# RESEARCH

**Open Access** 



# A survey on the management practices of graves' disease by Egyptian physicians and a comparison to similar reports from USA, Italy, China, and Brazil

Tamer Mohamed Elsherbiny<sup>1\*</sup> and Aliaa Aly El-Aghoury<sup>1</sup>

## Abstract

**Background** Graves' disease is the commonest cause of hyperthyroidism in iodine replete areas. Following universal salt iodization, most Egyptians are considered iodine sufficient. The present study aims to report a survey of real-life practices in the management of graves' disease among Egyptian physicians and compare them to other similar reports.

**Methods** An online survey was sent to members and affiliates of Alexandria thyroid association. Egyptian physicians were surveyed about initial diagnostics workup, management of an index case of uncomplicated graves' disease not desiring pregnancy. Two modified scenarios were proposed to the index case to survey the impact on treatment preferences. Anonymous responses were collected, analyzed, presented, and compared to other published similar reports.

**Results** Sixty-eight participated out of 120 invited physicians (56.67%). Initial workup included TSH receptor antibodies 46/68 (67.6%), thyroid ultrasound 45/68 (66.2%), and thyroid scintigraphy 25/68 (36.8%). Treatment preferences in the index case were antithyroid drugs (ATD's) 52/68 (76.5%), radioiodine 12/68 (17.5%), and surgery 4/68 (6%). Compared to other reports, treatment preferences were almost identical to Italian ones, ATD's (77.1%), radioiodine (16.2%), and surgery (4.5%). If the patient is complicated with graves' orbitopathy, treatment preferences would change into ATD's 37/67 (55%), radioiodine 1/67 (2%), radioiodine with corticosteroids 14/67 (21%), and surgery 15/67 (22%). If the patient is desiring pregnancy, treatment preferences would be ATD's 32/68 (47%), radioiodine 5/68 (7.4%), and surgery 31/68 (45.6%).

**Conclusion** A high participation rate was observed. Similar to other reports, medical treatment is the preferred modality of treatment in graves' disease and surgery is the least utilized modality. Similar treatment preferences to Italians were observed in the index case.

Keywords Graves' disease, Egypt, Survey, Orbitopathy, Pregnancy, Radioiodine, Thyroidectomy

## Background

Graves' disease (GD) is the most common cause of hyperthyroidism in iodine replete areas [1]. Universal salt iodization program was initiated in Egypt in 1996, and the latest national surveys conducted in 2014–2015 revealed that 75–91% of household salt is fortified with iodine [2, 3]. In a subnational survey of iodine status assessed by

\*Correspondence:

Tamer Mohamed Elsherbiny

Tamer\_elsherbiny@alexmed.edu.eg

<sup>1</sup> Endocrine Division, Alexandria Faculty of Medicine, Alexandria University, Khartoum Square, Azarita, Alexandria, Egypt



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

urinary iodine excretion, only 10% of 1879 school children were considered iodine deficient [4]. The prevalence of graves' disease in Egypt is unknown, however based on the current iodine status, it may be assumed to represent a common cause of hyperthyroidism in Egypt.

Establishing a diagnosis of graves' disease requires a combination of thyroid function testing, serological testing mainly TSH receptor autoantibodies (TRAb's), and imaging using thyroid ultrasound and/or thyroid scintigraphy or radioiodine uptake. The choice of investigations to establish the diagnosis may be influenced by the cost or the availability of the diagnostic test, the advice of evidence-based guidelines, and the acceptability by the patient [5].

The recommended initial line of treatment for graves' disease is medical treatment with antithyroid drugs (ATD's), followed by ablative therapy in the form of either surgery or radioiodine ablation. The treatment recommendations may be influenced by the presence of an active graves' orbitopathy (GO), by a medication adverse event, or by the patient's desire to achieve pregnancy in the short term [6].

The real-life practices in the management of graves' disease have been surveyed in different parts of the world. These surveys have demonstrated significant differences in the management of graves' disease in different countries and continents [7-10].

The present study aims to report real-life practices in the management of graves' disease in Egypt through an online survey conducted by Alexandria thyroid association, and to compare such practices to those reported from other countries in other continents.

#### Methods

Members of Alexandria thyroid association, and members of the endocrine divisions of several Egyptian universities have been invited to participate in an online survey to report their real-life practices managing a theoretical case of graves' disease, based on the survey originally used by Bartalena et al. in 2013, modified to fit the clinical practice in Egypt [11].

The survey was provided using Google forms, a link to the survey form (Supplementary file 1) was sent to 120 physicians on the contact list of Alexandria thyroid association, either by email or social media contacts (WhatsApp). The nature and purpose of the survey was explained at the first section of the survey, and consent to use the participants' responses anonymously was obtained from each participant. Two reminders were subsequently sent to invitees with no response.

The index case was a female patient of 42 years of age with a recent diagnosis of mild GD uncomplicated, and not desiring pregnancy in the short term. Later in the survey, two scenario modifications are proposed to the index case, the first modified scenario is when the index case is complicated by graves' orbitopathy, and the second modified scenario is when the patient desires pregnancy within 6-12 months.

The survey questions covered the following issues: initial diagnostics workup, the use of beta blockers in the initial management of GD, treatment preference in the index case, the initiation and discontinuation of antithyroid drugs, the use of ablative therapies in the index case, and finally the changes in handling the index case after applying the two modified scenarios, GD complicated with graves' orbitopathy (GO) and desire for pregnancy. Three questions were added from the Chinese survey by Wang et al. used in 2021, about smoking, items to consider discontinuation of ATD's, and follow up after stopping ATD's [9]. Since methimazole is not available in Egypt, all questions regarding the use of ATD's were including only carbimazole (CBZ) and propylthiouracil (PTU).

The survey was open for participation from April 2022 to April 2023. Only participants who answered at least 35 out of the 39 survey questions were included in the final results analysis. Answering such questions including year of graduation, seniority grade, and specialty were considered a must to include in the final results analysis. Anonymous responses were collected, and repeat submissions were omitted from the analysis.

Responses from participants of the present survey were then compared to those reported from other countries namely USA, Italy, China, and Brazil [7-10]. The comparison was limited to studies being reported from a single country, rather than continents or regions, considering that the present data reports practice patterns from a single African country, Egypt.

Approval was obtained from the ethics committee of Alexandria faculty of medicine, [IRB number 12098], in January 2022, serial number 0305441. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

#### Results

#### Participation rate and participant demographics

The Alexandria thyroid association invited 120 physicians to take the online survey, sixty-eight participated in the survey with a participation rate of 56.67%. Sixtyfive percent of participants were adult endocrinology consultants, 28% were adult endocrinology specialists, and 7% were general medicine consultants/specialists. Alexandria had most of the participants 25%, followed by Cairo 22%, Egypt' delta (5 governorates) 38%, and upper Egypt (4 governorates) 15%. Regarding years of experience after graduation, 10.5% had 40+years, 10.5% had 30 + years, 23% had 20 + years, 42% had 10 + years, and 14% had less than 10 years of experience. Finally, regarding volume of practice, 15% of participants treated 1-5 GD patients per year, 19% treated 6-10 GD patients per year, and 66% treated more than 10 GD patients per year.

#### Initial diagnostics work up for the index case

TSH Receptor antibodies was selected by 67.6% of participants, unfortunately stimulating and blocking bioassays of TRAb's are not available in Egypt. Thyroid ultrasound was selected by 66.2%, while thyroid scintigraphy including thyroid scan/radioactive iodine uptake was selected by 36.8%. TSH and Free T4 would be ordered by 82.4% and 89.7%, respectively. Antithyroid peroxidase antibodies (TPO) and antithyroglobulin antibodies (Tg) would be ordered by 25% and 11.8%, respectively. Liver panel and CBC would be ordered 27.9% and 39.7%, respectively (Fig. 1).

#### Use of beta blockers

95.5% of participants would start the index case on a beta blocker. 92.6% would prescribe propranolol, followed by metoprolol (4.4%), followed by atenolol (2.9%). 52.9% of participants would target a heart rate of <90 beats/minute, (25%) would target <80 beats/minute, (14.7%) would target <100 beats/minute, and the remaining participants would choose other targets.

#### Treatment preference in the index case

In the index case (uncomplicated graves' disease, and not planning pregnancy), (76.5%) of participants would choose medical treatment, (17.5%) would choose radioiodine ablation, and (6%) would choose surgery (Fig. 2A).

## **Medical treatment**

All participants would initiate medical treatment using carbimazole. Regarding the initial dose of CBZ, most participants (64.7%) would prescribe 30 mg daily, (17.7%) would prescribe 20 mg daily, (13.2%) would prescribe 40 mg daily, and the remaining (4.4%) would prescribe higher or lower doses or according to free T4.

## Monitoring

Regarding when to order the first thyroid labs, (50%) of participants would request it in 6 weeks, (36.8%) in 4 weeks, 4/68 (5.9%) in 8 weeks, and the remaining participants (7.3%) would request it in shorter or longer intervals. After achieving euthyroidism on ATD's, (51.5%) of participants would monitor thyroid function tests every 3 months, (45.6%) every 2 months, and the remaining participants (2.9%) would monitor patients more, or less frequently. Regarding routine lab monitoring during treatment with antithyroid drugs, (34.3%) of participants would use no routine monitoring, (3%) would routinely monitor liver associated enzymes, (18%) would routinely



Fig. 1 Initial diagnostics workup for graves' disease index case. TSH; Thyroid stimulating hormone, Free T4; Free thyroxine, Thyroid scintigraphy; thyroid scan and/or radioiodine uptake, CBC; Complete blood count



Fig. 2 Treatment preferences for a case of graves' disease. A Treatment preferences for the index case (uncomplicated graves' disease, not desiring pregnancy). B Treatment preferences for graves' disease case with risk factors for or complicated with active graves' orbitopathy, GO; Graves's orbitopathy, CS; Corticosteroids. C Treatment preferences for graves' disease case desiring pregnancy in 6–12 months

monitor complete cell count, and (44.7%) would routinely monitor both complete cell count and liver associated enzymes.

#### Adverse events management

Regarding the approach to persistent pruritic rash not improving with antihistamine, (59.7%) of participants would switch to the other antithyroid drug, (31.3%) would select an alternative mode of therapy (radioiodine or surgery), and (9%) would continue the same antithyroid drug plus antihistamine.

## Stopping ATD's and considering ablative therapy

Regarding time to consider stopping ATD's, assuming the patient achieved remission, (11.8%) of participants would stop ATD's after one year, (47%) after 18 months, (8.8%) after two years, and (32.4%) would stop ATD's according to the actual condition. Criteria to stop ATD's that were selected by more than 50% of participants were: normal TSH (51.5%), normal free T4 (60.3%), the dose of ATD's to maintain normal TSH has been the lowest (54.4%), and TRAb returns to negative (58.8%). The criteria that were selected by less than 50% of respondents were: the treatment course has reached 1.5 years (38.2%), thyroid ultrasound indicates normal arterial blood flow (11.8%), and the goiter has shrunk to normal (8.8%) (Fig. 3). After stopping ATD's, (56.7%) of participants would order thyroid function tests after 3 months, (29.9%) after one month, (11.9%) after 6 months, and (1.5%) after one year.

Regarding when to attempt an ablative therapy after starting medical treatment, (44%) of participants would attempt ablation within one year or less, (29.4%) after 18 months, (17.6%) after 2 or 3 years, (6%) would continue ATD's indefinitely, and (3%) would attempt ablation according to patient response and duration.

#### Surgery

The majority of participants (95.6%) would render the patient euthyroid using ATD's before surgery, and only (4.4%) would not. The routine prescription of either saturated solution of potassium iodide (SSKI) or Lugol's solution prior to thyroidectomy is done in only 25% of the patients. After surgery, the routine prescription of prophylactic vitamin D and calcium is done in 72% of patients upon discharge from hospital.

#### **Radioiodine ablation**

Pretreatment with ATD's prior to radioiodine ablation is done routinely by (41.2%) of participants, and only in selected cases by (53%) of participants. Regarding factors that determine the selective use of ATD's prior to radioiodine ablation (Age>65, Underlying heart disease, and Multiple comorbidities), a single factor was chosen by (35.6%), a combination of two factors was chosen by (24.4%), and a combination of all three factors was chosen by (40%) of participants. In patients receiving ATD's prior to radioiodine ablation, (76%) of participants would stop ATD's before giving radioiodine for a duration of 2-7 days as recommended by both ATA and ETA in their latest guidelines. After radioiodine, (19%) of participants wouldn't reinitiate ATD's, (25%) would reinstitute ATD's, and the remaining (56%) would only reinstitute ATD's in selected cases, using the same criteria previously mentioned.



Fig. 3 Criteria to stop ATD's assuming the patient achieved remission. Free T4; Free thyroxine, TRAb's; TSH receptor antibodies, ATD's; Antithyroid drugs, TSH; Thyroid stimulating hormone

#### Modified scenario one

If the patient had moderate active Graves' orbitopathy, additional investigations to be ordered would include Ophthalmologist evaluation (69.1%), MRI orbits (11.8%), CT orbits (noncontract) (10.2%), Visual field testing (5.9%), Orbital sonogram (1.5%), and CT orbit with contrast (1.5%). 98.5% of participants would ask their patients to stop smoking.

Treatment preferences according to different modifications in the clinical scenario: One, a patient with no baseline eye disease in the presence of risk factors for GO (smoking, high TRAb's titers, high T3 levels), ATD's (74.5%), surgery (12%), radioiodine with corticosteroids (7.5%), and radioiodine alone (6%). Two, a patient with mild active orbitopathy, ATD's (77.5%), surgery (9%), radioiodine with corticosteroids (12%), and radioiodine alone (1.5%). Three, a patient with moderate active orbitopathy, ATD's (55.2%), surgery (22.3%), radioiodine with corticosteroids (21%), and radioiodine alone (1.5%) (Fig. 2B). Finally, a patient with severe active orbitopathy, ATD's (32.8%), surgery (41.8%), and radioiodine with corticosteroids (25.4%).

If the patient's orbitopathy requires corticosteroid therapy, the most likely to administer this would be an endocrinologist by (75%) of participants, an oph-thalmologist by (23.5%), and primary care provider by (1.5%).

#### Modified scenario two

If the index case plans to become pregnant in the next 6–12 months, treatment preferences would be different as follows: (47%) of participants would recommend medical treatment, (45.6%) surgery, and only (7.4%) would recommend radioiodine (Fig. 2C). If the patient elects to use antithyroid drugs as the principal mode of therapy, (67.7%) of participants would prescribe CBZ, while (32.3%) would prescribe PTU. When the patient becomes pregnant, (97%) of participants would switch to PTU, while only (3%) wouldn't switch to PTU. If the patient was switched to PTU during the first trimester, (91%) of participants would switch to CBZ, as the patient enters the second trimester, assuming she still requires antithyroid drugs.

## Comparison to previously published studies from USA, Italy, China, and Brazil Participation rate

Although our study had the least number of invited participants, it had a high rate of participation (56.7%), second to China (60.2%), with the lowest rate being reported from Brazil (19.2%) (Table 1).

#### Initial diagnostics workup

TRAb's would be ordered in more than (90%) of GD patients in China, Italy, and Brazil, in two thirds of the patients by Egyptian practitioners (67.6%), and least to be ordered by USA participants (58.1%). Regarding imaging of GD patients, ultrasound thyroid would be ordered to support the diagnosis of GD more frequently than thyroid scintigraphy in all previous studies, as well as in our study, except in the USA where scintigraphy is more frequently used. In general, Tg antibodies were less frequently ordered compared to TPO antibodies in all previous studies, as well as in ours. Liver panel and CBC were least frequently utilized in our study compared to all other reports (Table 1) (Fig. 4).

#### Treatment preferences in the index case

A general pattern was observed regarding treatment preferences in the index case, ATD's were the most preferred in all reports, including ours, with the highest use in the Chinese study (98.5%), and the lowest use in the American study (53.9%), and similar rates of use in Egypt and Italy, (76.5%) and (77.1%), respectively. Surgery was the least preferred modality in in all reports, including ours, with the highest use in our study (6%), and the lowest use – almost none – in the Chinese and Brazilian studies, (0.1%) and (0%), respectively. An intermediate use of radioiodine in all reports, including ours, with the highest use in the American study (45%), and the lowest use in the Chinese study (1.3%), and similar rates of use in Egypt and Italy, (17.5%) and (16.2%), respectively (Table 1) (Fig. 5A).

# Treatment preferences in GD complicated with moderate active GO

A general pattern was observed regarding treatment preferences in this modified scenario. A decline in the rate of use of ATD's in all reports, with the exception of the American survey where the use of ATD's increased by 9%, yet ATD's remained the most preferred in all reports. A rise in the rate of use of surgery in all reports, with the highest use in the Italian study (31.6%), and the lowest use in the Brazilian study (2.8%), and close rates of use in Egypt and USA, (22.3%) and (18.5%), respectively. A rise in the rate of use of radioiodine in combination with glucocorticoids in all reports, with the exception of the American and Brazilian surveys where the use of radioiodine decreased by 26.2% and 2.5%, respectively (Table 1) (Fig. 5B).

#### Treatment preferences in GD patient desiring pregnancy

A general pattern was observed regarding treatment preferences in this modified scenario. A decline in the

	Egypt	USA [7]	ltaly [ <mark>8</mark> ]	China [9]	Brazil [10]
Participation rate	68/120 (56.7%)	648/1852 (35%)	947/1824 (51.9%)	756/ 1256 (60.2%)	573/3000 (19.1%)
Initial diagnostics					
TRAb's	67.6%	58.1%	93.9%	95.2%	93%
Ultrasound	66.2%	25.8%	92.1%	87.6%	82%
Thyroid scintigraphy	36.8%	41.9%	25.2%	21.7%	30%
TPO Ab	25%	42.4%	76.8%	54.0%	NR
Tg Ab	11.8%	23.7%	58%	48.9%	NR
Liver panel	27.9%	47.9%	52.7%	NR	61%
CBC	39.7%	49.7%	68.2%	NR	66%
Treatment preferences					
Index case Uncomplicated graves' disease	not desiring pregna	ncy			
ATD's	76.5%	53.9%	77.1%	98.5%	95%
Radioiodine	17.5%	45.0%	16.2%	1.3%	5%
Surgery	6%	0.7%	4.5%	0.1%	0%
Modified scenario 1 Graves' disease complicated w	ith moderate active C	GO			
ATD's	55.2%	62.8%	48.5%	73.9%	93.9%
Radioiodine	1.5%	1.9%			
Radioiodine + CS	21%	16.9%	19.9%	18.0%	2.5%
Surgery	22.3%	18.5%	31.6%	8.1%	2.8%
Modified scenario 2 Uncomplicated graves' disease	e desiring pregnancy				
ATD's	47%	49.9%	36%	NR	69%
Radioiodine	7.4%	29.8%	54.3%	NR	13.7%
Surgery	45.6%	20.3%	9.7%	NR	17.3%

**Table 1** A comparison of initial diagnostics workup and treatment preferences for graves' disease index case and in two modified scenarios from Egypt, USA, Italy, China, and Brazil

TRAb's TSH receptor antibodies, TPO Ab Thyroid peroxidase antibodies, Tg Ab Thyroglobulin antibodies, NR Not reported, CBC Complete blood count, ATD's Antithyroid drugs, CS Corticosteroids

rate of use of ATD's in all reports, yet ATD's remained the most preferred in all reports, with the highest use in the Brazilian study (69%), and the lowest use in the Italian study (36%), and close rates of use in Egypt and USA, (47%) and (49.9%), respectively. A rise in the rate of use of surgery in all reports, with the highest use in the Egyptian study (45.6%), and the lowest use in the Italian study (9.7%), and close rates of use in Brazil and USA, (17.3%) and (20.3%), respectively. A decreased rate of use of radioiodine was observed in both the Egyptian and American surveys, while an increased rate of use of radioiodine was observed in both the Italian study (54.3%), and the lowest use in the Egyptian study (7.4%) (Table 1) (Fig. 5C).

## Discussion

The present survey conducted by Alexandria thyroid association is the first to be conducted in Egypt to report real-life practices regarding the management of Graves' disease. Similar surveys have been previously conducted in other regions like Europe, Asia–Pacific region, and middle east [11-13], and in other countries like USA, Italy, China, and Brazil [7-10]. Such surveys clearly showed marked differences in the way a patient with graves' disease is initially investigated, and in the way treatment options are being utilized in the index case and in special situations which may affect the treatment preferences.

An almost identical pattern of treatment preferences for the index case was observed between Egypt and Italy, where medical treatment was chosen by 76.5% & 77.1%, radioiodine was chosen by 17.5 & 16.2%, and surgery was chosen by 6% & 4.5%, respectively [8]. This may be related to the fact that Italy is the nearest in distance to Egypt with mutual cultural and social relations, and also the exchange of clinical experience between Egyptian and European practitioners is much more compared to American and Asian ones. The lowest and highest preference of ATD's in the management of the index case was reported from USA (53.9%) and China (98.5%) respectively. The



Fig. 4 A comparison of initial diagnostics workup for graves' disease index case from Egypt, USA, Italy, China, and Brazil. TRAb's: TSH receptor antibodies, Thyroid scintigraphy; thyroid scan and/or radioiodine uptake, TPO Ab: Thyroid peroxidase antibodies, Tg Ab: Thyroglobulin antibodies, CBC; Complete blood count

relatively low preference of ATD's by North American participants reflects a long-standing preference to the use of radioiodine (69% in a previous 1990 survey), while the relatively high preference of ATD's by Chinese participants may reflect a low preference of ablative therapies used only in 1.5% of their patients [7, 9].

In the proposed scenario of GD complicated by moderate active GO, with the exception of Brazil, an almost identical rate of utilization of radioiodine with steroid prophylaxis was reported from Egypt, USA, Italy, and China of 21, 17, 20, and 18%, respectively with a general pattern of increased use of surgery at the expense of decreased use of ATD's compared to the index case [7–9]. In the proposed scenario of GD patient desiring pregnancy in the short term, a similar shift of treatment preferences was observed between Egypt and USA, with an increased use of surgery at the expense of decreased use of ATD's and a decreased use of radioiodine compared to the index case [7]. The decreased preference of ATD's in this scenario may be explained by the fact that both CBZ and PTU may cause birth defects with almost the same frequency, but less severe in the case of PTU [14].

Current clinical practice guidelines issued by the European thyroid association (ETA) recommend using TRAb's to confirm the diagnosis of graves' disease. In the present survey, 67.6% of Egyptian practitioners would order TRAb's when initially investigating a case with suspected graves' disease. A recent retrospective chart review of 390 GD patients' medical records from Alexandria, Egypt showed that 87.2% of patients were ordered TRAb's at initial presentation. This higher rate of utilization of TRAb's may be due to different practices – which may be related to the cost and availability of the test – in different parts of Egypt, as this retrospective study reported patients from Alexandria, whereas the present survey covered almost all areas from Egypt [15].

The same retrospective study reported that among 390 GD patients, 90% received medical treatment, 5.4% underwent surgery, and 4.3% received radioiodine ablation [14]. Treatment preferences for initial management reported in the present study were 76.5% for medical treatment, 6% for surgery, and 17.5% for radioiodine. These differences may be due to the fact that surveyed preferences were based on a theoretical uncomplicated index case not desiring pregnancy, whereas in the retrospective study, 17.7% were complicated with graves' orbitopathy and a record of 20 pregnancies were found in the patients' records, GO and pregnancy are both decision-making modifiers resulting in different treatment decisions [15].

ATD's is currently the recommended first line treatment for GD, recommended duration of medical treatment is 18–30 months before opting to an ablative therapy. Long-term ATD's have been considered in the latest ETA guidelines in elderly patients and in patients who prefer this modality of treatment [6]. Long term – more than 2 years – ATD's are associated with higher remission rates, safer than radioiodine and surgery, and considered to be appropriate for all age groups



Fig. 5 A comparison of treatment preferences for a case of graves' disease from Egypt, USA, Italy, China, and Brazil. A Treatment preferences for the index case (uncomplicated graves' disease, not desiring pregnancy). B Treatment preferences for graves' disease case complicated with moderate active graves' orbitopathy, GO; Graves's orbitopathy, CS; Corticosteroids. C Treatment preferences for graves' disease case desiring pregnancy in 6–12 months

[15]. Reports on long-term safety and efficacy of ATD's have covered periods of treatment up to 24 years [17]. However, only six percent of our surveyed participants chose to continue ATD's indefinitely.

Criteria for stopping medical treatment for GD assuming that the patient achieved remission in the current guidelines include a duration of 12–18 months of treatment, a normal TSH and determination of TRAb's status to guide whether to stop or extend ATD's treatment or to opt for a definitive treatment [6]. Other suggested criteria include euthyroidism using a minimal ATD's doses for a minimum of 6 months, a negative TRAb's, and a longer duration of ATD's treatment [18]. Criteria that were chosen by more than half of our surveyed physicians were euthyroidism evidenced by a normal TSH and free T4, achieved by the lowest dose of ATD's, and a negative TRAb's, without regard to the duration of treatment (Fig. 3).

Radioiodine ablation for GD has been proven to increase occurrence of new onset or progression of preexisting GO by about 20%. Use of oral glucocorticoid prophylaxis is safe and effectively prevents progression of preexisting GO [19]. Recent guidelines recommend using steroid prophylaxis in GD patients at risk of new onset or progression of preexisting GO [20]. For these reasons, when surveyed participants were presented with the modified scenario with GO, their preferences markedly changed - particularly in the proposed scenario of severe active GO - with a progressive increase in surgical ablation reaching 42% at the expense of a progressive decrease in medical treatment reaching 33%, and totally abandoning the sole choice of radioiodine and adopting the combined use of radioiodine and steroid prophylaxis in 25%.

The main limitation of the present study is the small number of invited physicians compared to similar previous reports. Considering that some subspecialities - like general practitioners and pediatric endocrinologists - were not represented among survey participants, the survey results may not fully capture the variability in management practices across the country. Yet, the present survey had the highest response rate, and also this is the first survey to be conducted from an African country, Egypt. The data from the present survey can be used to design continuous medical education programs for early career physicians and endocrinologists to provide better understanding of the rationale behind treatment preferences and practices, and future similar surveys can assess the impact of such programs on promoting evidence-based treatment practices.

## Conclusion

In conclusion, Egyptian treatment preferences were closest to Italian ones considering the management of the index case. A similar shift towards the use of steroid prophylaxis in combination with radioiodine and an almost identical rates of its use in all reports when managing GD with moderate active GO. A similar shift in treatment preferences was observed between Egypt and USA in the case of GD patient desiring pregnancy compared to the index case.

#### Abbreviations

- GD Graves' disease
- TRAb's TSH receptor antibodies
- ATD's Antithyroid drugs
- GO Graves' orbitopathy
- CBZ Carbimazole
- PTU Propylthiouracil
- TPO Thyroid peroxidase
- Tg Thyroglobulin
- CBC Complete blood count
- SSKI Saturated solution of potassium iodide
- ATA American Thyroid Association
- ETA European Thyroid Association
- MRI Magnetic resonance imaging

## **Supplementary Information**

The online version contains supplementary material available at https://doi. org/10.1186/s43162-024-00326-4.

Supplementary Material 1.

#### Acknowledgements

The Alexandria thyroid association is the first Egyptian scientific association concerned with thyroid related continuous education and research. This study is the first to be conducted by the association through inviting members and affiliates from Egyptian universities' faculty members. We would like to express our deepest gratitude to the participants in this survey for their contribution, time, and effort.

#### Authors' contributions

A.A.E. contributed to the study conception. T.M.E. contributed to the study conception, design, material preparation, data collection, and writing the manuscript.

#### Funding

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

#### Availability of data and materials

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

#### Declarations

#### Ethics approval and consent to participate

This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The protocol of the study was approved by the ethical committee of Alexandria faculty of medicine, [IRB number 12098].

#### **Competing interests**

The authors have no relevant financial or non-financial interests to disclose.

Received: 11 January 2024 Accepted: 30 May 2024 Published online: 06 June 2024

#### References

- 1. Zimmermann MB, Boelaert K (2015) lodine deficiency and thyroid disorders. Lancet Diabetes Endocrinol 3:286–295
- Ministry of Health and Population, Egypt. Global Alliance for Improved Nutrition (GAIN) UNICEF. National Survey of Household Iodised Salt Use and Iodine Status among Primary School Children and Pregnant Women in Egypt 2014/2015. United Nations Children's Fund (UNICEF); Cairo, Egypt: 2017.
- Ministry of Health and Population [Egypt], El-Zanaty and Associates [Egypt], and ICF International. 2015. Egypt Demographic and Health Survey 2014.
- Elsayed HH, El-Rahman MKA, ATawwfik A, (2015) lodine status of primary school children in different Egyptian environments. Egyptian J Hosp Med 61:451–458
- Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, Rivkees SA, Samuels M, Sosa JA, Stan MN, Walter MA (2016) 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Thyroid 26:1343–1421
- Kahaly GJ, Bartalena L, Hegedüs L, Leenhardt L, Poppe K, Pearce SH (2018) 2018 European thyroid association guideline for the management of graves' hyperthyroidism. Eur Thyroid J 7:167–186
- Burch HB, Burman KD, Cooper DS (2012) A 2011 survey of clinical practice patterns in the management of Graves' disease. J Clin Endocrinol Metab 97:4549–4558
- Negro R, Attanasio R, Grimaldi F, Guglielmi R, Papini E; AME (Associazione Medici Endocrinologi) and AACE (American Association of Clinical Endocrinologists) Italian Chapter (2016) A 2015 Italian Survey of Clinical Practice Patterns in the Management of Graves' Disease: Comparison with European and North American Surveys. Eur Thyroid J 5(2):112–119
- Wang X, Teng X, Li C, Li Y, Li J, Teng W, Shan Z, Lai Y (2021) A Chinese survey on clinical practice in hyperthyroidism management: comparison with recent studies and guidelines. Endocr Connect 10:1091–1100
- Villagelin D, Mazeto GMFS, Junior MCO, Ramos HE, Scheffel RS, Chiamolera MI, Perini N, Ronconi TL, Texeira P (2023) Treatment of Graves' disease in Brazil: results of a survey among endocrinologists. Arch Endocrinol Metab 67:e000657
- Bartalena L, Burch HB, Burman KD, Kahaly GJ (2016) A 2013 European survey of clinical practice patterns in the management of Graves' disease. Clin Endocrinol (Oxf) 84:115–120
- 12. Parameswaran R, de Jong MC, Kit JLW, Sek K, Nam TQ, Thang TV, Khue NT, Aye TT, Tun PM, Cole T, Miller JA, Villa M, Khiewvan B, Sirinvaravong S, Sin YL, Muhammad R, Jap TS, Agrawal A, Rajput R, Fernando R, Sumanatilleke M, Suastika K, Shong YK, Lang B, Bartalena L, Yang SP; Asian Graves Consortium Study (2023) 2021 Asia-Pacific Graves' Disease Consortium Survey of Clinical Practice Patterns in the Management of Graves' Disease. Endocrine 79(1):135–142
- Beshyah SA, Khalil AB, Sherif IH, Benbarka MM, Raza SA, Hussein W, Alzahrani AS, Chadli A (2017) A survey of clinical practice patterns in management of Graves disease in the Middle East and North Africa. Endocr Pract 23:299–308
- Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, Grobman WA, Laurberg P, Lazarus JH, Mandel SJ, Peeters RP, Sullivan S (2017) 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. Thyroid 27:315–389
- Elsherbiny TM (2023) Characterization, treatment preferences, and outcomes of 390 Egyptian Graves' disease patients: a retrospective study. Egypt J Intern Med 35:57
- Cooper DS (2021) Long-term antithyroid drug therapy. Curr Opin Endocrinol Diabetes Obes 28:510–516
- Azizi F, Abdi H, Amouzegar A (2021) Control of Graves' hyperthyroidism with very long-term methimazole treatment: a clinical trial. BMC Endocr Disord 21:16
- Chung JH (2021) Antithyroid Drug Treatment in Graves' Disease. Endocrinol Metab (Seoul) 36:491–499

- Ponto KA, Zang S, Kahaly GJ (2010) The tale of radioiodine and Graves' orbitopathy. Thyroid 20:785–793
- Bartalena L, Kahaly GJ, Baldeschi L, Dayan CM, Eckstein A, Marcocci C, Marinò M, Vaidya B, Wiersinga WM, EUGOGO, (2021) The 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy. Eur J Endocrinol 185:G43–G67

## **Publisher's Note**

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.