

Incidence and Etiology of Various Cancers in Kashmir Valley- A Comprehensive Review of Literature

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ABSTRACT

Cancer is a leading cause of morbidity and mortality all over the world. All types of cancers have been reported in Kashmir valley (India) including the cancers of skin, head and neck, gastrointestinal tract, genitourinary system, lungs, breast, thyroid, skin, blood etc. The interplay between genetic susceptibility and environmental factors is the basis of cancer etiopathogenesis. Cancer trends in Kashmir valley appear to be different from rest of the India, given its different socio-religious practices, food habits and may be geography (though not established yet). The aim of this article is to do a comprehensive review of literature about incidence and etiology of different types of cancers in Kashmir valley with identification of future research focus areas.

Keywords- Cancer, Kashmir, Etiology, Environmental factors.

I. INTRODUCTION

Cancer is one of the most dreadful diseases and second leading cause of death in world^[1, 2]. It accounted for an estimated 9.6 million deaths in 2018 (Figure 1)^[3]. Cancer is a condition in which a group of cells grow abnormally forming a tumor and invade to other parts of the body. Cancerous cells have the ability to bypass the checkpoints in cell cycle^[1]. A number of factors are responsible for the development of cancer through a series of mutations to proto-oncogenes or tumor

suppressor genes, which allow a cancerous cell to grow and divide uncontrollably^[1]. Some major risk factors of cancers include tobacco consumption, obesity, viral infections, radiation, stress, lack of physical activity, environmental pollutants and genetic factors^[1, 4].

Jammu and Kashmir (J&K) is the northern-most state of India. Over the last decade, an increasing trend has been observed in the incidence of cancer in J&K^[5]. The major sites of cancer in males are lungs, prostate, colon and rectum, stomach, esophagus and gastro-esophageal junction, while in females, major sites include breast, stomach, lungs, esophagus, colon and rectum, cervix and ovaries^[5-8].

Cancer profile varies in different parts of the world, and an epidemiological study will help us to know about the common cancer types prevalent in a particular segment of population of Kashmir valley along with the associated risk factors^[9]. The incidence and pattern of different types of carcinoma varies from country to country. It has been found that there is increased incidence of cancer in developed countries because of their different dietary habits, lifestyle and living conditions^[10]. Kashmir valley is distinct from rest of India with respect to its geography, climate, dietary habits and socio-religious practices. All the studies conducted with respect to cancer profile in Kashmir are derived from Hospital based cancer registries (HBCR), one of which is maintained in Regional Cancer Centre SKIMS Soura and another at SMHS Hospital Srinagar.

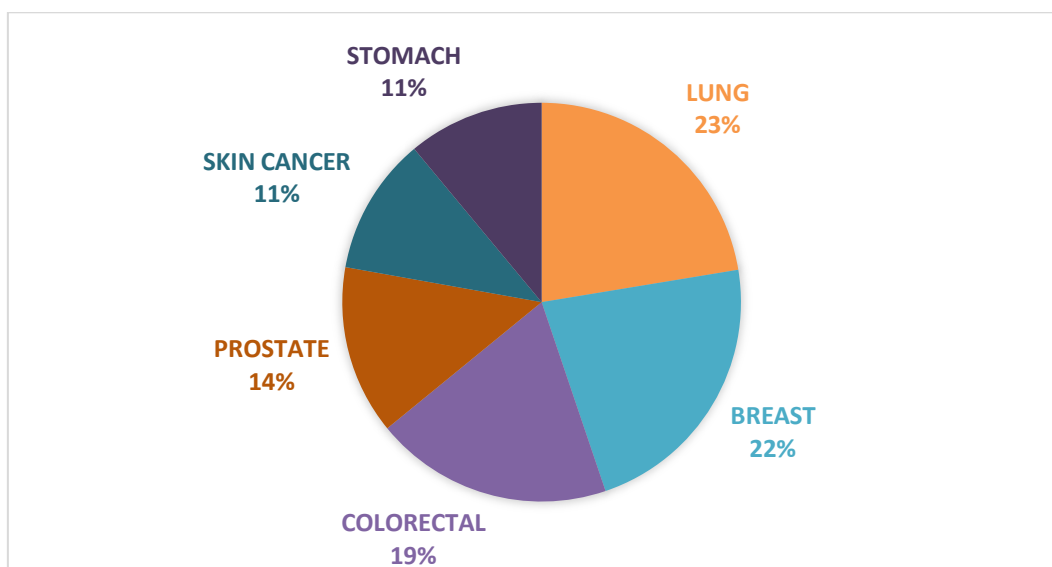


Figure 1: Pie chart represents the Leading cancer cases globally.

II. CANCER SCENARIO IN KASHMIR

In a study conducted by Wani *et al*^[5] the incidence of cancer was more in Kashmiri men than in women, with majority of patients falling in the age group 65-69. The study also revealed that carcinoma of esophagus, stomach and lungs have a high incidence both in men and women in Kashmir.

A. A. Pandith *et al*^[11] conducted a study which showed stomach cancer to be the leading one with an average frequency of 19.2% followed by esophagus and lung as 16.5% and 14.6% respectively. Stomach and lung are the leading cancer sites among men while, as esophagus and breast are the top cancer sites among women. This distribution of cancer types is markedly different from rest of India where oropharyngeal cancer tops the list.

Dhar *et al*^[12] concluded from his study that cancer of esophagus was the most frequent type in both sexes. The preponderance of esophageal cancer was attributable to the local practice of drinking hot salt tea.

The study by Rasool *et al*^[13] also reinforced the above study, concluding cancer of esophagus was the most common cancer in both the sexes combined with overall males affected more than the females.

Ayub *et al*^[14] made study on “*Epidemiological Distribution and Incidence of Different Cancers in Kashmir Valley 2002-2006*” which revealed that esophagus is the leading site of cancer in both sexes, followed by lung, brain, head and neck in males and breast and rectum in females.

Another study made by Qureshi *et al* on “*Gastric Cancer in Kashmir*” reveals that gastric cancer is the highly prevalent malignancy in Kashmir. Particular life style habits like consumption of salted tea and tobacco smoking by hukkah as well as *Helicobacter pylori* infection are main risk factors causing gastric cancer^[15].

III. CAUSES OF VARIOUS CANCERS IN KASHMIR VALLEY

Cancer causation is attributed to various risk factors that can be physical environment (climate, soil and water) and socio-cultural (individual behavior, lifestyle, food habits, alcohol, tobacco consumption, hygiene and occupation). Nearly 80% of all human cancers are environmental in origin^[16] and 10%-20% of them maybe associated with dietary factors^[17]. The cancer mortality rate among Kashmiri population have increased due to some leading behavioral and dietary risks, including high body mass index, low fruit and vegetable intake, lack of physical activity, tobacco use and lack of regular check-up. The changing life style and food habits among inhabitants of the Valley had caused surge in all the cancers especially in esophagus, colon and breast cancers. Some of the important causes of cancer in Kashmir valley are discussed in the following sub-sections briefly.

IV. LIFESTYLE RELATED FACTORS

1. Peculiar Food Habits

Improper diet is one of the main causes of cancer. The role of diet towards cancer varies greatly according to the type of cancers^[18,19]. The heavy consumption of red meat is the main cause of several cancers including gastrointestinal tract and colorectal^[20-22], prostate^[23], bladder^[24], breast^[25], stomach^[26] and oral cancers^[27]. Most probably, it is due to the production of heterocyclic amines during cooking of red meat. Heterocyclic amines are the most potent carcinogens. Pyrolysates, which are produced by charcoal cooking or smoke curing of meat, also exert a cancerous effect on our body cells^[28]. Almost 20% of total mutagenicity of fried beef is due to the presence of PhIP (2-amino-1-

methyl-6-phenyl-imidazo [4, 5-b] pyridine), which is the most abundant mutagen found in cooked beef. Food kept in plastic containers turns out to be carcinogenic because bis-phenol from the plastic containers gets dissolved and migrates into the food, increasing the risk of breast^[29] and prostate^[30] cancers. A low intake of fresh fruits and high cooking temperatures in Indian dishes may account for low levels of vitamin C, resulting into higher risks of stomach, mouth, pharyngeal, esophageal, lung, pancreas and cervical cancers^[31].

Consumption of high salt content and infection with *Helicobacter pylori* may be the possible reasons for the high incidence of gastric cancer in the Kashmiri population^[32]. The excess intake of hot salted alkaline tea (Noon Chai), prepared traditionally in a specially designed copper vessel called a 'Samawar' are some of the distinctive dietary habits for increased risk of gastric cancer in Kashmir^[33,34]. Other dietary risk factors which causes gastric cancer include pickled food, high rice intake, spicy food, excess chilly consumption, and intake of food at high temperature have emerged as significant risk factors and have been studied in other parts of India also, are prevalent in Kashmir as well^[33-35]. There has been a typical shift from intake of traditional food which was rich in complex carbohydrate to more of simple carbohydrates, which has increased the risk of obesity and obesity increases the risk of colorectal cancer^[36].

2. Smoking and Alcohol

The consumption of tobacco via cigarette smoking, hookah smoking, chewing, snuffing etc. is also the leading cause of cancers. The various cancers caused by the use of tobacco are of cancers of oral cavity, pharynx, larynx, esophagus, lungs and urinary bladder. Smoking is the most common risk factor for the causation of lung cancer^[37]. Use of tobacco in different forms is also quite prevalent in Kashmir. Though women do not generally smoke, however, Hookah smoking (a special cigar using raw tobacco) is practiced commonly by both males and females in rural Kashmir, hence, increasing the risk of lung cancer^[38]. Cigarette smoking and hookah smoking are largely responsible for passive smoking of other family members, especially during winter months, when soot, smoke, and fumes from kitchens and various types of heating appliances pollute the indoor air in ill ventilated and overcrowded dwellings^[38].

Chronic damage due to alcohol consumption can lead to liver cirrhosis and the development of hepatocellular carcinoma^[39]. World Health Organization has classified alcohol as a Group 1 chemical carcinogen. Alcohol consumption is also considered as one of the major risk factors for colorectal cancer^[40], but in Kashmir valley only a rare part of population is addicted to the consumption of alcohol.

3. Kangri cancer

Carcinoma of the skin in the form of "Kangri" cancer was a common cancer in Kashmir valley. Nearly 50% of the cancers of skin were of this type. Kangri cancer is a highly aggressive tumor with a propensity for

nodal metastasis. This malignancy is virtually non-existent in the rest of world. High incidence of this carcinoma is because of the chronic irritation of the skin due to the use of a fire pot (Kangri) by the Kashmiri people during the winter season, thus producing a premalignant lesion called *erythema-ab-ignae*^[41].

V. ENVIRONMENTAL FACTORS

4. Radiation

About 10% cancer occurrence is due to radiations, caused by both ionizing and non-ionizing radiations^[42]. High-energy radiation, including ultraviolet radiation (present in sunlight), x-rays, and gamma radiation, are generally carcinogenic, if received in sufficient doses. Ultraviolet (UV) radiation comes from the sun, sunlamps, and tanning booths. It causes early aging of the skin that can lead to skin cancer. The other major sources of radiations are radioactive compounds and pulsed electromagnetic fields. The main series of cancers induced by exposure to the adequate doses of the carcinogenic radiations include thyroid, skin, leukemia, lymphoma, breast and lung carcinomas^[43]. Irradiation of chest with X-rays (used for diagnostic and therapeutic purposes) during puberty increases the risk of breast cancer among girls. The major risk factor for various types of skin cancers viz. basal cell carcinoma, squamous cell carcinoma and melanoma is the exposure to ultraviolet light^[43].

5. Environmental Pollution

Air and water pollution are the results of biological, biochemical and atmospheric particles which cause damages to our living environment. Air pollution is a significant risk factor for respiratory infections, cardiac disease and lung cancer. The main cause of air pollution includes particulate matter, damaged ozone, nitrogen dioxide, sulphur dioxide, carbon dioxide, carbon monoxide, ammonia, radioactive decay of radon gas, methane, hydro-fluorocarbons and chlorofluorocarbons produced by combustion of fuels in automobiles and several industrial processes. Almost 3.5 million deaths are caused by both indoor and outdoor pollution worldwide^[44]. Water polluted by several organic compounds such as oil, plastics, detergents, chloroform, petroleum, polychlorinated bio phenyl, fertilizer, sulphur oxide, pesticides and trichloroethylene which cause various human diseases including cancer^[45]. An increased risk of cancer has been observed in people using chlorinated water for drinking purposes for a long time. N-Nitroso compounds that are mutagenic in nature are formed from nitrates present in drinking water and increase the risk of lymphoma, leukaemia, colorectal cancer and bladder cancers^[42].

6. Infections

Cancer can be caused by infectious agents. Today, experimental and epidemiological evidence indicates that a variety of infectious agents constitute one of the main causes of cancer worldwide^[46]. Viruses are

the principal ones, with at least eight different viruses associated with particular cancer types, with varying degrees of certainty. Other infectious agents involved in carcinogenesis are parasites and one bacterium^[47-51] (Table 1). The various infectious agents that cause cancer include viruses (Hepatitis B and C viruses, Human papillomavirus, Epstein-Barr virus, Human immunodeficiency virus, Human T-cell lymphotropic virus, Human herpes virus B), bacterium (*Helicobacter pylori*) and Parasites like *Schistosoma haematobium*, *Clonorchis sinensis*.

It has been estimated that chronic persistent infection with Hepatitis B virus (HBV) causes 60% of primary liver cancers worldwide and 67% of cases in developing countries^[46]. Hepatitis C virus (HCV) is the major cause of parenterally transmitted hepatitis worldwide. About 25% of cases of liver cancer in the world are attributable to HCV^[47].

Human papillomaviruses (HPV) are known to infect the genital tract^[49]. Epstein-Barr virus (EBV) has a causal role in nasopharyngeal carcinoma and sinonasal

angio-centric T-cell lymphoma. The association of EBV is associated with non-Hodgkin lymphoma mainly in patients with congenital or acquired immunodeficiency^[51]. The role of Human immunodeficiency virus (HIV) is probably as an immunosuppressive agent and hence enhances the risk of cancers^[49-51]. Human T-cell lymphotropic virus (HTLV-1) is the main etiological factor in adult T-cell leukaemia/lymphoma. This disease occurs almost exclusively in areas where HTLV-1 is endemic^[50]. Human herpes virus 8 (HHV-8) infections appear to be common agent in Kaposi sarcomas^[52]. *Helicobacter pylori* is the main cause of gastritis and peptic ulcer; infection may be lifelong if not treated with antibiotics^[53]. Chronic *H. pylori* infection is incriminated in gastric carcinoma. Parasitic infections are strongly associated with cancers and include *Schistosoma haematobium* (squamous cell carcinoma of the bladder) and the liver flukes, *Opisthorchis viverrini* and *Clonorchis sinensis* (Cholangiocarcinoma).

Table 1: Various types of cancers caused by infectious agents worldwide

Infectious agent	Cancer site
1. Viruses	
HPV	Cervix and other sites
HBV, HCV	Liver
EBV	Lymphomas and nasopharyngeal carcinoma
HHV-8	Kaposi sarcoma
HTLV-1	Leukaemia
2. Bacterium	
<i>H. pylori</i>	Stomach
3. Parasites	
<i>Schistosoma haematobium</i>	Bladder or intestines
Liver flukes, <i>Opisthorchis viverrini</i> , <i>Clonorchis sinensis</i>	Cholangiocarcinoma

7. Occupational carcinogens

The first report of association between risk of cancer and employment in particular occupations appeared during the 18th century, however, the majority of studies establishing a link between an increased risk of cancer and a particular working environment were published between 1950 and 1975^[54]. Occupational exposure to carcinogenic environments are increasing in developing countries as a result of transfers of hazardous industries and the establishment of new local industries as

part of a rapid global process of industrialization^[55]. Workplace exposures in farming that may be of etiologic importance for gastric cancer includes organic and inorganic dusts, pesticides and fertilizers. Studies have found that farmers & house wives had exposure to pesticides/insecticides, Fungicides, Chemicals, Fertilizer, Manure in daily routine works. Among these exposures, pesticides and fertilizers have been evaluated mainly in relation to gastric cancer risk, which supports the findings of Koutros S. et al^[56, 57].

VI. CONCLUSION

Etiology of various cancers in Kashmir valley has still many blanks to be filled by thorough population based studies as no such large population based epidemiological study has been done so far due to non-availability of population based cancer registries. The cancer mortality rate among Kashmiri people has increased due to some leading behavioral and dietary risks, including high body mass index, low fruit and vegetable intake, lack of physical activity, tobacco use and lack of regular check-up. The changing life style and food habits among the people has caused surge in all the cancers especially in Lung, GIT and blood cancers. The rise in cancer cases is also due to intake of spicy and pickled food and consumption of bulk of contaminated food items available in the market. There is huge adulteration in daily consumption food items that needs to be addressed and regulated. Due to increasing smoking rates in children and young adults, the incidence of lung cancers may further rise in near future.

The overall incidence of cancer in Kashmir valley shows an increasing trend. Future studies need to be focused on sources and causes of various cancers that may improve our understanding of risk factors for these malignancies in this region. This will also help in the allocation of available resources for prevention and treatment of these cancers.

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