



Epidemiology of Thyroid Cancer: Incidence and Mortality in China, 2015

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Objective: Using data from cancer registries to estimate thyroid cancer incidence and mortality in China, 2015.

Methods: Data submitted from local cancer registries were checked and evaluated according to the criteria of data quality control, a total of 368 cancer registries' data were qualified for the final analysis. Data were stratified by area (urban/rural, eastern/central/western), sex and age, combined with national population data to estimate thyroid cancer incidence and mortality in China, 2015.

Results: Approximately 200,700 new cases were diagnosed in 2015, accounting for 5.11% of all cancer cases. The crude incidence rate was 14.60/100,000. Age-standardized incidence rates by Chinese standard population (ASIRC) and world standard population (ASIRW) were 12.05/100,000 and 10.44/100,000, with the cumulative incidence rate (0–74 years old) of 1.00%. About 7,900 deaths of thyroid cancer were reported in 2015, accounting for 0.34% of all cancer deaths. The crude mortality rate was 0.58/100,000, age-standardized mortality rates by Chinese standard population (ASMRC) and world standard population (ASMRW) were 0.37/100,000 and 0.36/100,000. The age-standardized incidence and mortality in females were significantly higher than those in males ($P < 0.001$). The rates in urban areas were higher than those in rural areas ($P < 0.001$). The ASIRC in eastern areas was higher than that in central and western areas ($P < 0.001$), while the ASMRC in central areas was higher than that in eastern and western areas ($P < 0.001$).

Conclusions: The burden of thyroid cancer was heavy in China, cancer control faces the problem of the disparity between geographic areas, and the incidence and mortality rates were varied by sex and age. Targeted cancer preventive measures should be put into practice.

Keywords: cancer registry, thyroid cancer, incidence, mortality, China

INTRODUCTION

Thyroid cancer is the most common endocrine and head-and-neck malignancy globally. Since 1990s, the incidence rate of the disease has been increasing rapidly around the world excluding Africa for their limited diagnostic technology. Paes et al. reported in a research in 2010 that thyroid cancer incidence is rising at a rate that is the fastest of all malignancies (1). According to the Global Cancer Observatory (GLOBOCAN) 2018 from International Agency for Research on Cancer (IARC), about 567,200 new cases were diagnosed, and 41,100 deaths were caused by thyroid cancer in 2018 (2). The incidence rate of thyroid cancer is also increasing in China. According to the annual report of China Cancer Registry 2018, thyroid cancer has become one of the 10 major cancers threatening the health of Chinese residents (3). In some provinces (e.g., Zhejiang province), the incidence rate of thyroid cancer has dramatically risen to the top of all cancers in females (4). Some researchers have reported the incidence and mortality rates of thyroid cancer in the regional level (5–7), while the nationwide data is still lacked. As national cancer registration data were not publicly available in the same fashion as the Surveillance, Epidemiology, and End Results

Program in the USA, the National Central Cancer Registry of China (NCCRC) provides a status report on the cancer incidence and mortality regularly, with the focus on geographic, sex, and age variability throughout the country (8). In this study, we extracted the latest data of thyroid cancer from the database of the NCCRC and provide a nationwide epidemiology report of thyroid cancer in 2015.

MATERIALS AND METHODS

Data Source

NCCRC extracted cancer data through 501 cancer registries from 31 provinces in China, including 173 cancer registries in cities above the county level and 328 cancer registries in cities of the county level. A total of 368 cancer registries' data met the criteria of quality control and they were included in pooled data, of which 134 were located in urban areas and 234 were located in rural areas. A number of 309,553,499 populations (156,934,140 males and 152,619,359 females) were covered, accounting for 22.52% of the national population at the end of year 2015 (**Figure 1**). Among them, 148,804,626 (48.07%) were located in the urban areas, 160,748,873 (51.93%) located in the

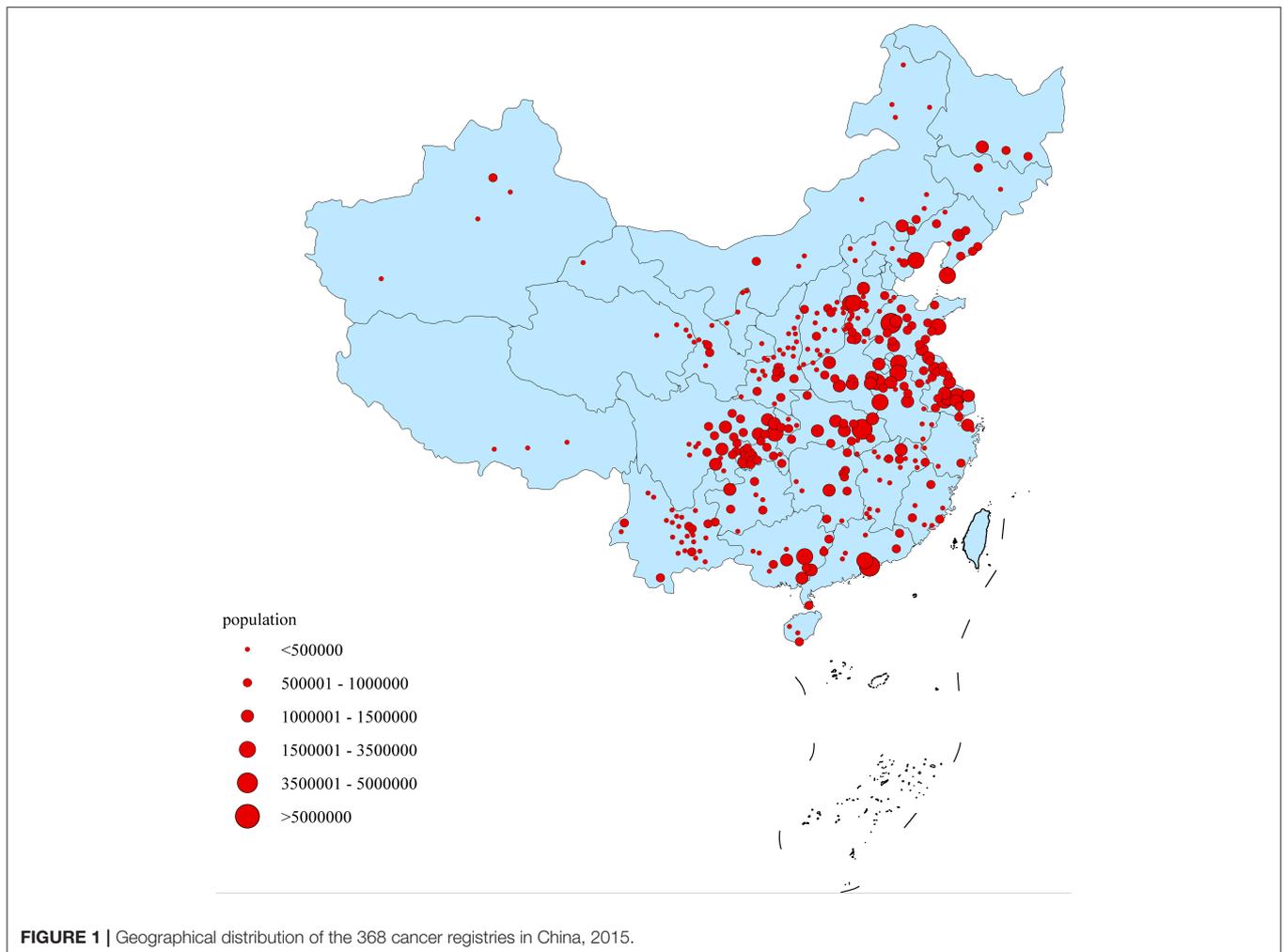


TABLE 1 | Quality evaluation of thyroid cancer in China, 2015.

Areas	Sex	M/I	%		
			MV	DCO	UB
Both	Both	0.04	93.18	0.10	0.09
	Male	0.07	92.71	0.17	0.12
	Female	0.04	93.33	0.08	0.08
Urban areas	Both	0.04	94.70	0.08	0.05
	Male	0.05	94.51	0.11	0.06
	Female	0.03	94.76	0.07	0.05
Rural areas	Both	0.06	89.99	0.16	0.18
	Male	0.11	88.40	0.30	0.27
	Female	0.05	90.44	0.11	0.15
Eastern areas	Both	0.03	94.82	0.09	0.09
	Male	0.05	94.49	0.18	0.11
	Female	0.03	94.92	0.06	0.09
Middle areas	Both	0.07	89.97	0.09	0.00
	Male	0.10	89.84	0.11	0.00
	Female	0.06	90.01	0.08	0.00
Western areas	Both	0.08	85.22	0.29	0.32
	Male	0.12	82.94	0.25	0.49
	Female	0.07	86.01	0.30	0.26

rural areas (9). According to International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), thyroid cancer cases, which are coded as C73, were extracted for analysis. The data inclusion criteria were focused on the authenticity, stability, and comparability of data quality. The quality of data was evaluated based on the characteristics of the corresponding regions. Aside from several important indexes such as MV%, DCO%, M/I, incidence and mortality, registries with proper range of each index were taken into consideration. Specifically, MV% ranged from 66 to 85%, DCO% < 15%, M/I ranged from 0.6 to 0.8 were included. Registries with poor data stability, fluctuation of incidence and mortality larger than 10% were defined as low quality and those data were excluded. To obtain the completeness of regional

coverage of the country, the standard of data inclusion was not such strict to western provinces, low socio-economic areas and the minority nationality regions, allowing a 10% fluctuation on the data inclusion criteria.

Quality Control

The “Guideline for Chinese Cancer Registration (2016)” (10) and requirement from IARC (11, 12) were used to build data inclusion criteria. Excel 2007 was used for data management, and IARCcrg Tools (Version 2.05) (13) issued by IARC/International Association of Cancer Registries’ (IACR) was used for data review and evaluation. The validity, reliability, completeness, and comparability of data were evaluated based on the percentage of morphologically verified cases (MV%), the percentage of death certificate-only cases (DCO%), the mortality to incidence (M/I) ratio and the percentage of the diagnosis of unknown basis (UB%). For all kinds of cancer reported by Zheng’s study, the total MV% was 69.34%, the DCO% was 2.09%, and the M/I was 0.61 (9), among which the MV%, DCO% and M/I for thyroid cancer was 93.18, 0.10, and 0.04, respectively (Table 1).

Statistical Analysis

The population by age, sex and area (urban/rural) in 2015 was calculated according to the 5th and 6th census data released by the National Bureau of statistics, combined with the population of China from 2000 to 2015, the change of urban-rural ratio, and the age composition of the Chinese population.

Crude incidence and mortality rates of thyroid cancer were calculated in each stratum by age group (0-, 1-4, 5-84 by 5 years and 85+ years old), sex and area (urban/rural). The number of new cases and deaths of thyroid cancer were estimated in China, 2015. Age-standardized rates by Chinese and world standard population were calculated using the population of China in 2000 and Segi’s population structure, respectively (14). Urban and rural areas were classified by the regulation of National Bureau of Statistics of the People’s Republic of China, and the incidence (death) rate, standardized incidence (death) rate, composition ratio, cumulative incidence (death) rate (0-74 years old) and truncated rate (35-64 years old) were calculated, respectively. SAS software (Version 9.4; SAS Institute Inc., Cary, USA) was used for statistical analysis. Formulae used are as follows:

$$\text{Incidence (mortality) rate per100,000} = \frac{\text{new cases (new cancer death) occurring during a given period}}{\text{population at risk at the same period} * 100,000} \tag{1}$$

$$\text{Age – specific incidence (mortality) rate per100,000} = \frac{\text{cases in a specific age group}}{\text{population in the age group} * 100,000} \tag{2}$$

$$\text{ASR per 100,000} = \frac{\sum (\text{standard population in corresponding age group} * \text{age – specific rate})}{\sum \text{standard population}} \tag{3}$$

$$\text{Cumulative rate(\%)} = (\sum (\text{age – specific rate} * \text{width of the age group})) * 100 \tag{4}$$

$$\text{Truncated incidence (mortality) rate per100,000} = \frac{\sum \text{truncated rate in a specific age group} * \text{standard proportion of the age group}}{\sum \text{standard population}} \tag{5}$$

RESULTS

Incidence of Thyroid Cancer

In 2015, the estimated new cases diagnosed with thyroid cancer were 200,700 in China, accounting for 5.11% of all new cancer cases, with the incidence rate ranked 7th in all kinds of cancer. The crude incidence rate was 14.60/100,000, the age-standardized incidence rate by Chinese standard population (ASIRC) and world standard population (ASIRW) were 12.05/100,000 and 10.44/100,000, and the cumulative rate (0–74 years old) was 1.00%. The incidence rate of thyroid cancer showed a gender variance in China, the ASIRC in males and females were 6.01 and 18.29/100,000, ranking 11st and 4th separately with the sex ratio of 3.04 (Table 2). In urban and rural areas, the estimated new cases were 151,000 and 49,700 cases, of which incidence rate in urban areas was 19.59/100,000 (9.80/100,000 in males, 29.79/100,000 in females), in rural areas was 8.24/100,000 (3.52/100,000 for males, 13.25/100,000 for females). The ASIRC in urban and rural areas were 15.60 and 7.06/100,000 with the ASIRC ratio of 2.21.

The new cases of thyroid cancer diagnosed were about 119,900, 53,500, and 27,200 cases in the eastern, central, and western areas. The incidence rate in the eastern areas was 23.26/100,000 (11.29/100,000 in males, 35.57/100,000 in females), much higher than 11.60/100,000 in the central areas (5.31/100,000 in males, 18.28/100,000 in females) and 6.85/100,000 in the western areas (3.56/100,000 in males, 10.36/100,000 in females). Eastern areas had the highest ASIRC (19.23/100,000), followed by central areas (9.32/100,000) and western areas (5.72/100,000). After adjusting age composition, the gap of incidence rate in different areas narrowed, but still remained the similar trend. In any areas, incidence in females was higher than that in males ($P < 0.001$) (Table 2).

Age-Specific Incidence Rate of Thyroid Cancer

Age-specific incidence rates increased with the growth of age. It remained relatively low before 15 years old and increased rapidly afterwards, reaching a peak in the age group of 50–54 years old. It began to decline after 55 years old, and dropped to 4.60/100,000 at 85+ years old. In the majority of age groups, incidence rates in females were higher than those in males with the sex ratio of about 3.00 at 15–70 years old. Age-specific incidence rates reached the peaks at the 50–54 years old both in males (12.40/100,000) and females (47.46/100,000). The incidence rates of urban and rural areas both reaching the peaks in the age group of 50–54 years old, while in most of age groups, age-specific incidence rates in urban areas were higher than those in rural areas (Table 3, Figure 2).

Mortality Rate of Thyroid Cancer

In 2015, thyroid cancer was 22nd leading cause of cancer-related deaths in China, ranking 19th in males and 20th in females. It is estimated 7,900 thyroid cancer deaths in 2015, accounting for 0.34% of all cancer deaths. The mortality rate of thyroid cancer was higher in females than that in males, the sex ratio of age-standardized mortality rate by Chinese standard population

(ASMRC) was 1.59 (ASMRC in males was 0.29/100,000 and in females was 0.46/100,000) (Table 4).

In urban and rural areas, the estimated thyroid cancer deaths were 4,900 and 2,900, respectively. The mortality rate of thyroid cancer in urban areas was 0.64/100,000 (0.48/100,000 in males, 0.81/100,000 in females), which was higher than that in rural areas (0.37/100,000 in males, 0.63/100,000 in females). The ASMRC in urban and rural areas were 0.40/100,000 and 0.34/100,000 with the ASMRC ratio of 1.18.

The new deaths of thyroid cancer were about 2,900, 3,100 and 1,700 cases in the eastern, central and western areas. Among them, the mortality rate in the central areas was 0.69/100,000 (0.48/100,000 in males, 0.91/100,000 in females), slightly higher than 0.58/100,000 in the eastern areas (0.44/100,000 in males, 0.71/100,000 in females) and 0.45/100,000 in the western areas (0.35/100,000 in males, 0.55/100,000 in females). Central areas had the highest ASMRC (0.47/100,000), followed by eastern areas (0.34/100,000) and western areas (0.30/100,000). The gap of mortality rates in different areas significantly narrowed after adjusting age composition, but still remained the similar trend. In any areas, the mortality rates of thyroid cancer in females were also higher than that in males as incidence rates showed above (Table 4).

Age-Specific Mortality Rate of Thyroid Cancer

Age-specific mortality rates increased with the growth of age, reaching a peak in the age group of 85+ years old. In different genders, the mortality rate of thyroid cancer also increased with the growth of age. The mortality rates reached their peaks in the age group of 85+ years old in males (4.25/100,000) and 80–84 years old in females (5.40/100,000). In each age group, however, differences in mortality rates in different genders were not statistically significant, so as in different areas. In urban and rural areas, mortality rates reached their peaks in the age group of 85+ years old in urban areas (5.44/100,000) and 80–84 years old in rural areas (4.14/100,000) (Table 5, Figure 3).

Histologic Subtypes Distribution of Thyroid Cancer

Thyroid cancer contains papillary thyroid carcinoma (PTC), medullary thyroid carcinoma (MTC), follicular thyroid carcinoma (FTC), and poorly differentiated thyroid cancer (PDT), etc. In 2015, about 84.25% cases of thyroid cancer had morphological verification. The most common type of thyroid cancer is PTC (92.38%), whereas FTC and MTC comprise only ~1.37 and 0.30% of thyroid cancer, and other less common variants encompass the small subset of remaining cases (Figure 4).

DISCUSSION

According to GLOBOCAN 2018, it was estimated that there were 567,200 new diagnosed cases of thyroid cancer in 2018 around the world. The ASIRW and cumulative rate in 0–74 years old of thyroid cancer were 6.7/100,000 and 0.68%. The number

TABLE 2 | Estimated new cases and incidence rate of thyroid cancer in China, 2015.

Areas	Sex	New cases ($\times 10^4$)	Crude incidence ($1/10^5$)	Ratio (%)	ASIRC ($1/10^5$)	ASIRW ($1/10^5$)	Cumulative rate 0–74 (%)	Truncated rate 35–64 ($1/10^5$)	Rank	P-value
All areas	Both	20.07	14.60	5.11	12.05	10.44	1.00	23.30	7	<0.001
	Male	4.94	7.03	2.30	6.01	5.12	0.49	10.90	11	
	Female	15.12	22.56	8.51	18.29	15.94	1.53	36.05	4	
Urban areas	Both	15.10	19.59	6.42	15.60 ^a	13.47	1.28	29.33	6	<0.001
	Male	3.85	9.80	3.06	8.09	6.85	0.64	14.21	8	
	Female	11.24	29.79	10.29	23.38	20.34	1.94	45.04	3	
Rural areas	Both	4.97	8.24	3.15	7.06 ^a	6.24	0.61	14.07	7	<0.001
	Male	1.09	3.52	1.22	3.11	2.73	0.27	5.78	15	
	Female	3.87	13.25	5.66	11.13	9.85	0.95	22.48	8	
Eastern areas	Both	11.99	23.26	7.36	19.23 ^b	16.45	1.56	36.46	6	<0.001
	Male	2.95	11.29	3.41	9.76	8.18	0.76	17.35	7	
	Female	9.04	35.57	11.83	28.80	24.83	2.36	55.71	3	
Central areas	Both	5.35	11.60	4.09	9.32 ^b	8.21	0.80	18.93	7	<0.001
	Male	1.26	5.31	1.75	4.41	3.84	0.37	8.51	13	
	Female	4.09	18.28	6.99	14.43	12.75	1.24	29.72	6	
Western areas	Both	2.72	6.85	2.75	5.72 ^b	5.03	0.49	10.82	8	<0.001
	Male	0.72	3.56	1.29	3.05	2.64	0.26	5.37	15	
	Female	1.99	10.36	4.66	8.55	7.56	0.73	16.55	7	

ASIRC, age-standardized incidence rate adjusted by Chinese standard population; ASIRW, age-standardized incidence rate adjusted by world population.

^aASIRC between urban and rural areas, $P < 0.001$.

^bASIRC between eastern, central and western areas, $P < 0.001$.

TABLE 3 | Age-specific incidence rate of thyroid cancer in China, 2015 ($1/10^5$).

Age group	All areas			Urban areas			Rural areas			P-value ^a	P-value ^b
	Both	Male ^a	Female ^a	Both ^b	Male	Female	Both ^b	Male	Female		
Total	14.60	7.03	22.56	19.59	9.80	29.79	8.24	3.52	13.25	<0.001	<0.001
0–	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	–	–
1–	0.01	0.00	0.01	0.00	0.00	0.00	0.01	0.00	0.03	0.284	0.376
5–	0.05	0.03	0.07	0.08	0.06	0.10	0.02	0.00	0.05	0.236	0.055
10–	0.35	0.15	0.58	0.37	0.13	0.64	0.33	0.18	0.52	<0.001	0.65
15–	1.44	0.68	2.34	1.78	0.83	2.88	1.09	0.53	1.76	<0.001	<0.001
20–	4.36	2.13	6.91	6.06	2.92	9.61	2.81	1.41	4.42	<0.001	<0.001
25–	10.78	5.84	16.11	16.22	9.35	23.67	6.02	2.75	9.52	<0.001	<0.001
30–	18.03	10.07	26.16	24.27	14.26	34.15	8.50	3.95	13.41	<0.001	<0.001
35–	20.57	11.52	29.70	26.37	15.28	37.49	10.77	5.22	16.43	<0.001	<0.001
40–	22.32	10.83	34.12	28.18	14.19	42.47	13.13	5.58	20.94	<0.001	<0.001
45–	22.12	9.98	34.72	27.79	12.93	43.49	14.07	5.70	22.54	<0.001	<0.001
50–	29.58	12.40	47.46	36.36	15.98	58.15	19.20	6.73	31.64	<0.001	<0.001
55–	25.30	10.88	40.38	31.83	13.67	51.02	15.04	6.42	23.89	<0.001	<0.001
60–	20.75	9.62	31.90	26.51	12.89	40.17	13.08	5.25	20.91	<0.001	<0.001
65–	14.51	7.01	21.98	18.18	8.79	27.46	9.92	4.79	15.06	<0.001	<0.001
70–	10.27	6.23	14.11	12.75	7.45	17.67	7.14	4.75	9.50	<0.001	<0.001
75–	6.74	4.52	8.73	7.99	5.33	10.32	4.98	3.42	6.43	<0.001	<0.001
80–	5.31	4.39	6.05	5.83	4.96	6.56	4.55	3.55	5.33	0.012	0.045
85+	4.60	3.98	5.00	5.66	4.96	6.15	3.04	2.36	3.43	0.166	<0.001

of newly diagnosed cases in China is 194,200, accounting for 34.23% of the overall new cases worldwide. The distribution of thyroid cancer showed geographically variance globally, 59.98% occurred in Asia, 13.82% occurred in Europe, 12.44% occurred in North America, and Africa accounted for only 3.22%. The highest estimated incidence rate was found in Korea, with the incidence rate of 60.7/100,000 (2).

This study estimated thyroid cancer burden in China in 2015 using the data of 368 local cancer registries that met the inclusion criteria, accounting for ~22.52% of the Chinese population. The calculation of incidence and mortality rates were based on the census data released by the National Bureau of Statistics, which was more accurate than the data from GLOBOCAN2018 and could better describe the current status of cancer epidemics in China. The estimated number of thyroid cancer cases newly diagnosed in China in 2015 was about 200,700, ranking 7th among new cases of malignant tumors and had become one of the top 10 cancers threatening health of Chinese residents. This increase is most probably linked to diagnostic progresses and more neck scans in China. Since 2010, some provinces in China start to incorporate the neck routine scan into the regular examination for urban employees, as well as the improvement of public awareness toward cancer prevention have led to the “high incidence” of thyroid cancer in recent years. In 2015, the incidence rates of thyroid cancer in China (ASIRW: 10.44/100,000) were higher than the world average (ASIRW: 6.7/100,000) and ranked 19th worldwide. The ASIRW in 2015 estimated by our team was higher than that estimated by GLOBOCAN2018(ASIRW: 10.1/100,000) (15), which further confirmed the strength of our study, for we have a much larger data source than any other studies also investigating the incidence and mortality of thyroid cancer in China. Thyroid cancer had relatively low mortality rates in

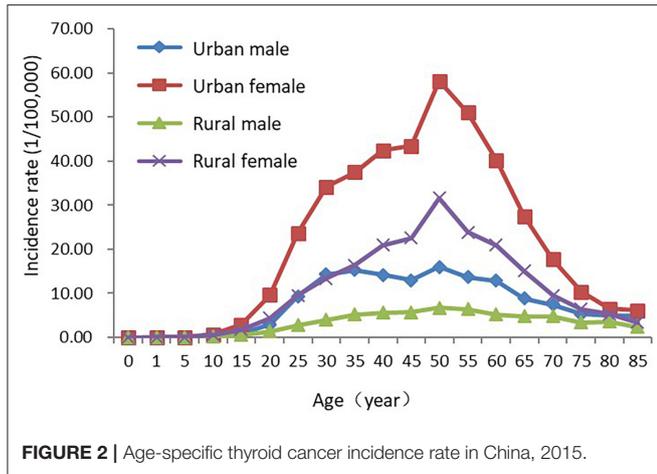


TABLE 4 | Estimated deaths and mortality rate of thyroid cancer in China, 2015.

Areas	Sex	Deaths (x 10 ⁴)	Crude mortality (1/10 ⁵)	Ratio (%)	ASMRC (1/10 ⁵)	ASMRW (1/10 ⁵)	Cumulative rate 0–74 (%)	Truncated rate 35–64 (1/10 ⁵)	Rank	P-value
All areas	Both	0.79	0.58	0.34	0.37	0.36	0.04	0.53	22	
	Male	0.30	0.43	0.20	0.29	0.28	0.03	0.43	19	<0.001
	Female	0.49	0.73	0.57	0.46	0.44	0.05	0.64	20	
Urban areas	Both	0.49	0.64	0.37	0.40 ^a	0.38	0.04	0.56	22	
	Male	0.18	0.48	0.22	0.31	0.30	0.03	0.44	19	<0.001
	Female	0.30	0.81	0.62	0.48	0.46	0.05	0.68	20	
Rural areas	Both	0.29	0.50	0.30	0.34 ^a	0.33	0.04	0.50	22	
	Male	0.11	0.37	0.18	0.26	0.26	0.03	0.41	19	<0.001
	Female	0.18	0.63	0.51	0.41	0.40	0.04	0.59	20	
Eastern areas	Both	0.29	0.58	0.32	0.34 ^b	0.33	0.04	0.45	23	
	Male	0.11	0.44	0.20	0.28	0.27	0.03	0.38	19	<0.001
	Female	0.18	0.71	0.52	0.40	0.39	0.04	0.53	20	
Central areas	Both	0.31	0.69	0.40	0.47 ^b	0.44	0.05	0.71	22	
	Male	0.11	0.48	0.22	0.33	0.32	0.03	0.56	19	<0.001
	Female	0.20	0.91	0.69	0.60	0.56	0.06	0.86	20	
Western areas	Both	0.17	0.45	0.29	0.30 ^b	0.30	0.03	0.43	22	
	Male	0.07	0.35	0.18	0.25	0.25	0.03	0.34	19	<0.001
	Female	0.10	0.55	0.49	0.36	0.36	0.04	0.53	20	

ASMRC, age-standardized mortality rate adjusted by Chinese standard population; ASMRW, age-standardized mortality rate adjusted by world standard population.

^aASMRC between urban and rural areas, P < 0.001.

^bASMRC between eastern, central and western areas, P < 0.001.

TABLE 5 | Age-specific mortality of thyroid cancer in China, 2015 (1/10⁵).

Age group	All areas			Urban areas			Rural areas			P-value ^a	P-value ^b
	Both	Male ^a	Female ^a	Both ^b	Male	Female	Both ^b	Male	Female		
Total	0.58	0.43	0.73	0.64	0.48	0.81	0.50	0.37	0.63	<0.001	<0.001
0–	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	–	–
1–	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	–	–
5–	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	–	–
10–	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	–	–
15–	0.03	0.01	0.05	0.04	0.03	0.06	0.02	0.00	0.05	0.156	0.414
20–	0.03	0.01	0.05	0.01	0.00	0.02	0.05	0.02	0.09	0.053	0.059
25–	0.05	0.04	0.07	0.06	0.08	0.03	0.05	0.00	0.11	0.264	0.796
30–	0.14	0.06	0.22	0.16	0.07	0.26	0.11	0.05	0.16	0.001	0.289
35–	0.21	0.15	0.26	0.24	0.17	0.31	0.15	0.12	0.18	0.052	0.109
40–	0.28	0.20	0.36	0.29	0.21	0.37	0.26	0.19	0.34	0.013	0.651
45–	0.37	0.24	0.52	0.41	0.27	0.55	0.33	0.19	0.46	<0.001	0.253
50–	0.64	0.47	0.81	0.66	0.44	0.90	0.61	0.54	0.69	0.001	0.574
55–	0.75	0.69	0.81	0.75	0.64	0.86	0.76	0.78	0.74	0.311	0.936
60–	1.30	1.12	1.47	1.35	1.24	1.46	1.22	0.97	1.47	0.034	0.402
65–	1.73	1.23	2.24	1.98	1.54	2.41	1.43	0.84	2.02	<0.001	0.017
70–	2.22	1.86	2.57	2.12	1.71	2.50	2.35	2.03	2.67	0.019	0.457
75–	3.24	2.58	3.84	3.56	2.64	4.37	2.80	2.50	3.08	0.002	0.073
80–	4.72	3.87	5.40	5.12	4.43	5.68	4.14	3.03	5.00	0.009	0.129
85+	4.73	4.25	5.04	5.44	4.41	6.15	3.70	3.99	3.54	0.256	0.028

the past few decades, and it was the 22nd leading cause of cancer in China. The age-standardized mortality rate standard population (ASMRW) in China was 0.36/100,000, lower than the world average of 0.42/100,000 in 2015(3). In our study, the incidence and mortality rates of thyroid cancer varied by sex, age groups, and areas. The results were consistent with the findings of incidence rates are usually higher in higher Human Development Index (HDI) vs. lower HDI settings, while mortality rates, in contrast, are rather similar (15). The explanation for the differences in incidence among different sex and areas are controversial, and several causes have been hypothesized; increased diagnostic intensity as well as “over-diagnosis” in females (16), and tumourigenesis in thyroid tissues is influenced by endocrine function and hormones, particularly oestrogen (17). In addition to, the environmental exposures in different HDI settings may be contributing to the observed variance in different areas (18). Priority should be placed on research to identify modifiable risk factors for females and populations in high HDI areas (e.g., urban areas, eastern areas), as well as improvement of public awareness for cancer prevention in males and populations in low HDI areas (e.g., rural areas, western areas). It is of note that the mortality rates in central areas (0.47 per 100,000) were significantly higher than those observed in other areas [e.g., in eastern areas [0.34 per 100,000], despite central areas [9.32 per 100,000] had a substantially lower incidence than eastern areas [19.23 per 100,000]]. As previous studies only focused on the differences between urban and rural areas when measuring regional variations (19, 20), the trend of mortality rates in central areas cannot be obtained. The results

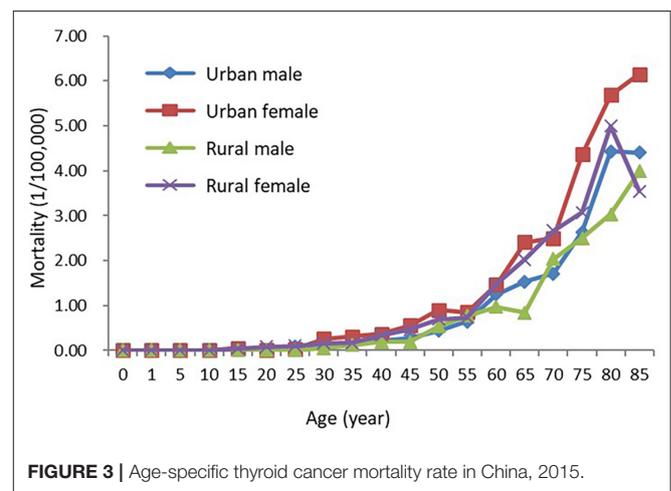
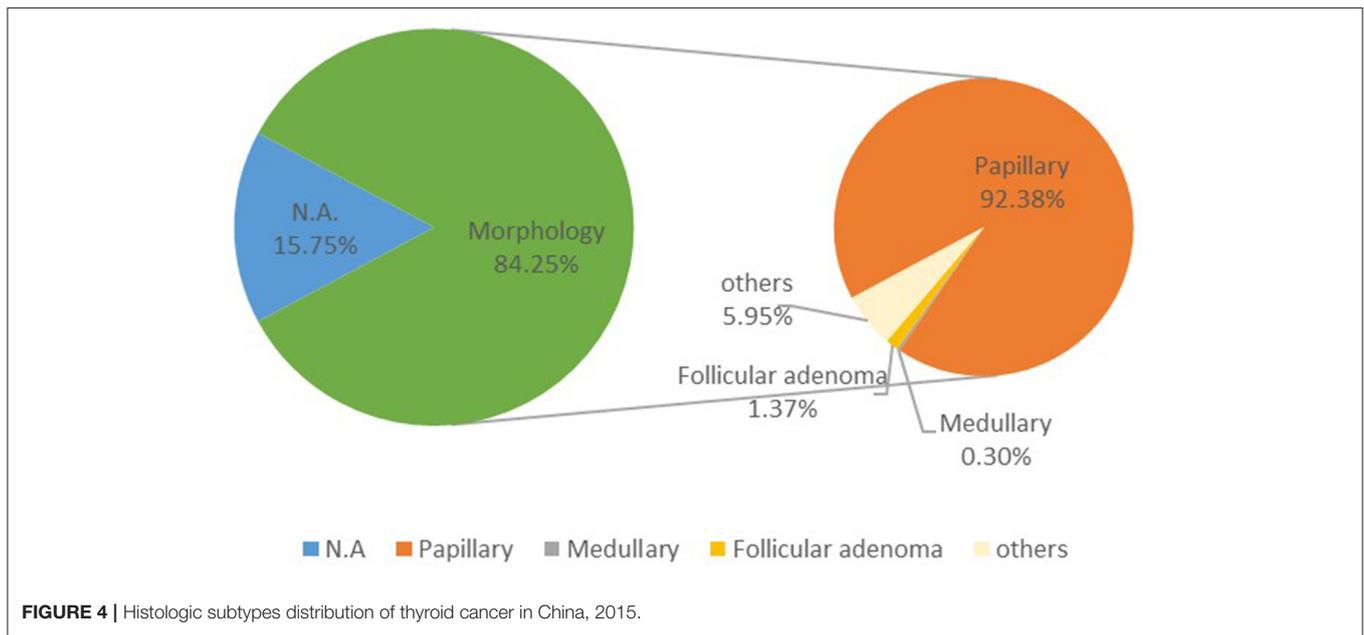


FIGURE 3 | Age-specific thyroid cancer mortality rate in China, 2015.

prompt the need of prudent consideration for greater focus on the cause of the relatively high mortality rate in central areas in China. The mortality rates of thyroid cancer increased with age like other most common cancer types. And they increased reaching a peak in the age group of 80–84 years old (in males and urban areas) and a peak in the 85+ years old (in females and rural areas).

Thyroid cancer incidence has been rising with the fastest speed over the last decades worldwide (21, 22), the ASIRC increased dramatically by 4.73 times between 2003 and 2012,



from 2.40/100,000 to 13.75/100,000 in China (23). Compared with the data in recent years, the incidence and mortality rate of thyroid cancer in China also showed an increasing trend, with the incidence rising from 8.82/100,000 in 2013 to 12.05/100,000 in 2015. The mortality rate slightly rose from 0.33/100,000 in 2013 to 0.37/100,000 in 2015. The same trend was observed in different areas and genders (20).

Based on our past work, we observed a rapid increase in the proportions of PTC in 12,508 patients with thyroid carcinoma identified in the Zhejiang Cancer Hospital from 1972 to 2014 while the proportions of MTC, FTC, and PDTC decreased over the decades. In the PTC cases, the proportion of patients with maximum tumor diameter (MTD) <1 cm dramatically and significantly increased from 0 in 1972–1985 to 32.1% in 2000–2014 (24). A higher PTC proportion was also observed in 2015 (PTC: 92.38%) compared to 2010 (PTC: 86%) (16), consistent with our previous finding. In 2015, it was estimated that there were 200,700 thyroid cancer incident cases and 7,900 deaths with the M/I of 0.04 in China. In the United States, ~62,450 new cases of thyroid cancer were predicted to be diagnosed in 2015 by the American Thyroid Association (ATA), with the predicted deaths number of 1,950. The M/I were 0.04 and 0.03 for China and the United States (25), which demonstrates thyroid cancer is usually highly treatable and is often cured with surgery. Based on the report from National Cancer Center in China, the 5-year survival for thyroid cancer increased significantly from 67.5% in 2003–05 to 84.3% in 2012–15 (26). However, the 5-year survival in China was still much lower than the United States (98.7%) (27). Similar or larger survival gaps were also found between China and other developed countries (28). Thus, much remains to be done to reduce the survival gap between China and developed countries.

There are debates over the increasing incidence of thyroid cancer internationally, doubting if the mass application of imaging technology that makes the thyroid cancer over diagnosed (29). An International Age-Period-Cohort Analysis

reported that global long-term declines in thyroid cancer mortality have been accompanied by downward trends in both period and cohort effects, indicating lack of evidence of a possible major contribution of “real” risk factors in thyroid cancer mortality, and indirectly confirming the main role of over diagnosis in the epidemic of thyroid cancer incidence (30).

However, another very influential factor, the tumor sizes at the time of diagnosis, should have been considered as well but that information was not available for all analyzed cases. The investigation of tumor sizes at diagnosis could partly answer whether the recent rapid growth of thyroid cancer should be attributed to over-diagnosis. If large tumors were observed to have similar increasing trend like small tumors, then risk factors other than diagnostic progresses may have also been responsible for the increase in the incidence of thyroid cancer.

CONCLUSIONS

Although thyroid cancer was found burdened with the high incidence, the mortality rate remained relatively low in China in 2015. The incidence and mortality rates of thyroid cancer varied by sex, age groups, and areas. Notably, mortality ASRs seem to now be high in central areas of China compared to others. This calls for further investigation of related risk factors to avoid harm in a growing number of populations. It remains utmost important to put targeted prevention and treatment programs into practice to curb the rapid growth of thyroid cancer.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

WW and JH initiated, planned, and designed the study. LD had full access to all the data in the study. SZ conducted

the data acquisition, management, and analysis. HL provided the statistical input for the data analysis. LD and ZZ drafted the manuscript. All authors interpreted the study results and critically revised the manuscript.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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