

## **Kashmiri Diet and Gastric Carcinoma Epidemiology and Risk Factors: A Review**

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### **ABSTRACT**

Kashmiri population has distinct dietary habits owing to the long winter spells prevalent in the valley which has accustomed the population to preserve the food in the form of smoked, pickled and dried foods. These peculiar dietary habits contribute to the intake of many N-nitroso compounds (NOCs) which are responsible for DNA damage, Cytotoxicity, gene mutation, DNA methylation, and unscheduled DNA synthesis. At the molecular level, these changes are responsible for the pathogenesis of cancer. This paper presents a review of the relation between the Kashmiri diet and gastric carcinomas, highly prevalent in the valley. This study creates an initial study base and enlists the number of potential factors responsible for the alarming rate of gastric carcinoma in the valley.

**Keywords:** Kashmir, Kashmiri diet, gastric cancer, N-Nitrosodimethylamine, dietary habits

### **1. INTRODUCTION**

Stomach cancer also known as gastric carcinoma is an abnormal uncontrolled division of cells that form a mass in any part of the stomach. This process happens slowly and may develop over time. Majority of the people suffering from it are usually diagnosed at the stage of metastasis. A Study conducted on a large scale in America reported that gastric cancer in around 65 % of cases was diagnosed at metastasis stage with about 85 % cases being reported when a tumor starts to affect the lymph nodes. <sup>[1]</sup> Metastasis is a stage when cancer starts to spread to other parts from the area where it has started. <sup>[2]</sup>

Majority of stomach cancers are of adenocarcinoma type. <sup>[2]</sup> In this type, the carcinoma starts from the mucosa layer which produces mucus. This is the fifth most common type of cancer throughout the world. <sup>[3]</sup> Diagnosis of this type of cancer is hard since the symptoms are quite relatable

with the non-serious issues that may occur in the GI tract like a sense of fullness in the stomach, difficulties while swallowing, frequent burps, heartburn, stomach ache, vomiting etc. Cancer at later stages causes serious symptoms like anemia, black stools, tiredness and fatigue, loss of appetite and weight loss etc. <sup>[2]</sup> Although the reasons for the growth of cancer in some and not in others is not known, there are certain risk factors which make some patients more prone to gastric cancer. These risk factors include dietary habits including salty, smoked or pickled food, H-Pylori bacterial infection, tumors in other body parts, smokers, people with family history of cancers, people of Asian subcontinent (especially Japan) and Americans, Type-A blood group etc. <sup>[2]</sup>

Several dietary factors are found to be responsible for the occurrence of gastric carcinoma across the world, when studied in detail; A case-control study revealed that

diet including high salt, smoked or food that is poorly preserved, rich in nitrates, nitrites are associated with high risk of gastric carcinoma, [4] this is because of the change in the gastric environment because of the generation of the carcinogenic N-nitroso compounds. [5] However some studies revealed in contrast that the intake of a large number of fruits and vegetables can reduce the risk of cancer in the human body. [6] Vitamins and minerals like calcium, vitamin A and C have a protective effect on the mucosa lining that decreases the effect caused by the carcinogenic compounds. [5,6]

A study done in detail reported that smokers are 2-3 times more prone to gastric carcinoma than non-smokers. [6] Reports also suggest the identification of the E-Cadherin mutation to avoid the occurrence from one generation to another as heredity non-polyposis colon cancer (HNPCC) syndrome. [7] Gastric carcinoma has also been associated very strongly to H-Pylori infection. This infection is found to induce changes in the gastric mucosa and flora resulting in gastric cancer in the human body. [8-11] Apart from this H.Pylori is found to have an adhering capacity with the Lewis blood group antigen which may cause chronic infection resulting in an increased risk in patients with Type A blood group. [8] Gastric cancer is 40 % more in Kashmir than any other form of cancer making this three to six times more than that the metro cities of India. [12] Gastric cancer attains the position of top five cancers in the valley with a Male: Female ratio of 3.17:1. [13] Dietary Habits of the population contribute to the high gastric cancer prevalence in the valley. [14] Many genetic factors and other socio-economic factors which are distinct to each community have a close association with the gastric cancer load on the community. [15-17] Many epidemiological studies conducted across Asian countries reveal that high salt intake in the diet is responsible for this increasing rise in the gastric Cancer. [18,19] The peculiar dietary habits of the Kashmir valley like intake of hot salt (alkaline tea; Kashmiri salt tea),

high intake of Brassica Olerecea (Haakh), Common picked vegetables, dried smoked fish (Hoch gade), dried vegetables and extra spicy spice cakes commonly called as Wur are found to be one of the reasons for the increased risk of gastric cancer in the valley. [20, 21]

## 2. Review methodology:

A predefined criteria was set to review the related literature. A thorough search was done on the required literature using popular keywords like gastric cancer, diet, dietary habits of Kashmir, N-nitroso compounds, carcinogens, and risk factors. Pub med and Google scholar were extensively used to collect the data.

## 3. Epidemiology:

Around 85 % of cases of gastric carcinoma were detected in 2016 which were mainly in the pancreas followed by duodenum across the world. [22] In North America, the probability of developing the gastric carcinoma is reported to be 1.5%. [22] However, the mortality rates in Canada have decreased from 21.2 % to 9.1 % in males. [23] It has been reported that in the United States the annual deaths caused by gastric cancer are 14,000. [24] The areas highly prone to gastric carcinoma include East Asia; areas like China and Japan Eastern part of Europe, Central America. While the low-risk areas include Southern Asia, North Africa, Australia, and New Zealand. [25]

In cultures of the world where food with the high salt intake is consumed gastric carcinomas are quite prevalent. Many research studies have proven that salt has a dampening effect on the body and may cause some serious chronic issues. [26] Studies prove that as per an epidemiological survey when a Japanese group of nationals migrated from their homeland and changed the habit of high salt intake in food, the sample revealed low incidences of gastric carcinomas. [26] In areas like Hawaii where the common dietary intake was that of salted fish the gastric carcinomas wherein high numbers [27] same is the case with Lithuania where a high intake of salted mushrooms became a reason for high

prevalence of gastric carcinomas. [28] Same results are found for Serbia, [29] Costa Rica where the most consumed item is of salted black bean, which reports the highest amount of gastric cancers in the world literature. [30] It is the fifth and seventh most prevalent disease in the males and females respectively in India. [3] Certain geographical areas of the country are more prone to gastric cancer like the north eastern states and the southern areas of India. [31] Although there is a declining trend in the disease all across the globe in certain parts of India this decline is not prevalent and the state of Jammu and Kashmir especially the Kashmir valley is one of them. [32,12,20,33,21,34-36]

In a number of studies done in Kashmir, it was reported that carcinomas of esophagus and stomach account to more than 57- 60 % of cancer cases in the state including Oesophageal and gastric malignancies. [38,39] A case-control study conducted in Kashmir revealed the effect of dietary habits on the increasing numbers of gastric carcinomas in the valley which included common habits like drinking a large quantity of Kashmiri salt tea and its peculiar preparation methods etc. [37]

**4. Dietary Risk Factors in Kashmiri Population:**

Kashmiri population has distinct dietary habits owing to the long winter spells prevalent in the valley which has accustomed the population to preserve the food in the form of smoked, pickled and dried foods. [40] Some of the common and largely consumed peculiar foods of the valley include:

**4.1: Sun-dried vegetables (*Hukh Suen*):**

Vegetables like turnips, tomatoes, bottle gourd, and brinjal are commonly consumed in the dried form. Turnip is peeled and sliced which is then hung to dry in open air. Long thin variety of brinjal is also preserved in the same way, sliced lengthwise, it is hung in straight ropes and left to sundry. Tomatoes are simply sliced and spread on a large surface to sundry. Bottle gourd is the most preferred and largely consumed dried vegetable of the valley which is cleaned and sliced, then left to dry.

It has also been reported that drying vegetables in the sun, exposing to uncontrolled U.V radiations makes the vegetables more prone to Aflatoxins and Fungi which may be detrimental to human health. [41]

**4.2: Brassica oleracea (*Haakh*):**

It is the most commonly consumed green leafy vegetable of the valley, owing to its affordable price people of all economic strata consume it as a staple diet. These are best cooked with a bit of green and red chili and tastes best when freshly off-stoved. [40]

Studies found that these preserved and peculiar foods have a significant amount of N-Nitroso compounds in them. [34] There are enough literature and evidence to prove the carcinogenic effect of N-Nitroso compounds. Studies done on experimental animals by exposing them to doses of N-Nitroso compound prove their toxicity and carcinogenetic effect in humans. [40] Some of the Foods commonly consumed in the valley contain the following N-Nitroso compounds as listed in Table 1. [40]

**Table1. Showing Typical Food Products Consumed by Kashmiri Population and Type of NOCs Contained in These Diet**

Type of Food Products	Description	N-Nitroso compound
Sundried foods	Different vegetables sundried in summers and consumed over a period of time during different seasons	NDMA (35.6 µg/kg)
Dried fish	Fresh water fish dried in sun and available in the markets; they are consumed over a period of time	NDMA (20 µg/kg)
Kehwa	Traditional sweet drink , with no tea	NDMA (9.2 µg/kg).
Traditional pickle	Mixed vegetable fermented with specific spices and consumed all round the year	NDMA (7.3 µg/kg)
<i>Brassica oleracia</i>	Commonly used green leafy vegetable.	NDMA (69.9 µg/kg), & NMU
Tobacco	In the form of cigarette/Hubble bubble - Hukka	NDMA, NPYR & NPIP
Kashmiri salt tea	Tea treated with bicarbonate, brewed at high temperature and diluted for drinking	NPRO & NPIC

Source: [40, 34]

### 4.3: Kashmiri Salt Tea (*Noon Chai*):

Referred to as *noon chai* in Kashmir and *sheer chai* in Central Asia, it is the prime traditional salted beverage of Kashmir. Its consumption by masses is daily. [12, 20, 33, 21, 34-36,42]

This most popular tea consumed from generation to generation is either in a brass utensil (samovar) which keeps tea warm by burning coal inside or a Modern thermos Flask

Its peculiar method of preparation includes brewing in sodium bicarbonate until a rich thick brown colour is obtained which is commonly called as *tueth*, for the correct red colour the right constituent of sodium bicarbonate is necessary; More the sodium bicarbonate darker the colour. It takes 45 min to 2 hours until the brown colour is truly obtained. It is then diluted with water where salt and milk is added. it is served hot and some may also add cream on the top depending on the consumers personal liking. It may be reheated as a personal requirement. It is the first beverage taken by the consumers in the morning and at the afternoon usually with Kashmiri flatbread brought from the local bakers. This local naan is made by the addition of white flour with salt and baking soda which further adds to the salt intake along with the Kashmiri salt tea. It is also believed that Kashmiri salt tea has a good digestibility because of the soda bicarbonate content. [34]

The per capita consumption of this Kashmiri salt tea range is 200 to 2500ml and is generally preferred hot by the consumers. [35] The intake of Kashmiri salt tea is more prevalent during winter seasons and generally preferred for indoor warmth, usually taken during morning and afternoon, it is also taken during working hours by the majority of the population.

**4.3.1: Salt and Kashmiri salt Tea:** The amount of salt ones uses in the tea is dependent on the consumer's perception of salty taste while some prefer high salted Kashmiri salt tea others may like low salted Kashmiri salt tea. Depending upon this perception the salt intake is based on the number of cups taken per day and their

frequency. More than 4 cups per day have been related to the risk of gastric cancer. [33]

Additionally the intake of *Girda* (Kashmiri special naan) which also has an additional salt value, with the Kashmiri salt tea adds to the intake of salt with it.

**4.3.2: Kashmiri salt tea and its Effects:** The internal mucosa lining of the GIT can be damaged by drinking frequent hot beverages. [43-45] Similarly consuming Kashmiri salt tea at a high temperature (hot in nature) may cause the damage of gastric epithelial cells. [12,35] This damage eventually leads to the formation of many free radicals of oxygen and nitrogen which can ultimately lead to carcinomas. [28] as reported in Mongolia by a case-control study individual habitual of drinking hot tea and beverages are more prone ( 3 times) to gastric carcinomas. [46] On average those individuals who are prone to drinking hot tea are more prone to gastric cancers than others. [47, 48]

**4.3.3: Reported Carcinogens present in Kashmiri salt tea as evident by previous studies:** Kashmiri salt tea can lead to very high exposure towards:

1. Methylamine: Causes burning of gastric mucous membrane which in turn causes early gastric cancer symptoms [51]
2. Ethylamine: causes irritation in the gastric mucous membrane and shows high toxicity towards pancreas [51]
3. Diethylamine: The acidic environment of the stomach causes diethylamine to react between nitrites and secondary amines which produce potent Nitrosamines. [51]
4. Pyrrolidine: Forms N-nitrosopyrrolidine, which is a potent carcinogen by reaction between sodium nitrate and pyrrolidine. Causes severe damage to liver and kidneys and formation of multiple tumors in the body. [51]
5. Methylbenzylamine, an animal carcinogen: results in oesophageal cancer by increasing the cell growth resulting a large number of tumors. [53, 34, 49]

Besides these during the preparation of Kashmiri salt tea following carcinogens are formed.

1. N-nitrosodimethylamine (NDMA):
2. N-nitrosoproline (NPRO) (360 µg/kg) and
3. N-nitroso pipercolic acid (NPIC) (5870 µg/kg) [50]

These are formed by the occurrence of intragastric nitrosation in which NDMA involves biotransformation by liver microsomal enzymes which generate methyl diazonium ion. This forms DNA adducts pointing at O6 –methyl guanine as a potent carcinogenic agent. [62] Presently studies report that overall nitrites and nitroso/nitroso amine compounds have a positive co-relation with gastric carcinoma. [52]

It is worth mentioning that along with these carcinogens some unidentified N-nitroso compounds are also present because of the local preparatory method of the Kashmiri salt tea. [34] Human resistance to nitroso compounds as carcinogens is negligible. [50] Presence of tannins in Kashmiri salt tea that have given positive effects to ribosomal degradation and have shown high toxicity in rats also proves that they can also be a contributing factor in the increasing carcinomas of the valley. [34]

#### 4.3.4: Effect of salt on Stomach Mucosa:

Salt acts as an initiator and the promoter in the process of gastric carcinomas. In some cases, it can also lead to loss of some glandular tissue and causes early gastric cancer symptoms which eventually leads to an advanced stage [54] A high salt intake diet can lead to chronic active gastritis. [55, 56] High salt intake can also cause helicobacter infection. [37] Chronic hypergastrinemia by high salt intake can synergize with Helicobacter infection and lead to eventual parietal cell loss and progression to gastric cancer. [57] A high salt intake may strip the lining of the stomach and may make infection with H. pylori more likely or may exacerbate the infection.

On the molecular level, high dietary salt intake may potentiate CagA (H. pylori

gene) expression and enhance the ability of CagA to translocate into gastric epithelial cells and enhance the ability of H. pylori to alter gastric epithelial cell function. [58]

Other potential reasons for Gastric cancer:

1. Smoked and cured foods: Kashmiri population enjoys a large variety of smoked foods like mutton and beef barbecues popularly called as *Tujji* in the valley. This smoked meat has a large amount of N-nitroso compounds in them which in turn result in the production of many potent carcinogenic compounds that are positively co-related to gastric cancer. [59]

2. Type-A blood group: Control studies reported that people of Type –A blood group are more prone to gastric cancer than non-type A and are hence more prone to H-Pylori infection as compare to non A type. [60]

3. Medical history: Heredity diffuse gastric cancer (HDGC) is a rare genetic condition in which the mutated gene (cancer gene) passes from one generation to another thus making the generation inheriting it more prone to gastric cancer as compared to others. [61] Pre-natal genetic diagnosis is the best way to diagnose the probability of the cancer gene in the embryo.

## 5. CONCLUSION

Peculiar dietary habits are related to the risk of gastric cancer in Kashmir. A dietary modification involving less Kashmiri salt tea, dried vegetables etc could be a practical strategy to decrease gastric cancer in Kashmir. People should be made aware about the ill effects of potential carcinogenic dietary compounds that are present in food and its consumption on empty stomach. This study creates an initial study base and enlists a number of potential factors responsible for the alarming rate of gastric carcinoma in the valley.

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