IDENTIFICATION OF RISK FACTORS IN THE DEVELOPMENT OF VARIOUS TYPES OF CANCERS AND COMMON CHEMO DRUGS USE PATTERN IN BANGLADESH

A thesis report, submitted to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

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CERTIFICATE BY HEAD OF THE DEPARTMENT

This is to certify that the dissertation entitled

"Identification of Risk Factors in the Development of Various Types of Cancers and Common Chemo Drugs Use Pattern in Bangladesh." is a cancer survey research work done by **Md. Shamsuzzaman** (2008-1-70-047) under the guidance of Farjana Khatun, Lecturer, Department of Pharmacy, East West University, Dhaka. No part of the thesis has been submitted for any other degree. I also certify that all the sources of information availed of this connection is duly acknowledged.

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CERTIFICATE BY THE SUPERVISOR

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Dedicated

To

My Loving Parents,

My Elder Brother

ABSTRACT

Purpose: The present research was a comprehensive study that was conducted to identify risk factors involved with various types of cancers and common drugs to cure cancers.

Methods: This was a survey based study where cancer patients of different genders, locations, occupations were taken as volunteers. A questionnaire was made to complete this survey. Information was collected by taking interview of the patients, observing diagnostic reports and prescriptions and also consulting with in charge doctors of the patients over a period of four months. Data was analyzed using Microsoft Excel 2010.

Results: From this study it was found that adults (60%) are more susceptible to cancer rather than any other age group. Males (71.25%) are very susceptible to cancer rather than woman (28.75%). Housewives (25%) and businessmen (23%) were mainly affected by different type of cancers. Mental stress (55%) is the major cause of cancer rather than the physical stress (45%). Smoking habit (42.1%) has large impact on causing cancer in males. Respiratory cancers (33.3%) and gastrointestinal cancers (33.3%) were most common in males. Taking betel nut (51.25%) habitually can cause various kinds of cancers, among them respiratory cancers (19.5%) and gastrointestinal cancers (24.5%) were most common. Cisplatin (42.5%) and etoposide (31.25%) these two anticancer drugs were given to most of the cancer patients.

Conclusion: The results of the study clearly indicate avoiding tobacco may be one of the best health decisions to prevent cancers. To raise public awareness regarding serious health ailments like cancer.

Keywords: *Cancer, gene, tumor, mechanism, TNM system, risk factors, chemotherapy, smoking.*

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Introduction

1. Introduction

The body is made up of hundreds of millions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries. Cancer begins when cells in a part of the body undergo abnormal cell division (1). There are many kinds of cancer, but they all start because of out of control cell division or growth of abnormal cells. Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to divide and form new, abnormal cells. Cancer cells can also invade other tissues (2). Cells become cancer cells because of the abnormal gene expression of DNA. DNA is present in every cell and directs all actions of the cell. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies by following programmed cell death (1). Apoptosis, or programmed cell death, is a normal component of the development and health of multicellular organisms. In cancer cell, the damaged DNA is not repaired, but the cell does not die like it should (programmed cell death). Instead, this cell goes on making new abnormal cells which are not recommended for the body. These new cells will all have the same damaged or genetically over expressed DNA as the first genetically damaged mother cell does. People can inherit damaged or over expressed DNA, but most DNA damage is caused by accidentally or pollution or environmental factors that happen while the normal cell is reproducing (2). Sometimes the cause of the DNA damage is something obvious, like cigarette smoking, nuclear radiation. But in most of the cases, no clear cause is found. In most cases the cancer cells form a tumor. Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is

called metastasis. It happens when the cancer cells get into the bloodstream or lymph vessels of our body. Different types of cancer can behave very differently (2).

1.1 Demographic facts for the world population

1.1.1 Population size and density

The estimated population of the world in 2008 was 6.75 billion people, increasing by around 79 million people each year. The world population is forecast to reach 7 billion people by late 2011, and 9.1 billion by 2050. Around four-fifths of the world's population live in the less developed regions of the world, and the vast majority of the world's population growth are expected to occur in these areas. By 2050, some 87% of the world's population is expected to reside in the developing countries (3).

Table – 1.1: Population Measures and Cancer Incidence and Mortality in Asia, Estimates between 2005 and 2010 (3).

	Population			Life Expectancy	Number of New Cancer Cases*		Number of Cancer Deaths*	
	2008 Estimates [Total] 2010 Estimates [by Age]			2005-2010 estimates	2008 estimates		2008 estimates	
	Total (1000's)	% Under 15	% Over 60	Years	Total	% of World Total	Total	% of World Total
Africa	987,092	40%	5%	54	715,571	6	541,779	7
Eastern Africa	310,570	44%	5%	53	221,076	2	173,676	2
Middle Africa	122,501	45%	5%	48	66,895	1	53,229	1
Northern Africa	205,814	31%	7%	68	164,350	1	120,801	2
Southern Africa	56,936	31%	7%	52	79,179	1	54,818	1
Western Africa	291,270	43%	5%	51	184,071	1	139,255	2
Asia	4,075,309	26%	10%	69	6,092,359	48	4,072,332	54
Eastern Asia	1,546,825	19%	14%	74	3,720,658	29	2,440,351	32

South-Central Asia	1,728,752	31%	7%	64	1,423,213	11	979,914	13
South-Eastern Asia	575,626	27%	9%	70	725,446	6	501,046	7
Western Asia	224,106	32%	7%	71	223,042	2	151,021	2
Europe	731,568	15%	22%	75	3,208,882	25	1,715,240	23
Central and Eastern Europe	293,488	15%	19%	69	983,408	8	626,007	8
Northern Europe	97,918	17%	23%	79	482,080	4	242,422	3
Southern Europe	152,316	15%	24%	80	713,401	6	382,773	5
Western Europe	187,846	16%	24%	80	1,029,993	8	464,038	6
Latin American and Caribbean	576,102	28%	10%	73	906,008	7	542,051	7
Caribbean	41,629	27%	12%	72	79,347	1	47,842	1
Central America	149,580	30%	9%	75	176,564	1	108,328	1
South America	384,892	27%	10%	73	650,097	5	385,881	5
Northern America	345,053	20%	18%	79	1,603,870	13	638,328	8
Oceania	34,937	24%	15%	76	135,864	1	55,072	1
More Developed Regions	1,229,219	17%	22%	77	5,555,281	44	2,744,840	36
Less Developed Regions	5,520,843	29%	9%	66	7,107,273	56	4,819,962	64
World	6,750,062	27%	11%	68	12,662,554	100	7,564,802	

China and India are by far the most populated countries in the world, accounting for 20% and 18% of the world's total population in 2008, respectively. Between 2003 and 2008, approximately a third (32%) of the world's population growth of around 400 million people occurred in India and China, and India is expected to overtake China to become the world's most populated country by 2030 (3).

1.1.2 Cancer incidence and mortality

An estimated 12.66 million people were diagnosed with cancer across the world in 2008 (Table 1.1). This equates to around 188 cases for every 100,000 people. The number of new cases found about 3.72 million in Eastern Asia. As expected from the size of Asia's population, the majority of cases (48%) occurred there. Just four cancer sites – lung, female breast, colorectal and stomach – accounted for two-fifths (41%) of the world's total. Cancer incidence worldwide is more than a fifth higher in men than in women, with World age-standardized incidence rates of

204 and 165 per 100,000, respectively, in 2008. Cancer was estimated to account for around 14% of all deaths (due to any cause) worldwide in 2008 (3).

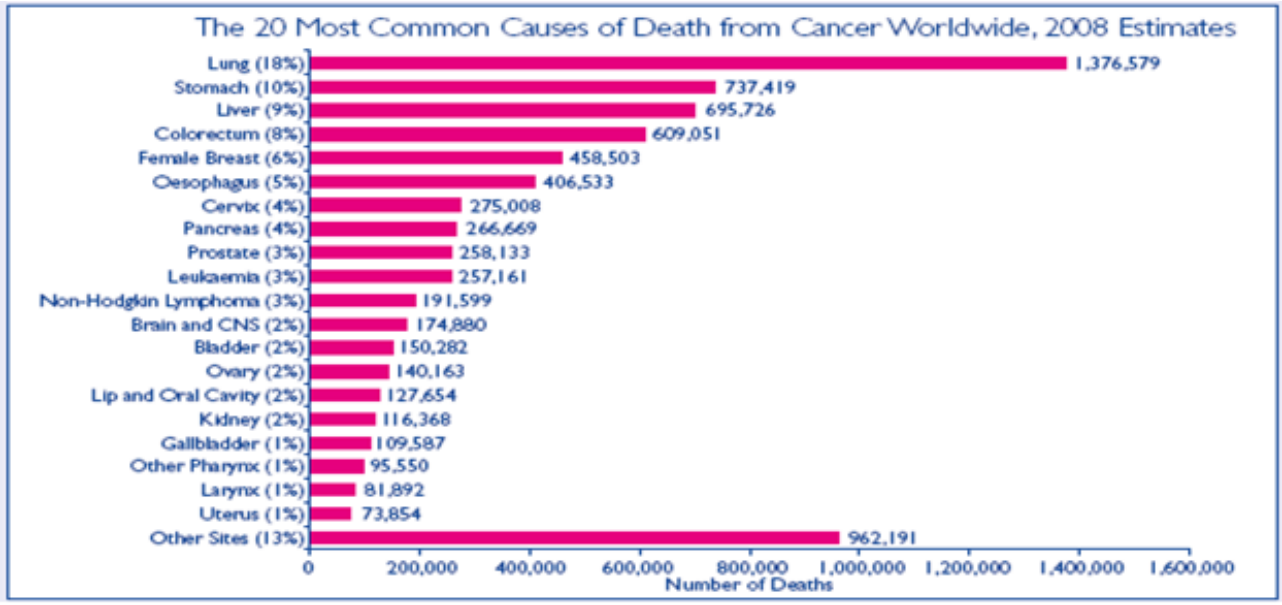

Figure- 1.1.1: The 20 Most Common Causes of Death from Cancer Worldwide, 2008 (3)

An estimated 7.56 million people died from cancer across the world in 2008. The four most common sites of cancer death – lung, stomach, liver and colorectal – accounted for 45% of the world's total cancer mortality (3).

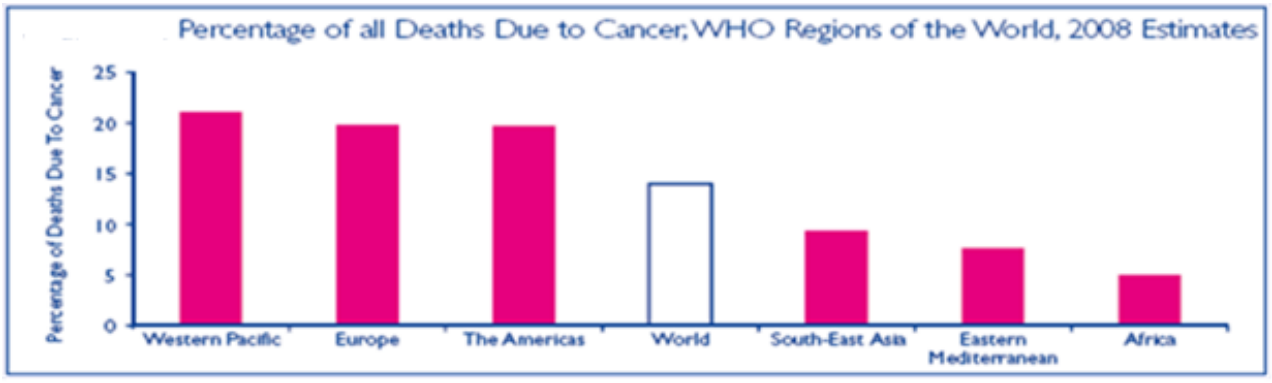

Figure- 1.1.2: Percentage of all Deaths Due to Cancer, WHO Regions of the World, 2008 Estimates (4).

1.2 Classification of Cancers

Table- 1.2: Classification of cancers according to the involved body location and organ system (5) (6).

Class	Sub class
Breast Cancer	Infiltrating (invasive) breast cancer Pre-invasive breast cancer (DCIS, LCIS) Inflammatory breast cancer Paget's Disease Metastatic breast cancer Recurrent breast cancer
Gastrointestinal / Digestive	Bile Duct Cancer Colon Cancer Gallbladder Cancer Gastric Cancer Intestinal Cancer Liver Cancer Pancreatic Cancer Rectal Cancer Stomach Cancers
Genitourinary / Urinal	Adrenal Cancer Bladder Cancer Kidney Cancer Penile Cancer

		Prostate Cancer Testicular Cancer Urinary Cancer
Gynecologic		Cervical Cancer Endometrial Cancer Fallopian Tube Cancer Ovarian Cancer Uterine Cancer Vaginal Cancer Vulvar Cancer
Head & Neck		Eye Cancer Head and Neck Cancer Laryngeal Cancer Oral Cancer Pharyngeal Cancer
	Oral Cancer	Salivary Gland Cancer Throat Cancer Thyroid Cancer Tongue Cancer Tonsil Cancer Jaw Cancer
	Pharyngeal Cancer	Sinus Cancer Nasal Cavity Cancer

Hematological / Blood	Hodgkin's Disease Leukemia Acute Lymphocytic Leukemia - ALL Acute Granulocytic Leukemia Acute Myelogenous Leukemia - AML Chronic Lymphocytic Leukemia - CLL Chronic Myelogenous Leukemia - CML Multiple Myeloma Lymphoma B-Cell Lymphoma Lymph Node Cancer (Lymphoma)
Musculoskeletal / Soft Tissue	Bone Cancer Osteosarcoma Melanoma Skin Cancer Basal Cell Squamous Cell Sarcoma Ewing's Sarcoma Kaposis Sarcoma
Neurological	Brain Tumor, Adult Brain Tumor, Childhood Astrocytomas

	Brain Stem Glioma Central Nervous System Atypical Teratoid/Rhabdoid Tumor Central Nervous System Embryonal Tumors Central Nervous System Germ Cell Tumors, Childhood -Craniopharyngioma -Ependymoma -Medulloblastoma -Spinal Cord Tumors Supratentorial Primitive Neuroectodermal Tumors -Pineoblastoma Neuroblastoma Pituitary Tumor Primary Central Nervous System (CNS) Lymphoma
Respiratory / Lung	Lung Cancer Adenocarcinoma Oat Cell Non-Small Cell Small Cell Squamous Cell

	Malignant Mesothelioma Thymoma and Thymic Carcinoma
Endocrine	Adrenocortical Carcinoma Gastrointestinal Carcinoid Tumor Pancreatic Neuroendocrine Tumors Islet Cell Tumors Parathyroid Cancer Pheochromocytoma Pituitary Tumor Thyroid Cancer
Eye	Intraocular Melanoma Retinoblastoma
Germ Cell	Childhood Central Nervous System Germ Cell Tumors Extracranial Germ Cell Tumor (Childhood) Extragonadal Germ Cell Tumor Ovarian Cancer Testicular Cancer
Skin	Cutaneous T-Cell Lymphoma Kaposi Sarcoma Melanoma Merkel Cell Carcinoma Skin Cancer

	T-Cell Lymphoma, Cutaneous

1.3 Mechanism of Developing Cancer

The process of replicating DNA and dividing a cell can be described as a series of coordinated events that compose a "cell division cycle," In each cell division cycle, chromosomes are replicated once (DNA synthesis or S-phase) and segregated to create two genetically identical daughter cells (mitosis or M-phase). These events are spaced by intervals of growth and reorganization (gap phases G_1 and G_2) (7). Cells can stop cycling after division, entering a state of quiescence (G_0). Commitment to traverse an entire cycle is made in late G_1. Progress through the cycle is accomplished in part by the regulated activity of numerous CDK–cyclin complexes, indicated here (7). At least two types of cell cycle control mechanisms are recognized: a cascade of protein phosphorylations that relay a cell from one stage to the next and a set of checkpoints that monitor completion of critical events and delay progression to the next stage if necessary (7). The first type of control involves a highly regulated kinase family (8). Kinase activation generally requires association with a second subunit that is transiently expressed at the appropriate period of the cell cycle; the periodic "cyclin" subunit associates with its partner "cyclin-dependent kinase" (CDK) to create an active complex with unique substrate specificity. Regulatory phosphorylation and dephosphorylation fine-tune the activity of CDK–cyclin complexes, ensuring well-delineated transitions between cell cycle stages.

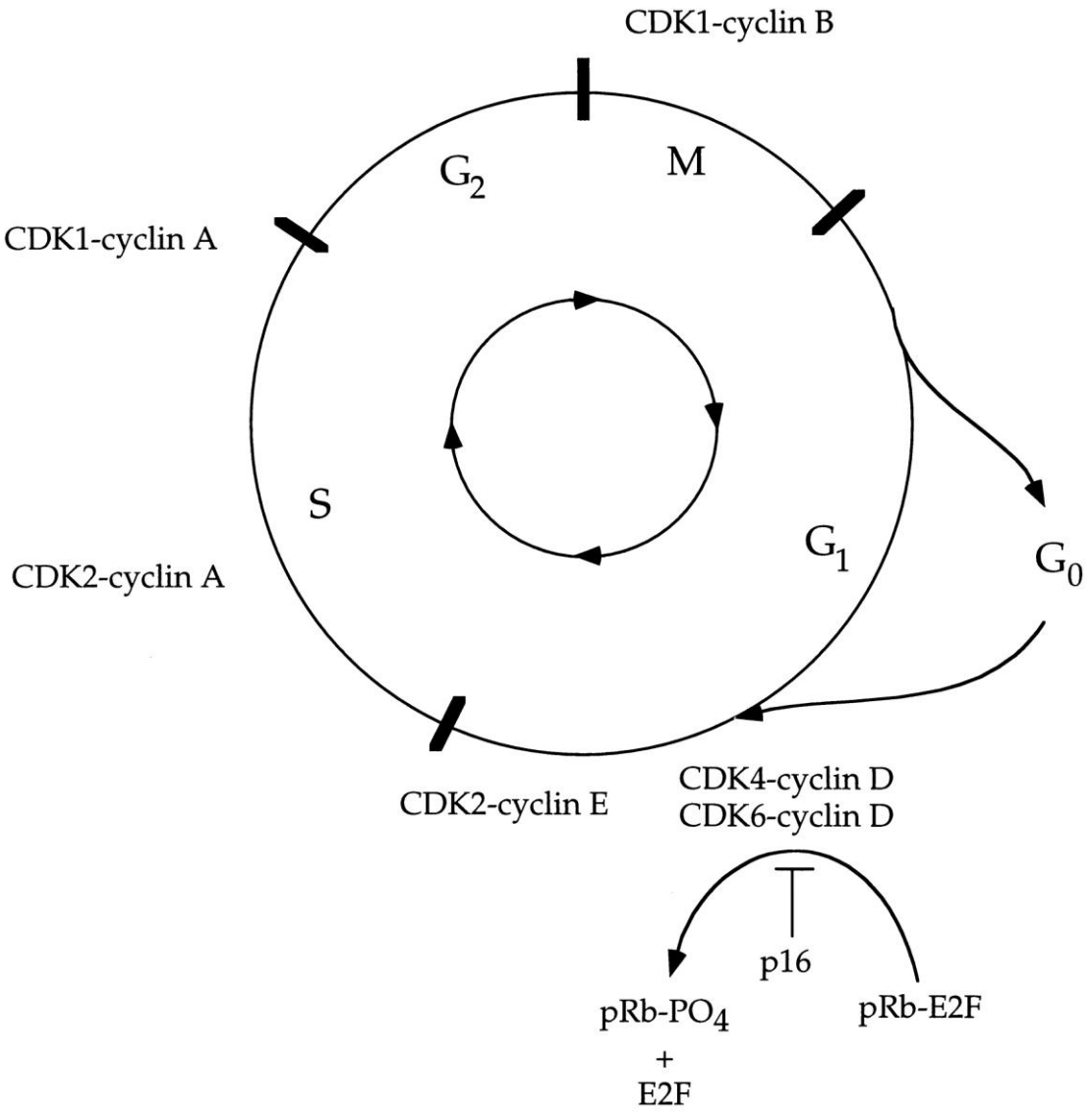

Figure 1.3: A schematic representation of the mammalian cell cycle (7).

A second type of cell cycle regulation, checkpoint control, is more supervisory. It is not an essential part of the cycle progression machinery. Cell cycle checkpoints sense flaws in critical events such as DNA replication and chromosome segregation (9). When checkpoints are activated, for example by under replicated or damaged DNA, signals are relayed to the cell cycle-progression machinery. These signals cause a delay in cycle progression, until the danger of mutation has been averted. Because checkpoint function is not required in every cell cycle, the

extent of checkpoint function is not as obvious as that of components integral to the process, such as CDKs (7).

Superficially, the connection between the cell cycle and cancer is obvious: cell cycle machinery controls cell proliferation, and cancer is a disease of inappropriate cell proliferation (7). Fundamentally, all cancers permit the existence of too many cells. However, this cell number excess is linked in a vicious cycle with a reduction in sensitivity to signals that normally tell a cell to adhere, differentiate, or die. This combination of altered properties increases the difficulty of deciphering which changes are primarily responsible for causing cancer (7).

The first genetic alterations shown to contribute to cancer development were gain-of-function mutations (10). These mutations define a set of "oncogenes" that are mutant versions of normal cellular "protooncogenes." The products of protooncogenes function in signal transduction pathways that promote cell proliferation. However, transformation by individual oncogenes can be redundant or can be cell type-specific. This suggests that multiple, distinct pathways of genetic alteration lead to cancer, but that not all pathways have the same role in each cell type.

More recently, the significance of loss-of-function mutations in carcinogenesis has become increasingly apparent (11). Mutations in these so-called "tumor suppressor" genes were initially recognized to have a major role in inherited cancer susceptibility (7). Because inactivation of both copies of a tumor suppressor gene is required for loss of function, individuals heterozygous for mutations at the locus are phenotypically normal. Thus, unlike gain-of-function mutations, loss-of-function tumor suppressor mutations can be carried in the gene pool with no direct deleterious consequence. However, individuals heterozygous for tumor suppressor mutations are more likely to develop cancer, because only one mutational event is required to prevent synthesis of any functional gene product (7).

It now appears that tumor suppressor gene mutations are highly likely to promote, and may even be required for, a large number of spontaneous as well as hereditary forms of cancer (12). But what are the functions of tumor suppressor gene products in a normal cell? There is suggestive evidence that several tumor suppressor genes encode proteins that negatively regulate cell cycle progression. Loss of function of the tumor suppressor gene product pRb, for example, would be predicted to liberate E2F transcriptional activators without requiring phosphorylation and thus bypass a normal negative regulation controlling entry into the cycle (Fig. 1.3). Loss of the tumor suppressor gene p16 would have a similar consequence, liberating E2Fs by increasing pRb phosphorylation (Fig. 1.3). In addition, cell cycle progression can be halted at several points by the tumor suppressor gene p53, activated in response to checkpoints sensing DNA and possibly also chromosome damage; loss of p53 would remove this brake to cycling (13).

The function of p53 in sentencing inappropriately growing cells to death has implications for cancer development and chemotherapy. Murine tumors with functional p53 respond to chemotherapy by promoting their own demise, but those lacking p53 typically do not (14).

Although p53 may serve many roles in the cell, its best-characterized function is as a transcriptional activator. The residues of p53 that are frequently mutated in cancer cells are critical for DNA binding (15). A p53–DNA co-crystal structure revealed that these frequently mutated residues fold together into one region of the surface of the protein (16). Thus, cancer-promoting mutations that occur throughout the primary sequence of the protein are in fact clustered in one functional domain.

Recent studies have focused on the structural basis for regulation of the CDKs, using CDK2 as a model system (8). In mammalian cells, CDK2 functions in S-phase with cyclin A as a partner (Fig.1.3). The association of cyclin A modifies the previously determined CDK2 structure (17)

by reorienting a catalytically critical glutamic acid into the catalytic cleft and moving away the regulatory loop that can block access of a protein substrate to bound ATP (18). Cyclin A binding stimulates CDK2 activity, but phosphorylation of threonine-160 is required for full activation. The crystal structure of threonine-phosphorylated CDK2 complexed with cyclin A reveals conformational change in the substrate-binding site and also a strengthening of CDK2–cyclin A interaction (19).

Finally, one mechanism for the inactivation of the CDK2–cyclin A complex was examined: binding of the inhibitor p27 (20). Co-crystals of CDK2–cyclin A with the N-terminal inhibitory domain of p27 reveal that bound p27 physically blocks the active site, inserting itself into the catalytic cleft. Also, p27 association modifies the structure of the "roof" of the ATP-binding site and blocks a putative protein substrate docking region on cyclin A (7). With these structural modifications in mind, it may be possible to design small molecules that will have the same effect: blocking CDK activity, thus halting the cancer cell cycle in its tracks.

1.4 Cancer Staging

1.4.1 TNM system

The staging system used by doctors is the TNM system from the American Joint Committee on Cancer (AJCC). TNM is an abbreviation for tumor (T), node (N), and metastasis (M), or cancer that has spread to other areas of the body. The TNM system uses three criteria to describe the stage of the cancer: the tumor itself, the lymph nodes around the tumor, and if the tumor has spread to other parts of the body (21) (22) (23) (24) (25).

T: The letter "T" plus a letter and a number (0 to 4) is used to describe the size of the tumor, including how much the tumor has grown into the nearby tissue. A larger tumor or a tumor that

has grown more deeply into the surrounding tissue is given a larger number (21) (22) (23) (24) (25).

N: The letter "N" plus a number (0 to 3) describes whether there is cancer in the lymph nodes, and, in some types of cancer, how many of these lymph nodes contain cancer. Lymph nodes are the tiny, bean-shaped organs that help fight infection (21) (22) (23) (24) (25).

M: The letter "M" indicates whether the cancer has metastasized (spread) to other parts of the body from where it started. Each cancer is assigned either M_0, meaning the cancer has not spread to other parts of the body, or M_1, meaning the cancer has spread to other parts of the body (21) (22) (23) (24) (25).

1.4.2 Cancer stage grouping

Doctors assign the stage of cancer by combining the T, N, and M classifications. Most cancers have four stages, stages I to IV. Some cancers also have a stage 0 (zero) (22) (23).

Stage 0: This is used to describe cancer in situ, meaning that the cancer is still near the place it started and has not invaded nearby tissues. It is often highly curable (22) (23).

Stage I: This is usually a small cancer or tumor that has not grown deeply into the nearby tissues and has not spread either to lymph nodes or other parts of the body. It is often called early-stage cancer (22) (23).

Stage II: At this stage, cancer growth is described as 'regional'. Stage II suggests that the cancer has been detected beyond the primary site. The size of the tumor is increased and the number of tumors might also be increased. When the cancer spreads to the nearby lymph nodes, tissues or organs, it is described as 'stage II cancer'. It is still possible to curb the growth of cancer with proper treatment (22) (23).

Stage III: When size of the cancer tumor is significantly large and/or when number of tumors

has increased considerably, the stage is described as stage III. During this stage, the cancer usually spreads to nearby lymph nodes, organs or even to distant lymph nodes and organs.

Stage IV: This stage means that the cancer has spread to other organs or parts of the body. It may be called advanced cancer (22) (23).

In addition to the T, N, and M staging system, we may use other information about a cancer to help determine the prognosis and the best available treatment. For some cancers, this information is used in addition to T, N, and M to determine the stage group (22) (23).

1.5 Causes, incidence, and risk factors

There are many different kinds of cancers. Cancer can develop in almost any organ or tissue, such as the lung, colon, breast, skin, bones, or nerve tissue. There are many causes of cancers, including (26) (27) (28) (29) (30) (31) (32) (33) (34) (35) (36) (37) (38) (39):

- Benzene and other chemicals
- Drinking excess alcohol
- Environmental toxins, such as certain poisonous mushrooms and a type of poison that can grow on peanut plants (aflatoxins)
- Excessive sunlight exposure
- Genetic problems/disorders
- Obesity
- Radiation (like seen after an atomic
- Diabetes
- Pancreatitis (inflammation of the pancreas)
- Infection with hepatitis B virus or hepatitis C virus
- Exposure to asbestos
- Exposure to radon or other radioactive chemicals
- Exposure to dioxin, nitrosamines, or polychlorinated biphenyls (PCBs)

bomb explosion)
- Viruses
- Tobacco Smoke
- Gender
- Race
- Age
- Family history
- Lifestyle
- Environmental factors
- Chronic use of medicines
- Auto-immune diseases like lupus (systemic lupus erythematosus) and rheumatoid arthritis.
- Workplace exposures
- Chronic irritation and infections
- Heavy metals poisoning
- Multiple enchondromatosis
- Not cancerous (benign)
- Invasive (spread to nearby areas)
- Located in only a small area
- Cancerous (malignant)
- Hormone replacement therapy (HRT)
- Iron overload in the body (hemochromatosis)
- Radon gas

1.6 Symptoms

Symptoms of cancer depend on the type and location of the cancer. For example, lung cancer can cause coughing, shortness of breath, or chest pain. Colon cancer often causes diarrhea, constipation, and blood in the stool. Some cancers may not have any symptoms at all. In certain cancers, such as pancreatic cancer, symptoms often do not start until the disease has reached an advanced stage.

The following symptoms can occur with most cancers (26) (27) (28) (29) (30) (31) (32) (33) (34) (35) (36) (37) (38) (39):

- Chills
- Abdominal pain (for cancer spread to

- Fatigue
- Fever
- Loss of appetite
- Malaise
- Night sweats
- Weight loss
- Weight gain, usually greatest around the chest and abdomen
- Fat deposits behind the neck and shoulders
- Purple stretch marks on the abdomen
- Excessive hair growth on the face, chest, and back in women
- Menstrual irregularities
- Weakness in the legs
- Easy bruising
- Depression and/or moodiness
- Weakened bones (osteoporosis), which can lead to fractures
- High blood sugar, often leading to diabetes
- High blood pressure
- Loss of energy and feeling tired

the liver).

- Shortness of breath, especially when a cancer has spread to the lungs.
- Nausea/vomiting
- Itching
- Swelling
- Fractures
- Spinal cord compression
- Hypercalcemia
- Changes in personality and behavior
- Impaired concentration
- Increased sleep
- Memory loss
- Problems with reasoning
- Gradual loss of movement or feeling in an arm or leg
- Hearing loss, with or without dizziness
- Speech difficulty
- Unexpected vision problem (especially if it occurs with a headache), including vision loss (usually of peripheral vision) in one or both eyes, or double vision

- ❖ Pain, such as back pain (for cancer spread to the spinal cord).
- ❖ Weakness or numbness
- ❖ Unsteadiness and problems with balance

1.7 Diagnosis

Like symptoms, the signs of cancer vary based on the type and location of the tumor. Common tests include the following (26) (27) (28) (29) (30) (31) (32) (33) (34) (35) (36) (37) (38) (39):

- Biopsy of the tumor
- Blood tests (which look for chemicals such as tumor markers)
- Bone marrow biopsy (for lymphoma or leukemia)
- Chest x-ray
- Complete blood count (CBC)
- Computed Tomography (CT) scan
- MRI (Magnetic Resonance Imaging) scan
- Radionuclide scans
- Imaging tests
- Somatostatin receptor scintigraphy (SRS)
- Ultrasonography
- Needle biopsies
- Surgical biopsies
- Thoracotomy
- Thorascopy
- Urine tests
- Pulmonary function tests (PET)
- Laproscopy
- Cholangiography
- Angiography
- Cholangioscopy
- Cystoscopy
- Bone scan
- Positron emission tomography (PET)

Most cancers are diagnosed by biopsy. Depending on the location of the tumor, the biopsy may be a simple procedure or a serious operation. Most patients with cancer have CT scans to determine the exact location and size of the tumor or tumors.

1.8 Treatment

Treatment varies based on the type of cancer and its stage. The stage of a cancer refers to how much it has grown and whether the tumor has spread from its original location (21).

1.8.1 Surgery

Surgery is the oldest form of cancer treatment. Advances in surgical techniques have allowed surgeons to operate on a growing number of patients and have good outcomes (40). When a surgeon has to cut into the body to operate, it's called invasive surgery. Today, operations that involve less cutting and damage to nearby organs and tissues (less invasive surgery) often can be done to remove tumors while saving as much normal tissue and function as possible (41). Surgery offers the greatest chance for cure for many types of cancer, especially those that have not spread to other parts of the body. Most people with cancer will have some type of surgery.

1.8.1.1 Preventive (prophylactic) surgery

Preventive surgery is done to remove body tissue that is likely to become cancer, even though there are no signs of cancer at the time of the surgery (42).

1.8.1.2 Staging surgery

Staging surgery is done to find out how much cancer there is and how far it has spread (43).

1.8.1.3 Curative surgery

Curative surgery is done when cancer is found in only one area, and it's likely that all of the cancer can be removed (44). In this case, curative surgery can be the main treatment. It may be used alone or along with chemotherapy or radiation therapy (45).

1.8.1.4 Debulking (cytoreductive) surgery

It is done when removing the entire cancerous tumor would cause too much damage to an organ or nearby tissues (46). In these cases, the doctor may take out as much of the tumor as possible and then try to treat what's left with radiation or chemotherapy (47).

1.8.1.5 Palliative surgery

This type of surgery is used to treat problems caused by advanced cancer. It is not done to cure the cancer (48).

1.8.1.6 Supportive surgery

Supportive surgery is done to help with other types of treatment (49).

1.8.1.7 Restorative (reconstructive) surgery

This type of surgery is used to improve the way a person looks after major cancer surgery, or to restore the function of an organ or body part after surgery (50).

1.8.2 Radiation treatment

Radiation therapy uses high-energy radiation to shrink tumors and kill cancer cells. X-rays, gamma rays, and charged particles are types of radiation used for cancer treatment. Two types of Radiation therapy are used (51).

1. **External-beam radiation therapy:** The radiation may be delivered by a machine outside the body (51).

2. Internal radiation therapy (also called brachytherapy): It may come from radioactive material placed in the body near cancer cells (51).

Systemic radiation therapy uses radioactive substances, such as radioactive iodine, that travel in the blood to kill cancer cells (51).

Radiation therapy kills cancer cells by damaging their DNA (the molecules inside cells that carry genetic information and pass it from one generation to the next) (51).

Some examples of palliative radiation therapy are:

- Radiation given to the brain to shrink tumors formed from cancer cells that have spread to the brain from another part of the body (metastases) (51).
- Radiation given to shrink a tumor that is pressing on the spine or growing within a bone, which can cause pain (51).
- Radiation given to shrink a tumor near the esophagus, which can interfere with a patient's ability to eat and drink (51).

1.8.3 Chemotherapy

Chemotherapy is the use of anti-cancer drugs that are injected into a vein or taken by mouth. These drugs enter the bloodstream and reach all areas of the body. Chemotherapy is mainly used for carcinoid tumors that have spread to other organs, are causing severe symptoms, and have not responded to other medicines. In some cases it may be given after surgery because chemotherapy does not always shrink carcinoid tumors (52) (53) (54) (55) (56) (57).

Some of the chemotherapy drugs that may be used for advanced lung carcinoids include:

1.8.3.1 Antimetabolites

Antimetabolites are structurally related to normal compounds within the cell. They generally interfere with the availability of normal purine or pyrimidine nucleotide precursors either by

inhibiting their synthesis or by competing with them in DNA or RNA synthesis. Their maximal cytotoxic effects are S-phase specific (58). Most commonly used antimetabolites are (58):

• Methotrexate

• 6-Mercaptopurine

• 5-Fluouracil

• Cytarabine

• Gemcitabine

1.8.3.2 Antibiotics

The antibiotics owe their cytotoxic action to their interaction with DNA, leading to disruption of DNA function (58). They are cell cycle specific. Most commonly used antibiotics as anticancer drugs are (58):

• Doxorubicin

• Daunorubicin

• Bleomycin

1.8.3.3 Alkylating Agents

Alkylating agents exert their cytotoxic effects by covalently binding to nucleophilic groups on various cell constituents (58). Alkylation of DNA is probably the crucial cytotoxic reaction that lethal to the tumor cell (58). Alkylating agents do not discriminate between cycling and resting cells, but they are most toxic to for rapidly diving cells (58). They are used in combination with other agents to treat a widely variety of lymphatic and solid cancers (58). In addition to being cytotoxic, all are mutagenic and carcinogenic and can lead to a second malignancy, such as leukemia (58). Most commonly used alkylating agents (58):

• Streptozotocin

• Cisplatin

• Cyclophosphamide

1.8.3.4 Topoisomerase Inhibitors

Topoisomerase inhibitors are agents designed to interfere with the action of topoisomerase enzymes (59) (topoisomerase I and II), which are enzymes that control the changes in DNA structure (60) by catalyzing the breaking and rejoining of the phosphodiester backbone of DNA strands during the normal cell cycle.

In recent years, topoisomerases have become popular targets for cancer chemotherapy treatments. It is thought that topoisomerase inhibitors block the ligation step of the cell cycle, generating single and double stranded breaks that harm the integrity of the genome. Introduction of these breaks subsequently lead to apoptosis and cell death. Most commonly used topoisomerase inhibitors:

• Etoposide

• Teniposide

1.8.3.5 Microtubule Inhibitors

The mitotic spindle is part of a larger, intracellular skeleton that is essential for the movements of structures occurring in the cytoplasm of all eukaryotic cells (58). The mitotic spindle consists of chromatin plus a system of microtubules composed of the protein tubulin. The mitotic spindle is essential for the equal portioning of DNA into the two daughter cells that are formed when a eukaryotic cell divides (58). Several plant-derived substances used as anticancer drugs disrupt this process by affecting the equilibrium between the polymerized and depolymerized forms of the microtubules, thereby causing cytotoxicity (58). Most commonly used microtubule Inhibitors (58):

• Vincristine

• Paclitaxel

In most cases, several chemotherapy drugs are used together, often in combination with other types of medicines. If we are going through chemotherapy, we should eat right. Chemotherapy causes our immune system to weaken, so we should avoid people with colds or the flu. We should also get plenty of rest, and don't feel as though we have to accomplish tasks all at once (52) (53) (54) (55) (56) (57).

1.8.4 Others

Allogeneic stem cell transplant, Immunosuppressive therapy, Transfusion, Antibiotics, Growth factors, Androgens, Treatment to lower iron levels these are performed for the treatment of aplastic-anaemia (52) (53) (54) (55) (56) (57).

Chapter: 2

Methodology

2.1 Objective

The cancer situation in Bangladesh is extremely alarming which is evident from some basic facts and figures. According to conservative estimate, presently there are over 1 million registered cancer patients in Bangladesh. Every year another additional 200,000 people are diagnosed with cancer. More than 50% of the affected people's lives are slowly but surely being snuffed out due to the cancer not being diagnosed on time and due to lack of proper treatment.

This research was conducted to identify cancer-related risk factors and its determinants among the general population of Bangladesh.

The main objectives of this study to-

1. To identify the most common cancer in Bangladesh.
2. To determine the socio-demographic variables age, gender, occupational status, education level, area of living, sources of information about cancer.
3. To identify various environmental factors like chemical substances, radiation, sun rays, and exposure to the carcinogens.
4. To identify lifestyle related risk factors for cancer incidences like tobacco smoking, gull, jorda, betel nuts, tea, coffee, alcohol consumption and alcoholic beverages (beer).
5. To identify widely used chemo drugs or anticancer drugs are given to cancer patients in Bangladesh.

2.2 Study Protocol

The study protocol consisted of the following steps:

a) Designing a questionnaire for survey

b) Selection of the study area

c) Survey work

d) Data compilation

e) Data analysis

f) Result and discussion

2.3 Inclusion Criteria

- Data were collected from cancer patients whom were given chemotherapy.
- Data were collected from in-patients only.
- Data were collected from both male and female patients
- Data were collected from all age group patients

2.4 Exclusion Criteria

- Cancer patients came for radiation therapy or surgery were excluded.
- Unwilling to participate or unable to comply with protocol requirements.

2.5 Research Design and Methods

This was a survey based study where cancer patients of different genders, locations, occupations were needed as volunteers. A questionnaire was made to complete this survey.

2.4 Study Area

The study was conducted at National Institute of Cancer Research and Hospital Mohakhali, Dhaka- 1212. The research study was carried out by maintaining the national laws and

regulations of the country and "WMA declaration on Helsinki-Ethical Principles for Medical Research Human Subjects, amended, October 2008."

2.5 Survey Method

All the information was collected by taking interview of the patients, observing diagnostic reports and prescriptions and also consulting with in charge doctors and physicians from the patients over a period of four months. The data was taken from in-patients who had come for chemotherapy. Data was analyzed using Microsoft Excel 2010. Data were collected prospectively from 80 patients from February 2012 to June 2012.

Chapter: 3

Results and Discussions

3.1 Distribution of patients according to age

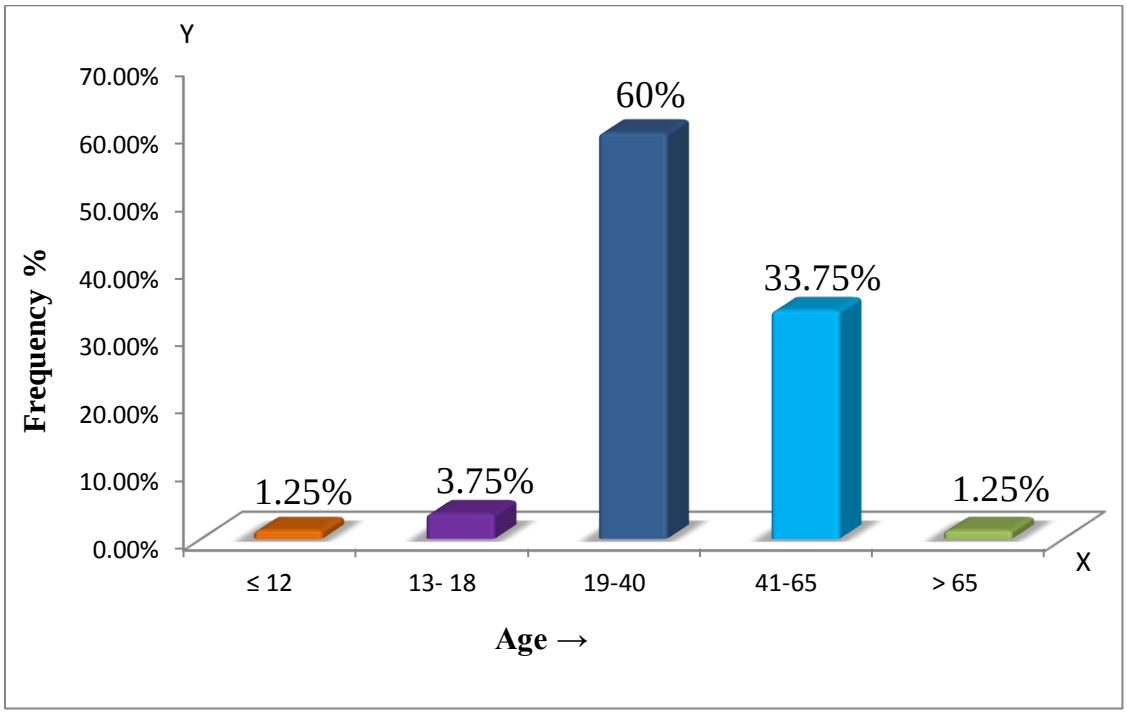

Figure 3.1: Distribution of patients according to age

In this survey based study, data were collected from 80 cancer patients (volunteers), 60% of the total cancer patients were between the ages of 19 to 40 years, 33.75% of the total patients were between the ages of 41 to 65 years, 3.75% patients were between the ages of 13 to 18 years, 1.25% patients were less than 12 years and higher than 65 years (Figure 3.1). From this study it was determined that adults were more susceptible to cancer rather than geriatrics, teenagers and pediatrics. The death rates from cancer rise with increasing age, and more than three-quarters (77%) of cancer deaths occur in those aged 65 and over in USA (61) (62) (63).

3.2 Distribution of patients According to Gender

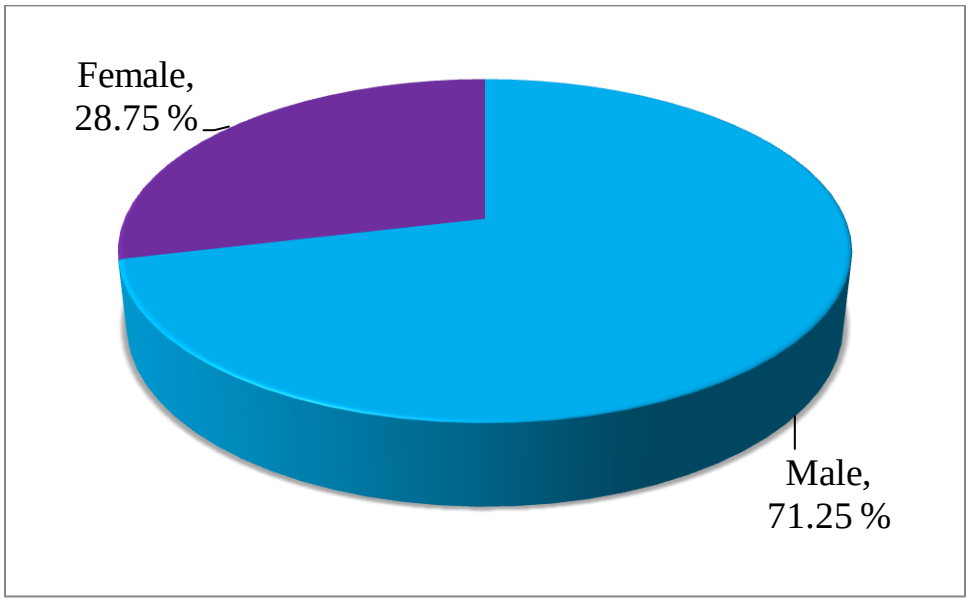

Figure 3.2: Distribution of patients According to Gender

Among 80 cancer patients, 71.25% were male patients and 28.75% were female patients (Figure 3.2). From the study it was come to know that males were very susceptible to can rather than females in Bangladesh. Men get cancer more than women, in USA, an estimation showed that from 2000 to 2004 total 745,180 new cancer cases occurred in men and 692,000 new cancer cases occurred in women, and estimated deaths in men were 294,100 and in women were 271,530 (64).

3.3 Distribution of patients according to Marital Status

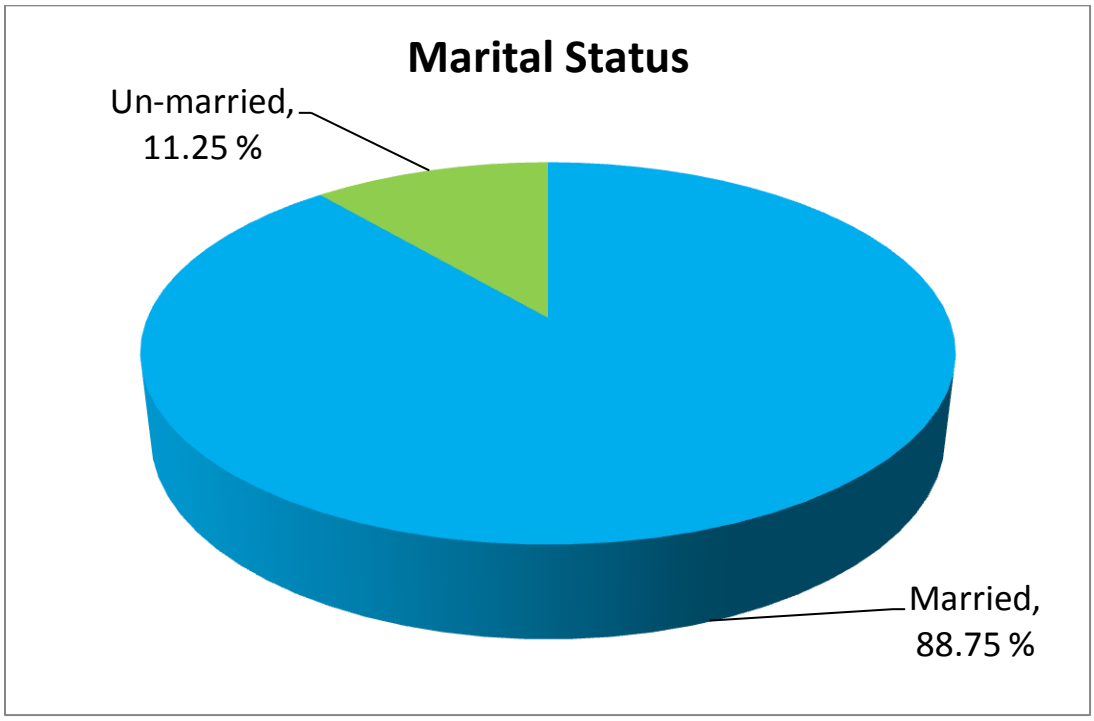

Figure 3.3: Distribution of patients according to Marital Status

Among 80 cancer patients, 88.75% were married patients and 11.25% were unmarried patients (Figure 3.3).

3.4 Distribution of patient according to living area

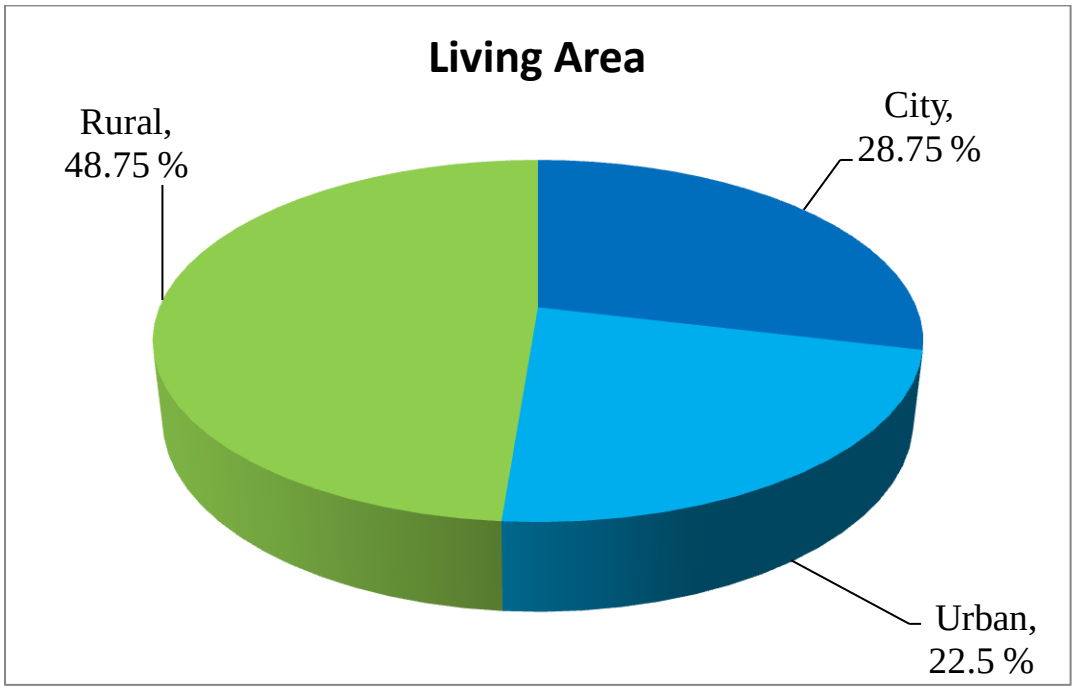

Figure 3.4: Distribution of patient according to living area

In this study data was collected from 80 cancer patients and these patients came from different districts of Bangladesh. Their living areas were divied in three categories:

- City
- Urban
- Rural

Among those 80 patients, 48.75% of the total patients came from rural areas, 28.75% of the total patients came from cities, and 22.5% of the patients came from urban areas.

3.5 Distribution of patient according to sites of living areas

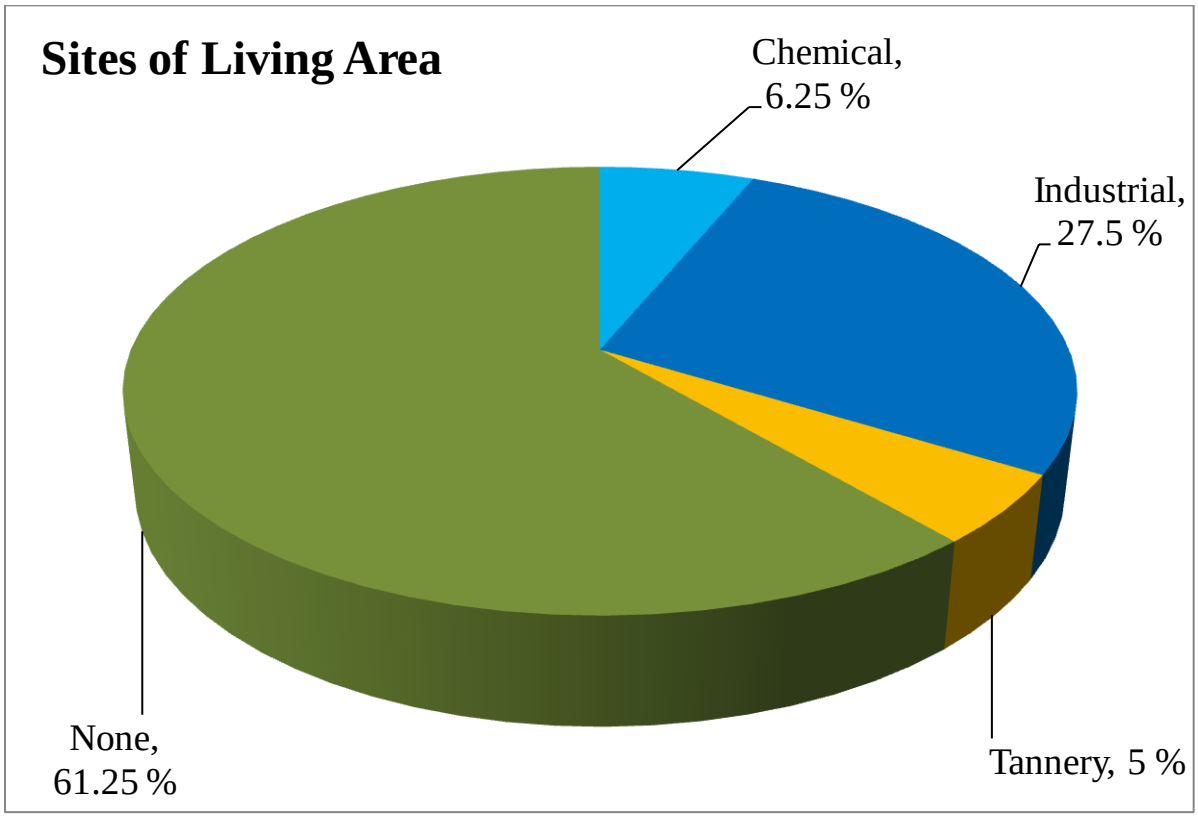

Figure 3.5: Distribution of patient according to sites of living areas

The sites of living areas of those 80 cancer patients were divided, according to their personal information given by the patients, written documents and hospital authorities. It was decided to divide the sites of living area into four categories, they are given below:

- Chemical
- Industrial
- Tannery
- Not applicable/None

It was found that 6.25% of the total cancer patients lived in the chemical areas for a long time and most of them were the workers of the chemicals based factories and a few were the only city dwellers.

27.5% lived in industrial areas, 5% lived in the tannery areas and 61.25% were from nonchemical, nonindustrial and no tannery areas. From this result it was determined that Environmental factors may have little effect on cancer incidences occurring in Bangladesh. Environmental factors may have harmful effects because patients from the chemical, industrial and tannery areas have severe cancerous conditions (65) (66).

3.6 Distribution of patients according to education

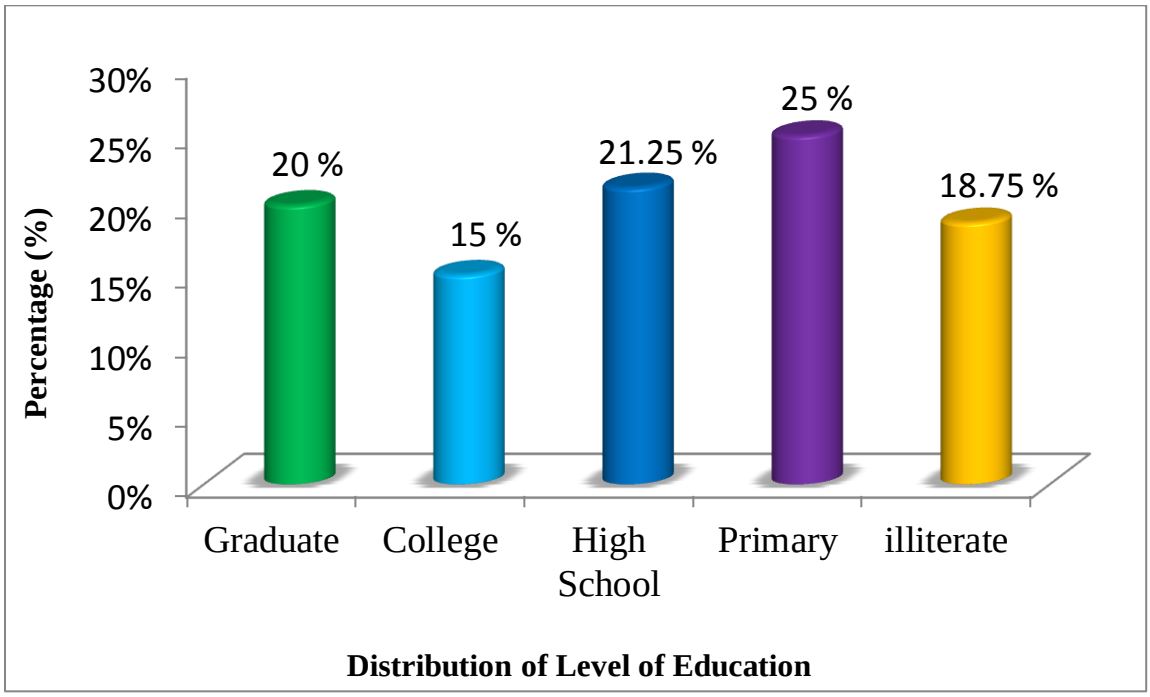

Figure 3.6: Distribution of patients according to Education

Among 80 volunteers (cancer patients), 20% were graduate persons, 15% attended college, 21.25% have passed high school, 25% finished primary education and 18.75% of them were illiterate.

3.7 Distribution of patients according to occupation

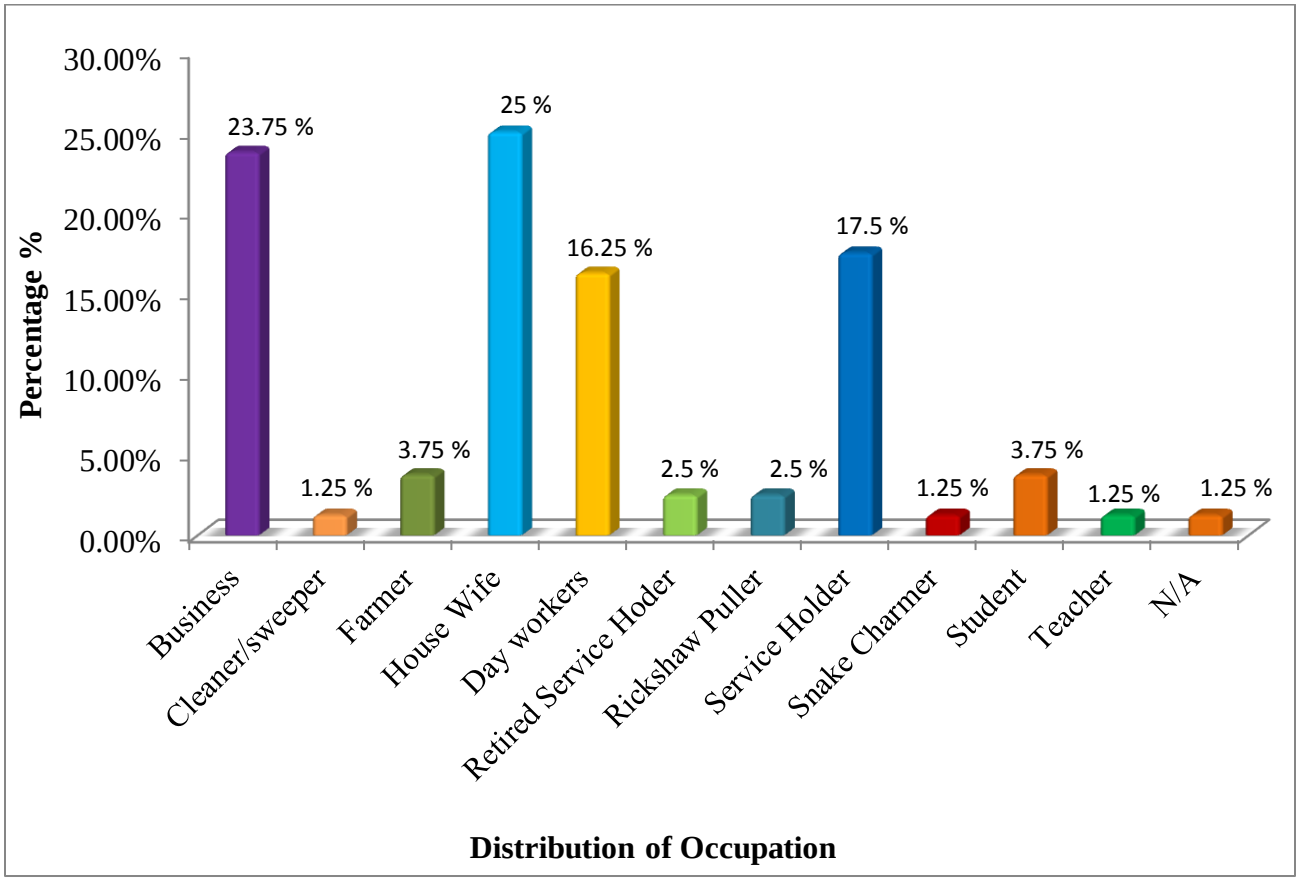

Figure 3.7: Distribution of patient according to occupation

Among 80 cancer patients, 23.75% were businessmen, 25% were housewives, 17.5% were Service holders, 2.5% were retired service holders, 16.25% were day workers, 1.25% were cleaner/sweeper, 3.75% were farmers, 2.5% were rickshaw pullers, 1.25% were snake charmers, 3.75% were students, 1.25% were teachers and 1.25 % of them were not able to do any work. From this study it was found that house wives, businessmen (mostly shopkeepers and vegetable sellers), service holders and day workers were mainly affected by different type of cancers.

3.8 Distribution of patient according to stress on work

Figure 3.8: Distribution of patient according to stress on work

Among 80 cancer patients, 55% of the patients had mental stress on work and 45% of the total cancer patients have physical stress on their work. From this result it can be said that mental stress was the major cause of cancer incidents rather than the physical stress.

3.9 Distribution of patient according to social class

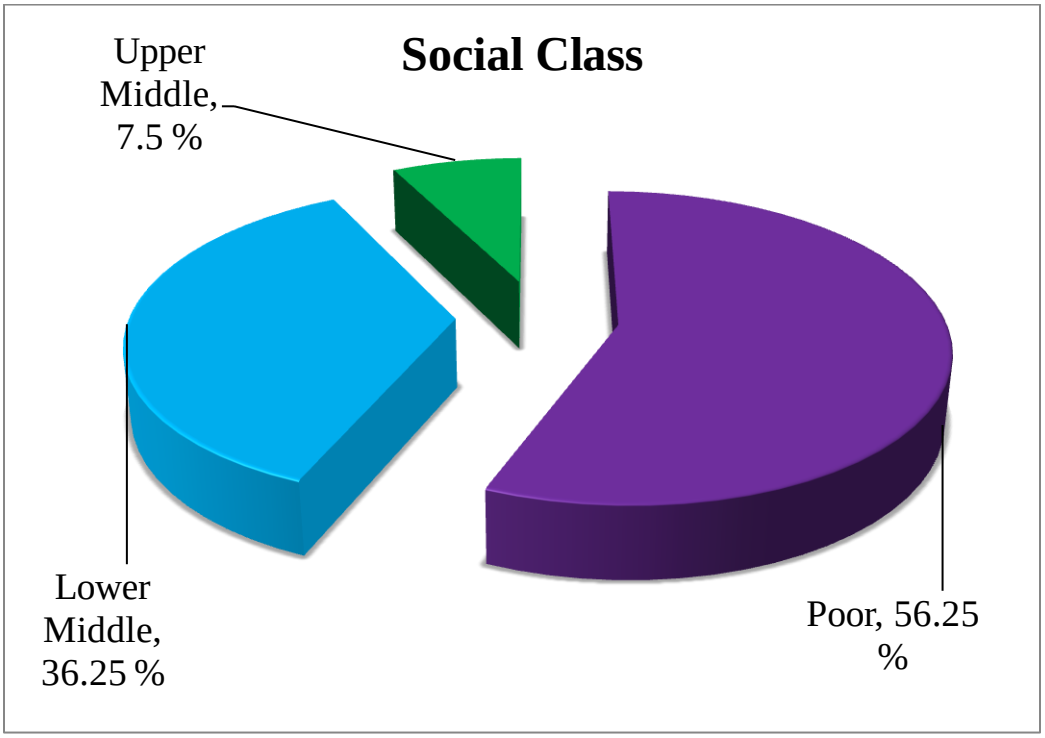

Figure 3.9: Distribution of patient according to social class

A survey based study was done on 80 cancer patients. These cancer patients came from different social class, society and cultures. For better study purposes, it was decided to create a social class. According to the plan the social class was divided into four major categories. They were:

- Rich
- Upper middle
- Lower middle
- Poor

Selected 80 cancer patients have been distributed in different categories according to their financial condition, monthly & yearly incomes, income sources and solvency. Among all of the

patients we did not find any rich patients. 7.5% patients who came from upper middle class, 36.25% of the cancer patients came from lower middle class and 56.25% of the patients were poor. From this study it was found that poor people were mainly affected by cancer in Bangladesh.

3.10 Distribution of patients according to water Source

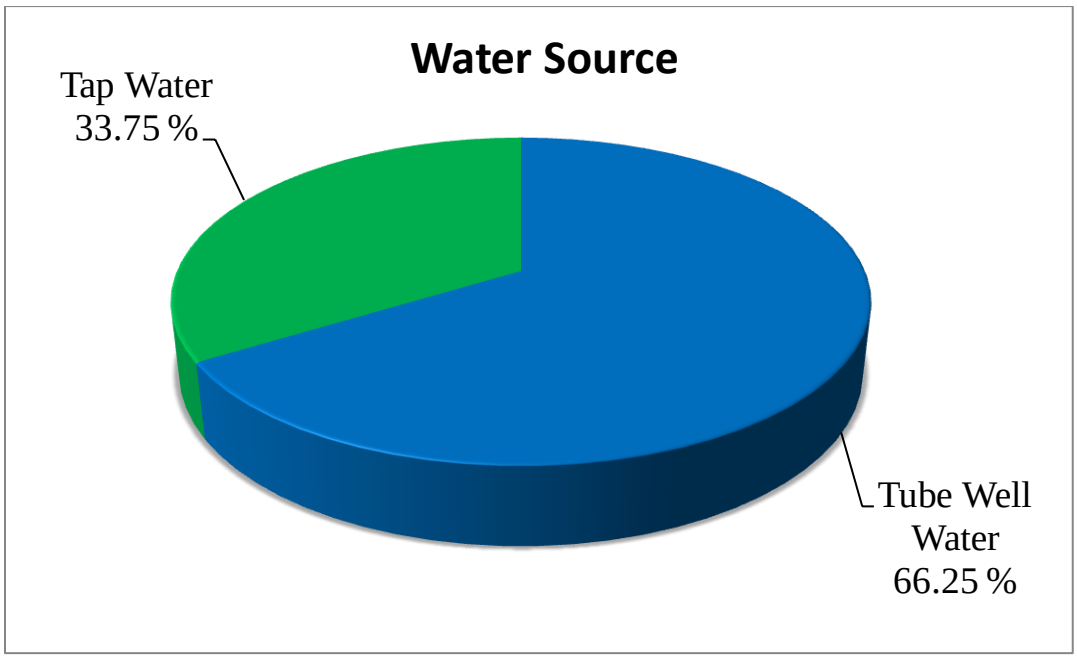

Figure 3.10: Distribution of patients according to water source

Among all 80 cancer patients, 66.25% of them have regularly used tube well water for drinking, washing clothes and dishes, and other domestic works and another 33.75% of them have used tap water for their daily life (Figure 3.10). Source-water contaminants of concern include arsenic, asbestos, radon, agricultural chemicals, and hazardous waste (67). Of these, the strongest

evidence for a cancer risk involves arsenic mainly found in tube well or underground water, which is linked to cancers of the liver, lung, bladder, and kidney (67). Chlorine is used for the treatment of water which is mainly supplied as tap water. The use of chlorine for water treatment to reduce the risk of infectious disease may account for a substantial portion of the cancer risk associated with drinking water (68). The by-products of chlorination are associated with increased risk of bladder and rectal cancer (69).

3.11 Distribution of patients according to food intake

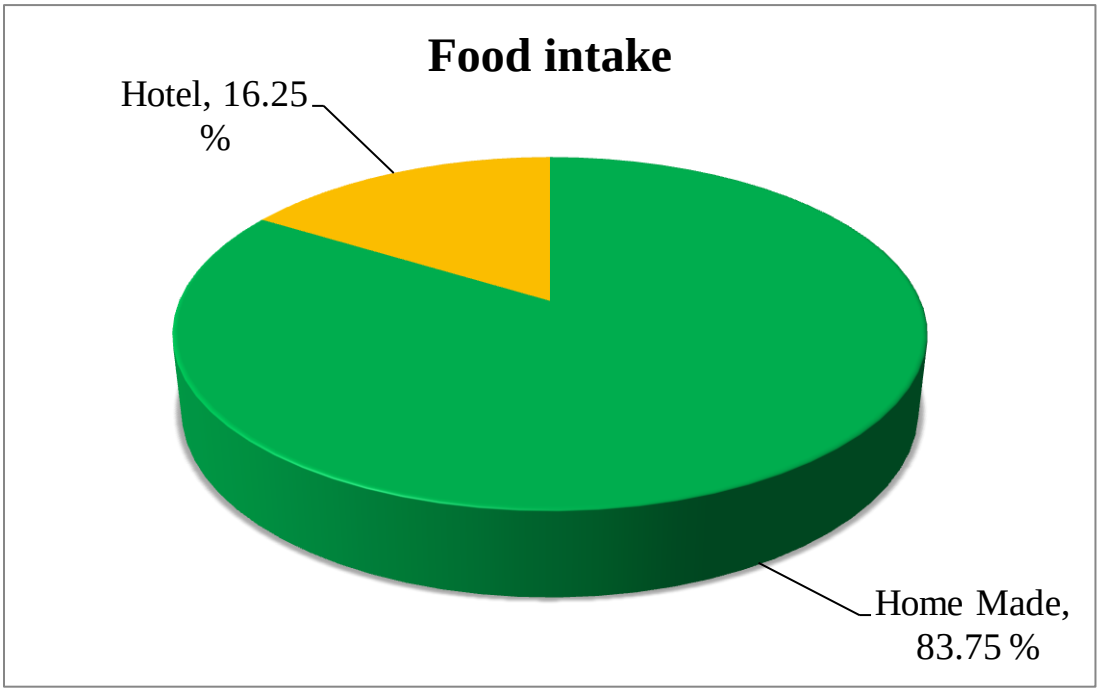

Figure 3.11: Distribution of patients according to food intake

Among 80 cancer patients, 83.75% have taken home food regularly and only 16.25% have taken hotel foods (Figure 3.11). From this study, it was clearly seen that most of the cancer incidents

occurring in Bangladesh are not closely related to food poisoning because still people of Bangladesh are not completely dependent on readymade food or fast food or hotel or restaurant made food. Potato chips and French fries were found to contain higher levels of acrylamide compared with other foods (70). High-temperature cooking methods, such as frying, baking, or broiling, have been found to produce acrylamide (71). A series of case-control studies have investigated the relationship between dietary intake of acrylamide and the risk of developing cancers of the oral cavity, pharynx, esophagus, larynx, large bowel, kidney, breast, and ovary (72) (73) (74) (75) (76). Among women with higher levels of acrylamide bound to the hemoglobin in their blood, there was a statistically significant increase in risk of estrogen receptor-positive breast cancer. This finding suggests an endocrine hormone-related effect, which would be consistent with the results of a questionnaire-based cohort study in the Netherlands that found an excess of endometrial and ovarian cancer (77). Another cohort study from the Netherlands suggested a positive association between dietary acrylamide and the risk of renal cell cancer (78).

3.12 Distribution of male patients according to smoking habit

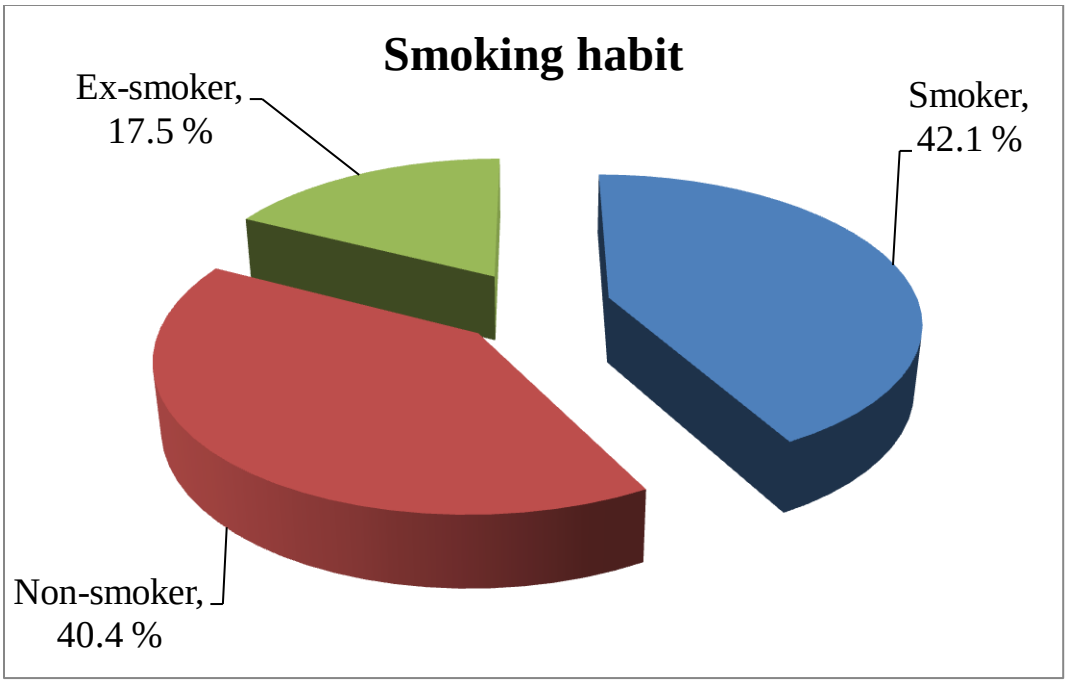

Figure 3.12: Distribution of male patients according to smoking habit

Among 80 cancer patients, 23 of them were female and they were also non-smokers. 57 cancers patients were male, among them 42.1% were smokers, 40.4% were non-smokers and 17.5% were ex-smokers. From this study, it was found that smoking habit has large impact on cancer incidences. Male smoking prevalence is among the world's highest, and mortality rates from smoking-caused cancers, particularly lung cancers (79). Smoking also increases the risk of over a dozen other cancers including cancers of the mouth, larynx, pharynx, nose and sinuses, esophagus, liver, pancreas, stomach, kidney, bladder, cervix and bowel, as well as one type of ovarian cancer and some types of leukemia (80) (81) (82) (83) (84).

3.13 Distribution of patient according to other habits

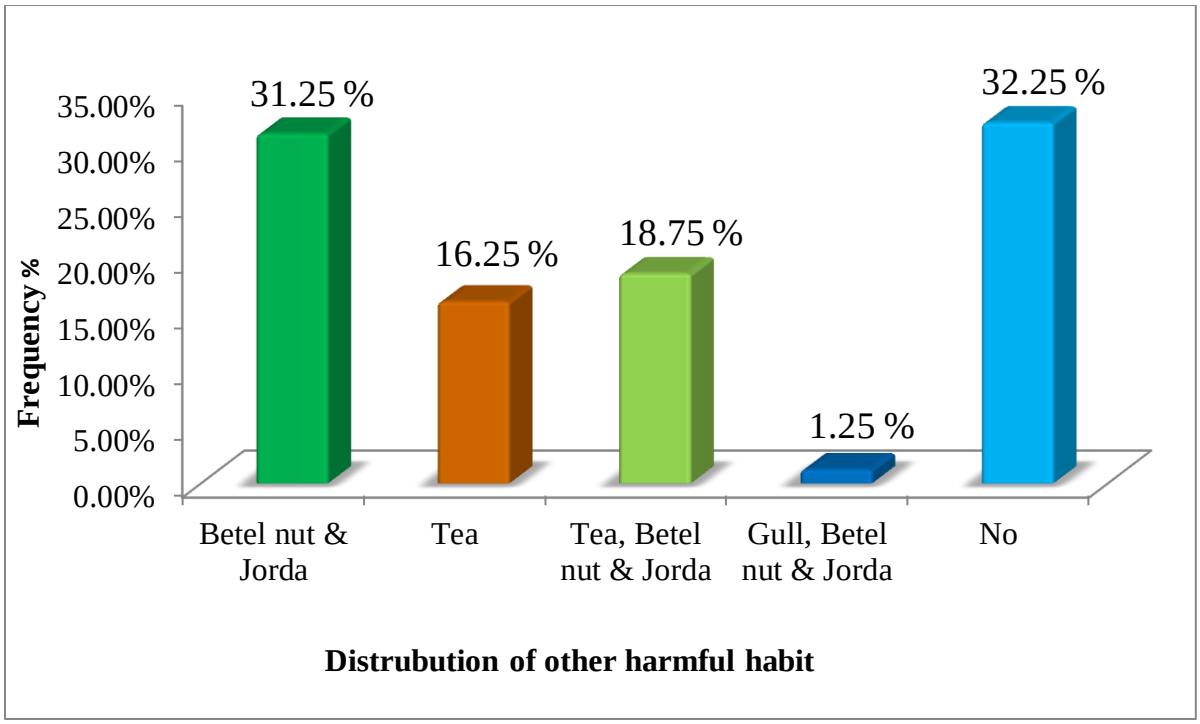

Figure 3.13: Distribution of patient according to other habits

Among 80 patients, 31.25% used to take betel nuts & jorda, 16.25% used to take only tea, 18.75% used to take tea, betel nuts & jorda, 1.25% used to take gull, betel nuts & jorda and 32.25% did not have any those harmful habits. From this study it was determined that taking betel nut regularly or habitually can cause various kinds of cancers.

3.14 Distribution of patient according to type of sleep

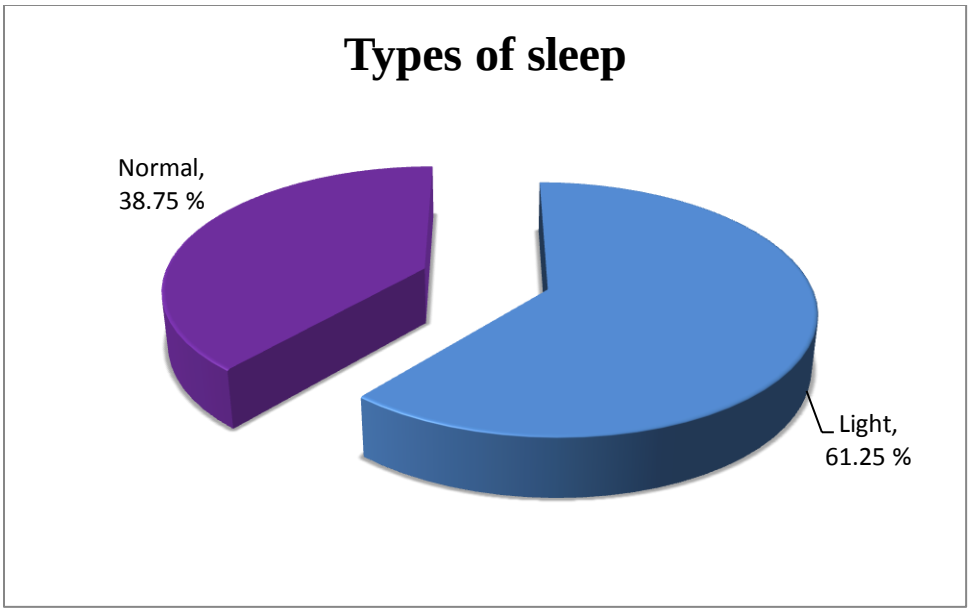

Figure 3.14: Distribution of patient according to type of sleep

Among 80 cancer patients, only 38.75% had no problem in sleeping or normal sleeping and 61.25% had light sleeping disorder. From this study, the result has been found that most of the cancer patients have the light sleeping disorder. It has been estimated that one-third to one-half of people with cancer experience sleep disturbance (85) (86). Physical illness, pain, hospitalization, drugs and other treatments for cancer, and the psychological impact of a malignant disease may disrupt the sleeping patterns of persons with cancer (87).

3.15 Distribution of patient according to family history

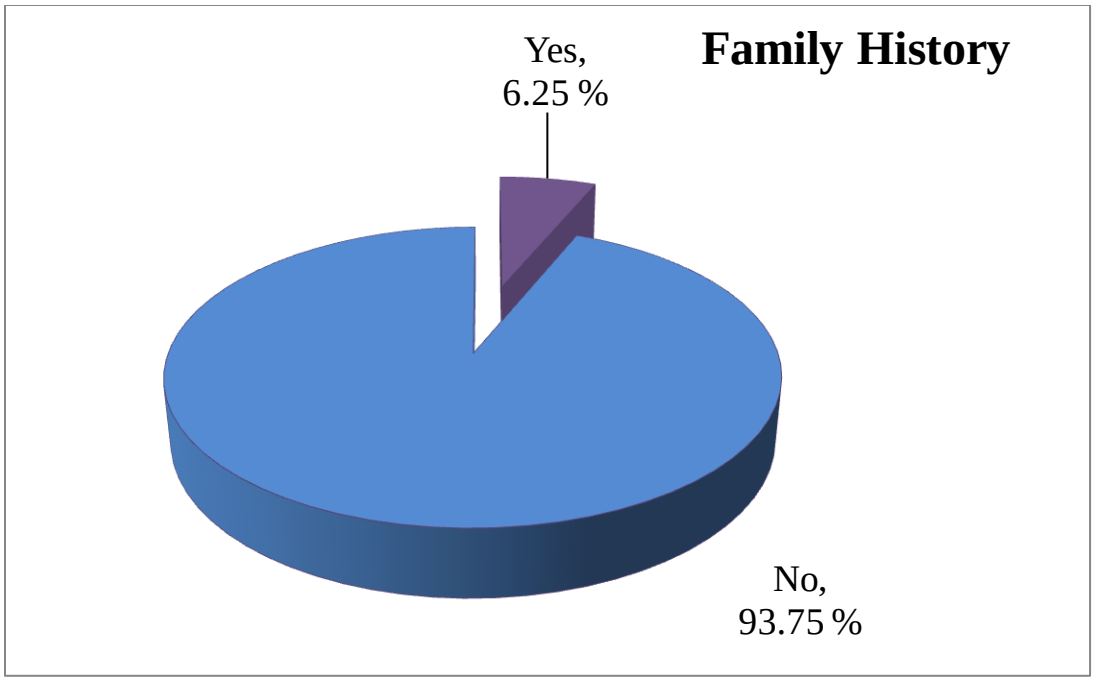

Figure 3.15: Distribution of patient according to family history

Among 80 cancer patients, only 6.25% had the family history of cancer incidences and 93.75% had no family history of cancer. From this study, it was found that family history or hereditary did not have direct influence in causing cancer incidences. Hereditary cancer is a cancer that has developed as a result of a gene mutation passed down from a parent to a child (88) (89) (90) (91) (92) (93). Inheriting a gene mutation does not necessarily mean that person will develop cancer, but increases their risk factor. Research and studies have found that certain gene mutations increase the chances of a person to develop certain kinds of cancers, depending on family history (88) (89) (90) (91) (92) (93). The most common hereditary cancers are (88) (89) (90) (91) (92) (93):

- Breast Cancer
- Ovarian Cancer

- Prostate Cancer
- Colorectal Cancer

3.16 Distribution of patients according to types of cancer

Type of Cancers according to the origin, location and organ system	Number of Patients	Percentage (%)
Gastro Intestinal Cancers	19	23.75
Blood Cancers	7	8.75
Breast Cancers	2	2.5
Genitourinary Cancers	17	21.25
Endocrine Cancers	3	3.75
Head & Neck Cancers	4	5
Lung Cancers/Respiratory Tract Cancers	15	18.75
Soft Tissue/ Musculoskeletal Cancers	11	13.75
Neurological Cancers	1	1.25
Germ Cell Cancers	1	1.25
Skin Cancer Cancers	1	1.25

Table 3.1: Distribution of patients according to types of cancer

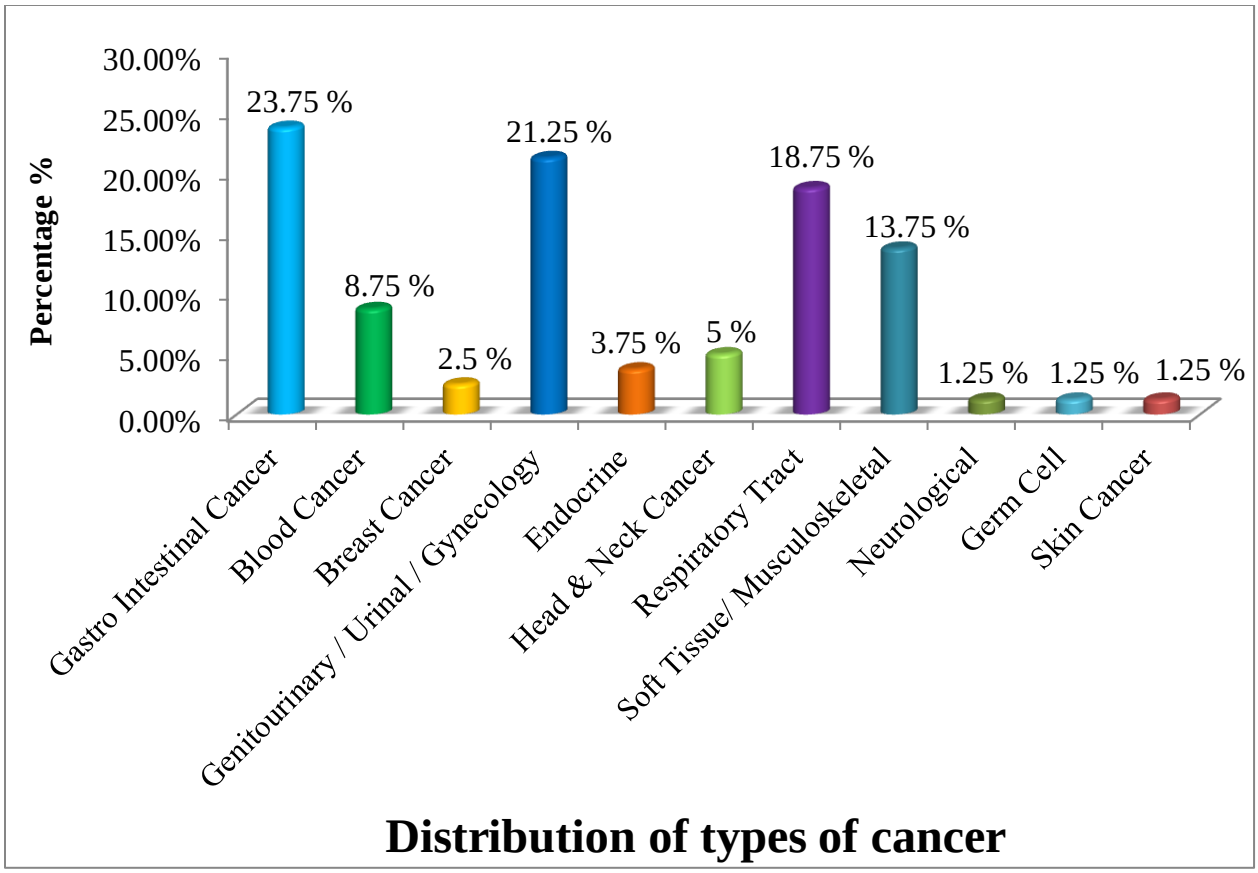

Figure 3.16: Distribution of patients according to types of cancer

Among 80 cancer patients, 23.75% had digestive/gastro intestinal cancers, 8.75% was blood cancer patients, 2.5% had breast cancer, 21.25% had genitourinary/urinal/gynecological cancers, 3.75% had endocrine cancers, 5% had head& neck cancers, 18.75% had respiratory tract cancers, 13.75% had soft tissue/musculoskeletal cancer, 1.25% had neurological cancers, 1.25% had germ cell cancers, 1.25% had skin cancers.

3.17 Distribution of patients according to smoking habits and types of cancers

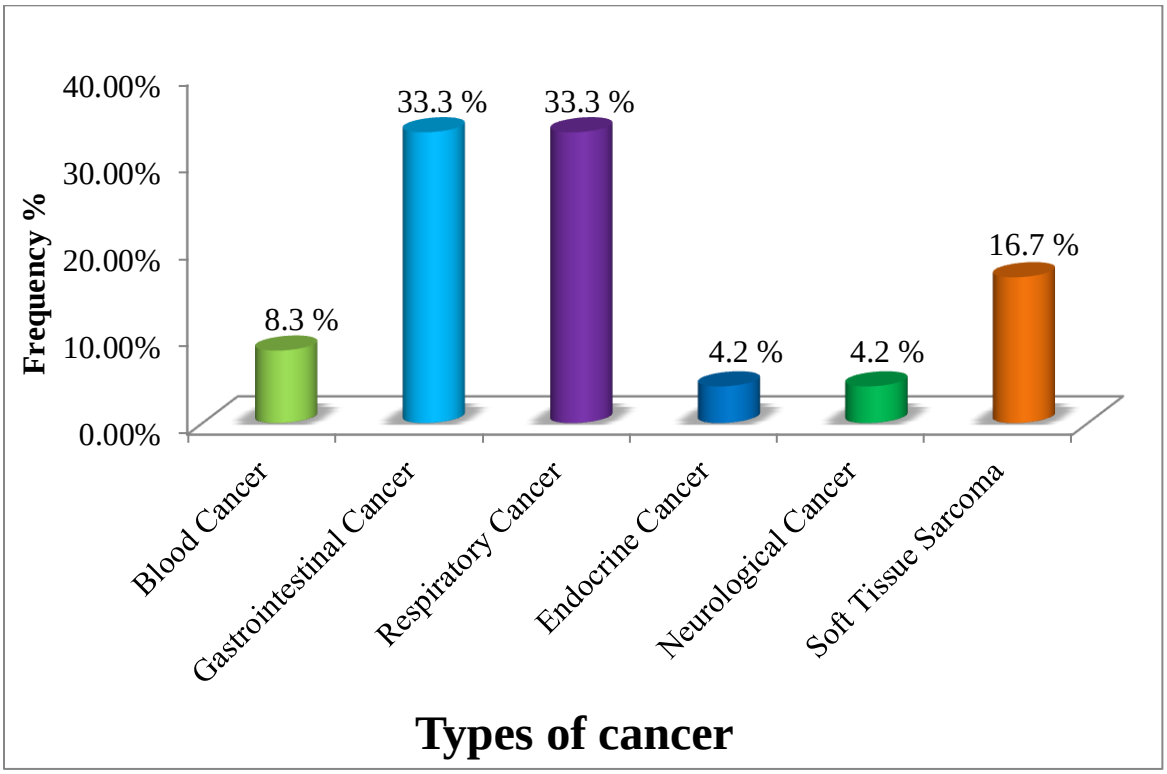

Figure 3.17: Distribution of patients according to smoking habits and types of cancers

Among 80 cancer patients, 24 cancer patients were smokers. Among these 24 cancer patients, 8.3% had blood cancers, 33.3% had gastrointestinal cancers, 33.3% had respiratory cancers, 4.2% had endocrine cancers, 4.2% had neurological cancers and 16.7% had soft tissue sarcomas. From this result, it was found that most of the cancer patients with the smoking habit had mainly gastrointestinal cancers and respiratory cancers. Tobacco leaf contains chemicals that are harmful to both smokers and nonsmokers. Breathing even a little tobacco smoke can be harmful (94) (95) (96). Of the more than 7,000 chemicals in tobacco leaf, at least 250 are known to be

harmful, including hydrogen cyanide, carbon monoxide, and ammonia (94) (97). Smoking is a leading cause of cancer and death from cancer. It causes cancers of the lung, esophagus, larynx, mouth, throat, kidney, bladder, pancreas, stomach, and cervix, as well as acute myeloid leukemia (94) (95).

3.18 Distribution of patients according to types of cancer and habits of taking betel nuts

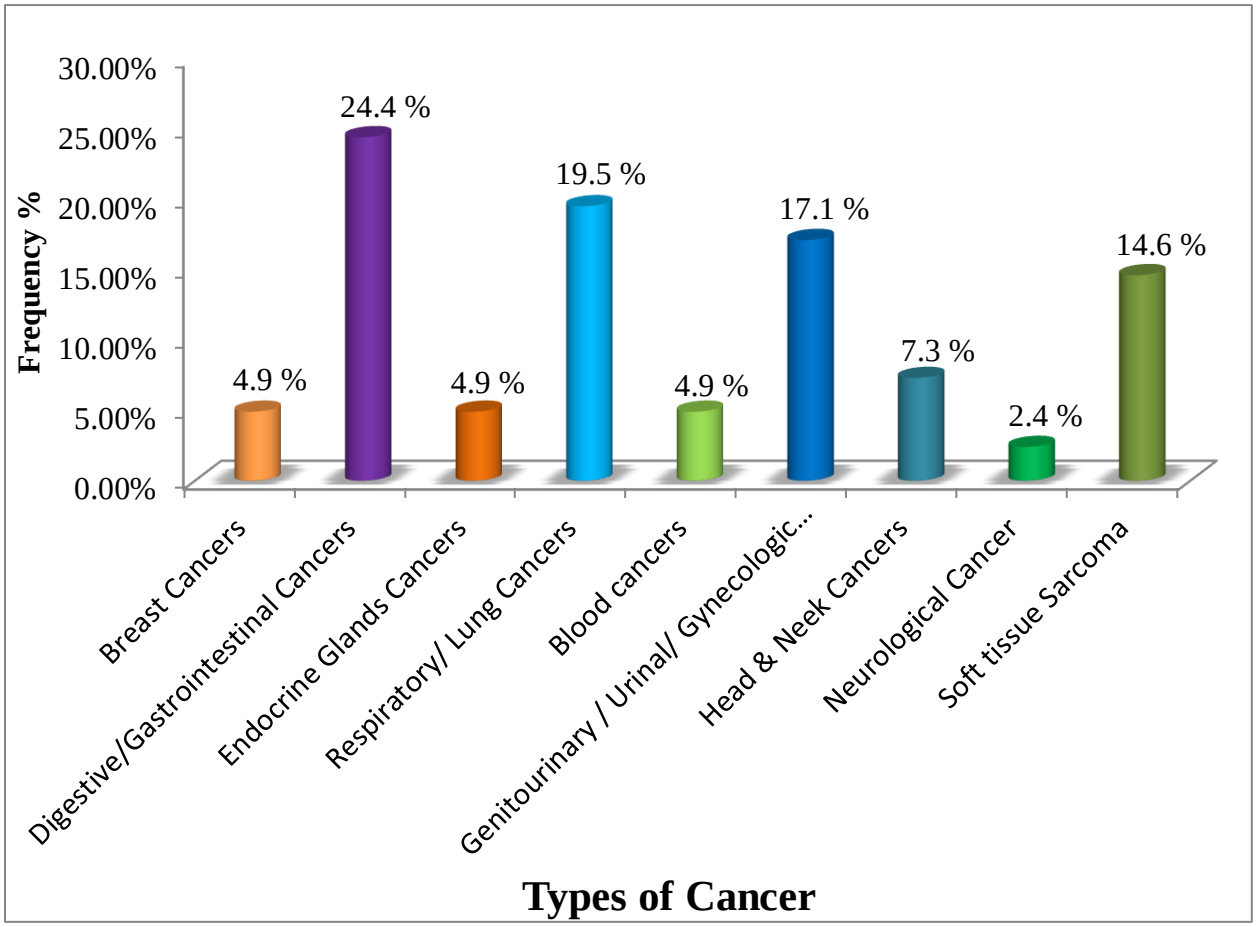

Figure 3.18: Distribution of patients according to types of cancer and habits of taking betel nuts.

Among 80 cancer patients, there were 41 cancer patients who were addicted to betel nuts or who had frequently taken betel nuts. Among these 41 cancer patients, 4.9% had breast cancers, 24.4% had digestive/gastrointestinal cancers, 4.9% had endocrine cancers, 19.5% had lung/respiratory cancers, 4.9% had blood cancers, 17.1% had genitourinary cancers, 7.3% had head & neck cancers, 2.4% had neurological cancers, 14.6% had soft tissue sarcomas. From this study, it was found that most of the cancer patients who had the habit of taking betel nuts were suffered from mainly digestive/gastrointestinal cancers and respiratory cancers.

3.19 Distribution of patients according to blood groups

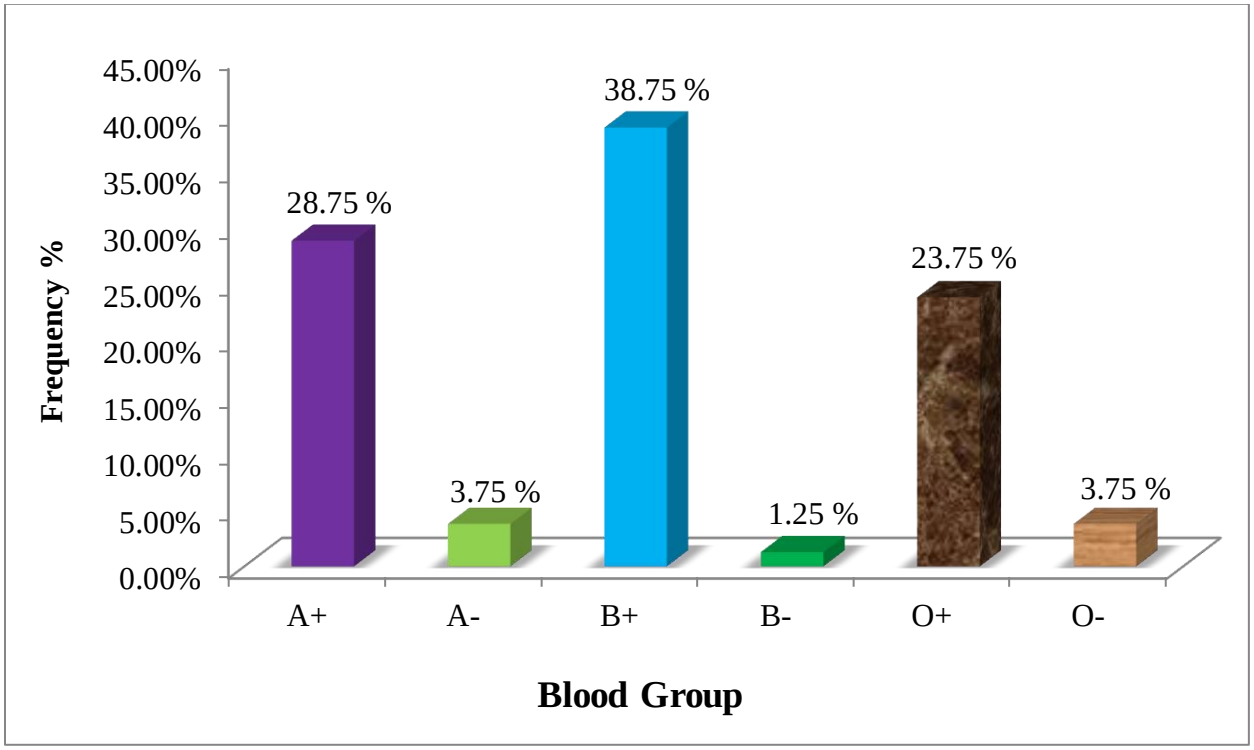

Figure: Distribution of patients according to blood groups

Among 80 cancer patients, 28.75% had A+ve blood group, 3.75% had A-ve blood group, 38.75% had B+ve blood group, 1.25% had B-ve blood group, 23.75% had O+ve blood group, 3.75% had O-ve blood group. Patients with B+ve and A+ve blood groups were mostly affected.

3.20 Distribution of patients according to chemotherapy or anticancer drugs

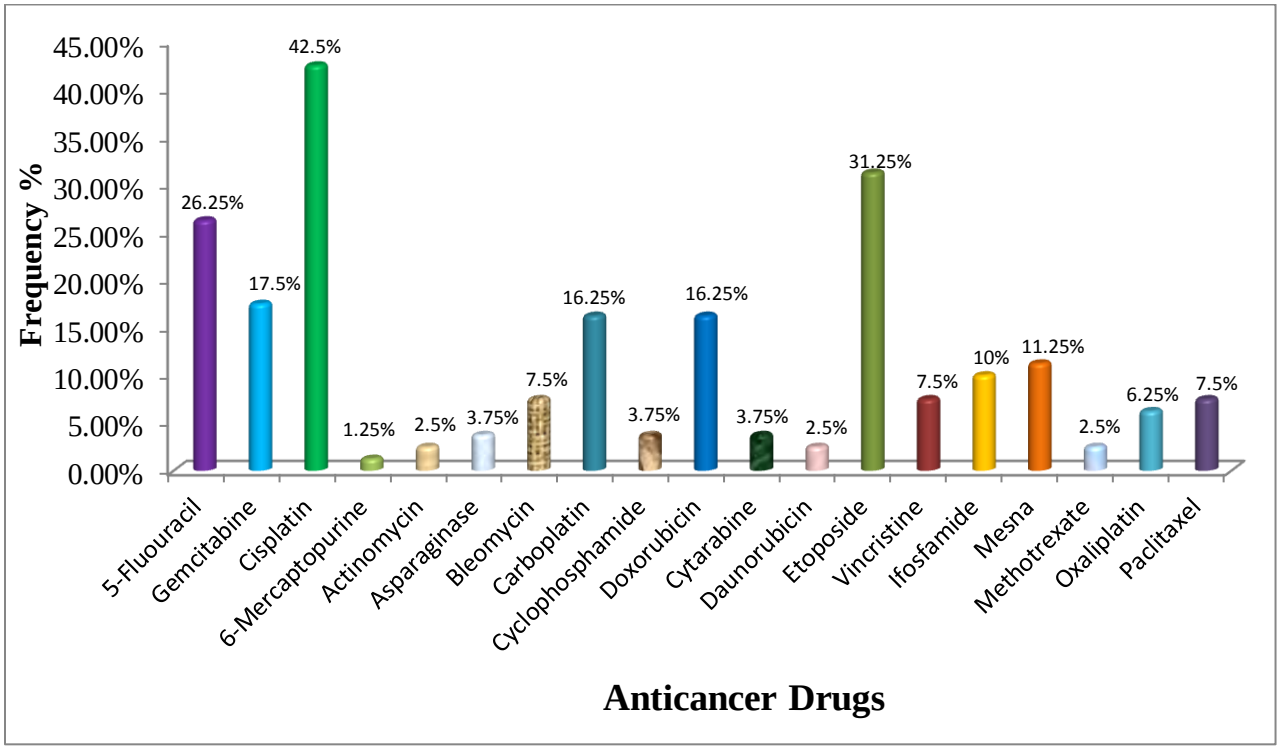

Figure 3.20: Distribution of patients according to chemotherapy or anticancer drugs

19 different types of chemotherapeutic agents or anticancer drugs were given to those 80 cancer patients by following the chemo schedules.

From the figure 3.20, it was found that cisplatin was given to 42.5% patients, which was the highest. Etoposide was given to 31.25% patients, which was the second highest and 5-fluouracil was given to 17.5% patients which was the third highest.

Chapter: 4

Conclusion

Conclusion

Cancer is potentially the most preventable and the most curable of the major chronic and life threatening diseases, unfortunately, it remains a leading killer worldwide. From the survey, it was found that the higher percentage of cancer cases in male rather than to female. Most of the male patients have tobacco smoking history. So, avoiding tobacco may be one of the best health decisions to prevent cancer. From the survey it was also observed that most of the cancer patients have no idea about cancer and its risk factors. It needs to increase public awareness regarding this matter and government needs to come forward. Mass education is necessary to raise public awareness regarding serious health ailments like cancer. Cancer treatment is expensive because most of the chemo drugs or anticancer drugs are imported from foreign countries and they are expensive due to patent ship. Almost all the patients said that they have approximately expensed 200,000 to 300,000 taka for their cancer treatment and they have been in great trouble to pass their livelihood and management of money for their treatment. Government must give subsidy on anticancer drugs that people of every class can get anticancer drugs at a cheap price. The present research was a comprehensive study that was conducted to identify rick factors involved with various types of cancers and chemotherapy use to treat various types of cancers. However, this study has not been able to establish the linkage and the levels of association between the identified risk factors and various cancers reported. The main limitation of this study was that it was only carried out taking information from below poverty leveled people of Bangladesh, which require in depth study to get a scenario of cancer status of Bangladesh.

Chapter: 5

Reference

Reference

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Appendix

East West University
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A Diseases Based Study: Cancer
(A Project Report to Be Submitted in the Department of Pharmacy for the Partial Fulfillment of the Degree of Bachelor of Pharmacy)

Date: **Report no:**

Personal Information

1. Name

2. Age yrs

3. Gender: □ Female Male

4. Marital Status □ Married □ Unmarried

□ Others

4. Living area: □ City □ Rural □ Urban □ Others

5. Site of the living area: □ Industrial

□ Chemical area

□ Tannery area □ N/A

6. Education: □ Illiterate □ Primary

□ High School □ College

□ Graduate or higher

7. Occupation: □ Student □ Business

□ Service holder □ Clinical

□ Housewife □ Others:

8. Stress on work □ Physical □ Mental □ Social

9. Social class □ Poor □ Lower middle

□ Upper middle □ Rich

10. Source of water used daily

11. Source of food intake daily □ Home made

□ Hotel □ Street

□ Others

12. Smoking habit □ Non smoker □ Ex-smoker

□ Smoker

13. Other addiction □ Betel nuts □ Tea □ Coffee

□ Gull □ Jorda □ Others

14. How long time on sleep

15. Types of sleep □ Normal □ Light sleep □ sound sleep

16. Awareness about Cancer: □ No □ Yes

Diseases Information:

17. Family History □ No □ Yes

18. Type of cancer?

19. Physical problem you may faced

A)…… **B)……** **C)……**

D)…… **E)……**

20. How long you are faced these

21. How long you know that it is cancer

22. Patient status □ Out-patient □ In-patient

23. Length of hospital stay

24. Impact of disease on income □ Small □ Large □ None

25. Are you satisfied by treatment? □ Yes □ No

Investigation

26. Physical Investigation:

Height	
Weight	
Pulse/min	
Temperature	
Blood pressure	
Complexion	

27. Haematological and Biochemical Investigation:

Blood Group	
RBC	
ESR	
Hb%	
WBC	
Platelets	
Biochemical	

28. Histopathological Investigation:

29. Radiological Investigation:

Disease Stage and Treatment:

30. Stage:

31. Treatment Cycle:

32. Duration of taking chemo-drugs:

33. Chemo-drugs details (Name, dose, name and amount of infusion)

34. Ancillary drugs: