Identification of the risk factors of the thyroid cancer by using logit model in Lahore

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Abstract: Thyroid Cancer is a disease, which becomes a cause of death in developing countries. The aim of this study is to investigate all the possible risk factors of thyroid cancer in Pakistan. This study was consisting of 320 individuals, including 160 cases and 160 controls. These subjects were interviewed from the INMOL hospital and Sheikh Zayed Hospital, Lahore. The information was collected regarding the characteristics like age, gender, family history of thyroid cancer, use of iodine-diet, radiation therapy, etc. Descriptive and inferential statistics were used to explore the risk factors of the thyroid cancer. Odds ratio and 95% confidence interval (CI) were computed by using logistic regression model. The result showed that the odds ratio and 95% CI for family history of cancer are 2.222 and (1.281-3.853), for use of iodine diet are 2.619 and (1.492-4.596), for acromegaly disease are 1.947 and (1.123-3.374), for oxidative stress are 6.229 and (3.473-11.172), for red meat are 2.601 and (1.421-4.762), for fast food are 3.177 and (1.745-5.785), for fried food are 2.357 and (1.268-4.382), for the use of fats are 2.531 and (1.265-5.064) and for sea food are 2.050 and (1.127-3.729), respectively. It can be concluded that oxidative stress has 6 times high risk of thyroid cancer with the odd ratio 6.229 and CI (3.473, 11.172). Moreover, fast food, the use of iodine diet, red meat and the seafood are also increased the risk factor of thyroid cancer.

Keywords: Thyroid cancer, cases, confidence interval, risk factors, logistic regression, odds ratio.

INTRODUCTION

Thyroid cancer is the disease in which the cancer cells are found in the tissues of thyroid gland. It is diagnosed after its symptoms appear in the patient (Thyroid Cancer Survivors Association, 2011). Thyroid cancer is more common endocrine tumor. It is mostly found in the female as compared to the male (Hussain *et al*., 2005; Hodgson *et al*., 2004; Haselkorn *et al*., 2000).

In North American, children ratio of thyroid cancer is 0.9 per million in boys and 2.2 per million in girls. According to American Cancer Society, the ratio between female and male may be high as 6:1. In 2009, 37,200 new cases of thyroid cancer were diagnosed in USA and 1600 out of them died due to the disease. The rate of thyroid cancer in Hawaii is higher than the other region of Japan (Wartofsky, 2010). The ratio of malignant thyroid tumor in Pakistan is recorded as 1.2%. It is also seems that papillary thyroid cancer is more common in Karachi, Pakistan. The ratio of male and female patients in Karachi is 2.5 to 4:1 and most of the patients suffered from multi nodular goiter (Zuberi *et al*., 2004). Thyroid cancer symptoms increased with age, because of the deficiency and excess of iodine and radiation exposure (Verkooijen *et al*., 2012; Hussain *et al*., 2005; Haselkorn *et al*., 2005). Thyroid cancer has many subtypes (i.e. papillary carcinoma, follicular carcinoma, anaplastic carcinoma and medullary carcinoma), among which papillary carcinoma is found with increasing trend in several decades (Verkooijen *et al*., 2012; Hussain *et al*., 2005). Haselkorn *et al*., (2005) explained the possible risk factors of thyroid cancer, which are high dose ionizing radiation, excess or shortage of iodine, occupational exposure, diet, weight gain, genetics and hormonal factors. Some genetics and environmental factors like radiation exposure, goiter and hormonal factors are also increased the risk of thyroid cancer (Sprague *et al*., 2012). Cigarette smoking and the use of alcohol is inversely associated with papillary and follicular carcinoma (Kitahara *et al*., 2012). The risk of thyroid cancer also increased if the first-degree relative had thyroid disease. There are 5-fold higher risks of thyroid cancer in these patients. High intake of fish, weight gain, personal history of thyroid disease, hormone and reproductive factors all of these increased the risk of thyroid cancer (Martin *et al*., 2013; Maso *et al*., 2013). A person who is suffering from goiter and having benign nodules/tumor is at the high risk of thyroid cancer (Franceschi *et al*., 2013; Maso *et al*., 2013). According to Rossing *et al*., (2013) physical activities like exercise reduce the risk of thyroid cancer. The factor oxidative stress is highly associated with thyroid cancer as it represents the instability between the production of oxidants and removal of the anti oxidative molecule in the body (Xing, 2012).

The risk of thyroid cancer is 3 times higher in women. The matters related to reproductive factors and menarche become the cause of enlarged thyroid gland, which

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increase the thyroid stimulating hormone and convert in thyroid tumor (Maso *et al*., 2013). Some vegetable are also considered the risk factor of thyroid cancer i.e. the high consumption of crucifer vegetable arise the risk of thyroid cancer among low iodine women. Acromegaly disease is the most common factor of thyroid cancer (Truong *et al*., 2010; Gullu, 2010).

MATERIALS AND METHODS

Permission of Ethical Committee Permission was obtained from ethical committee of the hospitals before starting the observational study and intervention. The committee was comprised of Consultant Medical Specialist, Consultant Oncologist, Consultant Nephrologist, and Director of the Hospital. (Ethical approval reference number: 1244-GCU-MPHIL-STAT-11). This case and control study was conducted in Lahore. In order to identify the risk factors of thyroid cancer, data was collected with the help of self-designed questionnaire from Sheikh Zayed and INMOL Hospital, Lahore, Pakistan. To measure the reliability of the questionnaire, Cronbach's Alpha test was used which was found to be 0.742. The sample of 320 subjects was obtained from the selected hospitals in different visits between the months of January to May, 2013. All the required information was obtained from the individual about the characteristics like age, gender, family history of thyroid cancer, use of iodine diet, radiation therapy, etc. Both the male and the female of all ages, admitted in the oncology wards of the two hospitals for treatment of thyroid cancer, were included in this study. The 160 cases (patients) and 160 controls (healthy persons) were taken in the sample. The binary variable was taken as dependent variable while the independent variables were nominal, ordinal and quantitative type. For the analysis, SPSS (Statistical Package for Social Sciences) version 16.0 was used. Descriptive and analytical results were obtained by using the different statistical tools including averages, percentages, chi-square test (to check the degree of association), Phi/v-statistics, Kendall's Tau-b and logistic regression models. Odds ratios and the 95% CI for the Odds ratios were estimated by using the binary logistic regression model.

RESULTS

This case-control study was based on 160 cases and 160 controls. This study contained 88 (27.5%)male patients and 232 (72.5%) female patients, out of which 88 (27.5%) belonged to rural areas and 232 (72.5%) belonged to urban areas. The 67 (41.9%) patients belonged to the age group 15-35, 63 (39.3%) belonged to the age group 36-55 and 30 (18.7%) belonged to the age group more than 56. The 87 (54.3%) cases were illiterate and 67 (41.9%) controls were illiterate, which showed that the thyroid cancer is common among illiterate people. The 58 (36.3%) number of cases belonged to group of living sedentary life. The 83 (51.9%) cases have a family history of cancer while the 77 (48.1%) did not have the family history of cancer. The 82 (51.3%) cases used iodine diet and suffered from thyroid cancer while 78 (48.8%) controls did not intake iodine diet. The 90 (56.3%) cases suffered from acromegaly disease and 98 (61.3%) cases had oxidative stress. Most of the cases would intake fats 108 (67.5%), fast food 91 (56.9%), fried food 108 (67.5%), vegetable 151 (94.4%), red meat 110 (68.8%) and sea food 124 (77.5%) in their diet for more than 2 days. Among 160 cases, 119 (74.4%) suffered from papillary carcinoma rather than the others. The 78 (48.8%) cases had goiter and 56 (35%) had nodules in thyroid.

For the analytical analysis, binary logistic regression model was run and the regression coefficients, odds ratio, *p*-value and 95% CI for odds ratio were computed. For the significance of the variables, p-value is used to compare with the predefined value. For the adequacy of the model, Omnibus test and Hosmer and Lemes how (HL) test are used (Hosmer and Leme show, 2000). The value of Omnibus test with chi-square 121.654 is significant at 0.000 p-value, which shows that at least one of the factor is significantly affecting the information explained by the model. The Hosmer and Lemeshow test (goodness of fit) is much better than the other traditional chi-square tests (Hosmer and Lemes how, 2000). In this study, it was observed that the HL test is insignificant with $\chi 2=5.338$ at $p=0.721$ showing that the model is adequately fitted. The Cox and Snell's R^2 statistics and Nagelkerke's R-square are used to observe the goodness of fit, the values of Cox and Snell's R^2 statistics and Nagelkerke's R-square are 0.316 and 0.422, respectively. From table 2, it is observed that 122 (76.2%) patients with thyroid cancer and 121 (75.6%) patients without thyroid cancer are correctly predicted. But 38 (23.8%) cases and 39 (24.3%) controls are misclassified as 38 (23.8%) patients are not having thyroid cancer and similarly 39 (24.3%) patients are observed to have thyroid cancer, respectively. The total number (percentages) of correctly classified and misclassified patients are 243 (75.9%) and 77 (24.1%), respectively**.** As the value of correctly classified is much higher, the fitted model is adequate.

The significant risk factors and their predictive strengths are observed from table 3. Nine risk factors, family history of cancer, use of iodine diet, acromegaly, oxidative stress, red meat, fast food, fried food, the use of fats and seafood are found to be significant towards thyroid cancer. The logit model of these factors is given below:

Z=4.854+0.798*(Family_Hist)+0.963*Iodine+0.666*Acromegaly+1.829*Stress+0.956*Meat+1.156*(Fast_food)+0.858*(Fried_ food)+0.929*(Fats_use)+0.718*(Sea_food

Table 1: Classification of Variables for Overall Observations

Variables	Categories	Thyroid Cancer	
		Yes	No
Age	15-35	67	90
	36-55	63	50
	56 >	30	20
Gender	Male	33	55
	Female	127	105
Monthly Income	< 20,000	136	119
	≥ 20,000	24	41
Residential Place	Rural	48	40
	Urban	112	120
Marital Status	Unmarried	35	69
	Ever Married	125	91
Education	Literate	73	93
	Illiterate	87	67
Lifestyle	Sedentary	58	26
	Normal	51	60
	Active	51	74
Family History of Cancer	Yes	83	51
	No	77	109
Family History of Thyroid Cancer	Yes	42	17
	No	118	143
Smoking Cigarette	Yes	12	17
	No	148	143
Use of Alcohol	Yes	2	0
	No	158	160
Radiation Therapy	Yes	39	24
	No	121	136
A Bowl Condition	Yes	44	21
	No	116	139
Use of Iodine Diet	Yes	82	51
	No	78	109
Acromegaly Disease	Yes	90	58
	No	70	102
Occupational Exposure	Yes	11	16
	No	149	144
Oxidative Stress	Yes	98	36
	No	62	124
Red Meat	Yes (>2 days)	110	90
	No (≤ 2 days)	50	70
Fast Food	Yes (>2 days)	91	69
	No (≤ 2 days)	69	91
Fried Food	Yes (>2 days)	84	109
	No (≤ 2 days)	76	51
Vegetable	Yes (>2 days)	151	137
	No (≤ 2 days)	9	23
Use of Fats	Yes (>2 days)	108	132
	No (≤ 2 days)	52	28
Sea Food	Yes (>2 days)	124	101
	No (≤ 2 days)	36	59
Profession	Teachers	9	21
	House wife	100	57
	Labor	26	42
	Business	4	8
	Student	14	25

Variables	Categories	Thyroid Cancer	
		Yes	No
Body Mass Index	<18.5	13	18
	18.5 to 25	62	72
	>25	85	70
Types of Cancer	Papillary	119	0
	Follicular	29	0
	Other	12	0
Symptoms of Thyroid Disease	Nodules	56	0
	Goiter	78	0
	Inflammation of Thyroid	26	0
	None	0	160

Table 2: Classification Table

		Predicted		
		Thyroid Cancer		Percentage Correct
		Yes	No	
Thyroid Cancer	Yes	122	38	76.2
	No	39	121	75.6
Overall percentage				75.9

Table 3: Variables in the Equation

Factors	ℵ	S.E	Wald	Df	Sig	Exp (β)	95% CI for Exp (β)	
							Lower	Upper
Family_ Hist	.798	.281	8.079	1	.004	2.222	1.281	3.853
Iodine	.963	.287	11.245	1	.001	2.619	1.492	4.596
Acromegaly	.666	.281	5.638	1	.018	1.947	1.123	3.374
Stress	1.829	.298	37.665	1	.000	6.229	3.473	11.172
Meat	.956	.309	9.597	1	.002	2.601	1.421	4.762
Fast_ food	1.156	.306	14.292	1	.000	3.177	1.745	5.785
Fried_ food	.858	.316	7.351	1	.007	2.357	1.268	4.382
Fats_ use	.929	.354	6.894	1	.009	2.531	1.265	5.064
Sea_ food	.718	.305	5.531	1	.019	2.050	1.127	3.729
Constant	-4.854	.628	59.745	1	.000	.008		

The subject, having family history of cancer, has 2.222 times higher risk of thyroid cancer as compared to the subjects not with family history. The odds ratio of use of iodine is 2.619 with the confidence limits (1.492, 4.596). It illustrates that an iodine patient has 2.619 times higher risk of having thyroid cancer as compare to those who don't intake iodine in their diet. A patient suffered from acromegaly disease has 1.947 times higher risk of thyroid cancer as compare to non acromegaly patients. The factor oxidative stress was observed as a highly significant factor of thyroid cancer. It has 6.229 times higher risk of thyroid cancer as compared to those who have no oxidative stress. The consumption of red meat more than 2 days in a week has 2.601 times higher risk of thyroid cancer as compared to the others. A subject who used fast food more than 2 days in a week has 3.177 times higher risk of thyroid cancer as compared to the subjects not used fast food. The subject used fried food more than 2 days in a week has 2.357 times higher risk of thyroid cancer as compared to those who consumed less on fried food. A person using fats more than 2 days per week has 2.531 times higher risk of thyroid cancer and a subject using sea food more than 2 days per week has 2.050 times higher risk of thyroid cancer as compared to the others.

DISCUSSION

Thyroid cancer is found to be one of the most common and rapidly increasing cancer in the world. It is mostly found in women than in men. In 2004, male and female ratio of thyroid cancer is 1:4 and the ratio of thyroid cancer is 2.2:1 in Pakistan. It is mostly observed between the age group of 30 to 60 years (Zuberi *et al*., 2004). The main objective of this study is to identify the significant risk factors which affecting the thyroid cancer. In Lahore, oxidative stress is found to be the highest risk factor of the thyroid cancer compared to the other risk factors. The odd ratio and 95%CI indicates that the oxidative stress

had 6.229 times higher risk of thyroid cancer as compared to the others. Oxidative stress is strongly associated with thyroid cancer (Xing, 2012). Consumption of iodine diet in food has 2.619 times higher risk of thyroid cancer, as it is directly related to thyroid cancer. Low level of Iodine is, in fact, strongly associated with thyroid cancer incidence, via benign thyroid conditions such as goiter and nodules, which are the cause of thyroid cancer (Maso, 2013).

The use of fast food items is positively significantly associated with thyroid cancer and the subjects who are using fast food items more than 2 days per week have 3.177 times higher risk of thyroid cancer as compared to those who consume fried items 2 or less days per week. It is also observed that thyroid cancer is common among those who have family history of the disease with 95% confidence interval of odds ratio (1.281-3.853), which indicated that the a person having family history of disease having 2.222 times higher risk of getting the disease. A case control study, based on 207 thyroid cancer cases, reported that the most of the cases had a first degree relative suffering from thyroid disease (Martin *et al*., 1993).

Consumption of fried food more than 2 days per week has 2.357 times higher risk of thyroid cancer with the CI (1.268, 4.382) and the consumption of fats more than 2 days per week has 2.531 times higher risk of thyroid cancer with the CI (1.265, 5.064). The use of butter and cheese is significantly associated with thyroid cancer, having OR=1.6, CI, 1.1-2.5 and OR=1.5, 1.0-2.4 (Galanti *et al*., 1997).

The consumption of seafood more than 2 days per week has 2.050 times higher risk of thyroid cancer with CI (1.127, 3.729). The high consumption of fresh water fish and dietary habits are positively associated with thyroid cancer risk (Martin *et al*, 1993). The red meat consumption also showed the positive association with (OR=2.601, CI; 1.421-4.762) which means that a person who used red meat 2 or more days per week has 2.061 times higher risk of getting the disease. The excess use of red meat, as well as chicken showed a positive association with thyroid cancer (Memon *et al*., 2002).

CONCLUSION

Thyroid cancer becomes a common cancer in Pakistan. It is mostly found in women than in men. Among the subtypes of thyroid cancer, ratio of papillary carcinoma is very high. Oxidative stress, the use of high iodine diet, acromegaly and family history of cancer, fried food, fast food, red meat and seafood increase the risk of thyroid cancer.

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