

The Current Scenario of cancer in Bangladesh on a global perspective

NazmirBintaAlam, Md.Waseque Mia, Md. Sajjad Hossain Sajib,
H. M. Syfuddin, Ajit Ghosh*

Department of Biochemistry and Molecular Biology, Shahjalal University of Science and Technology, Sylhet-3114, Bangladesh.

Corresponding Author: Ajit Ghosh, PhD

Abstract

Bangladesh is a developing country in the South East Asia region. Although having a scarcity of composition, but susceptible enough to challenge any life-threatening diseases such as AIDS, cancer, hepatitis b-g, and more. Currently, the prominent obstacle is cancer with a huge variability, exposed as a combination of more than 100 types of diseases accompanied by uncontrolled growth and proliferation of an abnormal/mutated cell, ultimately leads to death. The tumour is the initiation of this and manifest as cancer when it sprouts to the distant body parts through metastasis. Although all tumours are not cancerous; only the malignant ones do so. According to the world health organization Africa, Asia, Central and South America is the most affected zone with 60% new cancer cases with 70% of total death (Ferlay et al., 2015). A report revealed that about 2,00,000 people are affected by cancer and 1,50,000 people died per year in Bangladesh. A comprehensive update report of 2013 demonstrated the existence of 1.3-1.5 million patients with a 0.2 million new incorporation every year. Despite very less scientific information, the National Institute of Cancer Research and Hospital bulletin provides a short but overall idea about the current scenario in Bangladesh. Due to the insufficient diagnosis facilities, ignorance, costly treatment; only one-third of the cancer patients have the capability of primary care, treatment, and regular follow-up facilities. There are nineteen medical colleges and centers with sole association with the diagnosis and treatment; that is exclusively insufficient for a country having more than 180 million people.

Key words: Cancer, Bangladesh, Diagnosis and treatment.

Date of Submission: 28-10-2020

Date of Acceptance: 09-11-2020

I. Introduction

Although there is a positive advancement for diagnosis and treatment, currently, cancer is a significant health burden worldwide. It is the second most common disease after cardiovascular disorders with the maximum death penalty in the world (Jemal et al., 2010). Incidence and mortality rates of most cancers are increasing in undeveloped and less developed countries due to the adoption of unhealthy lifestyles like smoking, physical inactivity, and consumption of calorie-dense food (Jemal et al., 2010). Almost 25% of the global cancer burden was diagnosed in the low-income and lower-middle-income countries of the world in the 1960s (Uddin et al., 2013). According to the report of globescan (<https://globescan.com/>) 2010, an anticipated 12.7 million new cancer cases occurred with 7.6 million deaths (around 13% of all deaths) in 2008. By the year 2030, over 9 million cancer patients are assumed to die in the developing countries (Uddin et al., 2013).

According to 2008 data, the most prevalent types of cancers are breast (5.2 million), colorectal (3.2 million), prostate (3.2 million), lung (1.67 million), stomach (1.6 million), cervical (1.5 million), urinary bladder (1.1 million), liver (0.6 million), and oesophageal cancer (0.48 million) globally (Kotnis et al., 2005). Cancer is the sixth common cause of mortality in Bangladesh, and 60% of the cancer patients die within five years of diagnosis. Among them, Lung cancer in male, and cervical and breast cancer in female constitute 38% of all cancer cases in Bangladesh (http://dghs.gov.bd/bn/licts_file/images/Strategy/2009_NationalCancerControlStrategy2009-15.pdf). It has observed that cervical cancer is the most common cancer of women especially reproductive age in Bangladesh and most patients come for diagnosis at the late stages (Ahmed and Rahman, 2008).

The treatment facilities are progressing in this country along with all the limitation like only 150 clinical and 16 pediatric oncologists (total approximately ~180) in different hospitals or research institute like BSMMU hospital, ICDDR'B research institute, Ahsania Mission Cancer Hospital, Care Hospital, Chittagong University. Amader Gram runs different agency (56) and collaborative programs, Oncology club, CATSUP, Ashic Foundation, AK Khan Healthcare Trust, etc. are working along with Bangladesh government in different part conducting some vaccination program for cervical cancer with early detection of oral, breast and colorectal

cancer. Currently, facilities are provided only in 19 hospitals with limited facilities for chemotherapy by radiotherapy department, linear accelerators (15), brachytherapy (12) and Co-60 teletherapy (12) unit in Bangladesh. A plan (2009-2015) has been implemented by Unique National Cancer Control Strategy of Bangladesh to develop and overcome the future cancer care related problem with a massive control in collaboration with world health organization (WHO).

There is no population-based cancer registry in Bangladesh to provide reliable data on the incidence, prevalence, and mortality of cancer patients. Only some scattered statistical analysis is available from the National Institute of Cancer Research and Hospital (NICRH) and few other hospitals, but it can't give a full glance at the current situation. A survey-based study was conducted in 3 well-known hospitals of Dhaka from July to September 2012 (Sharmin et al., 2014). This study demonstrated the 1:1.2 ratio of male and female patients (Sharmin et al., 2014). A dominance of lung and stomach cancers (37.04%) for male and ovary cancer for female (39.39%) ranked as the top (Table 1). Therefore, the overall status of the cancer patients in Bangladesh is critical to imply advance measures with adequate control and get rid of this havoc in future. The primary aim of this study is to provide the glimpse of cancer scenario in Bangladesh with felicitous causes, treatment modalities as well as medicine, therapies used for different types of cancer patients, its detrimental effect on the national and global economy.

Table 1. A Cross-Sectional Survey revealed the prevalence of different types of cancer in Bangladesh

Male		Female	
Type	Incident	Type	Incident
Lung and stomach cancers	37.04%	Ovary cancer	39.39%
Thyroid cancer	25.93%	Breast cancer	27.27%
Sarcoma	14.81%	Rectum cancer	18.18%
Male genital tract cancer	7.41%	Duodenum cancer	9.09%
Eye cancer	7.41%		
Duodenum cancer	3.7%		
Rectum cancer	3.7%		

II. Global cancer scenario

According to WHO, the estimated death due to cancer was 8.2 million in 2012 with a predicted number of 12 million by the year 2030 (Torre et al., 2015). The utmost rising of number both in the developed and developing countries is directly proportional to the consumption of tobacco and alcoholic beverage (Jemal et al., 2011) as well as toxic pollutants of plastics and industrial wastes (Garcia-Perez et al., 2006). The global cancer statistics (GLOBOCAN) reported about 12.7 million cancer cases and 7.6 million died in the year 2008; that has been raised to 14.1 million cases and 8.2 million death in 2012. Thus, a jump of 1.4 million new cancer patient exposed with a considerable mortality number of 0.6 million within the time frame of four years (2008 – 2012). A 2012 report propagated that cancer patients comprised 65% of global and 57% of the total developed area with an alarming constitution (Jemal et al., 2011). Currently, lung and stomach cancer are the most ascending cancer in male and breast cancer in the female. The total number of the cancer patient is the highest in eastern Asia as compared to the other parts of the world (Table 2). Although the number of breast cancer affected patient is the maximum, the death rate is higher in case of liver, lung and stomach cancer. The predominant area for liver, lung and stomach cancer is Northern and Western Africa, Eastern Asia, south-east Asia, Central and Eastern Europe, and South America. On the other hand, the breast cancer-prone regions are Northern America, Australia/New Zealand, Northern and Western Europe. Based on the data of 2012, eastern Asia marked with the maximum number of cancer patients of 4,145,000 followed by northern America and south-central Asia among the 21 global regions (Table 3).

Table 2. The most affected areas of the world with different types of cancer

Type	Infected	Death	Area
Breast cancer	1,7000,000	521,900	High in Northern America, Australia/New Zealand, Northern and Western Europe. Intermediate in Central and Eastern Europe, Latin America, Caribbean. Low in most of Africa and Asia
Colorectal cancer	1,4000,000	693,900	High in Australia/New Zealand, Europe, Northern America Low in Africa and South-Central Asia
Stomach cancer	951,600	723,100	High in Eastern Asia (particularly in Korea, Mongolia, Japan, and China), Central and Eastern Europe, and South America. Low in Northern America and most parts of Africa.
Liver cancer	782,500	745,500	High in East and South-East Asia and Northern and Western Africa. Low in South-Central Asia; and Northern, Central, and Eastern Europe.
Cervical cancer	527,600	265,700	High in sub-Saharan Africa, Latin America and Caribbean, and Melanesia. Low in Western Asia, Australia/New Zealand, Northern America.

Esophageal cancer	455,800	400,200	High in Eastern Asia, and Eastern and Southern Africa. Low in Western Africa.
Urinary Bladder cancer	429,800	165,100	High in Europe, Northern America, Western Asia, Northern Africa Low in Eastern, Middle, and Western Africa.
Non-Hodgkin lymphoma	385,700	199,700	High in Australia, Western and Northern Europe and Northern America. Low in Asia and Eastern Europe.
Lip and oral cavity cancer	300,400	145,400	High in Melanesia, South-Central Asia, and Central and Eastern Europe. Low in Western Africa and Eastern Asia.
Nasopharyngeal cancer	86,700	50,800	High in South-Eastern Asia, Malaysia, Indonesia, and Singapore, South-Eastern China, and in Southern Asia. Intermediate in Micronesia/Polynesia, Eastern-Asia and Northern Africa.

Table 3. Number of new patients affected by cancer in 21 different areas of the world in the year 2012

Position	Regional area	Patients
1	Eastern Asia	4,145,000
2	Northern America	1,786,400
3	South-central Asia	1,514,000
4	Western Europe	1,110,300
5	Central and Eastern Europe	1,036,900
6	South-eastern Asia	807,700
7	South-western Asia	786,400
8	Southern Europe	769,200
9	Northern Europe	525,900
10	Western Asia	317,600
11	Eastern Africa	287,300
12	Northern Africa	220,600
13	Central America	197,600
14	Western Africa	182,100
15	Australia/ New Zealand	143,400
16	Caribbean	90,800
17	Southern Africa	82,900
18	Middle Africa	74,100
19	Melanesia	10,000
20	Polynesia	1,200
21	Micronesia	800

III. Cancer scenario in Bangladesh

Although cancer has been listed as the top cause of mortality, the statistical data of its prevalence and spread is superfluous. Many organization and research groups are now working tremendously to find the cause, an exact number of patients, types, diagnosis as well as defensive techniques for the disease. Still, government support is scanty to provide the latest facilities and support to the patients. Report of International Agency for Research on Cancer (IARC) proclaims that; about 7.5% death occurred from cancer in 2005. According to the National Institute of Cancer Research and Hospital (NICRH) report, 2007(Figure 1) the top listed cancer of male was lung cancer (25.5%), Lymphoma, esophagus, larynx, and stomach; and for female breast cancer (25.6%), cervix uteri, esophagus, lung, lymphoma and both sex it was lung (17.3%), Breast (12.3%), cervix, lymphoma & esophagus cancer (Uddin et al., 2013). According to the report, male is more prone to cancer (58%) as compared with the female (42%) (Table 4).

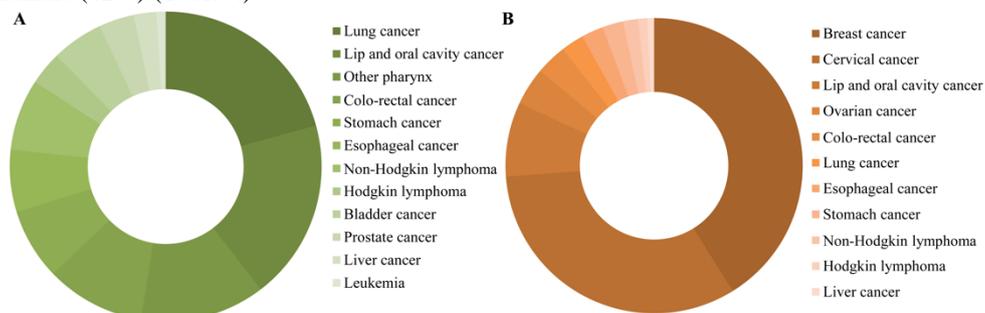


Figure 1. Cancer prevalence in Bangladesh for the last five years. Lung cancer is predominant in the male (A), while the breast cancer is predominant in the female (B).

Table 4. The state of cancer patients in the year 2005 to 2007 based on sex.

Year	2005		2006		2007		2005-2007	
Sex	Male	Female	Male	Female	Male	Female	Male	Female
Number	3,086	2,325	3,824	2,668	3,937	2,989	10,847	7,982
Percentage (%)	57	43	58.9	41.1	56.8	43.4	57.6	42.4

NICRH report 2012 stated that 12% (471) children out of 3360 were predominantly pediatric cancer patients among the admitted one (Uddin et al., 2013). An epidemiology report of 2012 (Hossain et al., 2016) by combining all the data from 2001-2012 on childhood and adolescent cancer patient, revealed that the infant mortality rate declined by 71% as compared to 1990s due to better infectious disease management (Sharmin et al., 2014). The report further added that nearly 84% of cases the patient's age is below 15 and these pediatric cancer patients are mostly from low and middle income-based countries (LMICS) (Magrath et al., 2013). Thus the expected number of childhood cancer will increase by 30% by 2020 (Rodriguez-Galindo et al., 2013). According to the health bulletin of NICRH 2014, a total of 3622 patient admitted in NICRH in 2013 including 577 pediatric patients. The number of suffered male and female patient was 1820 and 1225 out of 3045 cases with the death of total 118 patients including children. Within this year 15.74% (570 cases) suffered from C349 Bronchus or lung cancer, and 8.42% (305 cases) for C509 Breast cancer (Forouzanfar et al., 2011) (Table 5).

Table 5. Statistically the top ten cancers with the number of patients and the death rate.

No of cases	No and % of the patient	Death report (out of 110)
Bronchus or lung cancer	570 and 15.74%	34 and 30.91%
Breast cancer	305 and 8.42%	8 and 7.27%
Malignant neoplasm of ovarian cancer	200 and 5.52%	8 and 7.27%
Eye cancer	169 and 4.67%	
Cervix uteri cancer	167 and 4.61%	
Stomach cancer	152 and 4.20%	12 and 10.91%
Connective and soft tissue cancer	124 and 3.42%	6 and 5.45%
Bone and articular cartilage	95 and 2.62%	
Colon cancer	87 and 2.40%	6 and 5.45%
Malignant neoplasm of rectum	84 and 2.32%	5 and 4.55% or 3 and 2.73%
Lymphoid, hematopoietic and related tissue		4 and 3.64%
Brain cancer		4 and 3.64%

IV. The genetic basis of different types of cancer

Genetic switching is a hallmark event for the altered cancer manifestation at different parts of life (Tay, 1992). The major characteristics feature is the mutation to oncogene or amplification of proto-oncogene/ inactivation of tumour suppressor gene (Tay, 1992). Point mutation, chromosomal translocation, and nucleotide insertion-deletion are the main activation point towards the change of oncogenic expression and thus drive towards cancer. Even a single point mutation can lead to cancer by activating RAS p21 gene or inactivating tumour suppressor/ proto-oncogene like p53 (Anderson et al., 1992).

a) Lung cancer

Lung cancer holds its position on the top for the proclaiming life of both male and female. NICRH report 2014 stated that there was 29% lung cancer patient out of a total of 5622 patients (Zarogoulidis et al., 2015). The main cause of lung cancer is tobacco use that singly causes 30% cancer (Hossain et al., 2016). It comprises approximately 4000 chemicals, out of that 438 act as a cancer-causing agent (Hussain, 2013). Cigarette, biri, tarmac are the main risk factors for lung as well as oral, mouth and oropharynx cancer. Apart from this, genetic polymorphism of some gene located on chromosome 5p15.33, 6p21, and 15q24-25.1 are suspected of lung cancer through acetylcholine receptor blocking. Among them, the 5p15.33 region has been highly linked with lung adenocarcinoma (Yokota et al., 2010). While some other study identified 15q25.1 as the most sensitive region with 511,919 SNP genotypes in 1,952 cases and 1,438 controls (Wang et al., 2008). According to recently genome-wide association (GWA) study 6q21, 6q23-25 and 13q31.3 regions are also considered being responsible for lung cancer (Wang et al., 2008; Yokota et al., 2010).

b) Breast cancer

Breast cancer now is the most concerning one with 1.67 million new estimated patients in 2012 throughout the developing country with 62% mortality rate (Youlden et al., 2014). In 2010, 45% of new cancer was diagnosed in women between 15-49 ages (Forouzanfar et al., 2011). There were about 200,000 new breast

cancer patients in 2012 only in South Asia, from where 97,500 patient had died that year (Youlden et al., 2014). The major risk factors include reproductive, hereditary, and environmental causes. The most crucial hereditary factors are the mutations of several genes on loci includes- p54 gene, PTEN, ATM gene, her 2/3, BRCA1 and BRCA2 gene, estrogen and androgen receptor gene (AR), the HNPCC genes and many others. Among the responsible ones, BRCA1 and BRCA2 are alone responsible for 90% breast cancer (Bennett et al., 1999). Alcohol consumption might link to breast cancer as an external factor (Bennett et al., 1999; Key et al., 2001).

c) Colorectal cancer

GLOBOCAN report 2012 demonstrated that colorectal cancer is the second most diagnosed cancer in female and third in case of male where the estimated new cases were 1.4 million and the death was 693,900. Colorectal is the leading cause of cancer mortality in United States, mainly manifested by inactivation of tumour suppressor gene, e.g., adenomatous polyposis coli (APC) in 85% sporadic colorectal cancer (Kinzler and Vogelstein, 1996). Mutation to human mutS homolog 1 and 2 (MSH1 and MSH2) and PMS2 are also responsible for this with a percentage of about 15% (Kinzler and Vogelstein, 1996). Moreover, a mutation in DPC4/SMAD4 tumour suppressor gene and K-RAS oncogene play an impressive role in this cancer (Kinzler and Vogelstein, 1996; Miyaki and Kuroki, 2003).

d) Prostate cancer

As a diagnosed one, lies in the second position with the fifth leading cause of death worldwide. Men aged up to 70 are more prone to prostate cancer (Vellekoop and Loeb, 2013). Unfortunately, during diagnosis approximately 30% case the tumour starts spreading beyond the prostate gland results in prostate cancer (Shin et al., 2013). Although the specific cause is unknown 17p number chromosome carrying the HPC2/ELAC2 gene has a direct link to prostate cancer (Rebeck et al., 2000; Tavtigian et al., 2001). It was also noticed that mutation to a protein tyrosine phosphatase – PTEN, as well as some transcription factors, could lead to the prostate tumour and ultimately prostate cancer (Li et al., 1997; Sun et al., 1997).

e) Stomach cancer

Chromosomal instability, somatic gene mutation, microsatellite instability, functional SNP, and biomarker recognition may be helpful for the detection of the prognostic significance (French et al., 2004; Koo et al., 2004). Existence has been reported between the 17p (TP53) and loss of heterozygosity (LOH) biomarker in the precancerous gastric lesions; and then stomach cancer will be detected with the loss of LOH (Karaman et al., 2010). LOH level is higher in 1-9p, 11-14q, 17q, 18q, 21q and 22q chromosomal region during stomach cancer (Panani, 2008). BubR1 and AURKB show a low risk for stomach cancer whereas MAD1 and MAD2 induced Aurora kinase A (AURKA or STK15) situated on 20q13 region stimulate stomach adenocarcinoma (Osaki et al., 2007; Dar et al., 2008; Enjoji et al., 2009; Wang et al., 2010). Few other genes such as CCNB1, PTTG1, CCNE1, and PLK showed overexpression during stomach cancer with small prognosis (Wen et al., 2004; Kanaji et al., 2006; Hudler et al., 2011; Rossi et al., 2011). Recent studies suggested the positive benefits of antibiotics use to reduce the risk of stomach cancer (Herrero et al., 2014).

f) Liver Cancer

Liver cirrhosis, chronic hepatitis, and fatty liver cause chronic liver disease which may end with liver cancer. Diabetes, obesity and hemochromatosis and alcohol intake linked to liver damage ultimately lead to cancer and some viral infections like – Hepatitis B and C virus (HBV/ HCV), aflatoxin B are also associated with liver cancer (El-Serag, 2012). Various oncogenes like MYC, CCND1 and tumour suppressor gene like TP53, retinoblastoma (RB) are closely associated with the chromosomal alteration, and they can cause liver cancer (Shibata and Aburatani, 2014). Etiology-Independent chromosome aberrations, through amplification of MDM4 on 1q32.1 or gain of EEF1A2 on 20q13.33, are also involved in the hepatocyte cancer (HCC) (Schlaeger et al., 2008). Furthermore, mutations in some chromatin regulators e.g. ARID2, ARID1A, ARID1B, MLL3, and KMT2A are also reported to involve in ~50% case of the liver tumour (Fujimoto et al., 2012).

g) Cervical cancer

About 15 types of human papillomavirus (HPV) are responsible for cervical cancer leading to death as the second most prominent one in women. Innate and adaptive immunity mainly TH (helper T cell) is associated with HPV infection and high level of lesions (Hazelbag et al., 2001). The transcriptional blockage of the HPV DNA and tumour necrosis factor- α (TNF- α) cascade plays a major role in cervical cancer formation (Zur Hausen, 2002). IL-1 β gene is linked to this cancer type where its plasma levels upto 75% is associated with a 1.74-fold increased risk of cervical cancer (Tjong et al., 2001). Increased Th2 and decreased Th1 cytokine also involved in the premalignant cervical lesions (Mota et al., 1999; Zur Hausen, 2002). The recent study reveals that CTLA4 causes a 1.66-fold increased cervical cancer risk (Hu et al., 2010).

h) Mouth and oropharyngeal cancer

Alcohol consumption and tobacco smoking are the prominent causes although, the human papillomavirus (HPV), and some genetic mutation is closely related to this type of cancer (Williams, 2000; Smeets et al., 2009). B-cell lymphoma (BCL), C-myc, Epidermal growth factor receptor (EGFR), int-2, K-ras, Parathyroid adenomatosis 1 (PRAD-1) oncogenes related to oral cancer development along with transforming growth factor-alpha (TGF- α) (Wong et al., 1988; Sidransky, 1995).

i) Urinary Bladder Cancer

Mutation in the RAS gene family and FGFR3 gene is associated with the low-grade papillary/bladder cancer (Kompier et al., 2010). A cigarette component, Naphthylamine, acts as a carcinogenic agent for the urinary bladder cancer (Pong et al., 2006). There are mainly two pathways for the development of urinary bladder cancer – firstly, the association of oncogene Ras, ErbB2 and EGF receptor; and secondly, the cell cycle involved genes; tumour suppressor- Rb and p53 and DNA repair genes (Al Hussain and Akhtar, 2013).

j) Kaposi's sarcoma

It is an angioproliferative neoplasm, mostly associated with the opportunistic infection (Curtiss et al., 2016). The metastasis spreads through the lymphatic system and blood vessel and could grow in several body parts at the same time. It has four different types with different clinical parameters (Ziegler et al., 1984; Schwartz, 1996). The prevalence of KS (AIDs specific or non-specific) is associated with KSHV and it differs due to the geographical position (Gao et al., 1996; Lennette et al., 1996; Simpson et al., 1996; Orenstein et al., 1997; Belec et al., 1998; Qunibi et al., 1998; Whitby et al., 1998). Among the types; the multifocal AIDs are associated with KS mainly appears in the skin or visceral organs; and caused by PCP (pneumocystis carinii pneumonia) or other variety of infection (Friedman-Kien et al., 1981). Approximately 95% of cases it happens in homosexual person (Friedman-Kien, 1984). The classical form of KS ratio is 15:1 between men and women having lesions in the lower extremity (Hengge et al., 2002). The endemic form of KS, however, was most common among the men between the year 1989-1991 having 48.6 % but only 17.9 in women (Wabinga et al., 1993). The other form of KS mainly appears in transplant cases of the patient.

k) Leukemia

Children's are the main victim of this type of cancer with more than 100 types of alleles (Gilliland et al., 2004). Leukaemia cell originates from a rare group of leukaemia stem cell having self-renewal capacity. Like other cancer, some oncogene and anti-oncogene activation and inactivation are also related to leukaemia. The common leukaemia specific genes are c-abl, tal-1, Ttg-1, HRX and HOX-11 (Gilliland et al., 2004). Acute myeloid leukaemia (AML) is the frequent manifest leukaemia that accounts for more than 20% of normal karyotype through the mutation of CEBPA and encodes CCAAT DNA enhancer region binding protein of C/EBP α (Fung et al., 2013). The bi-allelic frameshift mutation of CEBPA (either N/C terminal) thus involves in the granulocyte differentiation and cancer (Fung et al., 2013).

V. Cancer diagnosis and treatment

Early diagnosis can be effective to prevent the prognosis of malignant cell transformation to cancerous one manifested by genetic or epigenetic events (Kumar and Pawaiya, 2010). Millions of people around the world can regain their life because of quick detection and diagnosis (Sudhakar, 2009). The most commonly used method for cancer screening, surveillance, and diagnosis includes digital mammography, computed tomography (CT) scans, magnetic resonance imaging (MRI), positron emission tomography (PET) scans, ultrasonography and magnetic resonance spectroscopy (Sudhakar, 2009; Kumar and Pawaiya, 2010). The biomedical test performed in the laboratory for the detection as well as diagnosis includes Fluorescent in Situ Hybridization (FISH), CSR, flow Cytometry, PCR/ Real-time PCR and microarray having high data extraction efficiency plus broad range application (Kumar and Pawaiya, 2010). These techniques are highly efficient to differentiate DNA, mRNA, as well as protein expression of an individual tumour, occupied patients. There are some specific tests like the Pap test for quick cervical cancer detection (Sudhakar, 2009).

Various tumour biomarkers are using as a dynamic process, with cytological, histopathological and serological methods like ELISA and RIA (Kumar and Pawaiya, 2010). As a biomarker, α -fetoprotein, prostate-specific antigen, carcinoembryonic antigen, CA 125, CA 19-9 is the tumour antigenic biomarker; granules of melanin, actin, factor III, cytokeratin recognized as the cytoplasmic protein biomarker; human chorionic gonadotropin, calcitonin renowned as the hormonal marker; and prostatic acid phosphatases, neuron-specific enolase, galactosyltransferase II used as the enzyme biomarkers (Kumar and Pawaiya, 2010). Recently a biomarker-based cancer scenario analysis was performed in the northeastern part of Bangladesh where carbohydrate antigen (CA) 15-3, CA 19-9, CA 125, PSA, CEA and AFP biomarkers are used to detect female-specific breast, pancreases, oesophagus, colon and ovary cancer; male-specific prostate gland cancer; and sex

nonspecific liver cancer in 1136 patients (Sony et al., 2018). The peak age range was 35-70 years where breast and ovarian cancers occur in the female at the early mid-age and men suffer from prostate cancer at a later stage of life (Sony et al., 2018).

Various research programs are conducted by researchers as well as doctors to dig up cheap treatment, technique, and biomarker to detect cancer. Laser treatment is getting renowned to cut tumour tissues of liver, skin, cervix, skin, larynx as well as some other specific tissues. Combination of chemotherapy/radiation and surgery is now getting effective and fruitful. Drugs like Anastrozole, Bevacizumab, Bleomycin, Cabazitaxel, Carboplatin, Chlorambucil, Dactinomycin, Daunorubicin Hydrochloride, Docetaxel, Doxorubicin Hydrochloride, Etoposide, Etoposide Phosphate, Everolimus, Filgrastim, Fludarabine Phosphate, Fluorouracil, Gefitinib, Decitabine, Gemcitabine etc. are available and used in cancer treatment in Bangladesh and other countries (Hussain, 2013). As radiation; confocal proton beam therapy, stereotactic surgery/therapy (for the brain tumour) and intra-operative radiation therapy is the most popular form. For the treatment of breast and prostate cancer, aromatase inhibitor and LHRH analogues are the most popular therapy (Sudhakar, 2009). Recently, immunotherapy has opened up a new era in this field where various biological agents like interleukin, cytokine, antigens as well as endogenous angiogenesis-inhibitors are used to block the tumour growth or signal transduction (Sudhakar, 2009). Use of monoclonal antibodies like rituximab and trastuzumab as therapeutics is impressive that targets lymphoma and cancer cells specifically. Recently antiangiogenic chemotherapy uses angiogenesis-inhibitors in a combination with chemotherapy (Sudhakar, 2009). Apart from that, new classes of molecules like siRNA, or antisense oligodeoxynucleotides are trying to be used for more specific treatment for cancer (Sudhakar, 2009).

VI. Existing treatment facilities in Bangladesh

Cancer diagnosis needs several modern types of equipment such as hemocytometer, flow cytometry, advanced microscope, molecular tools for DNA, RNA, and protein detection (Story et al., 2012; Hussain and Sullivan, 2013). As a developing country with an increasing number of cancer patients, the existing facilities are very low. As per the guidelines of International Atomic Energy Agency (IAEA), two teletherapy machines and one brachytherapy machine is essential for every 1 million population (Hussain and Sullivan, 2013). According to a 2013 report, there were 17 radiotherapy centres with 15 linear accelerators, 12 cobalt-60 machines and 12 brachytherapy machines were installed in Bangladesh (Hussain and Sullivan, 2013). Currently, there are around 20 medical hospitals and institutes where cancer can be diagnosed and provided the treatment, which is far less than the recommended number of World Health Organization (WHO) (Hussain, 2013). Among them, NICRH and Bangabandhu Sheikh Mujib Medical University (BSMMU) are the most renowned institutes that diagnose and provide cancer treatment in Bangladesh.

VII. Conclusion

Although Bangladesh is a small country with limited resources, it's getting ready to take challenges of all kinds of communicable as well as non-communicable diseases. Many researches on cancer is going all over the country and some with the collaboration and help of foreign countries. There are more than nineteen hospitals and research centers in Bangladesh with good cancer treatment facilities. Although small in quantity, some anticancer drugs and vaccines are manufactured by some of the local companies to cool down the current situation. The government should focus on this sector to tackle the massive need for discovering new drugs and diagnosis techniques with an affordable price.

References

- [1]. Ahmed, T., and Rahman, J. (2008). Development of a visual inspection programme for cervical cancer prevention in Bangladesh. *Reproductive health matters* 16, 78-85.
- [2]. Al Hussain, T.O., and Akhtar, M. (2013). Molecular basis of urinary bladder cancer. *Advances in anatomic pathology* 20, 53-60.
- [3]. Anderson, M.W., Reynolds, S.H., You, M., and Maronpot, R.M. (1992). Role of proto-oncogene activation in carcinogenesis. *Environmental health perspectives* 98, 13.
- [4]. Belec, L., Cancre, N., Hallouin, M.C., Morvan, J., Mohamed, A.S., and Gresenguet, G. (1998). High prevalence in Central Africa of blood donors who are potentially infectious for human herpesvirus 8. *Transfusion* 38, 771-775.
- [5]. Bennett, I.C., Gattas, M., and Teh, B.T. (1999). The genetic basis of breast cancer and its clinical implications. *ANZ Journal of Surgery* 69, 95-105.
- [6]. Curtiss, P., Strazzulla, L.C., and Friedman-Kien, A.E. (2016). An update on Kaposi's sarcoma: epidemiology, pathogenesis and treatment. *Dermatology and therapy* 6, 465-470.
- [7]. Dar, A.A., Zaika, A., Piazuolo, M.B., Correa, P., Koyama, T., Belkhiri, A., Washington, K., Castells, A., Pera, M., and El-Rifai, W. (2008). Frequent overexpression of Aurora Kinase A in upper gastrointestinal adenocarcinomas correlates with potent antiapoptotic functions. *Cancer* 112, 1688-1698.
- [8]. El-Serag, H.B. (2012). Epidemiology of viral hepatitis and hepatocellular carcinoma. *Gastroenterology* 142, 1264-1273. e1261.
- [9]. Enjoji, M., Iida, S., Sugita, H., Ishikawa, T., Uetake, H., Inokuchi, M., Yamada, H., Kojima, K., and Sugihara, K. (2009). BubR1 and AURKB overexpression are associated with a favourable prognosis in gastric cancer. *Molecular medicine reports* 2, 589-596.

- [10]. Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D.M., Forman, D., and Bray, F. (2015). Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *International journal of cancer* 136.
- [11]. Forouzanfar, M.H., Foreman, K.J., Delossantos, A.M., Lozano, R., Lopez, A.D., Murray, C.J., and Naghavi, M. (2011). Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. *The lancet* 378, 1461-1484.
- [12]. French, A.J., Petroni, G., Thibideau, S.N., Smolkin, M., Bissonette, E., Roviello, F., Harper, J.C., Koch, B.R., Anderson, S.A., and Hebbing, S.J. (2004). Allelic imbalance of 8p indicates poor survival in gastric cancer. *The Journal of Molecular Diagnostics* 6, 243-252.
- [13]. Friedman-Kien, A., Laubenstein, L., Marmor, M., Hymes, K., Green, J., Ragaz, A., Gottlieb, J., Muggia, F., Demopoulos, R., and Weintraub, M. (1981). Kaposi sarcoma and Pneumocystis pneumonia among homosexual men--New York City and California. *MMWR. Morbidity and mortality weekly report* 30, 305-308.
- [14]. Friedman-Kien, A.E. (1984). Kaposi's sarcoma: an opportunistic neoplasm. *The Journal of investigative dermatology* 82, 446.
- [15]. Fujimoto, A., Totoki, Y., Abe, T., Boroevich, K.A., Hosoda, F., Nguyen, H.H., Aoki, M., Hosono, N., Kubo, M., and Miya, F. (2012). Whole-genome sequencing of liver cancers identifies etiological influences on mutation patterns and recurrent mutations in chromatin regulators. *Nature genetics* 44, 760-764.
- [16]. Fung, T.K., Leung, A.Y.H., and So, C.W.E. (2013). Sox4you: A new player in C/EBP α leukemia. *Cancer cell* 24, 557-559.
- [17]. Gao, S.-J., Kingsley, L., Li, M., Zheng, W., Parravicini, C., Ziegler, J., Newton, R., Rinaldo, C.R., Saah, A., and Phair, J. (1996). KSHV antibodies among Americans, Italians and Ugandans with and without Kaposi's sarcoma. *Nature medicine* 2, 925.
- [18]. Garcia-Perez, J., Boldo, E., Ramis, R., Perez-Gomez, B., Pollan, M., Aragones, N., Lope, V., Rodriguez, S., Carrasco, J., and Gomez, D. (2006). Cancer Mortality and Industrial Pollution in Spain. *Epidemiology* 17, S307-S308.
- [19]. Gilliland, D.G., Jordan, C.T., and Felix, C.A. (2004). The molecular basis of leukemia. *ASH Education Program Book* 2004, 80-97.
- [20]. Hazelbag, S., Fleuren, G.J., Baelde, J., Schuurin, E., Kenter, G.G., and Gorter, A. (2001). Cytokine profile of cervical cancer cells. *Gynecologic oncology* 83, 235-243.
- [21]. Hengge, U.R., Ruzicka, T., Tyring, S.K., Stuschke, M., Roggendorf, M., Schwartz, R.A., and Seeber, S. (2002). Update on Kaposi's sarcoma and other HHV8 associated diseases. Part 1: epidemiology, environmental predispositions, clinical manifestations, and therapy. *The Lancet infectious diseases* 2, 281-292.
- [22]. Herrero, R., Parsonnet, J., and Greenberg, E.R. (2014). Prevention of gastric cancer. *Jama* 312, 1197-1198.
- [23]. Hossain, M.S., Begum, M., Mian, M.M., Ferdous, S., Kabir, S., Sarker, H.K., Karim, S., Choudhury, S., Khan, A., and Khan, Z.J. (2016). Epidemiology of childhood and adolescent cancer in Bangladesh, 2001–2014. *BMC cancer* 16, 104.
- [24]. Hu, L., Liu, J., Chen, X., Zhang, Y., Liu, L., Zhu, J., Chen, J., Shen, H., Qiang, F., and Hu, Z. (2010). CTLA-4 gene polymorphism+ 49 A/G contributes to genetic susceptibility to two infection-related cancers—hepatocellular carcinoma and cervical cancer. *Human immunology* 71, 888-891.
- [25]. Hudler, P., Repše, S., Juvan, R., and Komel, R. (2011). A genomic approach to investigate expression profiles in Slovenian patients with gastric cancer. *Oncology letters* 2, 1003-1014.
- [26]. Hussain, S.A., and Sullivan, R. (2013). Cancer control in Bangladesh. *Japanese journal of clinical oncology* 43, 1159-1169.
- [27]. Hussain, S.M.A. (2013). Comprehensive update on cancer scenario of Bangladesh. *South Asian journal of cancer* 2, 279.
- [28]. Jemal, A., Bray, F., Center, M.M., Ferlay, J., Ward, E., and Forman, D. (2011). Global cancer statistics. *CA: a cancer journal for clinicians* 61, 69-90.
- [29]. Jemal, A., Center, M.M., Desantis, C., and Ward, E.M. (2010). Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiology and Prevention Biomarkers* 19, 1893-1907.
- [30]. Kanaji, S., Saito, H., Tsujitani, S., Matsumoto, S., Tatebe, S., Kondo, A., Ozaki, M., Ito, H., and Ikeguchi, M. (2006). Expression of polo-like kinase 1 (PLK1) protein predicts the survival of patients with gastric carcinoma. *Oncology* 70, 126-133.
- [31]. Karaman, A., Eşref Kabalar, M., Nasir Binibi, D., Öztürk, C., and Pirim, I. (2010). Genetic alterations in gastric precancerous lesions. *Genetic Counseling* 21, 439.
- [32]. Key, T.J., Verkasalo, P.K., and Banks, E. (2001). Epidemiology of breast cancer. *The lancet oncology* 2, 133-140.
- [33]. Kinzler, K.W., and Vogelstein, B. (1996). Lessons from hereditary colorectal cancer. *Cell* 87, 159-170.
- [34]. Kompier, L.C., Lurkin, I., Van Der Aa, M.N., Van Rhijn, B.W., Van Der Kwast, T.H., and Zwarthoff, E.C. (2010). FGFR3, HRAS, KRAS, NRAS and PIK3CA mutations in bladder cancer and their potential as biomarkers for surveillance and therapy. *PLoS one* 5, e13821.
- [35]. Koo, S.H., Jeong, T.E., Kang, J.U., Kwon, K.C., Park, J.W., and Noh, S.M. (2004). Prognostic implications for gastric carcinoma based on loss of heterozygosity genotypes correlation with clinicopathologic variables. *Cancer genetics and cytogenetics* 153, 26-31.
- [36]. Kotnis, A., Sarin, R., and Mulherkar, R. (2005). Genotype, phenotype and cancer: role of low penetrance genes and environment in tumour susceptibility. *Journal of biosciences* 30, 93-102.
- [37]. Kumar, P., and Pawaiya, R. (2010). Advances in cancer diagnostics. *Braz. J. Vet. Pathol* 3, 142-153.
- [38]. Lennette, E.T., Blackbourn, D.J., and Levy, J.A. (1996). Antibodies to human herpesvirus type 8 in the general population and in Kaposi's sarcoma patients. *The Lancet* 348, 858-861.
- [39]. Li, J., Yen, C., Liaw, D., Podsypanina, K., Bose, S., Wang, S.I., Puc, J., Miliareis, C., Rodgers, L., and McCombie, R. (1997). PTEN, a putative protein tyrosine phosphatase gene mutated in human brain, breast, and prostate cancer. *science* 275, 1943-1947.
- [40]. Magrath, I., Steliarova-Foucher, E., Epelman, S., Ribeiro, R.C., Harif, M., Li, C.-K., Kebudi, R., Macfarlane, S.D., and Howard, S.C. (2013). Paediatric cancer in low-income and middle-income countries. *The lancet oncology* 14, e104-e116.
- [41]. Miyaki, M., and Kuroki, T. (2003). Role of Smad4 (DPC4) inactivation in human cancer. *Biochemical and biophysical research communications* 306, 799-804.
- [42]. Mota, F., Rayment, N., Chong, S., Singer, A., and Chain, B. (1999). The antigen-presenting environment in normal and human papillomavirus (HPV)-related premalignant cervical epithelium. *Clinical & Experimental Immunology* 116, 33-40.
- [43]. Orenstein, J.M., Alkan, S., Blauvelt, A., Jeang, K.-T., Weinstein, M.D., Ganem, D., and Herndier, B. (1997). Visualization of human herpesvirus type 8 in Kaposi's sarcoma by light and transmission electron microscopy. *Aids* 11, F35-F45.
- [44]. Osaki, M., Inoue, T., Yamaguchi, S., Inaba, A., Tokuyasu, N., Jeang, K.-T., Oshimura, M., and Ito, H. (2007). MAD1 (mitotic arrest deficiency 1) is a candidate for a tumor suppressor gene in human stomach. *Virchows Archiv* 451, 771-779.
- [45]. Panani, A.D. (2008). Cytogenetic and molecular aspects of gastric cancer: clinical implications. *Cancer letters* 266, 99-115.
- [46]. Pong, R.-C., Roark, R., Ou, J.-Y., Fan, J., Stanfield, J., Frenkel, E., Sagalowsky, A., and Hsieh, J.-T. (2006). Mechanism of increased coxsackie and adenovirus receptor gene expression and adenovirus uptake by phytoestrogen and histone deacetylase inhibitor in human bladder cancer cells and the potential clinical application. *Cancer research* 66, 8822-8828.

- [47]. Qunibi, W., Al-Furayh, O., Almeshari, K., Lin, S.-F., Sun, R., Heston, L., Ross, D., Rigsby, M., and Miller, G. (1998). SEROLOGIC ASSOCIATION OF HUMAN HERPESVIRUS EIGHT WITH POSTTRANSPLANT KAPOSI'S SARCOMA IN SAUDI ARABIA. *Transplantation* 65, 583-585.
- [48]. Rebbeck, T.R., Walker, A.H., Zeigler-Johnson, C., Weisburg, S., Martin, A.-M., Nathanson, K.L., Wein, A.J., and Malkowicz, S.B. (2000). Association of HPC2/ELAC2 genotypes and prostate cancer. *The American Journal of Human Genetics* 67, 1014-1019.
- [49]. Rodriguez-Galindo, C., Friedrich, P., Morrissey, L., and Frazier, L. (2013). Global challenges in pediatric oncology. *Current opinion in pediatrics* 25, 3-15.
- [50]. Rossi, E., Klersy, C., Manca, R., Zuffardi, O., and Solcia, E. (2011). Correlation between genomic alterations assessed by array comparative genomic hybridization, prognostically informative histologic subtype, stage, and patient survival in gastric cancer. *Human pathology* 42, 1937-1945.
- [51]. Schlaeger, C., Longerich, T., Schiller, C., Bewerunge, P., Mehrabi, A., Toedt, G., Kleeff, J., Ehemann, V., Eils, R., and Lichter, P. (2008). Etiology-dependent molecular mechanisms in human hepatocarcinogenesis. *Hepatology* 47, 511-520.
- [52]. Schwartz, R.A. (1996). Kaposi's sarcoma: advances and perspectives. *Journal of the American Academy of Dermatology* 34, 804-814.
- [53]. Sharmin, T., Parvin, S., Islam, M.A., Islam, M.M., Das, S.K., Gosh, B., and Al-Bari, M.a.A. (2014). Current Status and Prospective Of Cancer Disease in Bangladesh: A Cross-Sectional Survey. *IOSR Journal Of Pharmacy* 4, 41-47.
- [54]. Shibata, T., and Aburatani, H. (2014). Exploration of liver cancer genomes. *Nature Reviews Gastroenterology and Hepatology* 11, 340.
- [55]. Shin, S., Jing, K., Jeong, S., Kim, N., Song, K.-S., Heo, J.-Y., Park, J.-H., Seo, K.-S., Han, J., and Park, J.-I. (2013). The omega-3 polyunsaturated fatty acid DHA induces simultaneous apoptosis and autophagy via mitochondrial ROS-mediated Akt-mTOR signaling in prostate cancer cells expressing mutant p53. *BioMed research international* 2013.
- [56]. Sidransky, D. (1995). Molecular genetics of head and neck cancer. *Current opinion in oncology* 7, 229-233.
- [57]. Simpson, G.R., Schulz, T.F., Whitby, D., Cook, P.M., Boshoff, C., Rainbow, L., Howard, M.R., Gao, S.-J., Bohenzky, R.A., and Simmonds, P. (1996). Prevalence of Kaposi's sarcoma associated herpesvirus infection measured by antibodies to recombinant capsid protein and latent immunofluorescence antigen. *The Lancet* 348, 1133-1138.
- [58]. Smeets, S.J., Brakenhoff, R.H., Ylstra, B., Van Wieringen, W.N., Van De Wiel, M.A., Leemans, C.R., and Braakhuis, B.J. (2009). Genetic classification of oral and oropharyngeal carcinomas identifies subgroups with a different prognosis. *Analytical Cellular Pathology* 31, 291-300.
- [59]. Sony, S., Islam, M., Syeed Uddin, H., Ishma, T., Fariha, K., Hasnat, M., and Syfuddin, H. (2018). Biomarker-Based Cancer Scenario: A preliminary study of the northeastern region in Bangladesh. *BioResearch Communications* 4, 572-577.
- [60]. Story, H., Love, R., Salim, R., Roberto, A., Krieger, J., and Ginsburg, O. (2012). Improving outcomes from breast cancer in a low-income country: lessons from Bangladesh. *International journal of breast cancer* 2012.
- [61]. Sudhakar, A. (2009). History of cancer, ancient and modern treatment methods. *Journal of cancer science & therapy* 1, 1.
- [62]. Sun, Z., Pan, J., Bublely, G., and Balk, S.P. (1997). Frequent abnormalities of TSG101 transcripts in human prostate cancer. *Oncogene* 15, 3121.
- [63]. Tavtigian, S.V., Simard, J., Teng, D.H., Abtin, V., Baumgard, M., Beck, A., Camp, N.J., Carillo, A.R., Chen, Y., and Dayananth, P. (2001). A candidate prostate cancer susceptibility gene at chromosome 17p. *Nature genetics* 27, 172-180.
- [64]. Tay, J.S. (1992). The genetic basis of cancer. *J Singapore Paediatr Soc* 34, 126-135.
- [65]. Tjong, M.Y., Van Der Vange, N., Ter Schegget, J.S., Burger, M.P., Ten Kate, F.W., and Out, T.A. (2001). Cytokines in cervicovaginal washing fluid from patients with cervical neoplasia. *Cytokine* 14, 357-360.
- [66]. Torre, L.A., Bray, F., Siegel, R.L., Ferlay, J., Lortet-Tieulent, J., and Jemal, A. (2015). Global cancer statistics, 2012. *CA: a cancer journal for clinicians* 65, 87-108.
- [67]. Uddin, A.K., Khan, Z.J., and Johirul Islam, A. (2013). Cancer care scenario in Bangladesh. *South Asian journal of cancer* 2, 102.
- [68]. Vellekoop, A., and Loeb, S. (2013). More aggressive prostate cancer in elderly men. *Reviews in urology* 15, 202.
- [69]. Wabinga, H.R., Mugerwa, J.W., Parkin, D.M., and Wabwire-Mangen, F. (1993). Cancer in Kampala, Uganda, in 1989-91: changes in incidence in the era of AIDS. *International Journal of Cancer* 54, 26-36.
- [70]. Wang, L., Yin, F., Du, Y., Chen, B., Liang, S., Zhang, Y., Du, W., Wu, K., Ding, J., and Fan, D. (2010). Depression of MAD2 inhibits apoptosis and increases proliferation and multidrug resistance in gastric cancer cells by regulating the activation of phosphorylated survivin. *Tumor Biology* 31, 225-232.
- [71]. Wang, Y., Broderick, P., Webb, E., Wu, X., Vijayakrishnan, J., Matakidou, A., Qureshi, M., Dong, Q., Gu, X., Chen, W.V., Spitz, M.R., Eisen, T., Amos, C.I., and Houlston, R.S. (2008). Common 5p15.33 and 6p21.33 variants influence lung cancer risk. *Nat Genet* 40, 1407-1409.
- [72]. Wen, C.-Y., Nakayama, T., Wang, A.-P., Nakashima, M., Ding, Y.-T., Ito, M., Ishibashi, H., Matsuu, M., Shichijo, K., and Sekine, I. (2004). Expression of pituitary tumor transforming gene in human gastric carcinoma. *World journal of gastroenterology* 10, 481.
- [73]. Whitby, D., Boshoff, C., Weiss, R.A., Luppi, M., Barozzi, P., and Torelli, G. (1998). Human herpesvirus 8 seroprevalence in blood donors and lymphoma patients from different regions of Italy. *JNCI: Journal of the National Cancer Institute* 90, 395-397.
- [74]. Williams, H. (2000). Molecular pathogenesis of oral squamous carcinoma. *Molecular Pathology* 53, 165.
- [75]. Wong, D.T., Gallagher, G.T., Gertz, R., Chang, A.L., and Shklar, G. (1988). Transforming growth factor α in chemically transformed hamster oral keratinocytes. *Cancer research* 48, 3130-3134.
- [76]. Yokota, J., Shiraiishi, K., and Kohno, T. (2010). "Genetic basis for susceptibility to lung cancer: Recent progress and future directions," in *Advances in cancer research*. Elsevier, 51-72.
- [77]. Youlden, D.R., Cramb, S.M., Yip, C.H., and Baade, P.D. (2014). Incidence and mortality of female breast cancer in the Asia-Pacific region. *Cancer biology & medicine* 11, 101.
- [78]. Zarogoulidis, P., Tsakiridis, K., Karapantou, C., Lampaki, S., Kioumis, I., Pitsiou, G., Papaiwannou, A., Hohenforst-Schmidt, W., Huang, H., and Kesisis, G. (2015). Use of proteins as biomarkers and their role in carcinogenesis. *Journal of Cancer* 6, 9.
- [79]. Ziegler, J.L., Templeton, A., and Vogel, C.L. (Year). "Kaposi's sarcoma: a comparison of classical, endemic, and epidemic forms", in: *Seminars in oncology*: Elsevier, 47-52.
- [80]. Zur Hausen, H. (2002). Papillomaviruses and cancer: from basic studies to clinical application. *Nature reviews cancer* 2, 342.