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Original Article

Biomarker Based Cancer Scenario: A preliminary study of the northeastern region in Bangladesh

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ABSTRACT: Cancer, one of the major cause of mortality worldwide, has become a big threat to developing countries like Bangladesh because of its increased prevalence rate every year. Based on diagnosis and treatment modalities, this article inspects into various types of cancer incidences in a small sample from Sylhet, a city of Bangladesh, prior to any large-scale investigation representing the whole metropolis. Within the samples studied, the rate and frequency of cancer, incidences of each type of cancer in different genders and correlation of sex, age and malignancy are observed. Next, on the basis of reference values, the affected ones are separated from the entire samples. The highest number of the affected samples resides within an age range of 35-70 years where each type of biomarker indicates some specific type of cancer in a short age interval. Breast and ovarian cancers occur in the female at early mid-age and postmenopausal time whereas in men prostate cancer is mostly frequent after middle age e.g. from 71 to 80. Overall, since most of the samples are female, consequently cancer incidence rate is also noticeably higher in them compared to the males.

Keywords: Cancer biomarker, Age, Sex, Prevalence.

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INTRODUCTION

Cancer undoubtedly is the most pronounced disease in the biological field of the current world. It can be referred as a group of diseases initiating with abnormal cell growth and resulting in death. Cancer causes about half of all deaths per year worldwide and most frequently occurring cancers are lung, stomach, blood, GUT, prostate & female breast cancer.[1,2] The rate of cancer has been getting increased dramatically nowadays. Furthermore, it has remained as an incurable disease due to delay in detecting the stages. Though there are some common factors contributing to cancer development, appropriate early stage detection technique has become the main concern.

The cancer-induced mortality rate varies among sex, age, hormones and also among regional differences.[3] Age, which can be defined just as a unit of time, has become most studied risk factors for cancer and subsequently cancer has been considered as an age-related disease[4,5] due to incremental statistical proof of getting trapped by cancer after midlife. Statistically, it has been observed that approximately 75% of deaths due to colorectal cancer occur in people older than 65 years old[6]. Besides, sexual disparities can influence on the probability of having carcinoma[7]. Some types of cancers like esophageal adenocarcinoma occur nearly 6-10 times higher in men than women. Recent cancer

epidemiological investigation has pointed out that about ten types of cancer have the higher male to hypopharynx, oropharynx, esophagus, tonsil, urinary bladder and other urinary organs related cancers occur mostly in men. On the other hand, breast, mesentery, thyroid, gallbladder cancers are observed in women.

But there are still a limited number of data based on the population about how these two factors actually work on influencing cancer process. So, along with age and sex, some other cancer-causing factors had been considered which are accounted as tumor marker or biomarker. They are already being used as a potential tool for early detection of cancer stages. First and foremost, used markers are the members of glycoprotein Mucin family named CA15-3[9], CA-19-9[10], CA-125II[11]. Carcinoma/Carbohydrate Antigen 15-3 (CA15-3) is used for tracking many types of cancers e.g. liver, colon, small cell lung but most notably used for breast cancer. In that sense, it is a female-specific biomarker. CA15-3 is an epitope of the breast cancer-associated protein produced from MUC1 gene. An elevated level of CA15-3 is closely related to the early occurrence of breast cancer. As reference range of serum CA15-3 is less than 30 U/mL, a higher concentration than this can be correlated with more advanced stages of cancer or with larger tumor burden.[12] According to the point of view, in the metastatic stage, it increases at its highest. CA125, also denoted by the MUC16 protein that gets elevated beyond the normal in blood in response to the benign tumor. This test may be used to look for early signs of ovarian cancer. CA19-9 is a tumor surface marker used to observe the primary level of pancreatic cancer. At the same time, several other factors have been taken into consideration for a limited number of patients. The AFP (Alpha-fetoprotein) test helps to detect and diagnose the liver, ovaries and testicles cancers[13]. Prostate-specific Antigen (PSA) test reveals the blood PSA level. Increased level indicates the stages of prostatitis and benign prostatic hyperplasia.[14] The increased CEA (Carcinoembryonic Antigen) level in the blood may indicate the benign condition of liver cancer.[15]

In this article, a regional cancer epidemiological study had been conducted at Sylhet, a northeastern city of Bangladesh. The study was mainly executed on the basis of sexual disparity, age differences and level of CA15-3, CA19-9, CA125, PSA, CEA, and AFP in female incidence rate ratio (IRR)[8]. According to this analysis, Kaposi sarcoma, lip, mesothelioma, larynx, blood and serum in order to get a gross view of the circumstances of cancer incidence, rate of cancer in male and female, influence of age and sex on cancer occurrence.

MATERIALS AND METHODS

Study population and data collection

The population under study were the city dweller as well as rural people of Sylhet region, a northeastern metropolitan city of Bangladesh. The data was collected from a diagnostic center named MEDINOVA MEDICAL SERVICES LTD.-SYLHET, an approved medical center by Health minister's council for G.C.C (Gulf Co-operation Council) containing the Computer Code No. 05-03-01. Data were extracted from the archive of the medical center maintaining proper formalities and ethical issues. The time range of data is from March 2016 to March 2017 including patient's code number, principal assay name, age, sex, date of diagnosis and other related tests were taken where needed. Of total 1136 men and women under survey, there was diverse age ranges e.g. from 5 to 112 years old.

Calculation of cancer frequency and crude rate

Data of study people are separated from one another according to main biomarker assay. Five distinct biomarkers had been taken under consideration correlated to specific types of cancer as described above. Upon counting the total people undergoing diagnosis and the core set of people possessing a higher value of biomarker concentration than the references, the crude rate of malignancy were calculated. Alongside the crude rate, the distinct cancer frequency for male and female were also calculated as a percent value.

Graphical analysis

Heatmap, pie chart and bar diagrams were produced as the graphical representation of analyzed data. Graphs and diagrams were produced for each biomarker type based on age range and marker concentration in blood. Also, total population and positively diagnosed population were another factor for data analysis. Also, an attempt was taken to give a comparative view of cancer incidence in male and female through the analytical information of different biomarker.

RESULTS AND DISCUSSION

The total participants of collected data were 1136 during 1-year period, from March 2016 to March 2017. Data occupies only 0.21% of total folk of the Sylhet metropolitan city. Of the total, about 56.25% was women and 43.75% was men where 20.69% of women is thought to be cancer positive as well as 17.43% of men (Fig.1.A).

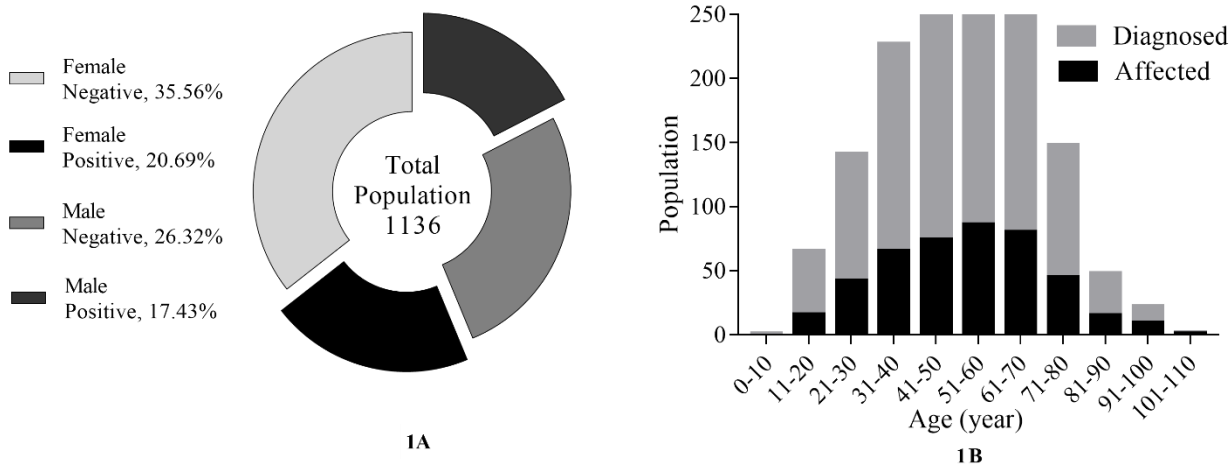

Fig.1: A pie chart showing total population under study, total percent of the male, female and the affected people (1A) Different age ranges showing affected population over the diagnosed (1B).

The age-specific rate of cancer incidence was calculated and depicted in a graph (Fig.1.B). A very diverse age ranges from 5 years to 112 years of the total study population was recorded. So, a graph was established showing an incidence of cancer (affected) in each 50 people (diagnosed) of certain age ranges e.g. 0-10, 11-20, 21-30….101-110. According to the graphical report, a maximum number of the diagnosed person fall within 40 to 70 years age range so as the affected percentage. It can be another proof about the increment rate of malignancy at the middle and late middle age. Detailed informations are distributed in Table2 to closely analyze the acquired relation between age range and cancer incidence. Here, the highest number of diagnosed and affected people are within 51-60 years age range. People of range 41-50 years are in position two based on diagnosis but 61-70 are the second age range where affected population is high. The ratio of affected versus diagnosed people is highest at the highest age range of 101-110 which is quite rare and there was a single case in our collected data. The ratio is also high after nineties. Surprisingly, nearly same ratio was found in young and after middle age.

The study has been enrolled with 5 major biomarkers e.g. CA15-3, CA19-9, CA125, PSA and CEA along with some other tests such as AFP. Each biomarker is related to some site-specific cancers. A total number of cases, cancer frequency for male and female and crude rate of cancer in case of each biomarker are shown in Table1

Table1: Potential biomarkers of site-specific cancer and frequency of male and female in Sylhet, 2016-2017.

Biomarker	**Probable site of cancer**	**Number of cases (male & female)**	**Cancer frequency female (%)**	**Cancer frequency Male (%)**	**Crude rate (%)**
CA 15-3	Breast (female specific)	94	13.82	N/A	13.82
CA 19-9	Pancreas, colon, esophagus	237	48.73	51.69	50.21
CA125	Ovaries (female specific)	288	39.93	N/A	39.93
PSA	Prostate gland (male specific)	266	N/A	33.08	33.08
CEA	Liver	251	36.22	41.13	39.04

Table 2: Distribution of affected incidences over diagnosed population ranging from age 1 to 110 years.

Age (year)	**1-10**	**11-20**	**21-30**	**31-40**	**41-50**	**51-60**	**61-70**	**71-80**	**81-90**	**91-100**	**101-110**
Diagnosed Population	1	49	99	162	232	243	200	103	33	13	1
Affected population	0	16	42	65	74	86	80	45	15	9	1
Ratio	0	0.33	0.42	0.40	0.32	0.35	0.40	0.44	0.45	0.69	1

CA-15-3 and CA-125 involve in breast and ovarian cancer respectively referring them as a female-specific marker and PSA is a male-specific marker for prostate cancer. Rest of two CEA and CA-19-9 are for both male and female. The reference value for each biomarker in serum is <31.30 U/ml[16], <35.00U/ml[17], <37.00U/ml[18], 0-4 ng/ml[19] and 0-10 ng/ml[20] for CA15-3, CA125, CA19-9, PSA and CEA respectively. An individual had been counted as the affected or at least the carrier of malignancy who crossed the reference values of the marker they tested. Out of total people, 628 was women and 232 was marked as the malignant carrier. For each biomarker, the diagnosed and seemingly affected number of women was plotted on the graph (Fig.2-left).

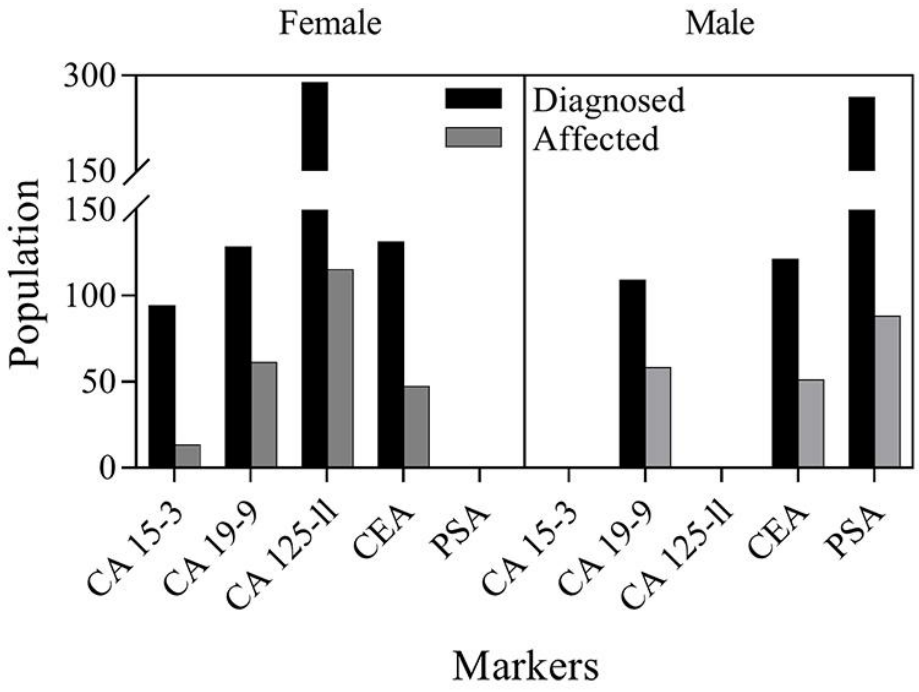

Fig.2: Diagnosed and affected population (male and female) for each marker. The number of affected was counted as expressing more than threshold concentration of marker in plasma.

The most prominent marker is CA-125II, female-specific and responsible for ovarian cancer. The cure rates would reach nearly 90% if early detection is possible but a very small percentage of this cancer is found at an early stage.

Statistically, 288 females were diagnosed and 115 of them were at a vulnerable range to malignancy. A quite high rate of CA-125II occurrence in a small city is an indication of the striking rate of ovarian cancer all over the world. Though breast cancer is more frequent than any other cancer type during middle age, superstition and introvert nature of maximum women in under developing countries like Bangladesh cause them to avert from proper diagnosis and monitoring. CA-15-3 is a most useful biomarker for breast cancer screening. Early detection of this biomarker increases the survival rate of patients from 80% to 92% where late or metastatic detection causes this rate down to 25%. Almost a significant number of malignancies were recorded as 13 out of 94 were counted as affected. High-level CEA and CA-19-9 were seen in 46 and 58 females out of 127 and 119 of total respectively. Prostate cancer seems to have an overgrowing rate in male so as seen in our data. PSA test is male-specific, and 88 individuals were suspected as affected out of total 266 diagnosed males. CEA test involving with liver malignancy provide data of 51 affected male where pancreas cancer rate is quite higher as 61 out of 118 males showed the high level of CA-19-9 (Fig.2-right).

There are huge shreds of evidence about the influence of age on cancer occurrence. It has been assumed that 70% of all cancer will occur at ≥65 age by 2030 on the basis of the current situation.[21] In Sylhet region, our study population data over 1-year time period gave a significant view about age and cancer occurrence which is explained through a heatmap (Fig.3).

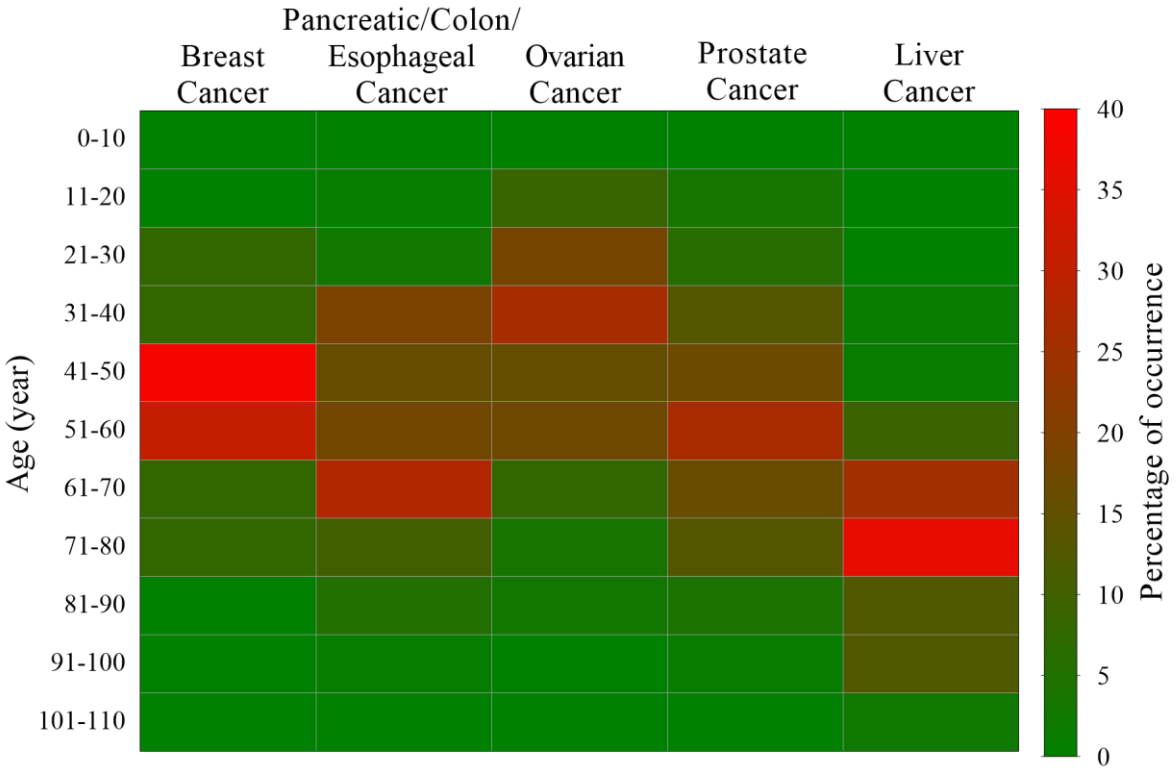

Fig.3: Heatmap showing percentile distribution of affected incidences for various cancers at specific age ranges (X axis implies cancer types and Y axis implies age ranges). Percentage of occurrence is marked using the bar-code labeling from 0 to 40.

It can be seen that breast cancer can be dominant at the stage of menopause (41-50) and the percentage of occurrence is highest (40%) at this age. Ovarian cancer can be flourished at 31-40 but the percent of occurrence is quite lower (nearly 30%) than breast cancer. Though both can be defined as the result of genetic predisposition but age range of 31-60 years is the most alarming for women. The manifestation of liver cancer involves mostly the lifestyle and viral infection rather than the age. But the outcome of data analysis couldn't be abdicated which showed an age range (71-80) when most of the liver cancer occurrence have been captured. Prostate cancer is mostly shown up at the middle age and probability of occurrence is directly proportional to age till sixty. Cancers related to pancreas, colon and esophagus start to progress during thirties and become dominant at sixties.

CONCLUSION

Biomarkers are used for diagnosis, prognosis, determination of the risk of diseases and so on. In this study, the outlooks of cancer incidence are analyzed by considering the age, sex and specific biomarker as the main parameter. A certain number of data was provided where female occupied the major portion. At first, the number of all diagnosed population and theoretically affected people were made an entry on the database. Then cancer frequency of male and female for specific cancer type were determined as well as the combined crude rate was calculated. Correlation between age and cancer was seen though it differs in ranges for sex. Female specific cancers are mostly observed at an adult age to postmenopausal stages which cause the decrease in total life expectancy. On the contrary, prostate-specific biomarker test revealed the occurrence of male-specific cancer takes place after midlife or old age which defines a quite chaos free middle age. It also suggests that maintaining a healthy lifestyle may prevent this later aged cancer frequency. Though the only biomarker-based early detection is quite old fashioned and less sensitive and genetic analysis and overlooking of family history are the major part of diagnosing cancer type, it mostly occupies the less invasive process thus can be conducted easily.

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