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ORIGINAL RESEARCH

Prevalence and Associated Factors of Thyroid Nodules Among 52,003 Chinese 'Healthy' Individuals in Beijing: A Retrospective Cross-Sectional Study

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Introduction: The prevalence of thyroid nodules has been increasing, and there are few research data on the risk factors of thyroid nodules in the Chinese population. In this study, we aimed to determine the prevalence and risk factors of thyroid nodules by retrospectively investigating the physical examination records of a cohort of "healthy" individuals in Beijing, China.

Methods: This was a retrospective cross-sectional study. The database of a Medical Examination Centre (MEC) was searched. Physical examination data, blood test data, and ultrasound examination data, etc., from 2015 to 2017 were accessed. Only those that recorded a thyroid ultrasound were included. Chi-square test and *t*-test were used to compare clinical features of individuals' age, gender, body mass index, blood pressure, blood glucose, blood lipids, uric acid, and presence of fatty liver. Risk factors for thyroid nodules were determined using multivariate logistic regression.

Results: A total of 52,003 records, which included 19,901 cases with thyroid nodules, were examined. The overall prevalence rate was 38.3% (19,901/52,003): 30.2% (6,726/22,305) and 44.4% (13,175/29,698) in men and women, respectively. Of 52,003 cases, only 35,420 cases had records of all nodule-related metabolic abnormalities and were selected for cross-sectional determination of related risk factors of thyroid nodules. In male, relationships were found between thyroid nodules and increased age ($p < 0.001$), impaired fasting glucose ($p = 0.044$), diabetes ($p = 0.047$), decreased HDL-C ($p = 0.018$) and prostatic hyperplasia ($p < 0.001$). And in female, relationships were found between thyroid nodules and increased age ($p < 0.001$) and decreased HDL-C ($p < 0.001$).

Conclusion: Thyroid nodules are common in China. This study found that thyroid nodules are associated with several metabolic indicators or metabolic diseases, although the mechanism is unclear. Further research is needed.

Keywords: thyroid nodule, prevalence, risk factor, logistic regression analysis

Introduction

Thyroid nodules are discrete lesions formed by local thyroid cells that grow abnormally.[1] Thyroid nodules are common, and the detection rate by palpation in the general population is 3% to 7%, while the detection rate by high-definition ultrasound is 20% to 76%.[2]

Studies have shown that the prevalence rate of thyroid nodules in 10 cities in China had increased from 10.2% in 2006 to 18.6% in 2010.[3] Between 5% and 15% of the nodules were malignant, ie, thyroid cancer,[4] which required attention. Recent literature suggests that nodule screening in healthy individuals should be avoided because of the potential risks associated with fine-needle aspirations.[5–7] It is nonetheless common in China to routinely screen healthy individuals because of the high prevalence. Cervical thyroid ultrasonography is used to confirm the existence of thyroid nodules, their location, number, size, shape, capsule, boundary, calcification, blood supply, texture (solid or cystic) and their relationship with surrounding tissues as well to assess the size, shape and structural characteristics of surrounding

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lymph nodes in the neck. Clinical treatment for benign and malignant thyroid nodules are very different and have a direct impact on the quality of life of these patients and the medical expenses involved.

Besides, iodine intake may affect the prevalence of thyroid disease. Since 1996, salt has been iodized throughout China so that iodine intake has increased countrywide. However, residents from different regions could still have different access and iodine intake. Teng et al had reported that the prevalence of single nodule or multiple nodules between people who had excessive iodine intake, people who had adequate iodine intake and people who had mildly deficient iodine intake differed significantly.[8] These findings concurred with other international research such as the study by Reiners et al in Germany that found iodine deficiencies impacted on the prevalence of diffuse and/or nodular thyroid disorders,[9] and a systematic review and meta-analyses conducted in 2017 confirmed the association between chronic exposure to excess iodine with thyroid diseases in different populations from around the world including USA, Japan, Korea and China.[10]

Therefore, it is of great clinical significance to determine the risk factors of thyroid nodules to aid in future health policy and planning about screening in China. In this paper, we report the retrospective analysis of the physical examination records of individuals who had thyroid ultrasound between 2015 and 2017 at a Medical Examination Centre (MEC) in Beijing to determine the prevalence of thyroid nodules and their related risk factors in the cohort.

Methods

This study has ethical approval from PUMCH Institutional Review Board (approval ID S-K569). All procedures in this study were performed in accordance with the ethical standards of PUMCH and ethics committee as well as with the 1964 Helsinki declaration and its later amendments.

Study Design and Study Population

This was a retrospective cross-sectional study. The database of a Medical Examination Centre (MEC) in Beijing was searched, and deidentified physical examination records from 2015 to 2017 were accessed.

MECs are either commercially operated or run by public hospitals in China to conduct annual health checks for people. The purpose of annual physical examination is to detect diseases early in healthy people, which is also one of the benefits provided by government agencies or companies to their employees. Therefore, lots of the customers of the MEC are employees from government and companies, but also can be any social individual. This study population was from the MEC, based on the privacy protection of customers, we could not get the details of their social background, such as occupation, income, education level, etc. However, according to the opinion from the administrator of the MEC, most of the customers were employees from various government agencies and companies.

Although thyroid ultrasound was routinely offered to all individuals who participated in the medical examinations, not all agreed to have one. Since this was a retrospective analysis, our approach was pragmatic, and we chose to extract data from all records that had recorded a thyroid ultrasound. Only those records that recorded a thyroid ultrasound were included in this study. The STROBE checklist[11] was used to guide this cross-sectional study report.

Data Extraction

Due to limitations and complications of data management, in our study, data extracted just included gender, age, body-mass index (BMI), blood pressure, blood glucose, blood lipids, uric acid and other blood test results as well as results of thyroid ultrasound, liver ultrasound and prostate ultrasound. Of these, we could find the parameters of metabolic abnormalities as one of our study points.

Diagnostic Criteria and Laboratory Test (Please See Supplementary Material 1)

Statistical Analysis

Excel software was used for data compilation and graphic production; SPSS software was used for statistical analysis.

In this study, age, BMI, BP, GLU, UA, TC, TG, LDL-C and HDL-C were calculated as continuous variables; and, gender, incidence rate of thyroid nodules, incidence rate of impaired fasting glucose and diabetes mellitus, incidence rate of fatty liver, incidence rate of low HDL-C, and incidence rate of prostatic hyperplasia were categorical variables.

For continuous variables, "mean ± standard deviation" was used to describe data in normal distribution. Statistical description of measurement data which did not satisfy normal distribution was expressed as "median (inter-quartile range)". Statistical description of categorical data and ranked data was expressed by percentage. The categorical data were compared using chi-square test. *t*-test was used to compare measurement data between two groups. F-test was used for comparison among multiple groups and to determine the model that best fitted the study population. Differences were considered statistically significant if $p<0.05$.

In the multifactorial analysis, we first conducted univariate testing using the presence of thyroid nodules as the dependent variable and the screened variables from single-factor analysis as the independent variables. Following consultation with our statistician, we then set the statistical significance at $p < 0.10$, to bring in more comprehensive variables to adjust key variables. In other words, any variable having a significant univariate test at $p < 0.10$ is selected as a candidate for the multivariate analysis. We base this decision on the Wald test from logistic regression which has a much higher p-value cut-off point. More traditional p levels such as 0.05 can fail in identifying variables known to be important.[12]

Binary logistic regression (LR) analysis was carried out. Backward LR method was used to screen independent variables. Odds ratio (OR) and confidence interval of each variable were calculated.

Results

A total of 90,000 records from 2015 to 2017 were searched; 52,172 cases had a thyroid ultrasound. Of these, the cases of 169 individuals who had thyroid surgery previously were excluded, leaving a study population of 52,003 cases.

Prevalence, age distribution, sex distribution, calcification ratio, site distribution and proportion of thyroid nodules were calculated based on the analysis of the study population of 52,003 cases. Of these, only 35,420 cases had records of all nodule-related metabolic abnormalities[13] (except prostate hyperplasia) and were selected for cross-sectional determination of related risk factors of thyroid nodule disease.

Study Population General Characteristics

In the study population of 52,003 cases, the average age was 41.68 ± 13.41 years, range 15–95 years; 22,305 (42.9%) were male, average age 41.58 ± 12.81 years; 29,698 (57.1%) were female, average age 41.76 ± 13.85 years.

Prevalence of Thyroid Nodules

In the study population of 52,003 cases, thyroid nodules were diagnosed by ultrasonography in 19,901 cases; the overall prevalence was 38.3%. Table 1 shows the prevalence in the study population stratified by age and gender.

Prevalence in different age groups was significantly different ($p < 0.001$). It was lowest in individuals younger than 30 years old (22.8%) and highest in individuals older than 80 years old (79.8%). (Figure 1)

In terms of gender distribution, prevalence was 30.2% in males and 44.4% in females, and significantly higher in the latter ($p < 0.001$).

Distribution of Thyroid Nodules

Of the 19,901 cases (6,726 males and 13,175 females) diagnosed with thyroid nodules, 202 (57 males and 145 females) were excluded because their ultrasound reports did not describe the location of the thyroid nodules. The remaining 19,699 (6,669 males and 13,030 females) cases had clear information about the site of the thyroid nodules. The incidence of nodules in both left and right sides of the thyroid was 44.6% and the incidence of nodules in the isthmus was only 0.4% (Table 2).

Representativeness of the Cross-Sectional Population

The population (35,420) was pragmatically selected for cross-sectional analysis, because its records had details of all nodule-related metabolic abnormalities (except prostate hyperplasia), was compared with the study population (52,003) to determine representativeness (Table 3).

Table 1 Prevalence of Thyroid Nodules in Study Population Stratified by Age and Gender (Visualized in Figure 1)

Age (Years)	Male Gender Individuals			Female Gender Individuals			Total (Male and Female Individuals)		
	No. with Nodules	**Total No.**	**Prevalence Rate (%)**	**No. with Nodules**	**Total No.**	**Prevalence Rate (%)**	**No. with Nodules**	**Total No.**	**Prevalence Rate (%)**
<30	640	3686	17.4	1569	5983	26.2	2209	9669	22.8
30–40	1704	8470	20.1	3369	10,309	32.7	5073	18,779	27.0
40–50	1356	4325	31.4	2583	5341	48.4	3939	9666	40.8
50–60	1444	3208	45.0	2401	3838	62.6	3845	7046	54.6
60–70	1206	2035	59.3	2181	2921	74.7	3387	4956	68.3
70–80	285	454	62.8	903	1107	81.6	1188	1561	76.1
>80	91	127	71.7	169	199	84.9	260	326	79.8
Total (all ages)	6726	22,305	30.2	13,175	29,698	44.4	19,901	52,003	38.3

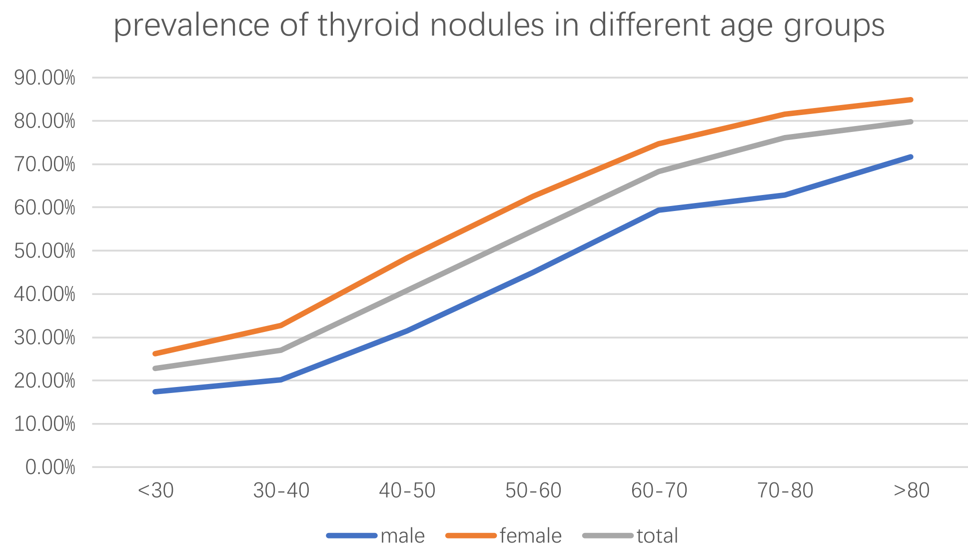

Figure 1 Prevalence of thyroid nodules increases with age.

Although there were statistically significant differences in age, BMI, systolic pressure, blood glucose, total cholesterol, triglyceride and no. of participants with fatty liver between the two groups, the large sample size of the populations meant that the actual numerical differences were very small. After comprehensive deliberation by the research team with our statistician, we considered the cross-sectional population to be adequately representative of the study population.

Table 2 Distribution of Thyroid Nodules

Location of Nodules	Male Gender Individuals (n=6,669)		Female Gender Individuals (n=13,030)		Total (Male and Female Gender Individuals) (n=19,699)	
	No.	%	No.	%	No.	%
Left thyroid	1944	29.25	3210	24.64	5154	26.16
Right thyroid	2151	32.25	3510	26.94	5661	28.74
Both sides	2541	38.10	6238	47.87	8779	44.57
Isthmus	23	0.35	53	0.41	76	0.38
Left and isthmus	2	0.03	11	0.08	13	0.07
Right and Isthmus	3	0.04	4	0.03	7	0.04
Both sides and isthmus	5	0.08	4	0.03	9	0.05

Table 3 Comparison of the Characteristics Between the Cross-Sectional Population and the Study Population

Variable	Study Population (52,003)		Cross-Sectional Population (35,420)	p-value
	No. of Cases with Records	Variable Value	Variable Value	
Age (years)	52,003	41.68±13.41	42.06±13.43	<0.001
Number of males	52,003	22,305(42.9%)	15,262(43.1%)	0.564
No. of participants with thyroid nodules	52,003	19,901(38.3%)	13,575(38.3%)	0.865
BMI (kg/m^2)	48,438	24.05±3.81	24.22±3.88	<0.001
Systolic BP (mmHg)	49,546	117.83±17.07	118.13±17.23	0.011

(*Continued*)

Table 3 (Continued).

Variable	Study Population (52,003)		Cross-Sectional Population (35,420)	p-value
	No. of Cases with Records	Variable Value	Variable Value	
Diastolic BP (mmHg)	40,545	69.01±11.06	69.15±11.17	0.066
GLU (mmol/L)	51,050	5.18±1.13	5.20±1.14	0.009
UA (mmol/L)	49,647	273.79±81.22	274.65±81.68	0.128
TC (mmol/L)	51,050	4.46±0.92	4.49±0.92	<0.001
TG (mmol/L)	51,050	1.25±1.06	1.28±1.08	<0.001
LDL-C (mmol/L)	43,483	3.42±0.86	3.42±0.85	0,823
HDL-C (mmol/L)	53,525	1.86±0.51	1.86±0.51	0.20
No. of participants with fatty liver	46,607	15,358 (33.0%)	11,938 (33.7%)	0.024
No. of participants with prostatic hyperplasia	21,645	3480 (16.1%)	*2445 (16.2%)	0.677

Notes: *Only 15,055 records in the cross-sectional population had information on prostatic hyperplasia.

1. Analysis of the Cross-Sectional Population (n = 35,420)

Multiple binary logistic regression was used to determine the relationship between the presence of thyroid nodules (dependent variable) and its potential risk factors (independent variables): age, gender, BMI, fasting glucose, blood pressure, blood lipids, uric acid, fatty liver and prostatic hyperplasia. In men, increased age, impaired fasting glucose, diabetes mellitus, reduced heavy-density lipoprotein and benign prostatic hyperplasia were determined to be independent risk factors for thyroid nodules ($p < 0.05$), while in women, relationships were found between thyroid nodules and increased age ($p < 0.001$) and decreased HDL-C ($p < 0.001$) (Table 4).

Discussion

Epidemiological studies have shown that the prevalence of thyroid nodules in some provinces in China was between 15.69% and 46.6%, but most of the study populations were small.[14–16] Our retrospective analysis of the physical examination records of 52,003 individuals who had thyroid ultrasound at a MEC in Beijing between 2015 and 2017

Table 4 Logistic Regression of Potential Risk Factors for Thyroid Nodules

Independent Variables	Male Gender Individuals			Female Gender Individuals		
	p-Value	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value	Odds Ratio (OR)	95% Confidence Interval (CI)
Increased age*	0.000	1.050	1.046–1.053	0.000	1.058	1.055–1.060
Fasting glucose**						
Normal (ref.)	-	1.0	-	-	1.0	-
Impaired fasting glucose	0.044	1.161	1.004–1.342	0.543	0.947	0.756–1.188
Diabetes mellitus	0.047	1.163	1.002–1.350	0.668	0.999	0.841–1.190
Low HDL-C***						
No (ref.)	-	1.0	-	-	1.0	-
Yes	0.018	1.288	1.044–1.590	0.000	2.206	1.512–3.263
Benign prostatic hyperplasia***						
No (ref.)	-	1.0	-	-	-	-
Yes	0.000	1.261	1.134–1.403	-	-	-

Notes: *Continuous variable. **Categorical variable. ***Binary variable.

reveals that the prevalence rate of thyroid nodules in this population was 38.3%, which was congruent with previous research findings.

Foreign studies have shown that the incidence of thyroid nodules increases with age.[17] In our study population, there were statistically significant differences in the prevalence of thyroid nodules in different age groups ($p < 0.001$). The incidence of thyroid nodules in people over 80 years was as high as 79.8%, and the trend remains even after stratification of males and females. This suggests that thyroid nodules have a definite correlation with age and may be related to degenerative changes of the thyroid gland.

There have been reports that thyroid nodules were significantly more prominent in females than in males.[18,19] Estrogen receptor expression in thyroid cells is presumed to play a role in the cell growth and nodule formation in thyroid glands since estrogen regulates the generation of thyroid-stimulating hormone,[20,21] this happens in both normal and neoplastic thyroid tissues.[22] Some in vitro studies have confirmed that 17β estradiol can stimulate normal thyroid cells[23] and the growth of thyroid follicular cells with estrogen receptors.[24] Findings from our study population similarly confirm the higher prevalence of thyroid nodules in females with overall prevalence rates of 44.4% and 30.2% in females and males, respectively, although the intrinsic mechanism of gender differences in thyroid nodules still requires further clarification.

Thyroid nodules are asymptomatic most of the times like hyperlipidemia and lung nodules, and it seems to be related to some metabolic diseases. In recent years, we could see more similar study published to make people notice this common problem. In China, Xinyu Chang et al had found that the detection rate of thyroid nodules was higher in prediabetes population. Hypertension, abnormal glucose and lipid metabolism, high TSH were risk factors, and the sample size was 2659 in this study.[25] In abroad, Vietnam carried out research this year with much bigger sample size (16784 cases) to explore the associated clinical characteristics of thyroid nodules. They found that advanced age, hypertension, and hyperglycemia were significantly associated with thyroid nodules in both genders. In men, significant risk also included increased body mass index, while increased total cholesterol and LDLc, hypertriglyceridemia and hyperuricemia were the significant risk in women. The data source was also come from Health Checkup Department like our study.[26]

In our cross-sectional population, we found that age and high-density lipoprotein reduction were independent risk factors for thyroid nodules in both genders through multivariate logistic regression analysis. In men, risk factor also included abnormal glucose and benign prostatic hyperplasia. While in women, we did not find the significant result for abnormal glucose. We thought abnormal glucose for just one time at health check-up could not reflex the long-term blood glucose status of those individuals. On the other hand, the presence of abnormal blood glucose and thyroid nodules detected at the same time point does not reflect the causal relationship between them. Some previous studies did not find the significant result for abnormal glucose either.[27,28] Again, the specific mechanisms of these metabolic factors are not clear and require further investigations.

In 2015 American Thyroid Association Management Guidelines and 2023 European Thyroid Association Clinical Practice Guidelines for Thyroid Nodules Management, they mentioned that thyroid sonography with a survey of the cervical lymph nodes should be performed in all patients with known or suspected nodules.[29,30] Although there is increasing recognition of the risks of screening for nodules in healthy individuals, as the prevalence of thyroid nodules is high even in a healthy Chinese population and the risk factors are complex, we suggest that routine physical examination and image examination of healthy individuals may still be necessary in China to achieve early detection and timely intervention for a condition that is typically without obvious symptoms. Both domestic and foreign research data indicate that the best detection method for thyroid nodules is high-resolution ultrasonography.

The strength of this study is that it examined reliable data of a "healthy" population and the sample size of the population was large. Nonetheless, there were challenges in scrutinizing the MEC database in the absence of comprehensive past medical and family histories.

Limitation

This article had some limitations. First, there may be a potential bias in this study population because most of the customers were employees from government agencies and companies (including the retired) according to the opinion of the administrator of the MEC. Second, this database included 6 teenagers aged 15–17, this may lead to the statistical result not so perfect, however, after consulted with statistician, considering that the sample size of these 6 cases is too small to analysis separately, whether they exist or not will not affect the results of the whole study. Furthermore, all 6 cases are teenagers, with a BMI between 19.8 and 31.3, who are basically treated as adults in clinical diagnosis and treatment. Third, as the diagnosis of diabetes and hypertension are made by examinations for two or more times, so abnormality of blood glucose and blood pressure for just one time in medical check-up center could not reflex the long-term status of the individuals, so it needs further study to verified.

Conclusion

The prevalence of thyroid nodules in 52,003 healthy individuals who had a physical examination and a thyroid ultrasound between 2015 and 2017 at a Medical Examination Center in Beijing, China, was high at 38.3%. Increased age, being female, impaired fasting glucose, diabetes mellitus, low HDL-C, prostatic hyperplasia were independent associated factors of thyroid nodules in this cohort. These findings support regular thyroid examination using high-resolution ultrasonography in at-risk Chinese population. Further research is needed to determine the specific mechanisms of each of these thyroid nodules related metabolic factors and the linear relationship between them and thyroid nodules after controlling for relevant biases.

Abbreviations

BMI, Body Mass Index; GLU, Glucose; BP, Blood Pressure; TC, Total Cholesterol; LDL-C, Low-Density Lipoprotein-Cholesterol; HDL-C, High-Density Lipoprotein-Cholesterol; TC, Total Cholesterol; TG, Triglyceride; UA, Uric acid.

Ethics Approval

Ethical clearance was obtained from the Peking Union Medical College Hospital Institutional Review Board (approval ID S-K569). Data collection consent was obtained from the Rich Healthcare Check-up Agency in Beijing, and all data were de-identified in accordance with ethics requirements to maintain confidentiality.

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Disclosure

The authors report no conflicts of interest in this work.

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