

Risk Factors Associated with Thyroid Cancer in Females Attending King Khalid University Hospital in Riyadh, Saudi Arabia

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ABSTRACT

Introduction: In Saudi Arabia, thyroid cancer constitutes 7% of all cancers. This study was undertaken to characterize women with thyroid cancer and to determine the associated risk factors.

Methods: This is a case control study of 90 Saudi women suffering from thyroid cancer were enrolled in King Khalid University Hospital of Riyadh, Saudi Arabia and follow up clinics and 178 of controls were selected from the same hospital matched by age within 5-year interval.

Results: In multivariable analysis the place of residence (OR 5.36), suffering from goiter during childhood or adolescence (OR 3.51), suffering from hypo & hyperthyroidism during their childhood or adolescence (OR 14.32), family had thyroid enlargement/nodules (OR 4.33), consumption of meat twice or more/week (OR 3.32), and cooking with iodized salt (OR 3.30) showed significant association with thyroid cancer.

Conclusion: The data from this study strongly conclude that many risk factors were associated with thyroid cancer in

females attending King Khalid University Hospital of Riyadh, Saudi Arabia including childhood goiter, hypo or hyperthyroidism, family history of thyroid enlargement or nodules and also meat intake.

Keywords: Thyroid Cancer, Females, Risk Factors, KKU Hospital, Saudi Arabia.

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INTRODUCTION

As the global incidence of thyroid cancer increased, the trend of the associated mortality showed a continuous decline. In 2012, the global reported death rate from thyroid cancer was 0.6 per 100,000 women and 0.3 per 100,000 men.¹ The 5-year and 10-year survival rates of thyroid cancer varies according to the type of thyroid cancer. Papillary carcinoma is the most frequent type representing 79% of all thyroid cancer has a 5-year survival rate of 96% and 10-year survival rate of 93%. Follicular carcinoma represents 13% of all thyroid cancer with a 5-year survival of 91% and 10-year survival rate of 85%. In Saudi Arabia, the 2010 report of the Saudi Cancer Registry showed that clinically diagnosed thyroid cancer accounts for 7% of all newly diagnosed cases of cancer.² The five regions with the highest age-standardized incidence rate were Al Jouf (8.4 per 100,000 population), the Eastern region (7 per 100,000 population), Riyadh region (6.9 per 100,000), Qassim region (5.1 per 100,000) and Najran region (4.8 per 100,000).²

Previous studies reported the higher likelihood of thyroid cancer in association with a number of risk factors including iodine deficiency^{3,4}, family history of thyroid cancer^{3,5,6} and obesity.^{3,7} Contradictory findings were reported in respect to reproductive factors, excess risk of thyroid cancer in association with irregular menstrual cycle, high parity and miscarriage was reported by

Truong et al (2005)⁸ whereas Akslen et al (1994) did not observe a significant association between thyroid cancer and reproductive variables namely parity and age at first birth.⁹ The meta-analysis of 17 epidemiological studies showed a weak and equivocal association between some hormonal and menstrual cycle factors and thyroid cancer risk.¹⁰

MATERIALS AND METHODS

The case control study was conducted in King Khalid University Hospital (KKUH) in Riyadh. The target population of the present study was women with an established diagnosis of thyroid cancer based on histopathological confirmation. The sample size was 90 cases and 178 controls.

Eligible participants were Saudi women treated in KKUH with an established diagnosis of thyroid cancer. Cases diagnosed within the last 5 years starting from January 2010 were enrolled in the study. The cases were recruited from those who are attending the clinic with new diagnosis till the number is completed. For each case enrolled, two controls were selected from attendant to outpatient clinics of the same hospital for the treatment of minor diseases such as skin and eye infection matched by age within 5-year interval. Non Saudi women and those with history of thyroid enlargement or nodules were excluded as the evaluation of the

nature of these nodules was not feasible. Data was collected from cases and controls using questionnaire interview and review of medical records. Questionnaire interview consists of (General

personal information, Personal medical history, Family history of thyroid diseases, Reproductive history, Hormonal replacement therapy, Smoking history, Dietary history).

Table 1: Types of thyroid cancer among Saudi women in KKHU from 2010-2016.

Type	Frequency	Percent
Papillary	85	94.4
Follicular	3	3.3
Medullary	2	2.2
Total	90	100.0

Table 2: Association between dietary history of Saudi women and their thyroid cancer

Variables	Thyroid Cancer (n=90)		Controls (n=178)		Odds ratio(OR)	95% CI for OR	
	No.	%	No.	%			
Fish	- Never& Occasional few times/year	47	52.2	84	47.2	1.0(ref.)	--
	- 1 to 3 times/month & once weekly	41	45.6	86	48.3	0.85	0.51,1.43
	- 2-4 times/week & 5-7 times/week	2	2.2	8	4.5	0.45	0.09,2.19
Chicken	- Never& Occasional few times/year	2	2.2	6	3.4	1.0(ref.)	--
	- 1 to 3 times/month & once weekly	8	8.9	19	10.7	1.26	0.29,7.95
	- 2-4 times/week & 5-7 times/week	80	88.9	153	86.3	1.57	0.31,7.95
Meat	- Never& Occasional few times/year	8	8.9	27	15.2	1.0(ref.)	--
	- 1 to 3 times/month & once weekly	32	35.6	94	52.8	1.45	0.47,2.78
	- 2-4 times/week & 5-7 times/week	50	55.6	57	32.0	2.96*	1.23,7.11
Cabbage	- Never& Occasional few times/year	38	42.2	81	45.5	0.58	0.30,1.11
	- 1 to 3 times/month & once weekly	27	30.0	66	37.1	0.51	0.25,1.01
	- 2-4 times/week & 5-7 times/week	25	27.8	31	17.4	1.0(ref.)	--
Cauliflower	- Never& Occasional few times/year	46	51.1	99	55.6	0.75	0.37,1.54
	- 1 to 3 times/month & once weekly	28	31.1	53	29.8	0.86	0.40,1.86
	- 2-4 times/week & 5-7 times/week	16	17.8	26	14.6	1.0(ref.)	--
Broccoli	- Never& Occasional few times/year	54	60.0	115	64.6	1.03	0.46,2.33
	- 1 to 3 times/month & once weekly	26	28.9	41	23.0	1.39	0.57,3.41
	- 2-4 times/week & 5-7 times/week	10	11.1	22	12.4	1.0(ref.)	--
Picked vegetables	- Never& Occasional few times/year	57	63.3	117	65.7	0.69	0.33,1.48
	- 1 to 3 times/month & once weekly	19	21.1	41	23.0	0.66	0.28,1.58
	- 2-4 times/week & 5-7 times/week	14	15.6	20	11.2	1.0(ref.)	--
Green vegetables	- Never& Occasional few times/year	3	3.3	7	3.9	0.78	0.19,3.09
	- 1 to 3 times/month & once weekly	12	13.3	35	19.7	0.62	0.30,1.27
	- 2-4 times/week & 5-7 times/week	75	83.3	136	76.4	1.0(ref.)	--
Fruits	- Never& Occasional few times/year	1	1.1	7	3.9	0.26	0.03,2.18
	- 1 to 3 times/month & once weekly	14	15.6	33	18.5	0.78	0.39,1.55
	- 2-4 times/week & 5-7 times/week	75	93.3	138	77.5	1.0(ref.)	--
Cooking with iodized salt	- Yes	71	78.9	98	55.1	3.058*	1.69,5.48
	- No	19	21.1	90	44.9	1.0(ref.)	--

*Statistically significant

Table 3: Independent risk factors of thyroid cancer using multivariate binary logistic regression

Risk factors	Adjusted odds ratio	95% C.I of Adjusted odds ratio	
▪ Place of residence (outside Riyadh)	5.36	2.73,10.49	
▪ Thyroid disease during childhood or adolescence	- Goiter - Hypo & Hypothyroidism	3.51 14.32	0.60,20.39 1.43,143.72
▪ Family had thyroid enlargement/nodules	- Yes	4.33	2.28,8.21
▪ Meat	- 1 to 3 times/month & once weekly - 2-4 times/week & 5-7 times/week	1.60 3.32	0.57,4.43 1.20,9.19
▪ Cooking with iodized salt	- Yes	3.30	1.66,6.57

Model $\chi^2 = 84.05$ ($p < 0.001$)

Nagelkerke Pseudo R2 = 0.373

Goodness of fit

Hosmer&Lemeshow = 1.35($p = 0.987$)

RESULTS

Table 1 shows that the predominant histological type of thyroid cancer was papillary carcinoma (94.4 %). The study included 90 cases and 178 controls in ratio 1:2. Table 2 shows that the mean age of 90 cases of Saudi women who were suffering with thyroid cancer is 41.2 years and 178 controls of Saudi women who were disease free are 42.9 years.

The data provides evidence of statistical association between consumption of meat by cases and their thyroid cancer. The consumption of meat frequency and its distribution is statistically significantly different between cases and controls. That is 55.6% (50 out of 90) of cases were consuming meat 2-4 times/week & 5-7 times/ week when compared with 32% (57 out of 178) of controls. Also 15.2% (27 out of 178) controls were never consuming & consuming occasionally few times/ year, whereas only 8.9% (8 out of 90) cases were never consuming & consuming occasionally few times/year, which is statistically significant. Responses of cases & controls towards the type of cooking salt (iodized salt) are statistically significantly associated with thyroid cancer (Table 2).

The Smoking indicates no statistically significant association with thyroid cancer. The analysis shows no statistically significant association between thyroid cancer and variables of mean age of menarche, current status of menopausal, pattern of menstrual cycle, mean duration of menstrual cycle, mean age at first pregnancy, mean number of pregnancies, mean number of deliveries, mean number of live births, used family planning methods, used intrauterine devices, used injectable and used oral contraceptives. This study shows no statistically significant association between the suffering from medical condition and thyroid cancer and between exposed to radiation and thyroid cancer. Whereas there is highly statistically significant association between 'suffering any thyroid disease during childhood or adolescence and thyroid cancer, in which 6.7% of cases and 1.1% of controls were suffered from Goiter and 5.6% of cases and 0.6% of controls were suffered from hypo & hyperthyroidism during their childhood or adolescence. Family had thyroid enlargement/nodules, family had hyperthyroidism, and family had thyroid cancer are statistically significantly associated with thyroid cancer among Saudi women. The corresponding odds ratio of 3.68 for the variable, family had thyroid enlargement/nodules, the corresponding odds ratio of 2.56 for the variable, family had hyperthyroidism.

In multivariable analysis, bivariate logistic regression was used to identify independent variables related to thyroid cancer. A model with the variables: the place of residence (OR 5.36), suffering from goiter during childhood or adolescence (OR 3.51), suffering from hypo & hyperthyroidism during their childhood or adolescence (OR 14.32), family had thyroid enlargement/nodules (OR 4.33), consumption of meat twice or more/week (OR 3.32), and cooking with iodized salt (OR 3.30) was statistically significant indicating that the above variables as a set distinguishing between the Saudi women who had thyroid cancer and the Saudi women who did not had thyroid cancer ($X^2=84.05$; $p < 0.001$; $df=7$). Hosmer and Lemeshow test which tests for the goodness of fit for logistic regression models (an alternative to model chi-square test) had a value of 1.35 ($p=0.987$; $df=7$). As the p-value is greater than 0.05, it can be inferred that the model's estimates fit the data at an acceptable level. This non-significance indicates that the model prediction does not significantly differ from the observed.

Nagelkerke's R^2 of 0.373 indicates a moderate relationship between prediction and grouping. The Wald criterion demonstrated that the variables in the model (as given in the table 3) made a significant contribution to the prediction of Thyroid cancer. The final model validation was carried out using classification table which summarizes the observed group and predicted group classification. The overall prediction success was 77.6% (56.7% for case and 88.2% for control) (Table 3).

DISCUSSION AND CONCLUSIONS

This case-control study shows no statistically significant association between the reproductive history of Saudi women and thyroid cancer. This finding is consistent with the report from a case-control study where they observe no association between thyroid cancer and reproductive factors.¹¹ Another meta-analysis of 17 epidemiological studies showed a weak and equivocal association between some hormonal and menstrual cycle factors and thyroid cancer risk.¹⁰ There is highly statistically significant association between 'suffering any thyroid disease during childhood or adolescence and thyroid cancer, the odds ratios of 6.46 and 11.07 for (i) Goiter and (ii) hypo & hyperthyroidism. This result is consistent with the results of previous studies. A case-control study conducted in Switzerland that reported a significant association between thyroid cancer and previous thyroid disease, the odds ratio was 25.2 if the patient had history of benign thyroid nodules and the odds ratio was 5.3 if the patient had history of goiter.¹² Another case-control study was conducted showed a significant association between thyroid cancer and benign thyroid disease, they found that the thyroid cancer is increased if the patients had history of thyroid disease with (RR=14.5).¹³ Our finding shows no statistically significant association between the suffering from medical condition and thyroid cancer. Inconsistent results exist between diabetes mellitus and the risk of thyroid cancer. A recent study by Paulus et al (2014) reported an association between diabetes mellitus and papillary carcinoma.¹⁴ This is in line with an earlier study conducted by Zivaljevic et al (2004) who reported a 4-fold increase in anaplastic thyroid cancer in relation to diabetes mellitus.¹⁵ This study shows an increased risk for thyroid cancer among Saudi women who had family history of thyroid enlargement/nodules (odds ratio of 3.68), family history of hyperthyroidism odds ratio of 2.56, family history of thyroid cancer the odds ratio of 3.71. This is in line with many epidemiologic studies, a case-control study showed increased risk of thyroid cancer associated with a family history of thyroid cancer OR, 4.1; 95% CI, (1.7-9.9) in first-degree relatives, the association of family history of papillary thyroid cancer in siblings was (OR, 7.4; 95% CI, 1.8-30.4).¹⁴ This study report shows no association between dietary factors (fish, chicken, Cabbage, Cauliflower, Broccoli, Picked vegetables, green vegetables, and fruits) and the thyroid cancer. Several studies showed no significant association between fish consumption and thyroid cancer.^{5,16,17} A study from the United States found an association between the consumption of poultry and thyroid cancer.¹⁸ Whereas the meta-analysis reported that the consumption of fish reduces the risk of thyroid cancer (OR 0.74, 95%CI: 0.59, 0.92) and the consumption of shellfish reduces the risk of thyroid cancer (OR 0.46, 95%CI: 0.27, 0.75).¹⁹ The limitation of this study is small sample size due to limitation of time. The result is exposed to recall bias, information

bias. The strength of this study is using histopathological record. In conclusion, many of the significant risk factors associated with thyroid cancer shown in the present study are preventable. This calls for planning the appropriate interventions to prevent the rising trend in cancer thyroid among Saudi women.

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