RESEARCH

A Chinese survey on clinical practice in hyperthyroidism management: comparison with recent studies and guidelines

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Abstract

Objective: To conduct a questionnaire survey of the current clinical practice for overt hyperthyroidism in China.

Methods: An online questionnaire survey was conducted in July 2020. The two questionnaires covered 35 and 8 questions about non-pregnancy and pregnancy clinical practice for overt hyperthyroidism, respectively.

Results: One thousand, two hundred fifty-six physicians participated. Chief physicians and associate chief physicians accounted for 58.6% of the participants. Approximately 95.2% of the respondents chose the thyrotropin receptor antibody (TRAb) test to clarify the etiology of thyrotoxicosis, while only 27.0% of them chose radioactive iodine uptake (RAIU). In terms of treatment for non-pregnant patients, anti-thyroid drugs (ATDs) were the first choice, and most of the clinicians chose methimazole. Compared with clinicians in recent studies, Chinese physicians used serum TRAb to diagnose Graves' disease more commonly, and there were obviously more physicians preferring ATDs. For maternal hyperthyroidism, most physicians preferred propylthiouracil administration before or during the first trimester, which is consistent with the 2016 American Thyroid Association (ATA) guidelines. In terms of the initial ATD dose, monitoring the treatment process, indications for ATD withdrawal and treatment of special cases, the preferences of Chinese physicians were generally consistent with the guidelines.

Conclusion: Chinese physicians can generally follow the ATA guidelines for the diagnosis and treatment of hyperthyroidism. Moreover, there are small differences from foreign studies or the guidelines with respect to particular problems. These findings provide evidence for future clinical research in China.

Key Words

- hyperthyroidism
- Graves' disease
- clinical practice
- questionnaire survey

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Introduction

Thyrotoxicosis refers to a clinical increase in serum thyroid hormones, including hyperthyroidism, thyroid destruction induced by thyroiditis and excessive intake of exogenous thyroid hormone (1). There are many types of hyperthyroidism, the most common of which is Graves' disease (GD); other types include toxic multinodular goiter (TMNG), toxic thyroid adenoma (TA) and Hashimoto's hyperthyroidism. According to the findings of the Thyroid Disease, Iodine Nutrition and Disease Epidemiology Study (TIDE study) in mainland China, the current prevalence of hyperthyroidism is 0.78%, and the GD is 0.53% (2). Thyrotoxicosis can affect all organs, leading to osteoporosis, cardiovascular disease, neuropsychiatric disorders, etc. (3, 4, 5), and hyperthyroid crisis can even be life-threatening.

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Treatment options for hyperthyroidism mainly include anti-thyroid drugs (ATDs), radioactive iodine (RAI) and thyroidectomy, as well as β-blockers as ancillary therapy. With the understanding of the pathology and accumulation of evidence in practice on hyperthyroidism, guidelines for the management of thyrotoxicosis and GD have been formulated or revised in China and abroad (1, 6, 7). In 2007, Chinese scholars formulated the first version of the Chinese guidelines for diagnosis and treatment of thyroid diseases, which has not yet been revised (6). In 2016, the American Thyroid Association (ATA) revised its 2011 guidelines. The new version of the guidelines contains many updates on the clinical practice of thyrotoxicosis, and the promotion and application of these guidelines have been changing the clinical practice (1, 7). However, the current Chinese status of clinical practice for thyrotoxicosis and GD is still unclear. The purpose of this survey was to analyze the Chinese patterns of diagnosis and treatment of hyperthyroidism, and to compare them with the guidelines and recent foreign investigations to provide a basis for updating the Chinese guidelines and guiding clinical practices.

Materials and methods

Collection of the questionnaire

A questionnaire survey was conducted during the 9th China Medical University Thyroid Forum held on July 18, 2020. Affected by the COVID-19 pandemic, the forum was conducted online. We distributed the two questionnaires on nonpregnancy and pregnancy issues during different topics on the live platform. All physicians could voluntarily participate in the surveys. Neither the forum organizer nor the authors directly contacted the participants, nor did they guide the physicians on their preferences during the survey.

The participants completed the questionnaires and uploaded their options. Repeated submissions from the same IP address were automatically blocked. The study was approved by the Ethical Committee of China Medical University. Consent has been obtained from each participant after full explanation of the purpose and nature of all procedures used.

Literature search strategy

An electronic search of PubMed, Embase and MEDLINE was performed to identify relevant investigations within the last ten years. We used the following search terms in "All fields": ((hyperthyroidism OR hyperthyroid OR Graves' disease OR GD) AND (survey OR questionnaire)). A manual check of the references from the initially included studies was also performed to identify eligible studies. Several specific studies on GO (Graves' ophthalmopathy) or relapsing GD were excluded.

Questionnaire design and survey implementation

Previously, a total of seven relevant studies on the diagnosis or treatment of hyperthyroidism were conducted in different countries (8, 9, 10, 11, 12, 13, 14). Several of the previous surveys were based on the same case (9, 10, 11, 13). According to our preliminary investigation, the rate of Chinese physicians who preferred ATDs was much higher than that of physicians abroad; therefore, our questionnaire for non-pregnant patients was more focused on ATD application and follow-up questions and less focused on RAI and surgery issues. The abovementioned questionnaire comprises 30 single-choice and 5 multiple-choice questions. Moreover, we selected eight questions from the questionnaire on thyroid diseases during pregnancy to assess the current Chinese practice on maternal hyperthyroidism. The detailed content of the 43 questions is shown in Table 1.

Results

Respondents' profiles

In total, 1256 Chinese clinicians from all 31 provinces participated in the survey, 756 of whom completed the non-pregnancy questionnaire and 536 of whom completed the pregnancy questionnaire. Among them were 352 (28.0%) chief physicians (i.e. specialists), 384 (30.6%) associate chief physicians (i.e. associate specialists), 357 (28.4%) attending physicians, 78 (6.2%) resident physicians and 85 (6.8%) clinicians with other professional titles. There were 874 (69.6%) physicians from tertiary hospitals (i.e. the highest level) and 359 (28.6%) physicians from secondary hospitals (i.e. the second highest level); the remaining physicians were from other medical institutions.

Diagnosis of hyperthyroidism

As shown in Table 2, regarding the choice of indicators for diagnosis, almost all the physicians chose serum thyroid-stimulating hormone (TSH), free thyroxine (fT4)

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Table 1 Details of the questions (except for the demographic information of the participants).

	Questions	Options
The non-pregnancy questionnaire covers a total of 35 questions		
1	Which of the following indicators do you obtain when diagnosing hyperthyroidism? (Multiple choice)	fT3, fT4, tT3, tT4, TSH, thyroid ultrasound, RAIU, thyroid radionuclide scan
2	Which of the following indicators do you obtain when diagnosing GD? (Multiple choice)	TRAb, TPOAb, TgAb, peak flow velocity of the superior thyroid artery, invasive exophthalmos, anterior tibial mucinous edema
3	Do you ask hyperthyroid patients not to smoke?	Yes, no
4	Do you ask hyperthyroid patients not to expose themselves to secondhand smoke?	Yes, no
5	Do you ask hyperthyroid patients to take a low-iodine diet?	Yes, no
6	Do you ask hyperthyroid patients to use noniodized salt?	Yes, no
7	Which one do you think is the first-line treatment for hyperthyroidism?	MMI, PTU, RAI, thyroidectomy
8	How do you choose the initial dose of ATD?	MMI 30 mg or PTU 300 mg per day, according to the actual situation
9	(If you choose the second option in the previous question) Which one do you refer to for selecting the initial dose of ATD? (Multiple choice)	fT3 and fT4, fT3, TSH, age of the patient, results of hepatic function and the WBC count at baseline
10	How often is it recommended for patients to test their thyroid function during the initial period of ATD therapy?	Monthly, bimonthly, trimonthly
11	How often is it recommended for patients to test their thyroid function during the reduction period of ATD therapy?	Monthly, bimonthly, trimonthly
12	How often is it recommended for patients to test their thyroid function during the maintenance period of ATD therapy?	Monthly, bimonthly, trimonthly
13	Do you recommend that patients test their WBC count before ATD therapy?	Yes, No
14	How long is it recommended to test the WBC count after taking an ATD for the first time?	For 1 week, for 1–2 weeks, for 1 month, for 1–3 months, according to the side effects
15	How often is the WBC test recommended three months after an ATD is initiated?	Monthly, bimonthly, trimonthly, every 6 months, no recommendation
16	Do you recommend that patients test their baseline hepatic function?	Yes, No
17	Do you think hepatic function should be monitored during ATD treatment?	Yes, No
18	How often is the hepatic function test recommended during the first three months of ATD treatment?	Weekly, every 1–2 weeks, monthly, every 1–3 months, according to the side effects
19	How often is the hepatic function test recommended three months after an ATD is initiated?	Monthly, bimonthly, trimonthly, every 6 weeks, no recommendation, according to the side effects
20	Do you recommend taking hepatoprotective drugs for high alkaline phosphatase during the ATD treatment?	Yes, no
21	Do you recommend monitoring ANCA after PTU is applied?	Yes, no
22	Which of the following symptoms or signs will you pay attention to during ATD treatment? (Multiple choice)	Shown in Fig. 1
23	When would you consider withdrawing the ATD after initiation?	One year, 1.5 years, 2 years, according to the actual condition
24	Which of the following items would you use to estimate whether ATD treatment can be withdrawn? (Multiple choice)	TRAb returns to negative. Normal TSH. Normal fT4 or fT3. The dose of ATD to maintain normal TSH has been the lowest. The treatment course has reached 1.5 years. The goiter has shrunk to normal. Thyroid ultrasound indicates normal arterial blood flow.
25	How long do you recommend patients to be followed after withdrawing ATDs?	One month, 3months, 6 months, 1 year
26	Do you recommend the use of a compound iodine solution?	Yes, no
27	Which of the following would you choose to manage recurrence after withdrawing the ATD?	ATD, RAI, thyroidectomy
28	What is your preferred treatment for inactive GO?	ATD, RAI, thyroidectomy
29	What is your preferred treatment for active GO?	ATD, RAI, thyroidectomy
30	What is your preferred treatment for hepatic damage in hyperthyroid patients?	ATD, RAI, thyroidectomy

(Continued)

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Table 1 Continued.

	Questions	Options
31	What is your preferred treatment when severe side effects of ATDs occur?	ATD, RAI, thyroidectomy
32	What is your preferred treatment for hyperthyroid patients with periodic paralysis?	ATD, RAI, thyroidectomy
33	What is your preferred treatment for hyperthyroid patients with TMNG?	ATD, RAI, thyroidectomy
34	What is your preferred treatment for hyperthyroid patients with TA?	ATD, RAI, thyroidectomy
35	What is your preferred treatment for elderly hyperthyroid patients with comorbidities?	ATD, RAI, thyroidectomy
The questions selected from the questionnaire on maternal thyroid diseases are listed below		
1	Does your institution carry out prepregnancy thyroid disease screening?	Yes, no
2	Do you approve of the screening for thyroid diseases during pregnancy?	Yes, no
3	How do you carry out the screening for thyroid disease during pregnancy?	Among all pregnant women, among high-risk women
4	Has your institution established a pregnancy-specific reference interval for TSH?	Yes, no
5	Which medication would you recommend to hyperthyroid patients planning to become pregnant?	MMI, PTU
6	If you have applied MMI before pregnancy, which medication would you prefer during early pregnancy?	MMI, PTU
7	If you have applied PTU during T1, which medication would you prefer during T2, assuming an ATD is still required?	MMI, PTU
8	Do you recommend stopping the drug in T1 hyperthyroid patients, if an ATD was applied prior to pregnancy?	Yes, no

ATD, anti-thyroid drug; fT3, free triiodothyronine; fT4, free thyroxine; GD, Graves' disease; GO, Graves' ophthalmopathy; MMI, methimazole; PTU, propylthiouracil; RAI, radioactive iodine; RAIU, radioactive iodine uptake; T1, the first trimester; TA, toxic adenoma; TgAb, thyroglobulin antibody; TMNG, toxic multinodular goiter; TPOAb, thyroid peroxidase antibody; TRAb, thyrotropin receptor antibody; TSH, thyroid-stimulating hormone; tT3, total triiodothyronine; tT4, total thyroxine; WBC, white blood cell.

and free triiodothyronine (fT3). Only half of them chose serum total thyroxine (tT4) and total triiodothyronine (tT3). In addition, 87.6% of the physicians chose thyroid ultrasound to assist the diagnosis. The thyroid radioiodine uptake (RAIU) rate and thyroid scan were not selected by most physicians.

We further investigated what kind of examinations should be arranged to confirm the diagnosis of GD. As shown in Table 2, nearly all physicians recommended testing for thyrotropin receptor antibody (TRAb), and half of them recommended thyroid peroxidase antibody (TPOAb), thyroglobulin antibody (TgAb) and peak velocity of the superior thyroid artery (to distinguish GD and destructive thyroiditis when RAI is contraindicated). In addition, most physicians diagnosed GD based on the presence of invasive exophthalmos or pretibial mucinous edema.

The comparison between the present and recent studies is shown in Table 2. Compared with foreigners, Chinese physicians were more inclined to use serum TSH levels and thyroid hormone levels (fT4 and fT3) to assess the existence of hyperthyroidism. Moreover, the corresponding rate of TRAb testing was also much higher than that abroad. Respondents considering RAI or ultrasound were comparable to those in recent studies. In addition, there were generally fewer Chinese clinicians who chose thyroid scans.

Treatment of hyperthyroidism

First choice of treatment plan

ATD therapy was the first choice for almost all of the clinicians for treating hyperthyroidism (Table 3). Meanwhile, RAI and thyroidectomy accounted for only a small portion of respondents. The application of compound iodine solution in the treatment of hyperthyroidism has been controversial for decades. In our survey, we found that 50.8% of the doctors considered applying iodine solution to treat the disease appropriately.

Similarly, we also listed the proportions of the preferred treatment options at home and abroad in Table 3. We found that in North America, the Middle East and North Africa, the rates of selecting RAI were higher than those in other regions, while fewer physicians preferred ATDs.

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Table 2 Summarized rates of laboratory or clinical examinations in each investigation (%).

	Burch, 2012	Bartalena, 2015	Negro, 2016	Beshyah, 2017	Wang, 2021
Region	North America	Europe	Italy	MENA	China
Respondents	730	147	947	352	756
TSH	89.1%	80.8%	68.5%	83%	98.8%
fT4	89.3%	81.5%	66.5%	80%	96.3%
fT3	40.5%	–	–	62%	95.2%
tT4	–	–	–	–	54.0%
tT3	31.8%	–	–	13%	54.4%
Ultrasound	25.8%	70.6%	92.1%	64%	87.6%
RAIU	47.0%	6.2%	11.5%	22%	27.0%
Thyroid radionuclide scan	41.9%	31.5%	25.2%	40%	21.7%
TRAb	58.1%	85.6%	93.9%	46%	95.2%
TPOAb	42.4%	64.4%	76.8%	50%	54.0%
TgAb	23.7%	30.1%	58.0%	36%	48.9%
Peak velocity of the superior thyroid artery	–	–	–	–	62.6%
Invasive exophthalmos	–	–	–	–	79.1%
Pretibial mucinous edema	–	–	–	–	64.3%

fT3, free triiodothyronine; fT4, free thyroxine; MENA, Middle East and North Africa; RAIU, radioactive iodine uptake; TgAb, thyroglobulin antibody; TPOAb, thyroid peroxidase antibody; TRAb, thyrotropin receptor antibody; TSH, thyroid-stimulating hormone; tT3, total triiodothyronine; tT4, total thyroxine.

ATD therapy was obviously more popular in Europe and China. Similar to the results in North America and Europe, methimazole (MMI) was the first choice of most Chinese physicians, while most physicians from the Middle East and North Africa preferred to choose carbimazole, which was not available in China.

Selection of the initial dose of ATD and monitoring during the treatment

Among the participants preferring to choose ATDs, 78% preferred an individualized initial dose according to the actual situation; the rest chose a fixed dose of MMI (30 mg/day) or propylthiouracil (PTU) (300 mg/day) as the initial dose. Among the abovementioned physicians selecting individualized initial doses, nearly 90% of them determined the initial dose based on the levels of serum fT3 and fT4, combined with the hepatic function tests and white blood cell (WBC) count. In addition, nearly 60% of them would refer to the TSH level, and nearly 70% of them also chose the initial dose based on the patients' age.

According to previous clinical experience, ATD application was divided into initiation, reduction and maintenance periods. The present survey found that 96.7% of the physicians recommended that patients review their thyroid function monthly during the initiation period, and a few physicians would recommend that patients review the function bimonthly (2.0%) or trimonthly (1.3%). Most of the participants (72.5%) still recommended the performance of a monthly review during the reduction period. For the maintenance period, the main feedback was once every 2–3 months (78.3%).

Monitoring and management of adverse reactions to ATDs

It is necessary for clinicians to inform patients of any possible adverse effects before medication administration and to monitor them. As shown in Fig. 1, we divided

Table 3 Summarized rates of treatment for non-pregnancy in each investigation (%).

	Burch, 2012	Bartalena, 2015	Negro, 2016	Beshyah, 2017	Goichot, 2017	Wang, 2021
Region	North America	Europe	Italy	MENA	France	Mainland China
Respondents	730	147	947	352	263	756
ATD	53.9%	83.8%	77.1%	53%	91%	98.5%
MMI	83.5%	79.3%	97.7%	9%	-	96.1%
PTU	2.7%	2.9%	1.4%	5%	-	3.9%
Carbimazole	13.8%	17.9%	0.9%	86%	-	-
RAI	45.0%	14.1%	16.2%	37%	6.1%	1.3%
Thyroidectomy	0.7%	2.1%	4.5%	3%	2.9%	0.1%

ATD, anti-thyroid drug; MENA, Middle East and North Africa; MMI, methimazole; PTU, propylthiouracil; RAI, radioactive iodine.

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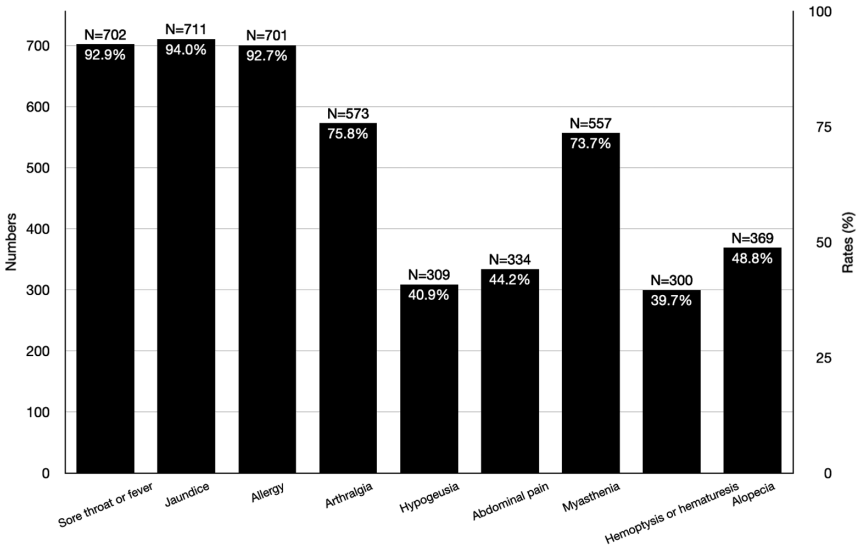

Figure 1
Rates of each anti-thyroid drug adverse reaction reported in the present survey.

ATD-related symptoms into nine items. The survey found that over 90% of the participants focused on sore throat or fever, jaundice and allergies; over 70% focused on the symptoms of arthralgia and myasthenia; another 40% of the physicians paid attention to other rare reactions, such as alopecia, hemoptysis and hematuria.

Only <1% of the physicians believed that the WBC count or hepatic function tests were unnecessary before the initiation of ATD treatment. Approximately 56% of the physicians recommended that patients test their WBC count 1 week after initiating the ATD, and 40.9% deemed that the frequency of WBC counting could be appropriately extended. Another 2.5% of the physicians believed that the timing of the WBC count should depend on the patient's symptoms. Regarding the frequency of hepatic function tests, the feedback given by the physicians was also different. A total of 38.5% of the physicians believed that hepatic function should be reviewed every 1–2 weeks after initiating the ATD, 30.6% of the physicians recommended that hepatic function be tested monthly and 19.3% of the physicians recommended that patients review their hepatic functions every 1–3 months. In addition, 3.6% deemed that the frequency of hepatic function tests should be specifically determined according to the patient's relevant symptoms.

Given that half of the hyperthyroid patients could have an isolated increase in serum total alkaline phosphatase (ALP) before or after treatment and that the downward trend is slow (15), we also investigated this clinical issue. Only approximately one-fourth of the physicians believed that hepatoprotective drugs should be taken, while the rest believed that hepatoprotection was unnecessary. ATDs might also have some rare adverse effects, such as anti-neutrophil cytoplasmic antibody (ANCA)-positive vasculitis. Approximately 72.6% of the physicians believed that ANCAs should be monitored after PTU was applied, while the rest of them believed that there was no need to monitor ANCAs. In general, if there were more serious adverse reactions in patients, 89.3% and 7.1% of the physicians would consider RAI and thyroidectomy as alternatives, respectively; another 3.6% would still consider maintaining the use of ATDs.

Withdrawal of ATD and post-withdrawal monitoring

In this survey, 0.9, 34.8 and 22.1% of the physicians respectively considered withdrawing the drug at 1 year, 1.5 years, and 2 years after an ATD was initiated, but 42.2% would appropriately extend the treatment course. TTRAb was the main indicator for deciding whether to stop ATD treatment (91.8%), whether TSH was normal (70.9%), whether the dose to maintain a normal TSH level was the lowest (78.2%), and whether the course of treatment exceeded 1.5 years (79.2%) were also taken into consideration by most of the participants. In addition, approximately half of the physicians decided the timing of discontinuation based on whether the fT3 and fT4 levels (57.3%), goiter (47.2%) and peak velocity of the superior thyroid artery returned to normal (49.9%).

Given that ATD treatment is not definitive for hyperthyroidism, we need to monitor patients regularly after withdrawing the drug. The survey found that 34.8, 47.1, 15.3 and 2.8% of the physicians recommended that patients review their thyroid function every 1 month, 3 months, 6 months, and 1 year, respectively, after withdrawing the drug. If hyperthyroidism relapsed, 42.5% recommended that ATDs should be

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continued, while 55.0 and 2.5% would consider RAI and thyroidectomy, respectively.

The choice of treatment in special cases

The survey showed that if hyperthyroid patients have inactive GO, 81.0% of the physicians would choose ATD, and RAI and thyroidectomy accounted for 16.1 and 2.9% of respondents, respectively. However, if active GO was present, the rate of ATD treatment was correspondingly reduced (73.9%), while the numbers of RAI treatments (18.0%) and surgeries (8.1%) were correspondingly increased. If hyperthyroidism was complicated by hepatic damage, 9.1, 80.8 and 10.1% selected ATD, RAI and thyroidectomy as the first option, respectively.

In addition, for periodic paralysis patients, 71.0, 22.0 and 7.0% of the physicians preferred ATD, RAI and thyroidectomy, respectively. For TMNG patients, 51.7% of the respondents preferred thyroidectomy, and ATD and RAI accounted for 25.4% and 22.9%, respectively. For patients with TA, thyroidectomy was the most preferred choice (68.9%), followed by RAI (24.3%) and ATDs (6.7%). For elderly hyperthyroid patients with comorbidities, ATD, RAI and thyroidectomy accounted for 62.8, 33.6 and 3.6% of respondents, respectively.

Lifestyle management of hyperthyroid patients

Most physicians inform hyperthyroid patients to avoid smoking and limit iodine intake. Specifically, 95.4% asked the patients not to smoke, and 90.1% asked the patients not to passively smoke. In addition, 97.2 and 72.5% of the physicians would recommend a low-iodine diet or non-iodized salt.

Screening and treatment options for maternal hyperthyroidism

The survey found that almost all physicians (99.4%) proposed implementing screening for thyroid diseases among pregnant women, most of whom (84.7%) were inclined to screen all pregnant women, while the rest preferred to screen high-risk individuals. Among the 536 respondents, 79.7% indicated that their institution provides pre-pregnancy screening services. However, 76.7% of the physicians admitted that their hospital had not established a pregnancy-specific TSH reference interval.

Regarding the treatment of hyperthyroidism during pregnancy, the results of our investigation are shown in Table 4. For hyperthyroid patients desiring pregnancy, most Chinese respondents (84.3%, much more than foreigners) preferred PTU for medication. During the first trimester (T1), approximately half (48.3%) of the respondents recommended discontinuing the drug. However, for T1 patients on MMI prior to pregnancy, the obvious proportion of Chinese physicians preferring PTU was similar to that in recent surveys. Moreover, the rate of switching to MMI in the second trimester (T2) accounted for approximately half of the respondents, which was similar to the corresponding proportion of foreigners.

Discussion

The questionnaire survey covered a total of 1256 clinicians in mainland China. By elucidating the current status of the diagnosis and treatment of hyperthyroidism, this study identifies the gap between the current guidelines and clinical practice, as well as between Chinese and foreign patterns, which would facilitate targeted continuous education and help to standardize the diagnosis, treatment and management of hyperthyroidism.

GD is the most common type of hyperthyroidism (2), and anterior tibial mucinous edema and infiltrating exophthalmos are the typical manifestations. The present survey found that only 60–80% of physicians focused on the above two typical signs to make a diagnosis. Due to a large demand for medical service in mainland China, excessive dependence on laboratory tests and examinations is currently a common problem. The ATA guidelines recommend that if the symptoms are obvious, GO or pretibial mucinous edema can be used as direct evidence for GD diagnosis. If the clinical manifestations are not sufficient to determine the cause of hyperthyroidism, further examinations should be performed, including TRAb and RAIU, and the peak velocity of the superior thyroid artery or tT3/tT4 ratio should also be arranged to distinguish GD and destructive thyroiditis, if necessary. In recent years, with its continuous improvement in sensitivity and specificity, TRAb detection has been increasingly preferred; compared with RAIU, it leaves patients radiation free. The 2016 ATA guidelines have recommended TRAb as the first choice for identifying the etiology of hyperthyroidism. A significant difference in the intention to detect TRAb between Chinese and international patients was revealed, suggesting that Chinese physicians are more inclined to choose economical and time-saving TRAb testing.

Overall, the frequency of applying ATD in China is much higher than in foreign countries. According to a

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Table 4 Summarized rates of treatment for pregnancy in each investigation (%).

	Burch, 2012	Poppe, 2012	Azizi, 2014	Bartalena, 2015	Negro, 2016	Beshyah, 2017	Wang, 2021
Region	North America	Europe	Asia	Europe	Italy	MENA	Mainland China
Respondents	730	210	310	147	947	352	536
Preferred ATD before pregnancy							
PTU	54.3%	42.1%	52%	48.9%	-	9%	84.3%
MMI	45.7%	36.2%	40%	42.3%	61%	36%	15.7%
Carbimazole	-			8.8%	-	54%	-
Switch to PTU in T1							
Yes	75.6%	86.5%	96%	75.3%	82.2%	92%	89.4%
No	24.4%	13.5%	4%	24.7%	17.8%	8%	10.6%
Switch to MMI (or CBZ) in T2							
Yes	45.9%	46.2%	42%	60%	-	66%	58.8%
No	54.1%	53.8%	58%	40%	-	34%	41.2%

ATD, anti-thyroid drug; CBZ, carbimazole; MENA, Middle East and North Africa; MMI, methimazole; PTU, propylthiouracil; T1, the first trimester; T2 the second trimester.

patient-based survey conducted by Brito *et al.* in 2016, the administration rate of ATD in the United States was 58%, of which MMI accounted for 87%; another 35% of the patients received RAI (16). The above results are similar to those of Burch *et al.* (11). Compared with mainland China, foreign physicians (especially in North America) are obviously more inclined to use RAI to treat hyperthyroidism, and the administration rate of ATD is generally lower than that in China. Although the guidelines recommend that ATD, RAI and surgery can be used as initial options for the treatment of hyperthyroidism, the differences in the proportions of the three therapies are also obvious, especially in China. According to the guidelines, excluding pregnant women in the first trimester, patients with thyroid crisis, and patients who have mild adverse reactions to MMI and refuse RAI or surgery, MMI should be the first choice for all patients who choose ATD for the treatment. Our results were consistent with the above recommendations. Additionally, in accordance with the guidelines, nearly 80% of the participants tend to individually choose the initial dose of ATD, and most of them will determine the initial dosage based on the multiple of serum-free thyroid hormone compared with normal.

Regarding the monitoring of ATD adverse reactions, there was a certain discrepancy between our results and the guidelines or foreign results. First, the guidelines recommend that the WBC count and hepatic function should be tested at baseline. This recommendation is also consistent with our survey results. Second, the guidelines point out that there is currently insufficient evidence to support monitoring WBC count or hepatic function during the treatment. Our results did not meet this recommendation. In addition, a European study also revealed that 57.8 and 42.3% of the physicians would monitor WBC count and liver function, respectively (9); and another North American study also found that 40.2% of the respondents would not monitor (11). There was a big difference between the physicians of mainland China and foreign countries on the question of whether it is necessary to monitor WBC count and hepatic function during the administration of ATD.

The recommended course of ATD treatment is 12–18 months, and serum TSH and TRAb are the main recommended indicators for discontinuation. This survey showed that only one-third of Chinese physicians stopped the medication after 12–18 months, which is much fewer than the corresponding proportion of foreigners (9, 11), and most Chinese physicians would extend the treatment course appropriately. A recent Iranian study also found that compared with the recommended course, a long-term small dose of MMI could significantly reduce the relapse rate of GD (17). However, the pros and cons of long-term MMI need to be evaluated by more RCTs. According to the recommendation, discontinuation can be considered if the treatment course was sufficient and both TSH and TRAb are normal. If TRAb reaches normal, the possibility of remission is greater. The preference of Chinese physicians is basically consistent with the above recommendations.

For GO patients, if the treatment is not appropriate, the condition may worsen. The guidelines recommend that for patients with mildly active GO, ATDs, RAI or thyroidectomy can be alternatively selected. After RAI treatment, it is necessary to determine whether glucocorticoids can be used at the same time according to the patient's situation. For patients with moderate-to-severe active GO, RAI is no longer recommended. This questionnaire survey found

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that Chinese physicians prefer ATD administration for both inactive and active GO.

Previous studies have found that in newly diagnosed hyperthyroid patients, the incidence of hepatic damage was 15–76% (18). The guidelines recommend that RAI be the first choice for the above situation and that RAI or surgery be the first choice for TMNG and TA. For elderly patients with comorbidities, both ATD and RAI therapy can be selected. The Chinese practice patterns in the above cases are consistent with the recommendations. For patients with periodic paralysis, RAI and surgery are regarded as the preferred treatment in the guidelines. Subsequently, ATD is merely listed as an acceptable treatment for periodic paralysis. However, only a small number of interviewed physicians were consistent with the preferred options.

A large number of previous studies have confirmed that smoking can promote the development of GO, promote relapse and affect the therapeutic effect on the disease (19). There is sufficient evidence to support the harm of smoking to GD patients, and our survey results were also consistent with the evidence. Considering that iodine is an essential element for the synthesis of thyroid hormones, most of the Chinese respondents recommended iodine restriction. However, the above feedback currently lacks evidence-based assessment. An RCT in China found that if GD patients were supplied with adequate iodine during medication, the relapse risk could be significantly reduced (20). A retrospective survey in South Korea found that GD patients with different clinical outcomes after drug withdrawal had no significant difference in urinary iodine levels, and GD patients with different iodine intakes had no significant differences in relapse or remission rate after drug withdrawal (21). The survey suggests that more in-depth studies are required in the future to confirm whether patients with hyperthyroidism need to limit their intake or be supplemented with iodine.

The survey showed that most medical institutions recognize the importance of thyroid screening before or during pregnancy, but most institutions have not implemented a pregnancy-specific TSH reference. Previous epidemiological investigations have confirmed the importance of the specific reference interval during pregnancy (22), so we need to strengthen this aspect in the future. It has been revealed that the first 6–10 weeks is the main period of drug-induced malformations during pregnancy (23). Therefore, to avoid malformation, the guidelines have recommended timely switching to PTU for patients desiring pregnancy and MMI administration if definitive therapy was not considered and ATDs could not be discontinued. The guidelines have also recommended that the application of PTU during T1, and MMI and PTU are both optional afterwards. The study found that most Chinese physicians can follow the guidelines to apply PTU regardless of whether it is before or during T1.

In summary, this survey reveals the current practice on hyperthyroidism in mainland China. The results show that compared with their foreign counterparts, Chinese physicians have widely adopted TRAb testing, and ATD therapy is still the first-line treatment option for hyperthyroidism. On one hand, this survey provides directions for future clinical research in China; on the other hand, it also suggests that continuing medical education should be strengthened to standardize the clinical diagnosis and treatment of hyperthyroidism.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Data availability statement

The database of the questionnaire survey is available on request to Prof Weiping Teng and Prof Zhongyan Shan.

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References

1 Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, Rivkees SA, Samuels M, Sosa JA, Stan MN, *et al*. American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid* 2016 **26** 1343–1421. (https://doi.org/10.1089/thy.2016.0229)

2 Li Y, Teng D, Ba J, Chen B, Du J, He L, Lai X, Teng X, Shi X, Li Y, *et al*. Efficacy and safety of long-term universal salt iodization on thyroid disorders: epidemiological evidence from 31 provinces of Mainland China. *Thyroid* 2020 **30** 568–579. (https://doi.org/10.1089/thy.2019.0067)

3 Feldman AZ, Shrestha RT & Hennessey JV. Neuropsychiatric manifestations of thyroid disease. *Endocrinology and Metabolism Clinics of North America* 2013 **42** 453–476. (https://doi.org/10.1016/j.ecl.2013.05.005)

4 Roffi M, Cattaneo F & Brandle M. Thyrotoxicosis and the cardiovascular system. *Minerva Endocrinologica* 2005 **30** 47–58.

5 Williams GR & Bassett JHD. Thyroid diseases and bone health. *Journal of Endocrinological Investigation* 2018 **41** 99–109. (https://doi.org/10.1007/s40618-017-0753-4)

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6 Endocrinology Branch of Chinese Medical Association. Chinese guidelines for diagnosis and management of thyroid diseases: hyperthyroidism. *Chinese Journal of Internal Medicine* 2007 **46** 876–882.

7 Bahn Chair RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, Laurberg P, McDougall IR, Montori VM, Rivkees SA, *et al*. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Thyroid* 2011 **21** 593–646. (https://doi.org/10.1089/thy.2010.0417)

8 Azizi F, Amouzegar A, Mehran L, Alamdari S, Subekti I, Vaidya B, Poppe K, Sarvghadi F, San Luis Jr T & Akamizu T. Management of hyperthyroidism during pregnancy in Asia. *Endocrine Journal* 2014 **61** 751–758. (https://doi.org/10.1507/endocrj.ej14-0145)

9 Bartalena L, Burch HB, Burman KD & Kahaly GJ. A 2013 European survey of clinical practice patterns in the management of Graves' disease. *Clinical Endocrinology* 2016 **84** 115–120. (https://doi.org/10.1111/cen.12688)

10 Beshyah SA, Khalil AB, Sherif IH, Benbarka MM, Raza SA, Hussein W, Alzahrani AS & Chadli A. A survey of clinical practice patterns in management of Graves disease in the Middle East and North Africa. *Endocrine Practice* 2017 **23** 299–308. (https://doi.org/10.4158/EP161607.OR)

11 Burch HB, Burman KD & Cooper DS. A 2011 survey of clinical practice patterns in the management of Graves' disease. *Journal of Clinical Endocrinology and Metabolism* 2012 **97** 4549–4558. (https://doi.org/10.1210/jc.2012-2802)

12 Goichot B, Bouee S, Castello-Bridoux C & Caron P. Survey of clinical practice patterns in the management of 992 hyperthyroid patients in France. *European Thyroid Journal* 2017 **6** 152–159. (https://doi.org/10.1159/000453260)

13 Negro R, Attanasio R, Grimaldi F, Guglielmi R, Papini E, AME (Associazione Medici Endocrinologi) & AACE (American Association of Clinical Endocrinologists) Italian Chapter. A 2015 Italian survey of clinical practice patterns in the management of graves' disease: comparison with European and North American surveys. *European Thyroid Journal* 2016 **5** 112–119. (https://doi.org/10.1159/000444482)

14 Poppe K, Hubalewska-Dydejczyk A, Laurberg P, Negro R, Vermiglio F & Vaidya B. Management of hyperthyroidism in pregnancy: results of a survey among members of the European thyroid association. *European Thyroid Journal* 2012 **1** 34–40. (https://doi.org/10.1159/000336101)

15 Cooper DS, Kaplan MM, Ridgway EC, Maloof F & Daniels GH. Alkaline phosphatase isoenzyme patterns in hyperthyroidism. *Annals of Internal Medicine* 1979 **90** 164–168. (https://doi.org/10.7326/0003-4819-90-2-164)

16 Brito JP, Schilz S, Singh Ospina N, Rodriguez-Gutierrez R, Maraka S, Sangaralingham LR & Montori VM. Antithyroid drugs-the most common treatment for Graves' disease in the United States: a nationwide population-based study. *Thyroid* 2016 **26** 1144–1145. (https://doi.org/10.1089/thy.2016.0222)

17 Azizi F, Amouzegar A, Tohidi M, Hedayati M, Khalili D, Cheraghi L, Mehrabi Y & Takyar M. Increased remission rates after long-term methimazole therapy in patients with Graves' disease: results of a randomized clinical trial. *Thyroid* 2019 **29** 1192–1200. (https://doi.org/10.1089/thy.2019.0180)

18 Piantanida E, Ippolito S, Gallo D, Masiello E, Premoli P, Cusini C, Rosetti S, Sabatino J, Segato S, Trimarchi F, *et al*. The interplay between thyroid and liver: implications for clinical practice. *Journal of Endocrinological Investigation* 2020 **43** 885–899. (https://doi.org/10.1007/s40618-020-01208-6)

19 Wiersinga WM. Smoking and thyroid. *Clinical Endocrinology* 2013 **79** 145–151. (https://doi.org/10.1111/cen.12222)

20 Huang H, Shi Y, Liang B, Cai H, Cai Q & Lin R. Optimal iodine supplementation during antithyroid drug therapy for Graves' disease is associated with lower recurrence rates than iodine restriction. *Clinical Endocrinology* 2018 **88** 473–478. (https://doi.org/10.1111/cen.13543)

21 Park SM, Cho YY, Joung JY, Sohn SY, Kim SW & Chung JH. Excessive iodine intake does not increase the recurrence rate of Graves' disease after withdrawal of the antithyroid drug in an iodine-replete area. *European Thyroid Journal* 2015 **4** 36–42. (https://doi.org/10.1159/000375261)

22 Gao X, Li Y, Li J, Liu A, Sun W, Teng W & Shan Z. Gestational TSH and FT4 reference intervals in Chinese women: a systematic review and meta-analysis. *Frontiers in Endocrinology* 2018 **9** 432. (https://doi.org/10.3389/fendo.2018.00432)

23 Laurberg P & Andersen SL. Therapy of endocrine disease: antithyroid drug use in early pregnancy and birth defects: time windows of relative safety and high risk? *European Journal of Endocrinology* 2014 **171** R13–R20. (https://doi.org/10.1530/EJE-14-0135)

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