).

Estimation of annual percentage change

APC is a summary measure of the trend over a prespecified fixed interval. APC was estimated independently for both the genders for the selected 18 registries, namely, Aurangabad, Bengaluru, Barshi, Bhopal, Cachar, Chennai, Delhi, Dibrugarh, Kamrup, Kolkata, Kollam, Manipur, Mizoram, Mumbai, Nagpur, Pune, Sikkim, and Thiruvananthapuram for the time period of 2001–2004 to 2012–2014.

Trend was estimated using Joinpoint trend analysis software by the National Cancer Institute.[4,5] APC was considered statistically significant if P value at 95% CI was ≤0.05.

Results

Tables 1 and 2 show gender-wise AAR for four time periods (2001–2004 to 2012–2014) in the 18 registries. There are substantial differences in the rates for both the genders, with high rates in Delhi, Cachar, Dibrugarh, and Kamrup and with lowest rates in Bengaluru, Barshi, Chennai, and Aurangabad. Among females, statistically significant increasing trends were observed in Bengaluru, Cachar, Delhi, Kamrup, and Pune, whereas the rates were decreasing in Aurangabad, Barshi, and Manipur. Among males, increasing but statistically nonsignificant trends were observed in Cachar, Dibrugarh, Kamrup, Nagpur, and Sikkim, whereas decreasing trends were observed in Bengaluru, Barshi, Bhopal, and Kolkata. Aurangabad showed a statistically significant decrease in trend (APC: −14.5, P < 0.001) among males.

As shown in Figure 1 [Supplementary Table 1], in the high-risk region, there was a statistically significant increase in AAR among females (APC: 5.4, P < 0.001), whereas the trend was increasing but statistically nonsignificant among females (APC: 6.3, P = 0.2). No significant increase in AAR was observed in the low-risk region (male – APC: −1.1, P = 0.8 and females – APC: −1, P = 0.5).

Table 3 shows the within-state variation of AAR (2004–2014) in Maharashtra, northeast region, and south region. In Maharashtra, Mumbai showed slightly higher rates than other three regions, for both genders. There was no variation observed in rates within the four regions in South India. Variability in rates was observed in northeast region, with Cachar, Kamrup, and Dibrugarh registries in Assam showing high rates.

Discussion

This trend analysis has shown that the rates of GBC incidence in the high-risk region are significantly increasing among females, whereas increasing but statistically nonsignificant trend was observed among males. Several factors such as diagnosis and completeness of reporting can affect the reported incidence of cancer.

In states with low risk of GBC, the rates of GBC were higher only in metro cities (Mumbai, Pune, and Bengaluru), whereas the rates were lower in small towns. This indicates the role of migration from high-risk areas to the metro cities. The role of migration in GBC was previously investigated.[2] It would be interesting to explore if the rising trend is because of high rates of migration

Table 1: Age-adjusted incidence rates of gallbladder cancer with annual percentage change in Indian registries (males)

Cancer registry	AAR by time period				APC	*P*
	2001-2004	2004-2008	2009-2011	2012-2014		
Aurangabad	NA	0.7	0.3	0.2	−14.5^	<0.001
Bengaluru	0.8	2.6	0.3	1.2	−4.6	0.75
Barshi rural	1.0	1.7	1.0	1.0	−1.7	0.67
Bhopal	2.8	3.4	3.3	2.6	−0.6	0.76
Cachar	2.1	4.7	5.1	5.2	7.4	0.19
Chennai	1.2	3.2	2.1	1.8	1.5	0.81
Delhi	3.7	6.5	4.2	5.3	1.2	0.76
Dibrugarh	2.4	3.7	3.2	4.1	3.6	0.23
Kamrup	3.0	7.3	7.4	8.8	8.5	0.17
Kolkata	NA	3.7	2.5	3.3	−2.0	0.72
Kollam	NA	0.9	1.1	1.4	5.5	0.15
Manipur	1.2	1.7	1.8	1.7	2.9	0.25
Mizoram	1.4	1.9	2.4	1.8	2.8	0.4
Mumbai	1.7	3.6	1.7	2.2	−0.7	0.9
Nagpur	NA	0.8	1.3	1.3	6.7	0.24
Pune	NA	0.9	0.9	1.1	2.2	0.55
Sikkim	0.6	3.7	2.1	2.2	8.1	0.5
Thiruvananthapuram	NA	0.9	0.7	1.2	2.8	0.71

Taken from NCRP database, P value for APC estimated at 95% CI. AAR – Age-adjusted incidence rate per 100,000; NA – AAR not available; APC – Annual percentage change; NCRP – National Cancer Registry Programme; CI – Confidence interval; ^ – Statistically significant

Table 2: Age-adjusted incidence rates of gallbladder cancer with annual percentage change in Indian registries (females)

Cancer registry	Time period				APC	*P*
	2001-2004	2004-2008	2009-2011	2012-2014		
Aurangabad	NA	0.3	0.1	0.1	−13.1	0.09
Bengaluru	1.0	1.4	1.5	2.0	5.7^	0.04
Barshi rural	0.5	0.6	0.2	0.2	−10.6	0.13
Bhopal	4.4	4.2	5.0	6.4	3.4	0.11
Cachar	5.1	6.5	10.1	10.2	7.0^	0.02
Chennai	0.9	1.2	2.0	1.5	5.7	0.17
Delhi	7.4	8.1	9.2	11.8	4.0^	0.04
Dibrugarh	5.8	7.5	7.7	8.6	3.1	0.09
Kamrup	10.2	12.6	14.0	17.1	4.3^	0.02
Kolkata	NA	4.5	5.6	7.7	6.7	0.14
Kollam	NA	0.6	0.8	1.0	6.4	0.09
Manipur	5.6	5.2	3.6	3.8	−4.1	0.06
Mizoram	4.1	2.7	2.9	3.6	−0.7	0.82
Mumbai	2.1	2.75	2.2	4.1	4.3	0.31
Nagpur	NA	0.8	1.0	1.4	6.9	0.21
Pune	NA	1.0	1.2	1.3	3.4^	0.04
Sikkim	2.4	5.2	6.8	6.7	9	0.12
Thiruvananthapuram	NA	0.8	1.3	1.1	4.7	0.47

Taken from NCRP database, *P* value for APC estimated at 95% CI. AAR – Age-adjusted incidence rate per 100,000; NA – AAR not available; APC – Annual percentage change; NCRP – National Cancer Registry Programme; CI – Confidence interval; ^ – Statistically significant

Table 3: Within-state variation in age-adjusted incidence rates of gallbladder cancer

State	Registry	2004-2008		2009-2011		2012-2014	
		Male	Female	Male	Female	Male	Female
Maharashtra	Nagpur	0.8	0.8	1.3	0.96	1.3	1.4
	Pune	0.9	1.0	0.85	1.2	1.1	1.3
	Mumbai	3.6	2.75	1.68	2.18	2.2	4.1
	Barshi	1.7	0.6	1.03	0.17	1.0	0.2
Northeast	Manipur	1.7	5.2	1.82	3.64	1.7	3.8
	Mizoram	1.9	2.7	2.44	2.94	1.8	3.6
	Cachar	4.7	6.5	5.11	10.13	5.2	10.2
	Kamrup	7.3	12.6	7.41	14.01	8.8	17.1
	Dibrugarh	3.7	7.5	3.24	7.7	4.1	8.6
	Sikkim	3.7	5.2	2.06	6.77	2.2	6.7
South India	Chennai	3.2	1.2	2.05	1.95	1.8	1.5
	Kollam	0.9	0.6	1.08	0.77	1.4	1.0
	Thiruvananthapuram	0.9	0.8	0.72	1.32	1.2	1.1
	Bengaluru	2.6	1.4	0.27	1.53	1.2	2.0

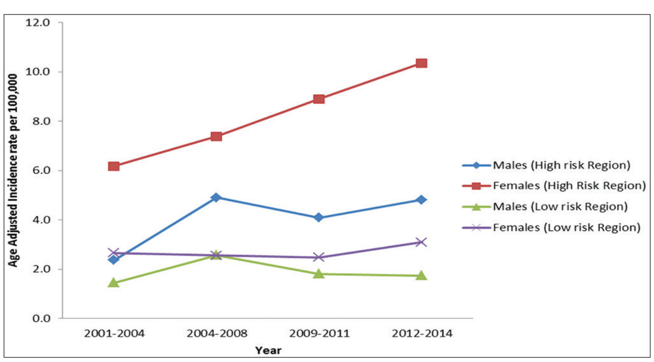

Figure 1: Trends in age-adjusted incidence rates of gallbladder cancer in the high- and low-risk regions. Data for Figure 1 are provided as supplementary table

from Northern states in India or there is a shift in lifestyle factors such as increase in obesity; consumption of fatty, spicy food; and reproductive factors for females which are contributing to develop GBC.

The time trend and pattern of GBC have striking differences even within state. For example, the rates are rising and are high only in Mumbai, Maharashtra, while among northeastern states, only Assam has high rates whereas Manipur, Mizoram, and Sikkim show low-to-medium rates of GBC. A detailed study about lifestyle patterns in Assam would thus be helpful to understand the reasons for high rates of GBC.

The risk factors of GBC are not widely studied. It has been estimated that the disease has high heritability component and risk loci surrounding ABCB4 and ABCB1 region on chromosome 7 has been identified.[6,7] The lifestyle factors which are generally considered to increase the risk of GBC are gallstone, obesity, and infection.[8-10] In addition, among females, high parity is a possible contributing factor for the increase in the risk of GBC.[9]

Conclusion

The time trend and pattern of GBC have striking differences within the country as well as in state. It would be important to conduct a large-scale study in the high- and low-risk regions of GBC to understand its etiology and to inform government regarding prevention strategies of this fatal disease.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Age-adjusted incidence rates of gallbladder cancer with annual percentage change in the high- and low-risk regions of India

Year	High-risk region		Low-risk region	
	Males (average AAR)	Females (average AAR)	Males (average AAR)	Females (average AAR)
2001-2004	2.4	6.2	1.4	2.7
2004-2008	4.9	7.4	2.6	2.6
2009-2011	4.1	8.9	1.8	2.5
2012-2014	4.8	10.4	1.7	3.1
APC	6.3	5.4^	1.1	1
P	0.2	0	0.8	0.5

AAR – Age-adjusted incidence rate; APC – Annual percentage change; ^ – Statistically significant