

## Identification of the Risk Factors of the Thyroid Cancer in Males, Lahore

Faiza Asif<sup>1</sup>, Muhammad Riaz Ahmad<sup>2</sup> and Jaffer Hussain<sup>3</sup>

### Abstract

Thyroid Cancer (TC) has become a common disease in the developing countries. A number of prognostic factors of thyroid cancer have been identified, such as age, gender, iodine deficiency, radiation exposure, food etc. The aim of this study is to explore the different risk factors of the occurrence of thyroid cancer in Pakistan. This study consisted of 88 males, including 33 cases and 55 controls. These individuals were interviewed from the INMOL Hospital and the Sheikh Zayed Hospital, Lahore and all the necessary information was collected. All the possible risk factors were observed descriptively and inferentially. For the Bivariate Analysis, the Chi-square, Phi/v statistics and Kendall's tau-B are used. For the purpose of Multivariate Analysis, Odds Ratio and 95% confidence interval of these factors were computed by using Logistic Regression model by using the SPSS. In Bivariate Analysis, five factors were found to be positively significant and one was found negatively significant. The Multivariate results showed that the Odds Ratio and 95 % confidence interval (C.I.) for oxidative stress were 10.081 and (2.681-37.902), for fast food they were 6.011 and (1.564-23.101) and for vegetables they were 8.896 and (0.830-95.340), respectively. It was concluded that oxidative stress has 10 time higher risk of thyroid cancer with the Odds Ratio 10.081 and C.I. (2.681-37.902). Moreover, fast food and cruciferous vegetables also increased the risk factor of thyroid cancer.

### Keywords

Thyroid cancer, Confidence interval, Risk factors, Logistic regression, Odds Ratio

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<sup>1</sup>Department of Statistics, GC University, Lahore, Pakistan.

Email: [fzmalik90@gmail.com](mailto:fzmalik90@gmail.com)

<sup>2</sup>Department of Statistics, Government Postgraduate College, Jaranwala, Pakistan.

Email: [mriaz1346@yahoo.com](mailto:mriaz1346@yahoo.com)

<sup>3</sup>Department of Statistics, GC University, Lahore, Pakistan.

Email: [jafferfarooq@hotmail.com](mailto:jafferfarooq@hotmail.com)

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**1. Introduction and literature review**

Thyroid cancer is the 20<sup>th</sup> most common cancer among males. In the last three decades, it is continuously increased all over the world (Pellegriti et al., 2013).

Thyroid cancer is the most common endocrine cancer. This incidence is high among the young population. The ratio of thyroid cancer among males and females is found to be 1: 9.5 (Musani et al., 2010). This cancer is rare in the males and it accounts roughly for about 0.5% of all cancers in men. It is frequently found in the form of nodular thyroid gland (Zuberi et al., 2004). In Pakistan, thyroid cancer is responsible for about 1.2 % cases of all malignant tumors, with patients usually presenting with neck mass (Shamim et al., 2008).

Thyroid cancer incidence is increased by age, time and birth cohort in Canada and the incidence rate was doubled among the males in 1996 than in 1972. Ionizing radiation was also found the mainly entrenched risk factor of thyroid cancer (Liu et al., 2001).

Thyroid cancer occurrence variation could be explained with the diet among ethnic groups, as the lack and excess of iodine was found to be possible risk factor of thyroid cancer. Thyroid cancer rate was also high among the people who intake goitrogenic vegetable (Haselkorn et al., 2000). Cruciferous vegetable and the thyroid cancer are positively associated with each other (Truong et al., 2010). Family history of thyroid cancer is also found as a risk factor. High weight and Body Mass Index (BMI) is also associated with thyroid cancer (Suzuki et al., 2008).

Most of the thyroid cancer patients have the history of benign thyroid nodules, goiter, and irradiation of neck and the starchy food, showed the direct association with thyroid cancer in Northern Italy (Franceschi et al., 1989). Radiation exposure is also the well-known risk factor of thyroid cancer. Radiation treatment at the lower age associated with a higher risk of thyroid cancer (Schneider et al., 1993).

**2. Material and method**

This case and control study was conducted to explore the risk factors of thyroid cancer among the males, in Lahore. For this purpose, data was collected with the help of self-designed questionnaire from the Sheikh Zayed and the INMOL Hospital, Lahore, Pakistan. The reliability of questionnaire was measured with the Cronbach's Alpha test, which was found to be 0.742. The questionnaire was

based on different questions like age, family history of cancer, residential area, life style, the use of iodine diet, oxidative stress, the use of fast food etc. The sample of 88 males was obtained from the selected hospitals in different visits between the months of January to May, 2013. The 33 cases (patients) and 55 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.

The independent variables used in this study were taken as nominal, ordinal and quantitative type but the response variable was Binary. For the Descriptive and Inferential Analysis, different statistical tools including averages, percentages, Chi-square test (to check the degree of association), Phi/v-statistics, Kendall's Tau-B, Odds Ratios, the 95% confidence intervals and Logistic Regression models were used.

Logistic Regression has been used to examine the relationship between independent variables and dichotomous responses variable. To represent the relationship among dependent and independent variable, there must be nonlinear relationship among the coefficient of both variables. If the estimated probability is greater than 0.50 then the results is happen otherwise no (Hair et al., 2008).

Let,  $Y$  be a Binary random variable to  $m$  independent variables is denoted by  $Y = X_1, X_2, X_3, \dots, X_m$  and the conditional probability of the model is  $p = P(Y=1)$  at the values of  $m$  predictors. Then by using the Maximum Likelihood method, Logistic Regression models of  $Y$  on  $X_1, X_2, X_3, \dots, X_m$  estimates the parameter  $\beta_0, \beta_1, \beta_2, \dots, \beta_m$  is,

$$\log \text{it}[p] = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_m x_m \quad (2.1)$$

which can be written as:

$$p = \frac{\exp(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_m x_m)}{1 + \exp(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_m x_m)} \quad (2.2)$$

The adequacy of the fitted model can be observed by using the Cox and Snell  $R^2$  and Nagelkerke  $R^2$ . Both the measures are the same, having range from 0 to 1 and similar to  $R^2$  in interpretation. Nagelkerke  $R^2$  can attain its maximum value one

but the Cox and Snell's  $R^2_{cs}$  can never attain its maximum value one (Hosmer and Lemeshow, 2000).

### 3. Result

This case-control study is based on 33 cases and 55 controls. From the Table 1, it is observed that among 33 cases, 42.2% of the patients are from middle age group (36-55) and 82% are belonged from urban areas. According to study of (Zuberi et al., 2004) it was found that the thyroid cancer in peak among the patients of 30 to 60 years of age. Thyroid cancer is found to be common among married patients, among labor and among those who's having family history of thyroid cancer.

The 19 (57.5%) cases are suffered from oxidative stress and 69.6% patients are intake red meat and fast food in their diet. Similarly as, 96.9% patients are intake cruciferous vegetables in their daily food and 75.7% cases consumed fats products. Among 33 cases, 81.8% patients are used sea food and 84.8% patients has body mass index greater than 25. Most of the patients are suffered from papillary thyroid cancer. In the study of Los Angeles country, it was seen that the ratio of male of all races patients were high among the papillary thyroid cancer with 1.74%, respectively (Haselkorn et al., 2000).

For the Analytical Analysis, Binary Logistic Regression model, the Regression coefficients, Odds Ratio, p-value and 95% confidence interval for Odds Ratio were computed and for the significance of the factors, predefined value was compared with p-value. To assess the overall significance of the model, Omnibus test and Hosmer and Lemeshow (HL) test were used (Hosmer and Lemeshow, 2000). The value of Omnibus test with Chi-square 42.408 is significant at 0.000 p-value, which showing that at least one of the factor is significantly affecting the information explained by the model. In order to observe the Goodness of Fitted model, Cox and Snell  $R^2$  and Nagelkerke  $R^2$  value are 0.382 and 0.521, respectively. From Analysis, it is observed that the HL test is insignificant with  $\chi^2 = 18.482$  at  $p = 0.118$ , indicates that the model is appropriate and adequately fitted. It is also observed from Table 2, that marital status and education are negatively associated with thyroid cancer, while family history of thyroid cancer, oxidative stress, use of vegetables and body mass index are positively associated with thyroid cancer. It is also observed from Table 2, that (72.7%) cases and (92.7%) were correctly predicted.

As from the Table 4 of male fitted model, four risk factors, oxidative stress (oxidative stress), fast food (Fastfood), vegetables (Vegetable\_use) and age are found to be significant towards thyroid cancer.

The Logit model of these factors is given below:

$$Z = 0.506 + 2.311 * (\text{Oxidative Stress}) + 1.794 * (\text{Fast\_food}) + 2.186 * (\text{Vegetable\_use}) - 0.060 * (\text{Age})$$

The three factors including oxidative stress (Oxidative Stress), fast food (Fast\_food) and cruciferous vegetables (Vegetable\_use) are found to be directly related to thyroid cancer, while the age is inversely related to thyroid cancer. From Table 4, this model explain that the subject having oxidative stress has 10.081 times higher risk of thyroid cancer as compared to non-oxidative stress subjects with the confidence limits are (2.681, 37.902), respectively. Similarly, as a subject who is used fast food 2 or more days per week having 6.011 higher risks of thyroid cancer than the other and the confidence limits of Odds Ratio at 95% are (1.564, 23.011), which is greater than 1. The value of Odds Ratio for the vegetables user shows that the subject has 8.896 times more chances of thyroid cancer as compared to those who has not used cruciferous vegetables in more than 2 days per week. The factor age and thyroid cancer has found negatively significant with the odds 0.942. The value of Odds Ratio showed that the patients at different ages have 0.942 times more chances of thyroid cancer. When 1 year age increased then 1.06 risk of thyroid cancer increased.

#### 4. Discussion

Thyroid cancer is found to be one of the most common and rapidly increased malignant in the world. It seen that the ratio of male patients is less than female patients. The ratio of thyroid cancer patients in Pakistan is 2.2:1. In this study, it is observed that 42.4% patients were found between the age group of 36 to 55 years and 36.4% were suffered from disease laying in the age group of above 56. The 5.1% patients, who were suffered from disease, were found in age group of 45-64 years and 7.5% were found between the age group of 65-84 (Hodgson et al., 2004). During the study of thyroid cancer in Sweden and Norway mostly male patients were found in the age group of 50-54 or in above 60 (Galanti et al., 1997). The main objective of this study is to identify the significant risk factors which cause the thyroid cancer. According to this study, oxidative stress is found to be the highest risk factor of the thyroid cancer compared to the other risk factor. Goiter is associated with the oxidative stress (Poncin et al., 2010). The

Odds Ratio and 95% C.I. indicates that the oxidative stress has 10.081 times higher risk of thyroid cancer as compared to the other. Oxidative stress is strongly associated with thyroid cancer (Xing, 2012). Due to the antioxidant deficiency mostly patients of thyroid cancer were suffered from oxidative stress (Metere et al., 202). Turnip and cruciferous vegetables also found as a risk factor of thyroid cancer. The subjects who use these vegetables more than 2 days per week have 8.896 times high risk of thyroid cancer. The consumption of the cruciferous vegetables considered a risk factor of the thyroid cancer. It showed a positive association with the disease (Choi et al., 2014). Similarly as, consumption of fast food items in more than 2 days per week is also positively associated with thyroid cancer with the Odds Ratio 6.011. Too much consumption of starchy food (i.e whole grains, potatoes, legumes, yams etc.) was associated with thyroid cancer (Truong et al., 2010). The use of cheese and butter with Odds Ratio and confidence interval (1.5, 1.0-2.4 and 1.6, 1.1-2.5) were highly associated with thyroid cancer. As well as, it was also concluded that cruciferous vegetables increased the risk of thyroid cancer (Galanti et al., 1997). Too much use of nutritional food which get from animals (e.g meat), in Chinese food showed a positive association with thyroid cancer (Choi et al., 2014).

## **5. Conclusion**

We may conclude from the above results that oxidative stress is play an important role in the rapid growth of thyroid cell and it is positively associated with thyroid cancer. Some goitrogenic food, such as turnip and cruciferous vegetables is also positively associated with thyroid cancer. All the dietary food which have nitrated and nitrite, used as a fast food is also raised the risk of thyroid cancer.

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**Table 1:** Classification of risk factors

Variables	Code	Categories	Male		
			Thyroid cancer		
			Yes	No	Total
Age	Age	Lower age (15-35)	7	35	42
		Middle age (36-55)	14	16	30
		High age (56 or >)	12	4	16
Residential place	Residence	Rural	6	14	20
		Urban	27	41	68
Residential area	Area	Industrial	14	17	31
		Non industrial	19	38	57
Marital status	Marital	Unmarried	8	25	33
		Ever Married	25	30	55
Education	Education	Literate	12	33	45
		Illiterate	21	22	43
Lifestyle	Life_style	Sedentary	5	6	11
		Normal	11	14	25
		Active	17	35	52
Family history of cancer	Family_History	Yes	17	18	35
		No	16	37	53
Smoking cigarette	Smoke_Cigarette	Yes	11	17	28
		No	22	38	60
Use of alcohol	Alcohol_use	Yes	1	0	1
		No	32	55	87
Radiation therapy	Rad_thrpy	Yes	7	6	13
		No	26	49	75
Use of iodine diet	Iodine	Yes	15	20	35
		No	18	35	53
Occupational exposure	Occup_Exposure	Yes	10	11	21
		No	23	44	67
Oxidative stress	Stress	Yes	19	5	24
		No	14	50	64
Red meat	Meat	Yes	23	32	55
		No	10	23	33
Fast food	Fast_food	Yes	23	29	52
		No	10	26	36
Fried food	Fried_food	Yes	17	36	53
		No	16	19	35
Vegetables	Vegetable_use	Yes	32	45	77
		No	1	10	11
Use of fats	Fats_use	Yes	25	47	72
		No	8	8	16
Sea food	Sea_food	Yes	27	36	63
		No	6	19	25

Profession		Teachers	0	3	3
		House wife	0	1	1
		Labor	25	35	60
		Business	3	7	10
		Student	4	9	13
Body Mass Index	BMI	<18.5	3	5	8
		18.5 to 25	2	25	27
		>25	28	25	53
Type of cancer	Type	Papillary	26	0	26
		Follicular	4	0	4
		Other	3	0	3
		None	0	55	55
Symptoms of thyroid disease	Symptoms	Nodules	11	0	11
		Goiter	12	0	12
		Inflammation of thyroid	10	0	10
		None	0	55	55

**Table 2:** Classification table of male patients

Observed		Predicted		
		Thyroid cancer		Percentage Correct
		Yes	No	
Thyroid cancer	Yes	97	30	76.4
	No	30	75	71.4
<b>Overall percentage</b>				74.1

**Table 3:** Bivariate Analysis of male patients

Factors	$\chi^2$ Value	P-value	Phi $\phi$	Tau-B
Marital Status	3.960	0.047	-0.212	-----
Education	4.611	0.032	-0.229	-----
Family History of Thyroid Cancer	5.043	0.025	0.239	-----
Oxidative stress	24.444	0.000	0.527	-----
Vegetables	4.329	0.037	0.222	-----
Body Mass Index	15.747	0.000	0.423	-----

**Table 4:** Fitted model of male patients

Factors	$\beta$	S.E	Wald	d.f.	Sig.	Exp( $\beta$ )	95% C.I. for Exp( $\beta$ )	
							Lower	Upper
Oxidative Stress	2.311	.676	11.693	1	.001	10.081	2.681	37.902
Fast_food	1.794	.687	6.819	1	.009	6.011	1.564	23.101
Veg_use	2.186	1.210	3.262	1	.071	8.896	.830	95.340
Age	-.060	.021	8.183	1	.004	.942	.904	.981
Constant	.506	1.070	.224	1	.636	1.659		



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