

Gallbladder Cancer and Its Trend in India

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Abstract: GBC (Gallbladder cancer) is ranked 5th amongst all cancers in India especially in females. The incidence rate of GBC is even higher in North India compared to South India. As India is fast developing country so the changes in life style of people have increased risk of GBC in recent years.

Key words: Incidence, cancer, India, risk factors.

1. Introduction

This article is an effort to study the trends of GBC (gallbladder cancer) in India. GBC was first described in 1777 [1]. More than 200 years later, even today delay in diagnosis and absence of effective treatment for many patients remain typical features of this disease

The GBC is uncommon but most common biliary tract cancer and lethal gastrointestinal tumour amongst all. The incidence of gallbladder varies in wide geographic and ethnic regions. This research study is undergoing in order to find possible new risk factors for this disease and also confirm our understanding for established causal agents. More early the patient approaches to get confirmation of disease the better are prognosis. However ambiguous clinical presentation and paucity of pathological and radiological features often create difficulty in identification of GBC and only 10% of GBC cases present a stage manageable to treat surgically. This paper reviews the current trends of GBCs in India. This paper also would enrich present available literature in gallbladder carcinoma to enhance awareness of GBC.

2. Methodology

A systematic review with a special emphasis on review article published in medical literature using search terms “gallbladder cancer OR carcinoma”. Secondary references obtained from these publications were identified by a manual search and reviewed as relevant. Case reports except for rare pathological entities were predominantly excluded. Articles discussing on Gallbladder cancer were included in this review, while those dedicated exclusively to biliary tract malignancies were excluded. Selected relevant abstracts from ICMR (Indian Council of Medical Research) and other relevant organisations have also been reviewed. We have predominately limited our search to publications since 1990 to review concepts of gallbladder cancer in the 21st century.

3. Epidemiology and Risk Factors

GBC, as its presenting symptoms are vague and likely to other diseases such as Gallstone and cholecystitis. GBC is usually diagnosed in advanced stage, with a 5-year survival rate of less than 5% in stage IV.

Incidences of GBC in other part of world and India can be clearly understood by the given map mentioned below which illustrates that how alarming situation is emerging for GBC in India.

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In describing the incidence of GBC, main sources of data have been used from ICMR (Indian Medical Council of Research) New Delhi India. The incidence of gallbladder cancer varies in different parts of the world and also within the Indian population.

The highest GBC incidence rates worldwide per 100,000 are in Delhi, India 21.5, South Karachi, Pakistan 13.8 and Quito, Ecuador 12.9 and high rates are reported in Chile (27/100,000) and Poland

(14/100,000), Japan (7/100,000) and Israel (5/100,000) [2].

In India GBC is more common in north and north east states of India i.e., Uttar Pradesh, Bihar, Orissa, West Bengal and Assam. It is the commonest digestive cancer in North Indian women. Incidence of GBC in women in northern India is as high as 9 per 100,000 per year as compared to 1 per 100,000 per year in southern India.



Fig. 1 Incidence of GBC (From National Cancer Institute. Surveillance, Epidemiology and End Results (SEER) Program. Source: <http://seer.cancer.gov>).

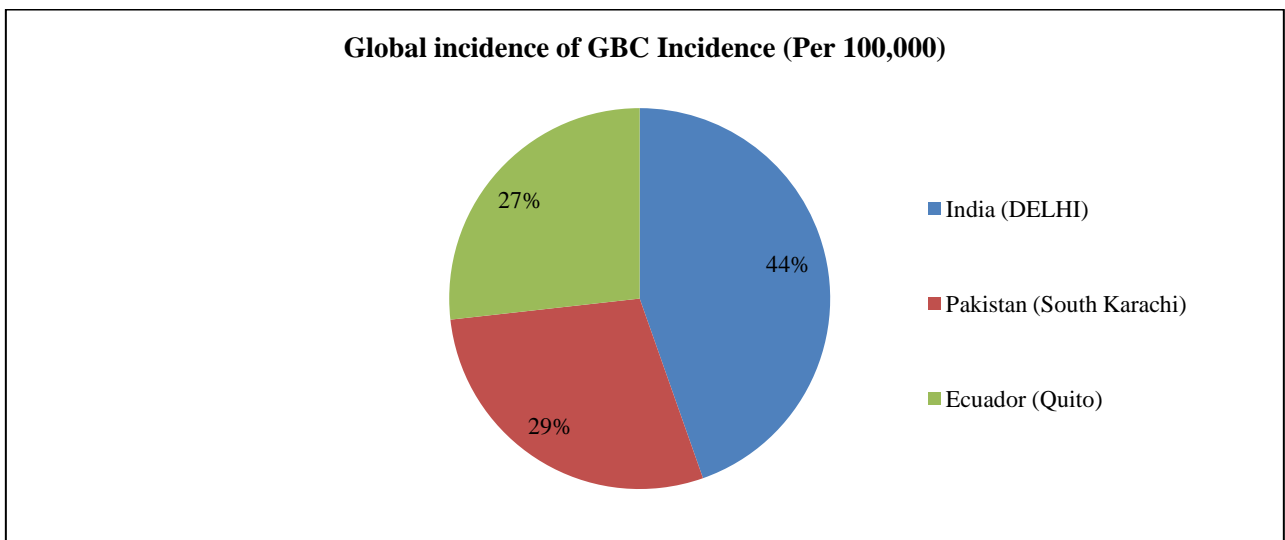


Fig. 2 Global incidence of GBC (Per 100,000*) . Source [3].

The Indian states and territories have been quantified on basis of geographical variation and in incidences of GBC. They are divided into two categories—a high and low risk region by using of incidence rates extracted from PBCRS (population based cancer registries). States having age-adjusted rates of > 0.5 per 100,000 persons considered high-risk region and all other considered low. There have been some states having no cancer registries, defined as microscopic age-adjusted incident rate. Accordingly states—Bihar, Delhi, Himachal Pradesh, Punjab, Chandigarh, Rajasthan, Uttarakhand, Uttar Pradesh, Assam, Tripura, Sikkim, Jharkhand, and West Bengal were categorized into high-risk regions (mainly North Indian states) the rest of states were into low-risk regions [2]

GBC ranks amongst the first 10 cancers in ICMR (Indian Council of Medical Research). Six cancer registries of Indian Council of Medical Research (1990-1996) show a 10 times lower incidence of GBC per 10,000 in South India compared with North, the age-adjusted incidence rate for females being 0.8 in Chennai in south and 9.0 in Delhi in the north [3].

In India, during 2001, the estimated number of gallbladder cancer was 14,986 and is likely to increase to 23,750 by 2016 as a result of aging and increase in

size of the population. As per data it has estimates that GBC burden in 2025, where India will alone represent 9.76% males and 11.15% females [3, 4].

In one the study done of 773 GBC patients coming to Tata Memorial Hospital, Mumbai India, a tertiary referral centre, over six years (1990-1995) depicts that maximum were from Uttar Pradesh (41.9%), Bihar (35.8%), West Bengal (8.1%) and parts of Madhya Pradesh (7.3%) and Assam (7.0%). There appears to be a higher incidence of GBC in the Gangetic basin, Uttar Pradesh (65%) and Bihar 51%. Though high prevalence of GBD is well documented and in both Uttar Pradesh and Bihar it had been predominantly more in rural population living in river belt of Ganga with few community based studies from this areas One of the factors of age associated with gallbladder disease and also GBC shows that the prevalence of GBD is more than 1.5 times in persons aged 50 and above compared to those aged 30-49 as also reported in previous studies [5].

As shown that it is much higher in the North part of India (e.g. incidence in Delhi is 3.7 per 100,000 for male and 8.9 per 100,000 for female and in Bhopal it is 1.6 and 2.5 per 100,000 for male and female respectively) compared with the Southern cities of India (e.g., in Chennai incidence is 0.5 per 100,000 for

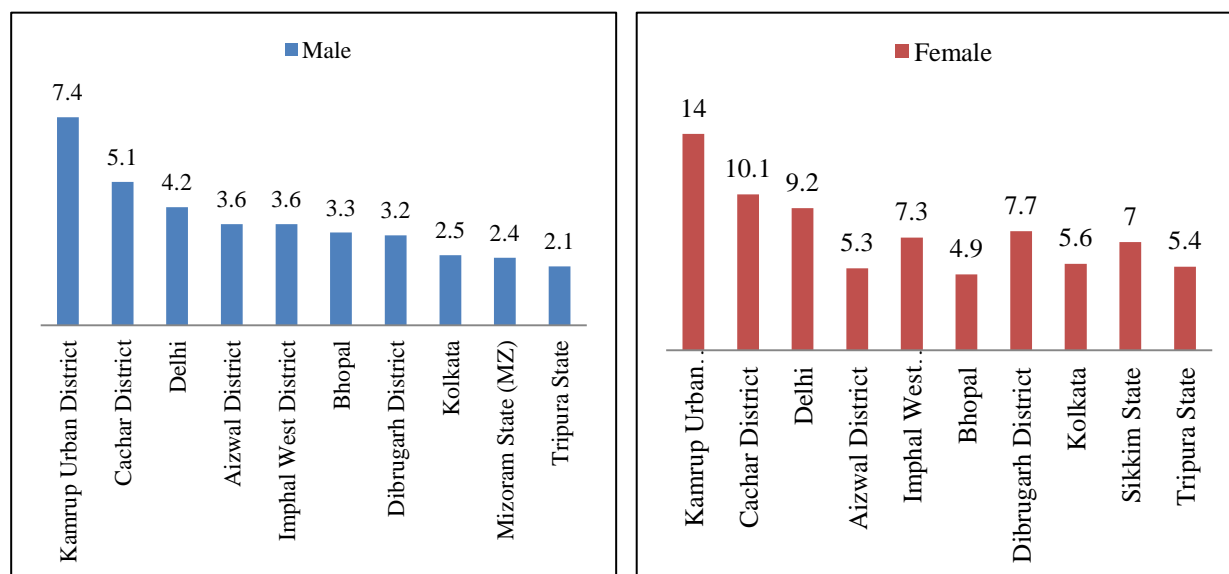


Fig. 3 National Comparison of AAR from Indian PBCRS* Source: [4].

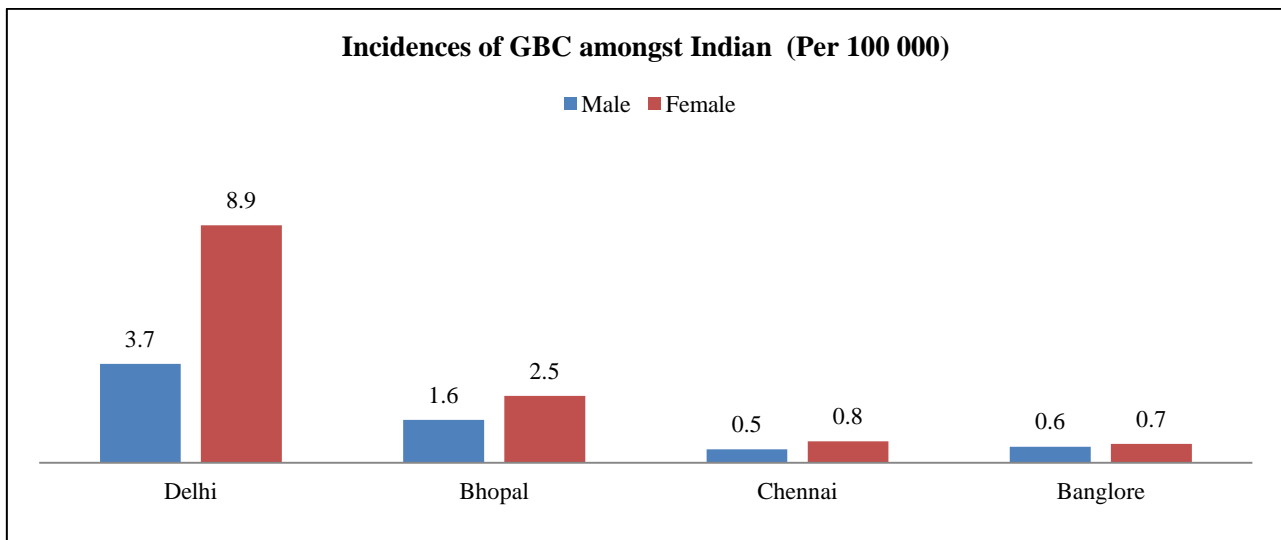


Fig. 4 Incidences of GBC amongst Indian (Per 100, 000). Source: [10].

Statement for Gallstone (Predominance to GBC)			
FAT	FAIR	FERTILE	FORTY

Fig. 5 Statement for Gallstone (Predominance to GBC).

male and 0.8 per 100,000 for female and in Bangalore incidence for male is 0.6 per 100,000 and for female it is 0.7 per 100,000 population).

Its geographical incidence has been increasing in the Ganges delta. The GBC incidence parallels the prevalence of GBD (gallbladder disease); chronicity and large GST (gallstones) have been associated with a higher risk of GBC. The GST has been reported to increase risk of four to seven times of GBC which occurs more commonly in elderly women in which 90% of the patients are above the age of 50 years. Peak incidence is between 70-75 yrs.; with the male: female ratio 1:3.2.

One of the largest door to door surveys had been done among the rural population of North India, where a high prevalence of GBC was reported. This survey was done to estimate all Gallbladder diseases including GBC and predisposing factors such gallstone disease along with environmental factors. Among the sample size of 13,334 the households had majorly low, approx. 36% medium and only 11% high SLI (standard of living index). Approx. 68% male and 18% females are literate, majorly all sample were

Hindu. A history of blood relative suffering from GBD depicts a positive association in both genders. In males, diabetes showed a positive association with GBD. As a dietary concern chickpeas (chana) had higher odds for GBD in all.

The study was amongst 3 districts of selected states of India, i.e. Patna, Vaishali, Varanasi. Dominancy of females was seen for GST. Prevalence of GBD was higher in symptomatic compared to asymptomatic population.

4. Main Risk Factor

Risk factors for gallbladder cancer can be divided into four broad categories. Amongst major risk factors, gallbladder stone (cholelithiasis) had been more relatively associated with GBC. Gallstone disease was at least 7 times more common in north India as compared to those in south India. Most of gall stones (> 80%) in north India are cholesterol stones while more than 60% of gall stones in south India are pigment stones and only less than 5% are cholesterol stones. Gall stone disease occurs at a younger age in Indian than in western populations. The overall prevalence of

gall stone disease in adult women in Kashmir was 9.6% but it was as high as 29% in women in the age a group of 51-60 years [6]. Gallstones are found in almost all cases of gallbladder cancer (78% to 85%). Over 90% of gallbladder carcinomas are adenocarcinoma.

It is seen that gallbladder stone cases in developed countries consist predominantly of cholesterol (> 85%), whereas the remainder constitutes black pigment stones (i.e., composed of calcium bilirubinate). Some recent studies have shown that almost 91% of the patient who had been on sedentary life style had more chances of having gallstone. Obese women having high BMI approx. 28.03 have linear association with prevalence of cholelithiasis [7].

One of the factors of age associated with gallbladder disease and also GBC shows that the prevalence of GBD is more than 1.5 times in persons aged 50 and above compared to those aged 30-49 as also reported in previous studies [7].

Obesity is also a public health burden in poorer countries, is also called as “New World Syndrome”. The World Health Organisation has described as most neglected public health problem globally [8]. One of the studies in USA found that gallbladder mortality

rates were associated with obesity in women [9]. According to NFHS (National Family Health Survey) women have been overweight or obese who were between the age of 15-49 years. The change in percentage is from 11% in NFHS-2 to 15% in NFHS-3 of women who had ever-married. Under nutrition is more prevalent in rural areas, whereas overweight and obesity are more than 3 times higher in urban areas. The percentage of overweight or obese women is highest in Punjab (30%), followed by Kerala (28%) and Delhi (26%) relatively richer states [10].

Due to some dietary factors, with diets high in calories, carbohydrates, red meats, oils, and red chilli peppers confer a higher risk. Intake of green leafy vegetables and fruits may be protective. There has been some suggestion of inverse association with fibre intake, vitamin C and vitamin E. There is reported variation of dietary habit in North and South parts of India. The pattern of difference in diet of North Indian are masticatory diet while sloppy diet of South Indians. The mucus concentration in saliva supports to increase with masticatory meals in comparison to sloppy meals. Mucus is precipitated by strong acid in the stomach and this state can produce less permeability to stimuli

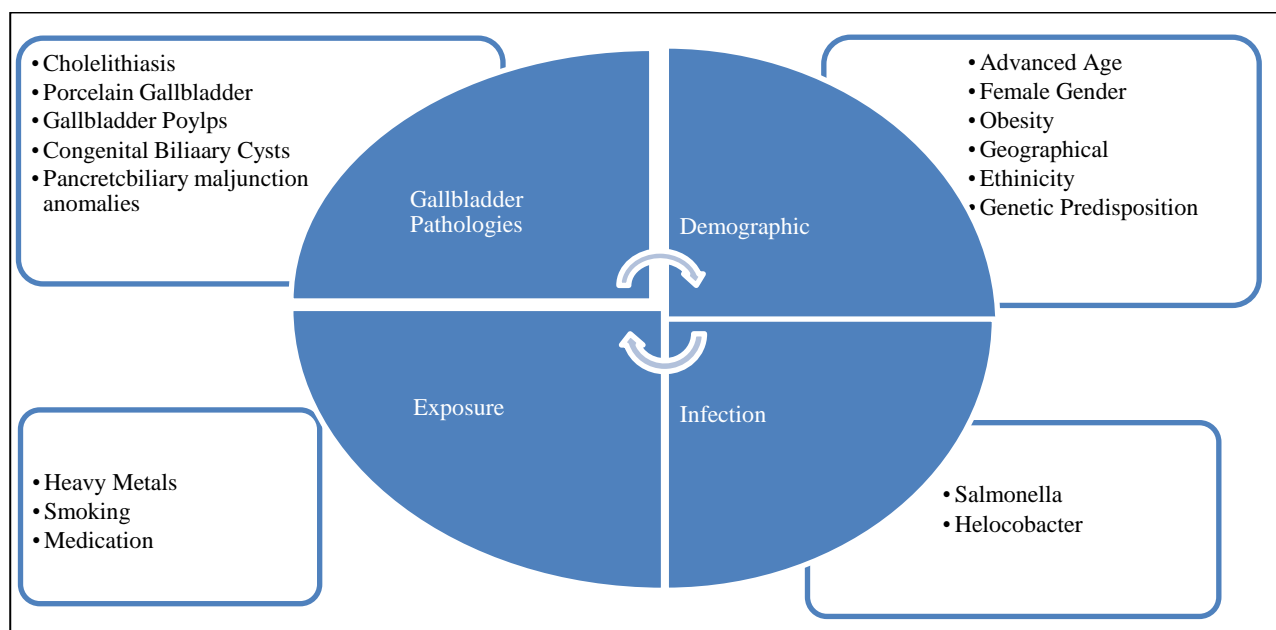


Fig.6 Risk Factors of GBCs.

which are responsible for CCK (Cholecystokinin) release, as CCK is responsible for gallbladder contraction. These dietetic variations affect changes in gallbladder contraction as well as the flow rate of bile. If gallbladder contraction decreases the bile remains for longer duration and biliary system. The most potent carcinogenic chemical is derivatives of cholic acid. It is still doubtful but intake of high fatty diet and wheat in North Indian life style might play some role. Different studies explain that consumption of fruits and vegetables lowers the risk of GBC. Consumption of sugar increases calorie intake without providing any of nutrients, whereas nutrients help to reduce risk cancer. While tea might have protection against cancer due to carrying antioxidant content but coffee has carcinogenic effect due to presence of mutagens. The major risk factor for GBC is history of gallstone and obesity [11]. GBC rates are higher than USA even though dietary fat intake is higher in US [12]. GBC is with diabetes, chickpea consumption, drinking unsafe water.

On gross examination, approximately 10% to 37% of the gallbladder carcinomas cannot be identified with certainty.

5. Conclusion

On reviewing different relevant article it shows that GBC is fast growing upper gastrointestinal cancer in last 2 decades. The predominant factor for its high incidences is gallbladder diseases i.e. gall stone as main.

Many research and articles have shown a major risk area of GBC is Northern part of India comprising mainly states Punjab, Delhi, Uttrakhand, Uttar Pradesh, Bihar, Assam, Arunachal Pradesh, Sikkim, Tripura, Meghalaya, West Bengal. The incidence of GBC increase in population has been due to age, gender female, obesity, gallbladder disease, some intake of drugs.

It has been seen that some major diet associations have some relation to increase incidences of GBC e.g. consumption of fibre, fat, sugar, egg, etc.

Amongst all cancer diseases the fundamental concept to prevent it, is adopting better life style where more of physical activity and less of mental stress, apart from that proper awareness health check-ups of individual health at particular age in regular interval. As GBC itself is said to be most hidden cancer among all, hence regular check up with ultrasound of abdomen can better help for early diagnosis of disease and easy intervention and treatment is possible. GBC as being said that it is difficult to treat if diagnosed later stage, it should be followed to adopt the thinking that early decision and precautionary surgery could provide better chance of survival.

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