Article

Lifestyle and heritability effects on cancer in Bangladesh: an application of Cox proportional hazards model

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Abstract: The burden of cancer is increasing very rapidly day by day all over the world, largely due to an increasing unhealthy lifestyle. Some cross-sectional studies have been conducted on lifestyle of cancer patients based on Sylhet city, Bangladesh. However, to the best of our knowledge, no study has been done based on longitudinal aspect considering whole Bangladesh, therefore, we aimed to conduct a longitudinal study to know the effects of lifestyle and heritability on cancer in Bangladesh. We selected total 384 cancer patients by using simple random sampling from eight divisions during December 2018, and created a cohort in each division in Bangladesh. After one year, we collected their survival data from four selected cohorts. We used a Cox proportional hazards model for survival data. It was found that overall female patient's survival rate is higher than male patients. It was also observed that the significant factors of the lifestyle dimension influence the hazard function of the cancer patients. It indicates that more consumption of beverages, fast food, chips/chocolates/ice-cream, smoking and betel nut increased the hazard of cancer. That is, changing lifestyle is needed to reduce the cancer diseases in future. Taken together, the findings of this study may be able to make awareness in the society about the cancer, afterwards it might be able to reduce the cancer diseases in future in regional, national and international level to improve public health sectors.

1. Introduction

Cancer is main killer diseases all over the world. The burden of cancer is increasing very rapidly day by day because of increasing unhealthy lifestyle. It is a major health problem in developed country and second highest cause of death in developing countries. In 2012 about 14.1 million people were attacked by cancer in the world. Among them 8.2 million people were deaths (Hussain and Sullivan, 2013; "WHO | World Cancer Report 2014," World Health Organization, 2014; Zaman and Baki, 2009). Cancer is caused by both internal factors such as inherited mutations, hormones and immures conditions and the important lifestyle factors or environmental factors that affect the incidence and mortality of cancer include tobacco, alcohol, diet, obesity, infectious agents, environmental pollutants, and radiation(Anand *et al*., 2008; Argos *et al*., 2014; Ashrafunnessa *et al*., 2005; Danaei *et al*., 2005; Fitzgerald *et al*., 2010; Khatun *et al*., 2009; McPherson *et al*., 2000; Mukti *et al*., 2014). The contributions of genes and environmental factors towards cancer risk is (5-10) % and (90-95) % respectively (Hussain and Sullivan, 2013).

According to cancer registry of NICRH (2009-2015) there are 2.5 lakh cancer patients in Bangladesh while approximately 2 lakh people develop and 1.5 lakh die of the disease (Hussain and Zaman, 2008). Based on the online literature and reports we have found only five different studies (Hasan *et al*., 2012; Hussain, 2013; Shahriar *et al*., 2011; Talukder *et al*., 2008; Uddin *et al*., 2013) where researchers have been investigated status of cancer disease in Bangladesh based on Dhaka city. As the studies did not use the same reference standard, the

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prevalence of cancer is varied. Studies show that males have been suffering from cancer mostly lung, stomach, colorectal, lymphoma, and oral etc. Among them most of the people have been sufferings from lung cancer. On the other hand among female, researchers have been found breast cancer is the highest one followed by carcinoma cervix, stomach, colorectal and cancer of ovary. The ratio of male and female patients is 1.4:1. According to their findings the underlying risk factors are smoking, betel leaf, obesity, HPV infection, Helicobacter pylori. Studies also show that most of the female patients are housewives and most of the male patients are agricultural workers. Most of the patients are illiterate and are in age group (30-65) years.

In 2016, Ullah *et al*. (2016) conducted a study based on Sylhet city to know the extent of environmental and heritability effects on cancer, we found that theextent of environmental effect (path coefficient = 0.37) is more than the heritability effect (path coefficient = 0.15) and it shows that higher BMI, less exercise, and taking more junk food and meat might be the more influential factors for cancer.

Many studies (Bruner *et al*., 2003; Coté *et al*., 2012; GBD 2015 Disease and Injury Incidence and Prevalence Collaborators, 2016; GBD 2015 Mortality and Causes of Death Collaborators, 2016; Global Burden of Disease Cancer Collaboration *et al*., 2018; Kampman, 2007; McGuire, 2016; Nelson *et al*., 2013; Shahriar *et al*., 2011; Soerjomataram *et al*., 2018; Sung *et al*., 2019; Wolin*et al*., 2009; Wu *et al*., 2013) have been conducted including status and lifestyle of cancer patients. However, none study has been conducted covering whole Bangladesh on lifestyle and heritability effects on cancer, therefore, we would like to extend the study including longitudinal concept including survival data in the perspective of Bangladesh. In this study, our primary objective is to find out the lifestyle and heritability effects on cancer in Bangladesh considering survival data using Cox proportional hazardsmodel.

2. Materials and Methods

To find out the extent of heritability and lifestyle (environmental) effects on cancer, a semi-structured questionnaire has been prepared to collect the data from the cancer patients. At first we selected some cancer patients randomly from each division/strata and created a cohort in each division. We collected total 384 cancer patients from the hospitals of 8 divisional cities in Bangladesh. Initially (T_0), for cross-sectional data, we collected the information (life style, food habits, height, weight and demographic variables etc. and different blood test results) from the selected patients based on a questionnaire.

2.1. Data Sources

We conducted a cross-sectional study during December, 2018 in Bangladesh and the study population was the cancer patients from all over Bangladesh. Bangladesh is divided into eight (8) divisions for administrative purpose and these are- Dhaka (Capital), Chattogram, Rajshahi, Sylhet, Barishal, Rangpur, Khulna, and Mymensingh. The participants were the cancer patients going to treat cancer at public/private hospitals in different divisions of Bangladesh and simple random sampling procedure was used to collect sample from the study population.

A structured questionnaire was used to collect information from the cancer patients and the questionnaire included socio-demographic information, family history of cancer, eating behavior, pathological information, therapeutic data, and costing details. Information was collected from patients who were willing to give their details and from their relatives if the patients were not in such state to answer all questions. The study was approved by the research Center of SUST, Shahjalal University of Science and Technology (SUST), Sylhet, Bangladesh. Data collection was conducted by approaching to cancer patients who were waiting to meet the oncologist at cancer unit of different hospitals or taking therapy in hospitals. At first, socio-demographic information, costing details, therapeutic data, and eating behavior were collected orally from patients. Then pathological information and measurement of human body (Height, weight before and after cancer) were collected from their medical reports file. In each division information was collected in 3-4 days from as many patients as found.

After one year (during December, 2019), we selected 4 (four) cohorts by using a simple random sampling from the total 8 (eight) divisions/cohorts and then followed the initially selected patients around 12 months. After 12 months (T_{12}) we collected information such as: survive(yes/no), survival time (duration of disease, that is difference between death time and detecting time of cancer) , weight status (increase, stable, decrease), food habits (better, as usual, worse) from 4 divisions(Dhaka, Chattogram Sylhet and Mymensingh). For the Cox model we used gender, factors of lifestyle and heritability dimensions. Factors of lifestyle and heritability dimensions have been selected by Principal component analysis (PCA) separately.

For data entry, processing and analysis we used Statistical Package for Social Sciences (SPSS) version 22.0. Exploratory data analysis, PCA and Cox proportional hazards model had been used to analyze the data.

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3. Results

The mean (±SD) of height for male patients were 64.40 (±4.78) and for female were 60.01 (±3.90). The mean (±SD) of weight before cancer for male patients were 57.33 (±13.68) and for female were 53.63 (±11.60) and of weight after cancer for male were 50.07 (±11.80) and for female were 49.11 (±12.39). The average amount of money spent by patients was 235677.08 BDT (±329599.11 BDT).

Among 384 cancer patients, 192 (50%) patients were male and 192 (50%) were female. 30.21% of patients were from age group 40-49 and 24.74% from 50-59 age group. 50 (13.02%) of them were job holder, 177 (46.09%) are housewife, 44 (11.46%) were businessman and 36 (9.38%) of them were farmer. Education level of 311 (80.99%) individuals were below SSC, 37 (9.64%) were HSC pass, 19 (4.95%) were illiterate and 10 (2.60%) individuals were graduate. 237 (61.72%) of them were in stage 1 of cancer, 105 (27.34%) of them were in stage 2, 33 (8.59%) in stage 3 and 9 (2.34%) of them were in stage 4 of cancer. 65 (16.93%) of them had throat cancer, 47 (12.24%) had stomach cancer, 44 (11.46%) had breast (Left) cancer, 42 (10.94%) had lung cancer, 33 (8.59%) had cervical cancer and 33 (8.59%) of them had other type of cancer like anal, bone, kidney cancer etc. Total 372 (96.88%) of them usually eat food at their home and rest of them at restaurant. Total 305 (79.43%) of them had no relative diagnosed with cancer, 18(4.69%) had brother having cancer, 16 (4.17%) had father having cancer and 13 (3.39%) had other relatives having cancer. Total 304 (79.17%) of them didn't like exercise and rest of them do like it. Among 384 cancer patients, 267 (69.53%) of them had no other disease and 117 (30.47%) of them had diagnosed with different disease other than cancer. Total 282 (73.44%) of them could not bear their cost and others could.

It was also observed that 16% of cancer patients went to hospitals of Chattogram city, 14% to Sylhet and 14% to Khulna for treatment. Location of cancer by Genderdisclosed that Throat, Stomach, Lung, Colon, and Liver cancer found mostly in male patients and also Skin cancer happened to male patients more than female but the difference was high for Lung and Throat cancer but Blood cancer found in female patients more than male.On the other hand, location of cancer by division demonstrated that most throat cancer patients (18) were in Mymensignh followed by 14 in Chattogram and 14 in Rangpur and most stomach cancer patients (15) were in Sylhet. In addition, most Lung (12) and cervical (13) cancer patients found in Dhaka and Khulna respectively and Lung, Throat and Stomach cancer patients had been seen in every division.We found that 21.35% male patients preferred smoking very much and 15.63% more than average. 35.94% male patients and 36.46% female patients preferred beef/mutton less than average and 38.54% male and 41.15% female patients favored chicken moderately.

3.1. Survival data analysis

After one year we collected information such as: survive(yes/no), survival time (duration of disease, that is difference between death time and detecting time of cancer) , weight status (increase, stable, decrease), food habits (better, normal, worse) from 4 divisions(Dhaka, Chattogram Sylhet and Mymensing). We found total 46 (22.2%) patients died out of 207, and 31.4 % patients are still survive and we did not get data from around 46.4% patients. Among the died patients most of them are form Chattogram division (37%) followed by Dhaka (23.9%) and among the surviving patients most of them are from Dhaka (33.8%) followed by Sylhet (29.2%) and Chattogram (23.2%).

We also observed that patients who are still survive- among them around 30% patients' weights are increased, stable 29% and decreased around 41% patients. Food habits also improved around 41%, as usual11% and getting worse around 48% patients (Table 1).

We found median survival time is highest in Sylhet (18 months) followed by Chattogram (15 months. However, overall survival time is 12 months in these four divisions. It is shown in confidence interval as the length of confidence interval is wider for Chattogram division and narrower in Dhaka division (Table 1). We found that more male patients (27%) died compare to female patients (14.4%) though median survival time of both male and female is 12 months.

3.2. Results of Cox proportional hazard model

In order to run the Cox-model or proportional hazard model we used gender, division and the factors of lifestyle/environmental dimension and factors of heritability dimension. Factors of lifestyle dimension and heritability dimension were selected by PCA. Initially we run the model with all 4 factors (selected from the scree plot) for lifestyle dimension and 8 factors (similarly selected from the scree plot) for heritability dimension and observed -2loglikelihood of Omnibus test. We run the model repeatedly for reducing the factors. Finally we found 4 factors from each dimension (smallest -2loglikelihood) then run the final model (Table 2).

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From the results of Cox-model it was observed that female patients are around 20% less hazard than male patients though there is no significant difference between them. We also found that factor-1 (p<0.05), factor-2 (p<0.05) and factor 3 (p<0.10) of the lifestyle dimension are significant effect on hazard of cancer and there is no factor was found significant in heritability dimension. It indicates that the variables with the highest loadings in the significant factors of the lifestyle dimension influence the hazard function of the cancer patients. In the factor analysis we observed more consumption of beverages, fast food, chips/chocolates/ice-cream, smoking and betel nut increased the hazard of cancer (Table 3).

Table 1. Median survival time of patients respect to division and gender.

	Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Dhaka	9.000	1.651	5.763	12.237
Chattogram	15.000	4.939	5.319	24.681
Sylhet	18.000	4.243	9.684	26.316
Mymensingh	12.000	2.183	7.722	16.278
Overall	12.000	1.121	9.803	14.197
Male	12.000	1.789	8.494	15.506
Female	12.000	1.587	8.889	15.111
Overall	12.000	1.113	9.818	14.182

Table 2. Results of the Cox proportional hazard model.

Covariates	B	SE	Wald	df	Sig.	Exp(B)
Gender	-.199	.377	.279	1	.597	.820
Lifestyle Dimension						
FAC1	-.402	.192	4.383	1	.036	.669
FAC2	.383	.171	5.041	1	.025	**1.467**
FAC3	.270	.148	3.317	1	.069	**1.310**
FAC4	-.211	.185	1.309	1	.253	.809
Heritability Dimension						
FAC1	.026	.189	.019	1	.890	1.027
FAC2	-.156	.208	.562	1	.453	.856
FAC3	-.149	.185	.654	1	.419	.861
FAC4	.220	.148	2.208	1	.137	1.246

Table 3. Loadings of the variables of the selected components/factors of lifestyle dimension.

	Component			
	1	2	3	4
How much do you prefer **Fast food**	.335	**.708**	.011	.208
How much do you prefer Vegetable	.598	-.301	.059	.299
How much do you prefer Fish	.652	-.192	-.170	.192
How much do you prefer **beverages**	.247	**.730**	-.118	-.069
How much do you prefer Chicken	.715	-.096	.004	.175
How much do you prefer Beef/mutton	.650	.214	.231	-.321
How much do you prefer **smoking**	.248	.213	**.628**	-.531
How much do you prefer **Chips/Chocolate/ice-cream**	.117	**.580**	-.528	.086
How much do you prefer **betel-nut**	.093	.133	**.697**	.524
How much do you prefer fruits	.537	-.289	-.244	-.381

4. Discussion

Cancer is the major accidental cause of dying in early stage of life especially in Bangladesh and it is becoming a major concern for health sector. To find out, how many factors are responsible for growing cancer in a body and which factors they are, many studies has been done by researchers and doctors all over the world. Though we are far away from the reasonable and flawless answer of these questions because of different cases, it has been revealed that heritability factors and lifestyle factors can be responsible for growth of cancer. To find out the

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level of lifestyle and heritability effects we have conducted a cross-sectional study on cancer patients of eight division of Bangladesh and collected information of 384 cancer patients where there are 192 male and 192 female patients, after one year we collected the survival information from the patients of 4 divisions. At first we get descriptive information of the data and then for further discovery we run PCA, survival probabilities and Cox model.

According to International Agency for Research on Cancer, the rate of occurring breast cancer (Incidence rate (IR): 46.3) was high followed by Prostate (IR: 29.3), Lung (IR: 22.5), and Colorectal cancer (IR: 19.7), among both male and female cases. On the other, among male patients lung cancer (IR: 31.5) found to be high followed by Prostate (IR: 29.3), Colorectal (IR: 23.6), and Stomach (IR: 15.7) and among female patients Breast cancer (IR: 46.3) was on high and then were Colorectal (IR: 16.3), Lung (IR: 14.6), and Cervix uteri (IR: 13.1) (Bray *et al*., 2018). From descriptive information, we found that among different cancer people throat and stomach cancer mostly and among female patients, Breast, Cervical and Ovary cancer rate is high whereas Throat and Lung cancer occurs highly among male patients. According to a study in USA for young age of people the risk of getting cancer which is obese-related was higher than older age (Sung *et al*., 2019). From our study we observed that people of aged 30-60 had higher chance of growing cancer than the other age group where age group 40-50 is the high-risk group. According to a study in hospitals of Dhaka city, 27% of cancer patients were from Dhaka, followed by Cumilla (17%) (Shahriar *et al*., 2011). In our study, we found that about 16% of cancer patients go to hospitals of Chattogram, followed by Sylhet (14%). As number of patients have not fixed for each division, so it is not clear that although having high facility hospitals and trained doctor, cancer patients don't go to hospitals of Dhaka. The reasons can be that most of cancer patients are not from well-to-do family and as a result most of the time they can't afford to stay in Dhaka and maintain their treatment cost. Along with that, sometimes they prefer not to go those hospitals where costly equipments are available to avoid high treatment cost. On the other hand, patients who have enough money to treat their cancer outside Bangladesh, they don't go any hospitals as they don't trust treatment procedure and doctors of Bangladesh. From our study we found that preference of sweetened items like beverages, ice-cream, chocolate is not that much high in both male and female patients but they consumes moderately these type of foods. Another study in North-western Iran depicted that high consumption of milk of high fat, yogurt and food item with heavy cheese, deep fried meet and using same oil for 2 days increased the chance of having gastric cancer (Somi *et al*., 2015). Our study discovers that although in less amount but patients prefer fast food moderately and it has been seen that company or shops that make fast food or fried items use Mobil oil to make food crispier and also most of the time same oil for 2 or 3 days. A case-control study on esophageal and gastric cancers found that consumption of herby cheese and smoking was higher in cancer patients group (P < 0.001) than the control group (Celik *et al*., 2015). In our study, most of the female patients don't prefer smoking at all and also for half of male patients it has been seen that smoking preference is not that much high but more than one-third of male patients prefer smoking too much while some of them may be chain-smoker. Studies found that about 10% of world's population consumed betel-nut and among them most people were from India because of its availability, low pricing etc. (Sharan and Choudhury, 2010; Sharan *et al*., 2012). Our study tells that about one-fifth of cancer patients prefer betel-nut strongly and rests of them chew it moderately. Another study in US found high association between colon cancer and eating main dish of beef, lamb, pork etc. every day with relative risk 2.49 comparing with eating these item once in a month among women (Willett *et al*., 1990) and another study in Japan stated that consumption of red meat was highly associated with the risk of having colon cancer among women (Takachi *et al*., 2011). Our study shows that 40% of females prefer red meat items highly which indicates slight influence of it on Cancer and same for male patients. A study on nasopharyngeal carcinoma (NPC) in China discovered that risk of having NPC was highly effected (P (trend) <0.01) by having first relative with any cancer and many members suffering from cancer (Bruner *et al*., 2003). In our study we detect that about 80% of cancer patients have no family history of cancer and whom having family history of cancer, most of them has first relative- father, mother, brother with cancer.

Survival data shows that around 22% patients died in Dhaka, Chattogram, Sylhet and Mymensing divisions. Among them most people died in Chattogram followed by Dhaka. However, median survival time is higher in Chattogram and lower in Dhaka division. Considering all cancer diseases, we observed that female survival rate is higher than male patients, however, considering only stomach and colon cancer, survival rate is found higher for male than that of female (Ahammed *et al*., 2020). Patients who are still survive, among them most of the patients' weights are decreased as well as most of their food habits are getting worse. That is, they are suffering the diseases severely. From the Cox model it is clear that more consumption of beverages, fast food, chips/chocolates/ice-cream, smoking and betel nut increased the hazard of cancer.

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5. Conclusions

Although there are many studies which are similar to our study conducted in Bangladesh as well as many other countries in the world, this study can give a rough idea about the effects of lifestyle and heritability factors on cancer diseases in Bangladesh and possible idea about precautions that can be adopted in terms of different factors. It is true that the discoveries from this study may not explain or present the real scenario of different effects which are responsible for cancer but it might be help us to take further this study by studying different factors for different types of cancer individually. Taken together, the findings in this study may be able to make awareness in the society about the cancer, afterwards it may be able to reduce the cancer diseases in future in regional, national and international level. Finally, we recommend that- changing lifestyle is very essential to prevent the cancer diseases as we found lifestyle plays important role for cancer. So we should do exercise daily and avoid oily and junk food. We should take more fresh vegetables and fruits daily.

Conflict of interest

None to declare.

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