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RESEARCH

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Real-world derived weight-based levothyroxine doses to achieve optimal thyrotropin target in different degrees of autoimmune hypothyroidism

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Abstract

Purpose All patients with overt and severe subclinical hypothyroidism (SCH), and some with mild SCH require levothyroxine (L-T4) therapy. The present study aims to report real-world derived weight-based L-T4 doses to achieve optimal–low normal–thyrotropin target in different degrees of autoimmune hypothyroidism.

Methods This was a retrospective study of patients with autoimmune hypothyroidism. Inclusion criteria were consistent achievement of optimal TSH target (0.3 to 2.5 μIU/L) using a stable L-T4 dose for at least 6 months. Patients were classified into 4 groups: group 1; mild SCH, group 2; severe SCH, group 3; overt hypothyroidism, and group 4; hypothyroidism with unknown initial TSH and free T4. Weight-based L-T4 doses were calculated for each group.

Results Eighty-seven, 95, 75, and 91 patients met the inclusion criteria for groups 1–4, respectively. Weight-based L-T4 dose was the lowest in group 1 (1 ± 0.25 μg/kg/day), was the highest in group 3 (1.4 ± 0.29 μg/kg/day), while in groups 2 (1.2 ± 0.26 μg/kg/day), and 4 (1.2 ± 0.31 μg/kg/day) were not statistically different from each other. There was a significant decrease in weight-based L-T4 dose with increasing body weight categories in groups 1 and 2, and a significant difference between those less than 60 or ≥ 60 years of age in group 3.

Conclusion Real-world derived weight-based L-T4 doses to achieve optimal TSH target are 1, 1.2, and 1.4 μg/kg/day for patients with mild, severe SCH, and overt autoimmune hypothyroidism, respectively. Age and body weight subcategories can better fine-tune required doses.

Keywords Levothyroxine, Hashimoto thyroiditis, Autoimmune hypothyroidism, Subclinical hypothyroidism, Overt hypothyroidism

Background

Chronic autoimmune or Hashimoto thyroiditis is the most common cause of hypothyroidism. All patients diagnosed with overt hypothyroidism, as well as patients with subclinical hypothyroidism with severely increased thyrotropin—thyrotropin (TSH) of 10 μIU/L or greater—should be treated using levothyroxine (L-T4), due to increased cardiovascular morbidity and mortality. For patients with subclinical hypothyroidism with mildly increased TSH–TSH less than 10 μIU/L—some patients may benefit from treatment in cases requiring fertility or patients with high risk of progression to overt hypothyroidism [1–4].

For initiation of L-T4, several parameters have been used including age, thyrotropin at the time of diagnosis, physiological state of the patient, and body weight.

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However, weight-based L-T4 dose determination has been recommended by both the American and European thyroid associations for L-T4 initiation. Race, ethnicity (African Americans versus Caucasians), and obesity (obese versus non-obese) may influence weight-based L-T4 dose determination [1, 5–10].

Thyrotropin of less than 2.5 μIU/L was suggested as a more appropriate therapeutic target in hypothyroid patients requiring L-T4 because most healthy subjects have a TSH of less than 2.5 μIU/L [8]. In hypothyroid patients on L-T4 treatment, TSH of less than 2.5 μIU/l was considered optimal to rule out depression in this high-risk group [11]. A preconception TSH of less than 2.5 μIU/L was associated with better pregnancy outcomes compared to higher values [12].

Both the European Thyroid Association (ETA) and the Italian Association of Clinical Endocrinologists recommend L-T4 dose titration to target TSH of less than 2.5 μIU/L and less than 3 μIU/L respectively in young hypothyroid patients [5, 13].

The present study aims to provide a guide for weight-based L-T4 dosing to achieve the optimal TSH target of 0.3–2.5 μIU/L in different degrees—mild and severe subclinical, and overt—of autoimmune hypothyroidism.

Methods

This was a retrospective study of patients attending the endocrinology outpatient clinic, at Alexandria Faculty of Medicine, Alexandria University, Egypt. The medical records of all patients who received a diagnosis of autoimmune hypothyroidism were reviewed. All autoimmune hypothyroidism patients attending the clinic in the period from January 2022 to June 2023 were included in the review.

The inclusion criteria were Hashimoto thyroiditis as evidenced by positive thyroperoxidase (TPO) and/or thyroglobulin (Tg) autoantibodies and/or sonographic evidence of autoimmune thyroid disease namely hypoechogenicity or coarse echotexture. Consistent achievement of optimal TSH target of 0.3 to 2.5 μIU/L using a stable L-T4 dose for at least 6 months. Exclusion criteria included pregnancy, patients with thyroid cancer requiring TSH suppression, liver cirrhosis, chronic kidney disease, and acute illness within 2–3 months to avoid non-thyroidal illness syndrome.

Patients were classified according to degrees of hypothyroidism into 4 groups. Group 1: mild subclinical hypothyroidism (mSCH) when initial TSH is elevated but less than 10 μIU/L and free T4 is normal. Group 2: severe subclinical hypothyroidism (sSCH) when initial TSH is elevated ≥ 10 μIU/L and free T4 is normal. Group 3: overt hypothyroidism (OH) when initial TSH is elevated and free T4 is low. Group 4: hypothyroidism unknown (HU) when initial TSH and free T4 were not available (Roche Diagnostics, Mannheim, Germany on Cobas E 411 analyzer [normal 0.27–4.2 μIU/L]).

Demographic data including sex and age of the patient at the time of review. TSH at inclusion was calculated by averaging the last 2 or 3 TSH readings from the last 2 or 3 documented visits covering a minimum of 6 months or more. The duration of achieving target TSH was reviewed. The average body weight of included patients was calculated using the patient's body weight from the last 2 or 3 documented visits while achieving the target TSH. Weight-based L-T4 doses were calculated by dividing the patient's daily L-T4 doses by the patient's body weight and expressed as μg/kg/day.

The protocol of the study was approved by the ethical committee of Alexandria Faculty of Medicine [IRB number 12098], on November 2023, serial number 0306375.

Statistical analysis

Data was fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Categorical data were represented as numbers and percentages. The chi-square test was applied to investigate the association between the categorical variables. Alternatively, Fisher's exact correction or Monte Carlo correction test was applied when more than 20% of the cells were expected to count less than 5. For continuous data, they were tested for normality by the Kolmogorov–Smirnov test. Quantitative data were expressed as a range (minimum and maximum), mean, standard deviation, and median one-way ANOVA test was used for comparing the four studied groups, while the Mann–Whitney test for abnormally distributed quantitative variables, to compare between two studied groups. The Kruskal–Wallis test was used to compare different groups for not normally distributed quantitative variables and followed by a post hoc test (Dunn's for multiple comparisons test) for pairwise comparison. Spearman coefficient was used to correlate between quantitative variables. The significance of the obtained results was judged at the 5% level.

Results

Three hundred forty-eight patients met the inclusion criteria and were classified as follows: group 1 (mSCH) 87 patients, group 2 (sSCH) 95 patients, group 3 (OH) 75 patients, and group 4 (HU) 91 patients. Most of the patients in the four groups were females, 98.9%, 95.8%, 90.7%, and 97.8% respectively, with no significant difference between the four groups. The mean age of the patients in group 4 (49.5 ± 13.5 years) was significantly higher compared to group 1 (41.1 ± 11.1 years), and group 2 (43.5 ± 14.6 years), but not significantly different compared to group 3 (45.6 ± 15.4 years). The mean body

weight was not significantly different between the four groups (Table 1).

TSH at inclusion was significantly lower in group 3 (1.2 ± 0.50 µIU/L) compared to group 1 (1.5 ± 0.51 µIU/L), and group 2 (1.5 ± 0.49 µIU/L), but not significantly different compared to group 4 (1.4 ± 0.50 µIU/L). Daily L-T4 dose was the lowest in group 1: mSCH (83.4 ± 24.6 µg/day) and significantly lower compared to all three other groups. Daily L-T4 dose was the highest in group 3: OH (116.1 ± 31.7 µg/day) and significantly higher compared to all three other groups. Daily L-T4 doses in groups 2: sSCH (97.7 ± 24.7 µg/day), and group 4: HU (106.5 ± 32.1 µg/day) were not statistically different from each other (Table 2).

Weight-based L-T4 dose was the lowest in group 1: mSCH (1 ± 0.25 µg/kg/day) and significantly lower compared to all three other groups. Weight-based L-T4 dose was the highest in group 3: OH (1.4 ± 0.29 µg/kg/day) and significantly higher compared to all three other groups. Weight-based L-T4 doses in groups 2: sSCH (1.2 ± 0.26 µg/kg/day), and group 4: HU (1.2 ± 0.31 µg/kg/day) were not statistically different from each other. The mean duration during which the patients maintained the reported L-T4 dose—27.3, 25.8, 27.1, and 25.9 months for groups 1, 2, 3, and 4 respectively—did not differ significantly between the 4 studied groups (Table 2).

There was a strong positive correlation between body weight and daily L-T4 dose in all 4 studied groups, while age did not correlate with daily L-T4 dose in any of the studied groups. However, age significantly and negatively correlated with weight-based L-T4 dose only in group 3: OH [spearman coefficient – 0.296, $p = 0.010$] (Table 3, Fig. 1).

When patients were classified according to their body weight into 3 subcategories: less than 70 kg, between 70–100 kg and greater than 100 kg, there was a statistically significant difference between the three weight subcategories regarding weight-based L-T4 doses in groups 1 and 2. Weight-based L-T4 doses in group 1 were 1.14 ± 0.26 µg/kg/day, 0.97 ± 0.19 µg/kg/day, and 0.93 ± 0.32 µg/kg/day for body weight subcategories < 70 kg, 70–100 kg, and > 100 kg, respectively [$p = 0.024$]. Weight-based L-T4 doses in group 2 were (1.29 ± 0.27 µg/kg/day), (1.17 ± 0.26 µg/kg/day),

Table 1 Comparison between the different studied groups according to demographic data

Demographic data	Group 1 ($n = 87$)	Group 2 ($n = 95$)	Group 3 ($n = 75$)	Group 4 ($n = 91$)	Test of Sig	*p*
Sex						
Female	86 (98.9%)	91 (95.8%)	68 (90.7%)	89 (97.8%)	$\chi^2 = 6.871$	$^{MC}p = 0.064$
Male	1 (1.1%)	4 (4.2%)	7 (9.3%)	2 (2.2%)		
Age (years)						
< 60	79 (90.8%)	79 (83.2%)	56 (74.7%)	65 (71.4%)	$\chi^2 = 12.526^*$	0.006^*
≥ 60	8 (9.2%)	16 (16.8%)	19 (25.3%)	26 (28.6%)		
Mean ± SD	41.1 ± 11.1	43.5 ± 14.6	45.6 ± 15.4	49.5 ± 13.5	$F = 6.073^*$	$< 0.001^*$
Median (min.–max.)	38 (17–71)	41 (14–76)	43 (18–82)	50 (20–77)		
Sig. bet. grps	$p_1 = 0.638$, $p_2 = 0.154$, $p_3 < 0.001^*$, $p_4 = 0.744$, $p_5 = 0.016^*$, $p_6 = 0.269$					
Body weight (kg)						
< 70	22 (25.3%)	17 (17.9%)	18 (24%)	15 (16.5%)	$\chi^2 = 3.566$	0.735
70–100	48 (55.2%)	59 (62.1%)	45 (60%)	59 (64.8%)		
> 100	17 (19.5%)	19 (20%)	12 (16%)	17 (18.7%)		
Mean ± SD	84.5 ± 19	85 ± 18.1	83.7 ± 18.9	87.3 ± 17.9	$F = 0.620$	0.603
Median (min.–max.)	82 (51.7–161.7)	81.7 (53.7–151)	82 (36–146.5)	86.7 (52.7–134)		

Group 1 mild subclinical hypothyroidism, *Group 2* severe subclinical hypothyroidism, *Group 3* overt hypothyroidism, *Group 4* hypothyroidism unknown

SD standard deviation, *F F* for one-way ANOVA test, χ^2 chi-square test, *MC* Monte Carlo, *H H* for Kruskal–Wallis test, pairwise comparison between each 2 groups was done using post hoc test (Dunn's for multiple comparisons test)

p p value for comparing between the studied groups

p_1 *p* value for comparing between Group 1 and Group 2

p_2: *p* value for comparing between Group 1 and Group 3

p_3: *p* value for comparing between Group 1 and Group 4

p_4: *p* value for comparing between Group 2 and Group 3

p_5: *p* value for comparing between Group 2 and Group 4

p_6: *p* value for comparing between Group 3 and Group 4

* Statistically significant at $p \leq 0.05$

Table 2 Comparison between the different studied groups according to different parameters

	Group 1 (*n* = 87)	Group 2 (*n* = 95)	Group 3 (*n* = 75)	Group 4 (*n* = 91)	*p*
TSH					
Mean ± SD	1.5 ± 0.51	1.5 ± 0.49	1.2 ± 0.50	1.4 ± 0.50	0.001*
Median (min.–max.)	1.5 (0.41–2.5)	1.5 (0.36–2.4)	1.1 (0.37–2.3)	1.5 (0.32–2.5)	
Sig. bet. grps	$p_1 = 0.686$, $p_2 < 0.001^*$, $p_3 = 0.051$, $p_4 = 0.001^*$, $p_5 = 0.113$, $p_6 = 0.063$				
Daily levothyroxine dose					
Mean ± SD	83.4 ± 24.6	97.7 ± 24.7	116.1 ± 31.7	106.5 ± 32.1	< 0.001*
Median (min.–max.)	78 (50–165)	100 (50–200)	114 (43–250)	100 (53–215)	
Sig. bet. grps	$p_1 < 0.001^*$, $p_2 < 0.001^*$, $p_3 < 0.001^*$, $p_4 < 0.001^*$, $p_5 = 0.162$, $p_6 = 0.010^*$				
L-T4 dose (μg/kg/day)					
Mean ± SD	1 ± 0.25	1.2 ± 0.26	1.4 ± 0.29	1.2 ± 0.31	< 0.001*
Median (min.–max.)	0.99 (0.48–1.7)	1.1 (0.68–2.2)	1.4 (0.61–2.5)	1.2 (0.60–1.3)	
Sig. bet. grps	$p_1 < 0.001^*$, $p_2 < 0.001^*$, $p_3 < 0.001^*$, $p_4 < 0.001^*$, $p_5 = 0.150$, $p_6 < 0.001^*$				
Duration of reported dose (months)					
Mean ± SD	27.3 ± 19.8	25.8 ± 17.7	27.1 ± 18.3	25.9 ± 17.8	0.949
Median (min.–max.)	20 (6–95)	22 (6–75)	23 (6–96)	21 (6–90)	

Group 1 mild subclinical hypothyroidism, *Group 2* severe subclinical hypothyroidism, *Group 3* overt hypothyroidism, *Group 4* hypothyroidism unknown

SD standard deviation

p: *p* value for comparing between the studied groups

p_1: *p* value for comparing between Group 1 and Group 2

p_2: *p* value for comparing between Group 1 and Group 3

p_3: *p* value for comparing between Group 1 and Group 4

p_4: *p* value for comparing between Group 2 and Group 3

p_5: *p* value for comparing between Group 2 and Group 4

p_6: *p* value for comparing between Group 3 and Group 4

* Statistically significant at $p \leq 0.05$

Table 3 Correlation between levothyroxine dose with age and body weight in each group

		Levothyroxine dose			
		Group 1 (*n* = 87)	Group 2 (*n* = 95)	Group 3 (*n* = 75)	Group 4 (*n* = 91)
Age (years)	r_s	0.040	0.188	−0.064	−0.011
	p	0.710	0.068	0.584	0.918
Body weight (kg)	r_s	0.426*	0.521*	0.744*	0.538*
	p	< 0.001*	< 0.001*	< 0.001*	< 0.001*

Group 1 mild subclinical hypothyroidism, *Group 2* severe subclinical hypothyroidism, *Group 3* overt hypothyroidism, *Group 4* hypothyroidism unknown

r_s Spearman coefficient

* Statistically significant at $p \leq 0.05$

and (1.03 ± 0.21 μg/kg/day) for body weight subcategories < 70 kg, 70–100 kg, and > 100 kg, respectively [$p = 0.004$] (Table 4).

In group 3: OH, when patients were classified according to their age into less than 60 years of age or 60 years of age or older, weight-based L-T4 dose was significantly higher in patients less than 60 years of age (1.45 ± 0.31 μg/kg/day) compared to patients 60 years of age or older (1.27 ± 0.18 μg/kg/day) [$p = 0.030$]. (Table 5).

Discussion

The present study is the first to provide a real-world derived weight-based levothyroxine dosing scheme to achieve optimal—low normal—TSH target of 0.3–2.5 μIU/L in patients with autoimmune thyroiditis with different degrees of hypothyroidism, who represents the majority of patients with hypothyroidism. For patients with mild SCH, severe SCH, and overt autoimmune hypothyroidism, the dosing would be 1, 1.2, and 1.4 μg/kg/day respectively. For patients with mild SCH and severe SCH, differences exist according to body weight subcategories: < 70 kg, 70–100 kg, and > 100 kg. For mSCH it would be 1.14, 0.97, and 0.93 μg/kg/day, respectively, and for sSCH it would be 1.29, 1.17, and 1.03 μg/kg/day, respectively. For overt autoimmune hypothyroidism, age plays a role where patients < 60 years of age should receive 1.45 μg/kg/day, while patients ≥ 60 years of age should receive 1.27 μg/kg/day. In patients whose records are lacking initial thyroid function tests, an

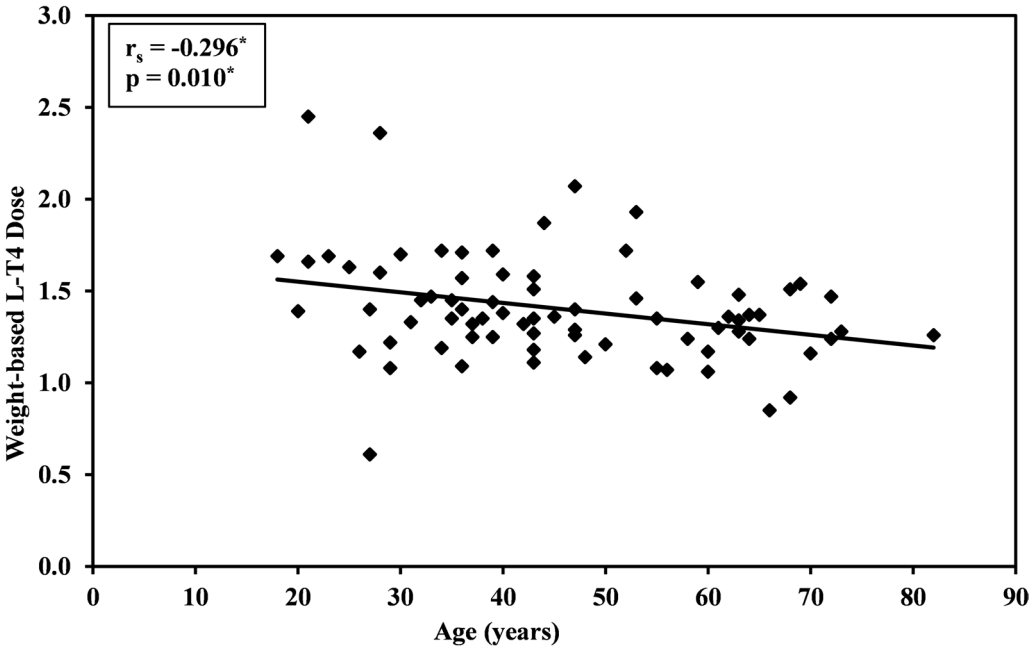

Fig. 1 Correlation between age and weight-based levothyroxine dose in group 3: overt hypothyroidism

optimal target is expected to be achieved using 1.2 μg/kg/day.

In the present study, patients with overt autoimmune hypothyroidism achieved optimal TSH target using a dose of 1.4 μg/kg/day of actual body weight. This dose is lower than the one recommended by the American Thyroid Association (ATA)—1.6–1.8 μg/kg/day—most probably due to the environmental and racial characteristics of our included patients [1].

Similarly, Southeast Asians seem to have lower L-T4 requirements to achieve euthyroidism compared to those recommended by the ATA. In two studies, one from Pakistan and the other from Singapore—including patients with a diagnosis of primary hypothyroidism—L-T4 requirements to achieve euthyroidism were 1.4 and 1.1 μg/kg/day respectively [9, 14]. Environmental and racial differences may account for different requirements. In both studies, the initial degree of hypothyroidism and the percentage of each degree was not reported.

Apart from racial and ethnic factors which may have contributed to different L-T4 requirements in the present study compared to those recommended by the ATA, a number of environmental factors may also have a role in affecting levels of TSH and thyroid hormones. These factors can be classified into either lifestyle factors or environmental pollutants. Lifestyle factors include smoking status, diet (including goitrogenic foods, Junk Food, beverages like tea and coffee, and micronutrients like vitamin D or selenium), and physical exercise. Pollutants include chemicals (including pesticides, polychlorinated and polybrominated biphenyls, or Bisphenol A), or heavy metals (including arsenic, lead, and mercury) [15]. The exact effect of these factors on current patients cannot be properly evaluated given the retrospective nature of the study.

In the present study, patients with mild and severe subclinical autoimmune hypothyroidism achieved optimal TSH target using doses of 1 and 1.2 μg/kg/day of actual body weight respectively. These doses are also lower than the one recommended by the European Thyroid Association (ETA), that is 1.5 μg/kg/day of actual body weight [5].

In a randomized controlled trial of 36 patients with mild SCH, the mean L-T4 dose required to achieve a target TSH of 0.5–1.5 μIU/L was 110 μg/day [16]. However, by the end of this study, 10 patients (28%) were actually over-replaced, which may explain why their dose is higher than the L-T4 dose required to achieve a target TSH of 0.3–2.5 μIU/L in the present study, in a similar group of patients with mild SCH, which was 83.4 μg/day.

In another randomized controlled trial of 18 patients with both mild and severe SCH, the mean L-T4 dose required to achieve a target TSH of 0.5–5.5 μIU/L was 68 μg/day [17]. The higher TSH target used in this study may explain why their patients required a lower dose compared to the doses required by our patients with mild and severe SCH which were 83.4 μg/day for mSCH and 97.7 μg/day for sSCH.

Table 4 Relation between body weight subcategories and daily Levothyroxine dose and weight-based L-T4 dose in each group

		Body weight (kg)			*p*
		< 70	**70–100**	**> 100**	
Group 1 (*n* = 87)	Daily L-T4 dose	(*n* = 22)	(*n* = 48)	(*n* = 17)	
	Mean ± SD	70.86 ± 17.53	81.98 ± 16.73	103.6 ± 36.86	0.002*
	Median (min.–max.)	67.50 (50.0 114.0)	85.0 (50.0–128.0)	100.0 (50.0–165.0)	
	L-T4 dose (µg/kg/day)	(*n* = 22)	(*n* = 48)	(*n* = 17)	
	Mean ± SD	1.14 ± 0.26	0.97 ± 0.19	0.93 ± 0.32	0.024*
	Median (min.–max.)	1.09 (0.77–1.71)	0.98 (0.52–1.36)	0.86 (0.48–1.58)	
Group 2 (*n* = 95)	Daily L-T4 dose	(*n* = 17)	(*n* = 59)	(*n* = 19)	
	Mean ± SD	79.65 ± 18.40	96.80 ± 20.82	116.5 ± 28.42	< 0.001*
	Median (min.–max.)	75.0 (50.00–107.0)	100.0 (50.00–171.0)	112.5 (85.00–200.0)	
	L-T4 dose (µg/kg/day)	(*n* = 17)	(*n* = 59)	(*n* = 19)	
	Mean ± SD	1.29 ± 0.27	1.17 ± 0.26	1.03 ± 0.21	0.004*
	Median (min.–max.)	1.32 (0.82–1.76)	1.13 (0.68–2.19)	0.98 (0.74–1.58)	
Group 3 (*n* = 75)	Daily L-T4 dose	(*n* = 18)	(*n* = 45)	(*n* = 12)	
	Mean ± SD	87.81 ± 15.78	118.8 ± 24.68	148.6 ± 38.16	< 0.001*
	Median (Min.–Max.)	89.0 (57.0–114.0)	114.0 (43.0–185.0)	139.0 (114.0–250.0)	
	L-T4 dose (µg/kg/day)	(*n* = 18)	(*n* = 45)	(*n* = 12)	
	Mean ± SD	1.44 ± 0.33	1.42 ± 0.29	1.30 ± 0.27	0.091
	Median (Min.–max.)	1.40 (0.85–2.36)	1.37 (0.61–2.45)	1.25 (1.08–2.07)	
Group 4 (*n* = 91)	Daily L-T4 dose	(*n* = 15)	(*n* = 59)	(*n* = 17)	
	Mean ± SD	87.67 ± 17.25	102.2 ± 27.09	138.2 ± 37.56	< 0.001*
	Median (Min.–max.)	85.0 (64.0–121.0)	100.0 (53.0–200.0)	143.0 (71.0–215.0)	
	L-T4 dose (µg/kg/day)	(*n* = 15)	(*n* = 59)	(*n* = 17)	
	Mean ± SD	1.43 ± 0.35	1.19 ± 0.29	1.20 ± 0.31	0.072
	Median (Min.–max.)	1.32 (1.05–2.14)	1.14 (0.60–2.27)	1.17 (0.71–1.83)	

SD standard deviation

p p value for comparing between the different body weight subcategories

* Statistically significant at $p \leq 0.05$

Table 5 Relation between age and daily Levothyroxine dose and weight-based L-T4 dose in group 3: Overt hypothyroidism

Group 3: OH (*n* = 75)	**Age (years)**		*p*
	< 60 (*n* = 56)	**≥ 60 (*n* = 19)**	
Daily L-T4 dose			
Mean ± SD	120.0 ± 33.73	104.8 ± 21.89	0.108
Median (min.–max.)	114.0 (43.0–250.0)	107.0 (57.0–143.0)	
L-T4 dose (µg/kg/day)			
Mean ± SD	1.45 ± 0.31	1.27 ± 0.18	0.030*
Median (min.–max.)	1.40 (0.61–2.45)	1.28 (0.85–1.54)	

SD standard deviation

p p value for comparing between patients < 60 and ≥ 60 years of age

* Statistically significant at $p \leq 0.05$

In a retrospective study of 200 patients with hypothyroidism—one-third of whom had autoimmune hypothyroidism—actual body weight was strongly and negatively correlated to weight-based L-T4 dose in both univariate and multivariate analysis [10]. In the present study, there was a significant decrease in weight-based L-T4 dose with increasing actual body weight categories, but only in patients with mild and severe SCH.

In another retrospective study of 504 patients with hypothyroidism, there was a significant decrease in weight-based L-T4 dose with increasing actual body weight categories [14]. In the present study, body weight categories may further guide weight-based L-T4 dosing

as follows: 1.14, 0.97, and 0.93 μg/kg/day for weight subcategories < 70 kg, 70–100 kg, and > 100 kg, respectively for mSCH, and 1.29, 1.17, and 1.03 μg/kg/day for weight subcategories < 70 kg, 70–100 kg, and > 100 kg, respectively for sSCH.

In a retrospective study of 586 patients with hypothyroidism—one-third of whom had autoimmune hypothyroidism—weight-based L-T4 dose showed no significant difference between different age groups in the whole group. However, only patients with autoimmune hypothyroidism showed a significant negative correlation between age and daily L-T4 dose, and L-T4 dose was significantly higher in patients younger than 45 years of age compared to patients of 45 years of age or older [18].

In the present study, a significant and negative correlation between age and weight-based L-T4 dose was present only in patients with overt hypothyroidism. There was a significant difference in the weight-based L-T4 dose required to achieve target TSH in the OH group between those less than 60 years of age and 60 years of age or older. Thus, age may further guide weight-based L-T4 dosing in OH as follows: 1.45 μg/kg/day in patients less than 60 years of age compared to 1.27 μg/kg/day in patients 60 years of age or older.

A difference in L-T4 requirements in hypothyroid elderly patients compared to younger hypothyroid patients was previously demonstrated in hypothyroid patients in general [19], in hypothyroid men [20], and in hypothyroid women [21]. These differences were explained on the basis of an age-related decrease in thyroid hormone clearance, a decrease in lean body mass, or hormonal differences between pre- and post-menopausal women. Other factors may be age-related comorbidities, polypharmacy commonly encountered in the elderly, and compliance issues [22].

The limitations of the present study include the retrospective nature of the study, lack of assessment—by a validated questionnaire—of adherence to L-T4, and the fact that the patients used more than one L-T4 brand/generic which may cause performance variabilities. Comorbidity and possible drug interactions are known determinants of L-T4 dose which were not studied in the present study. The major strength of the present study is that the suggested weight-based doses are based on real-world practice, and so it is achievable. The present study is the first to propose weight-based doses for both grades of subclinical hypothyroidism, mild and severe SCH.

In conclusion, the present study provides a real-world-driven algorithm for weight-based L-T4 dosing for different degrees of autoimmune hypothyroidism to achieve optimal TSH targets. 1, 1.2, and 1.4 μg/kg/day for patients with mild SCH, severe SCH, and overt autoimmune hypothyroidism, respectively. In both mild and severe SCH, body weight subcategories can further fine-tune the required doses. In overt hypothyroidism, age subcategories can help better determine the required doses.

Abbreviations

L-T4	Levothyroxine
TSH	Thyroid-stimulating hormone or thyrotropin
ETA	European Thyroid Association
mSCH	Mild subclinical hypothyroidism
sSCH	Severe subclinical hypothyroidism
OH	Overt hypothyroidism
HU	Hypothyroidism unknown
ATA	American Thyroid Association

Author's contributions

The author contributed to the study conception, design, material preparation, data collection, and writing the manuscript. The author read and approved the final manuscript.

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Availability of data and materials

The datasets generated during and/or analyzed 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. Approval was obtained from the ethics committee of Alexandria Faculty of Medicine, [IRB number 12098] on November 2023, serial number 0306375.

Competing interests

The author declares no competing interests.

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