

## RESEARCH ARTICLE

# Risk Factors for Thyroid Cancer in Females Using a Logit Model in Lahore, Pakistan

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### Abstract

**Background:** Thyroid cancer (TC) is a more common endocrine malignancy in females and is a major cause of death in developing countries. Therefore the aim of this study was to explore possible risk factors of thyroid cancer in females of Pakistan. **Materials and Methods:** This study covered 232 females, including 127 (54.7%) cases and 105 (45.2%) controls, from the INMOL Hospital and Sheikh Zayed Hospital, Lahore. Different risk factors were explored by the descriptive and inferentially statistics. Odds ratios and 95% confidence intervals for different risk factors were computed using logistic regression. **Results:** The results showed six risk factors, marital status, family history of thyroid cancer, iodine in the diet, oxidative stress, fast food and fried food, to demonstrate positive significant links to thyroid cancer (odds ratios and 95% confidence intervals of :2.152, 1.104-4.198; 2.630, 1.416-4.887; 2.391, 1.282-4.458; 4.115, 2.185-7.750; 3.656, 1.851-7.223; 2.357, 1.268-4.382; and 2.360, 1.199-4.643, respectively). **Conclusions:** The Oxidative stress, marital status, family history of cancer, fast food, use of iodine diet and fried food are the risk factors of thyroid cancer in females.

**Keywords:** Thyroid cancer - risk factors - logistic regression - odds ratio - oxidative stress

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### Introduction

Thyroid cancer is a relatively rare cancer than other but it is the most common endocrine malignancy worldwide. It is mostly found in females of almost all the geographic areas (Iftikhar et al., 2011). It is a disease in which the cancer cells are found in the tissues of thyroid gland. It is diagnosed after its symptoms appearing in patient (Thyroid Cancer Survivors Association, 2014). Thyroid cancer is more common endocrine tumor. It is mostly found in females as compared to males (Haselkorn et al., 2000; Hodgson et al., 2004; Hussain et al., 2005). According to American Cancer Society, the ratio between female and male may be high as 6:1. Approximately 2,700 new cases were found in UK each year with the female male ratio of 3:1 (Cancer Research UK, 2014). In 2014, 62,980 new cases were estimated in US and the estimated deaths due to thyroid cancer were 1,890 recorded. The female to male ratio in this part of world is 19.1 to 6.4 (National Cancer Institute, 2014). During the study in Baluchistan 58 (66.7%) cases of thyroid cancer were found among the females between the age of 12-70. Among the 58 cases, 48 (83%) cases were found of the papillary cancer (Iftikhar et al., 2011).

It was observed in the study of histopathological pattern of thyroid cancer in Saudi Arabia region, that 78.8% females were suffered from thyroid cancer. Among

these cases, papillary carcinoma was found to be most common tumor (Albasri et al., 2014). Overall percentage of thyroid cancer in Pakistan is 1.2%. Similarly, the ratio of male to female patients in whole Karachi, Pakistan is 2.6 to (Shah et al., 1999). During the study in Aga Khan University Hospital, Karachi the ratio of female to male patients was 2.2 to 1 (Zuberi et al., 2004). Papillary thyroid cancer more significantly found in females and iodine excess or deficit is a big cause of papillary and follicular thyroid cancer (Verkooijen et al., 2012). The 6235 (72.5%) female cases were found among the 8603 registered cases in Florida which was three times more than males. This study was concluded that radiation exposure, occupational exposure, reproductive factors often increase the risk of thyroid cancer (Hodgson et al., 2004). The possible risk factors of the higher ratio of thyroid cancer in women may be high dose ionizing radiation, excess or shortage of iodine, hormone replacement therapy and other hormonal factors (Haselkorn et al., 2005). Smoking and use of alcohol is inversely associated with papillary and follicular carcinoma (Kitahara et al., 2012).

### Materials and Methods

This case and control study of thyroid cancer was carried out in the Sheikh Zayed Hospital and INMOL Hospital, Lahore, Pakistan with the help of self-designed

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questionnaire. Reliability of the questionnaire was checked by Cronbach's Alpha test which was 0.74. The sample of 232 females was obtained from the selected hospitals in different visits between the months of January to May, 2013. All the requisite information was collected from the females about the characteristics like age, gender, family history of thyroid cancer, use of iodine

diet, radiation therapy, etc. The dependent variable of this study was binary while the independent variables were nominal, ordinal and quantitative type. For the descriptive and analytical purpose, SPSS (Statistical Package for Social Sciences) version 16.0 was used. For the analysis, bivariate analysis and binary logistic regression model were used. All the regression coefficients, odds ratio,

**Table 1. Classification of Variables**

Variables	Code	Categories	Female		
			Thyroid Cancer		
			Yes	No	Total
Age	Age	Lower age (15-35)	60	55	115
		Middle age (36-55)	49	34	83
		High age (56 or >)	18	16	34
Weight	Weight	30-60	51	42	93
		61-90	73	61	134
		91 or more	3	2	5
Monthly income	Income	<20,000	110	84	194
		≥ 20,000	17	21	38
Residential place	Residence	Rural	42	26	68
		Urban	85	79	164
Residential area	Area	Industrial	50	30	80
		non industrial	77	75	152
Marital status	Marital	Unmarried	27	44	71
		Ever Married	100	61	161
Education	Education	Literate	61	60	121
		Illiterate	66	45	111
Lifestyle	Life_style	Sedentary	53	20	73
		Normal	40	46	86
		Active	34	39	73
Family history of cancer	Family_hist	Yes	66	33	99
		No	61	72	133
Radiation therapy	Rad_thrpy	Yes	32	18	50
		No	95	87	182
A bowl condition	FAP	Yes	40	18	58
		No	87	87	174
Use of iodine diet	Iodine	Yes	67	31	98
		No	60	74	134
Acromegaly disease	Acromegaly	Yes	82	46	128
		No	45	59	104
Occupational exposure	Occup_expo	Yes	1	5	6
		No	126	100	226
Oxidative stress	Stress	Yes	79	31	110
		No	48	74	122
Red meat	Meat	Yes	87	58	145
		No	40	47	87
Fast food	Fast_food	Yes	68	40	108
		No	59	65	124
Fried food	Fried_food	Yes	67	73	140
		No	60	32	92
Vegetables	Veg_use	Yes	119	92	211
		No	8	13	21
Use of fats	Fats_use	Yes	83	85	168
		No	44	20	64
Sea food	Sea_food	Yes	97	65	162
		No	30	40	70
Profession		Teachers	9	18	27
		House wife	100	56	156
		Labor	1	7	8
		Business	1	1	2
		Student	10	16	26
Body Mass Index	BMI	<18.5	10	13	23
		18.5 to 25	60	47	107
		>25	57	45	102

**Table 2. Variables in the Equation**

Factors	$\beta$	S.E	Wald	Df	Sig	Exp ( $\beta$ )	95% CI for	
							Exp ( $\beta$ )	Upper
Marital Status	0.767	0.341	5.06	1	0.024	2.152	1.104	4.198
Family_Hist	0.967	0.316	9.359	1	0.002	2.63	1.416	4.887
Iodine	0.872	0.318	7.514	1	0.006	2.391	1.282	4.458
Stress	1.415	0.323	19.181	1	0	4.115	2.185	7.75
Fast_food	1.296	0.347	13.928	1	0	3.656	1.851	7.223
Fried_food	0.859	0.345	6.183	1	0.013	2.36	1.199	4.643
Constant	-3.522	0.551	40.874	1	0	0.03		

p-value and 95% confidence interval for odds ratio were computed. P-value is used to compare the significance of the variables with the predefined value. For the adequacy of the model, Omnibus test and Hosmer and Lemeshow (HL) test are used (Hosmer and Lemeshow, 2000).

## Results

This case-control female study was based on 232 patients. Out of 232, 127 (54.7%) patients were suffered from thyroid cancer. Table 1 describes all the classification of the risk factors. Among 232 females, 68 (29.3%) belonged to rural areas and 164 (70.7%) belonged to urban areas. The 60 (47.2%) cases were belonged to lower age group (15-35), 49 (38.5%) cases were belonged to middle age, while the 18 (14.2%) cases were belonged to high age (56 or above). The 66 (51.9%) cases were illiterate and 61 (48%) controls were illiterate, which showed that the thyroid cancer is common among illiterate people. Among 127 cases 53(41.7%) lived sedentary life while 40(31.4%) lived normal life and 34(26.8%) lived active life. The 66 (51.9%) cases have a family history of cancer while the 61 (48.1%) were not have family history of cancer. The 67 (52.8%) cases were used iodine diet and suffered from thyroid cancer while 60 (47.2%) controls were not intake iodine diet. The 82 (64.5%) cases were suffered from acromegaly disease and 79 (62.2%) cases were has oxidative stress. Most of the cases were intake fats 83 (65.4%), fast food 68 (53.5%), fried food 67 (52.3%), vegetables 119 (93.7%), red meat 87 (68.5%) and sea food 97 (77.6%) in their diet more than 2 days. Among 127 cases 93 (73.2%) were suffered from papillary carcinoma, 25 (19.7%) were suffered from follicular carcinoma while the rest of 9 (7.1%) were suffered from medullary and anaplastic thyroid cancer. The 66 (60%) cases were suffered from goiter disease and 45 (35.4%) cases were suffered from nodules in thyroid.

It was observed that 97 (76.4%) patients with thyroid cancer and 75 (75.1.4%) patients without thyroid cancer were correctly predicted. But 38 (23.8%) cases and 39 (24.3%) controls were misclassified as 30 (23.6%) patients were not having thyroid cancer and similarly 30 (23.6%) patients were observed as having thyroid cancer, respectively. The total numbers (percentages) of correctly classified and misclassified patients were 172 (74.1%) and 60 (25.9%), respectively. As the value of correctly classified was much higher, so the fitted model was adequate.

The significant risk factors and their predictive

strengths are observed in Table 2. Six risk factors including marital status, family history of cancer (Family\_Hist), use of iodine diet (iodine), oxidative stress (stress), fast food (Fast\_Food) and fried food (Fried\_Food) were found to be positively significant towards thyroid cancer. The logit model of these factors is given below:

$$Z = -3.522 + 0.767 * \text{Marital Status} + 0.967 * (\text{Family\_Hist}) + 0.872 * \text{Iodine} + 1.415 * \text{Stress} + 1.296 * (\text{Fast\_food}) + 0.859 * (\text{Fried\_food})$$

The subject having oxidative stress was observed as a highly significant factor of thyroid cancer. It had 4.115 times higher risk of thyroid cancer (OR: 4.115, 95% CI: 2.185-7.750, p=0.000). Similarly intake of fast food more than 2 days in a week was 3.656 time higher positively significant with thyroid cancer (OR: 3.656, 95% CI: 1.851-7.223, p=0.000). Same as the subject used fried food more than 2 days in a week had 2.360 times higher risk of thyroid cancer (OR: 2.360, 95% CI: 1.199-4.643, p=0.013). Family history of cancer was significantly associated with thyroid cancer (OR: 2.630, 95% CI: 1.416-4.887, p=0.002). Marital status was also positively significant with thyroid cancer (OR: 2.152, 95% CI: 1.104-4.198, p=0.024).

## Discussion

Thyroid cancer is found to be one of the most common and rapidly increased cancer in the world. It is mostly found in women than men. According to the study of Albasri, thyroid cancer has become the second most common tumor in the Saudi women. The male to female ratio in this region is 4:29 (Albasri et al., 2014). The ratio of thyroid cancer in male to female is 1:4 in Pakistan and in Karachi this ratio is 2.2:1. It is mostly observed between the age group of 30 to 60 years (Zuberi et al., 2004). The incidence of thyroid cancer was found high among the females of Baluchistan than males. Among 87 cases, 58 were females and among these 58 females, 53% cases belonged to 21-40 years age group (Iftikhar et al., 2011).

The main objective of this study is to identify the significant risk factors which cause of thyroid cancer. According to present study, oxidative stress is found to be the highest risk factor of the thyroid cancer as compared to the other risk factor. The odd ratio and 95% CI indicates that the oxidative stress had 4.115 times higher risk of thyroid cancer as compared to the other. Another study showed that the increased levels of oxidants and decreased

levels of antioxidants were exposed strong oxidative stress which provides the evidence of thyroid cancer in patients (Wang et al., 2011). High oxidative stress is a new and strongly associated risk factor of thyroid cancer. As, it represent the instability between the production of oxidants and removal of the anti-oxidative molecule in the body (Xing, 2012). The oxidation level disturbance in the blood of the thyroid cancer patients is due to the superoxide anion (free radical which produce during psychological cellular metabolism and inflammation). The excess of superoxide anion damage the DNA badly and also it showed the clearly involvement of oxidative stress in thyroid cancer (Metere et al., 2012).

According to this study, consumption of low and high iodine diet has 2.391 times higher risk of thyroid cancer, as it is directly related to thyroid cancer. Maso (2013) investigated low level 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. Excess and deficiency of iodine become the cause of autoimmune thyroid disorder like goiter and nodules (Prummel et al., 2004). Papillary carcinoma is mostly found in high iodide intake areas and low in areas with low dietary iodide (Williams et al., 1997). Like the other countries, iodine deficiency is the well recognized problem in Pakistan. Due to lack knowledge of consumption and intake of iodine nutrition thyroid hormones are affected. It also becomes the cause of pregnancy loss (Elahi et al., 2003). Different types of thyroid carcinoma are related to low and high iodine diet. Low iodine diet becomes the cause of follicular and anaplastic cancer and high iodine diet becomes the cause of papillary thyroid carcinoma. The incidence of thyroid cancer is similar to in iodine deficiency regions (Rasmussen, 2001). Thyroid cancer is directly significant to family history of thyroid cancer and intake of low iodine diet (Xhaard et al., 2014). Iodine is necessary for the production of thyroxine. Low level of iodine reduces the production of hormones. In such situation thyroid work harder to produce hormone which become the cause of enlargement and as well as goiter. In pregnancy iodine deficiency increased the risk of miscarriage (Park et al., 2005).

This study indicate the use of fast food items is positively significantly associated with thyroid cancer and the subject who are using fast food items more than 2 days per week have 3.656 times high risk of thyroid cancer. The use of butter and cheese in diet is positively associated with increasing the risk of thyroid cancer having OR=1.6, CI, 1.1-2.5 and OR=1.5, 1.0-2.4 (Galanti et al, 1997). The use of whole wheat and rye also contain iodine and the quantity of iodine among in these things depend on soil where these grown. Moreover the sea fish, shellfish, salad and pasta dishes have sufficient iodine intake (Vegetarian and Vegan Foundation, 2013). This study shows that consumption of fried food more than 2 days per week has 2.360 times higher risk of thyroid cancer with the CI (1.199, 4.643). The role of diet is positively associated with the thyroid cancer. Mostly nutritional factors are related with the risk of thyroid cancer (Galanti et al., 1997).

It is also seen from that study, thyroid cancer is

common among those whose has family history of cancer with 2.630 odds ratio (1.416-4.887), which indicated that the a person having family history of disease having 2.630 times risk of getting disease. According to the study of Martin et al, 1993 the most of the cases whose reported has a first degree relative suffered from thyroid disease. The genetic transformation is also responsible for the thyroid cancer incidence (Perrier et al., 1998). Genetics factors are 20-25% responsible for all the type of thyroid cancer. There is also a strong association among thyroid cancer and history of benign nodules and goiter (Maso et al., 2009).

In conclusion, thyroid cancer becomes a common cancer in Pakistan. It is mostly found among the female patients of age group (15-60). The ratio of papillary carcinoma is very high among all the types. It is concluded that oxidative stress, use of high and low iodine diet, genetic cancer history, excess of fast and fried food increase the risk of thyroid cancer.

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