Flaws of universal salt iodization programmes in nutrition transition contexts: is there a risk of a double burden of inadequate iodine intake and excess adiposity? A case study in Tunisia

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Abstract

Background In the Middle East and North Africa (MENA) region, universal salt iodization (USI) programs defaults were sometimes shown to increase the risk of iodine excess. Also, the nutrition transition which underlies the obesity epidemic in the MENA region is characterized by salt-rich diets, so that there could be a cumulative effect with respect to iodine status. We assess the within-subject co-existence of overweight and inadequate iodine intake, and associated factors.

Methods A national cross-sectional study used a stratified, clustered random sample and conducted among Tunisian school-age children aged from 6 to 12 y. (n = 1560). Overweight (Ow) was body mass index (BMI)-for-age ≥ + 1z. Iodine deficiency was UIC (Urinary Iodine Content) < 100 µg/L and iodine intake above requirements (IAR) UIC ≥ 200 µg/L. Association of covariables with the within-subject double burden Ow–IAR was assessed by multinomial regression.

Results The prevalences of Ow-ID or Obe-ID were marginal, but not so for excess adiposity and IAR as for example prevalence of Ow-IAR was 9.8% (95% CI: [7.7–12.3]). OW and IAR were found to co-occur independently (P = 0.29). Socio-economic patterning of Ow-IAR was mild. Nevertheless, prevalence were the lowest among children of mother with no formal schooling and in the South-East region. Beyond school-age children, we estimated that this double burden of overweight and excess iodine could concern a third of Tunisian adults (all the more for women).

Conclusions Among Tunisian children, iodine deficiency coupled with excess adiposity was quite marginal. Coexistence of overweight and excess iodine may affect a tenth of these children. More data would be needed to document a possibly even higher rate among adults. Cumulative effects of unhealthy lifestyle due to the nutrition transition interacting with metabolic pathways may be involved in this potential overweight-high iodine intake double burden. In the MENA region, obesity and salt reduction policies should continue to be monitored.

Introduction

Overweight and obesity are nowadays a major global public health problem as more than 1.9 billion adults were overweight and 650 million obese in 2016 worldwide [1]. In the framework of the epidemiological and nutrition transition, overweight, obesity and associated non-communicable diseases have increased especially rapidly in the low- and middle-income countries (LMICs), including the Middle East and North Africa (MENA) region where the prevalence of obesity and diabetes are among the highest worldwide [2]. Nevertheless, the rapid changes in lifestyles underlying the nutrition transition, including towards westernized and more energy rich diets have not always been exclusive of the persistence of micronutrient deficiencies [3]. This has resulted in some contexts, in a double burden of malnutrition resulting from the co-existence of excess adiposity and/or associated Noncommunicable diseases (NCDs) and undernutrition phenomena partly linked to micronutrient deficiencies, e.g. as documented for iron deficiency and anaemia [4–6].

As for micronutrient deficiencies, iodine deficiency (ID) is one of the most prevalent in the world at the rate of 27.8% or two billion of people in the general population [7]. In order to tackle ID, a number of countries, including the MENA region, have adopted universal salt iodization (USI) programme [7]. This USI programme achieved some success in reducing ID, in certain contexts ([8]), but defaults in the process of salt iodization, were also sometimes shown to increase the risk of iodine excess (IE) [7, 9]. Also, in the context of the nutrition transition, the salt-rich westernized diet which underlies the progression of excess adiposity in LMICs, could result in a cumulative effect with respect to iodine status [10]. Beyond, at the metabolic level, it also has been documented that iodine disturbances with consequences on thyroid function (hyfonction), can occur among obese subjects [11–13]. Although the links are not completely elucidated [14], it is possible that this association may be complicated in the framework of inadequate iodine status either deficiency or excess. In such nutrition transition context, it seems of interest to address the issue of the double burden of excess adiposity and iodine inadequate status. Double burden of over and under nutrition can arise from their co-occurrence at different aggregated levels, i.e. in different sub-populations in the same geographical area, or among different members within the same households [15]. But it is all the more an issue when both adverse conditions co-occur within the same subjects [4, 5]. Without strong hypotheses pertaining to independent co-occurrence of both conditions in the same subjects, assessing such a within-subject double burden necessitates all the relevant data on the same individuals. From a practical point of view, the monitoring of USI programme is mostly based on survey pertaining to 6–12 y., school-age children which is the internationally recommended target age class for the assessment of iodine status in populations [16]. Yet, this age class has not been spared from the worldwide progression of overweight and obesity, including the MENA region [14].

Tunisia is a typical MENA country undergoing the nutrition transition, featuring high prevalences of overweight and obesity including among children [17]. Also, a national survey among 6–12 y. to monitor the USI programme launched in 1995, documented that if only one in ten children featured ID, more than half were at risk of iodine excess [18].

Based on this national sample of 6–12 y. children in Tunisia, the objectives of the study were then to assess: - the magnitude of the within-subject co-occurrence of excess adiposity and inadequate iodine status, - the nature of that co-occurrence (independent, synergetic or antagonistic), - and the association with socio-demographic factors.

Methods

Study area

Tunisia is a North African country, located between Algeria at west and Libya at east, with about eleven million inhabitants of which two thirds are urban. It is ranked 95th out of 189 countries (i.e. at the lower end of the high development group of countries), according to the Human Development Index [19]. The level of economic development is much higher in the northern and eastern coastal regions, than in the mountainous western inland parts, especially the north- and central-west regions, or the mainly desert south-west. Due to the epidemiological and nutrition transition it has experienced in the last decades, Tunisia features high prevalences of overweight and obesity (especially among women) as well as related non-communicable diseases such as diabetes and hypertension [4, 5, 20, 21]. As for control of iodine deficiency, mandatory salt iodization had been implemented in specific areas since 1984, but the national USI program was adopted in 1995 and launched in 1996 [18, 22]. Its evaluation in 2012 showed some success regarding control of iodine deficiency, but also a high proportion of excess iodine intake, partly in relation with defaults in the salt iodization process and its monitoring [22].

Participants

The present study is a based on a secondary analysis of data collected in a previously documented national cross-sectional survey conducted in Tunisia between May and June 2012: 6–12 y. school-children (n = 1560) were surveyed using a random, stratified, clustered sample [18].

Measurements

Anthropometry

Anthropometric assessment was performed according to the World Health Organization (WHO) standards [23]. Height was measured using a wall-mounted stadiometer (Person-check®, Kirchner and Wilhelm, Germany) with a precision of 0.1 cm. Weight was measured using a calibrated scale (Detecto, Webb City, MO, USA. BMI (Body Mass Index = weight/height^2) for-age in z-scores was computed from the WHO reference for school-age children. Thinness was defined as BMI-for-age < − 2 z-scores, overweight as BMI-for-age ≥ + 1 z and obesity as BMI-for-age ≥ + 2 z.

Iodine status

Urine samples were collected according to standardized procedures [24]. The Sandell-Kholthoff method was used to assess urinary iodine concentration (UIC) [16]. Details related to technique precision and validation were previously published [18]. The WHO cut-offs for assessment of population iodine status based on the median UIC (µg/L) were used to classify school-age children as follow [16, 25]: UIC < 100 defined iodine deficiency (ID), UIC ≥ 200 defined iodine intake above requirements (IAR_{200}) and UIC ≥ 300 defined excess of iodine status(IE_{300}).

Co-occurrence of inadequate iodine and anthropometric status

Nine different co-occurrences were studied: ID and overweight (or obesity or thinness), IAR_{200} and overweight (or obesity or thinness), IE_{300} and overweight (or obesity or thinness), (Table 1).

Table 1
Prevalence of the co-occurrence of inadequate iodine status and thinness or excess adiposity among 6–12 y. Tunisian school children, by sex.

		All (n = 1560)		Co-occurrence of inadequate iodine and BMI status					
		Iodine status	BMI status	**All (n = 1560)**			**Girls (n = 780)**	**Boys (n = 780)**	*P*-Value[d]
		%[a]	%[a]	%[a]	95% CI [b]	P-Value[c]	%[a]	%[a]	
ID[e]	Thinness[f]	11.4	7.0	0.7	0.3–1.3	0.54	0.6	0.7	0.96
	Overweight[f]		18.4	2.5	1.3–4.8	0.48	2.2	2.9	0.46
	Obesity[f]		6.4	1.0	0.5–2.1	0.30	0.6	1.5	0.28
IAR_{200}[e]	Thinness[f]	52.2	7.0	4.1	2.9–5.6	0.63	4.0	4.2	0.87
	Overweight[f]		18.4	9.7	7.7–12.3	0.29	9.1	10.4	0.53
	Obesity[f]		6.4	3.2	2.0–5.5	0.43	3.9	2.4	0.17
IE_{300}[e]	Thinness[f]	25.1	7.0	1.7	1.1–2.4	0.74	1.4	2.0	0.37
	Overweight[f]		18.4	5.0	3.7–6.7	0.32	4.9	5.1	0.89
	Obesity[f]		6.4	1.8	1.1–2.8	0.48	2.2	1.4	0.35

a Weighted percentage

b 95% confidence interval taking into account the complex sampling design.

c Chi-square test of null hypothesis of independence between inadequate iodine status and inadequate BMI status

d Chisquare test for comparaison of % among girls vs. boys.

e ID : Iodine deficiency (UIC < 100 µg/L), IAR_{200} Iodine Above Requirements (UIC ≥ 200 µg/L), IE_{300} Iodine excess (UIC ≥ 300 µg/L).

f Thinness: BMI-for-age <-2 z-score, overweight: BMI-for-age ≥ + 1 z-score, obesity: BMI-for-age ≥ + 2 z-score

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Each double burden was coded as a categorical variable with four categories, e.g. for “iodine intake above requirements (UIC ≥ 200) and overweight”: iodine intake above requirements and overweight($IAR_{200}\&Ow$), iodine intake above requirements and not overweight ($IAR_{200}\&\overline{Ow}$), no iodine intake above requirements and overweight ($\overline{IAR}_{200}\&Ow$), no iodine intake above requirements and no overweight ($\overline{IAR}_{200}\&\overline{Ow}$).

Socio-demographic characteristics

A self-administered questionnaire was used to collect information on the parent’s occupation, instruction level and age.

Statistical analysis

Data management and statistical analyses were carried out with Stata software (version 14·0; StataCorp, College Station, USA). The type I error risk was set at 0·05 for all analyses. All estimates, standard errors, P-values and confidence intervals take into account the complex sampling plan (*svy* prefix in Stata).

Descriptive results are expressed as means for interval variables, and as proportions for categorical variables. For each of the nine combinations of iodine x anthropometric status, the null hypothesis of independence between the iodine and anthropometric status binary variables was assessed using chi-square tests. Associations between the double burdens in four categories and socio-demographic factors were quantified by relative prevalence ratios (RPR) estimated within multinomial logistic regression models using the *mlogit* Stata command [26]: the response reference category was that of both not inadequate iodine and no excess adiposity (e.g. for the “Iodine Above Requirements and Overweight” double burden, this was the $\overline{IAR}_{200}\&\overline{Ow}$ category).This analysis, using double burdens coded as 4 category response variables, enabled to estimate associations with co-variates of single and double burdens from the same model (*v.* the same response reference category i.e. subjects with none). For each covariable (milieu, region, sex, age, mother’s and father’s level of education and professional activity), crude associations were estimated in univariate models featuring one covariate at a time. Adjusted associations were derived from a multivariate model including all covariables.

Descriptive analyses were first performed separately for girls *v.* boys. But as we did not observe meaningful differences, multivariate analyses were ultimately ran and presented for girls and boys together.

Results

Sample characteristics

The population characteristics have been previously published [18]: 1560 school children were included in the study, and their mean age was 9.3 ± 0.04 y. More than 90% of children’s parents had attended at least primary school (94.6% for fathers *vs.* 86.2% for mothers) and 94.3% of fathers but only 25.2% of mothers had a professional activity. Mean weight of the children was 30.4 ± 0.4 kg, mean height 134.3 ± 0.5 cm and mean BMI 16.5 ± 0.1 kg/m² (-0.18 z-scores ± 0.06). Prevalence of thinness was 7.0% (95% CI: 5.6–8.7); 18.4% (95% CI: 15.5–21.7) were overweight and 6.4% (95% CI: 4.8–8.4) were obese (Table 1). Median UIC was 220 µg/L, prevalence of ID was 11.4% (95% CI: 8.6–14.9), while 52.2% (95% CI: 50.1–62.2) had UIC ≥ 200 and 25.1% (95% CI: 19.6–31.4) featured UIC ≥ 300 (Table 1).

Co-occurrence of inadequate iodine and anthropometric status

There was no difference in prevalence between girls and boys, whatever the co-occurrence of inadequate iodine and anthropometric status considered (Table 1). The highest overall prevalence of double burden was observed for the co-occurrence of IAR_{200} & Ow at 9.7% (95%: 7.7–14.3). Also, 5.0% (95%: 3.7–6.7) of the children featured both IE_{300} & Ow. Other types of inadequate iodine and anthropometric status double burdens were rare. Our data did not provide any evidence at the 0.05 alpha level against the null hypothesis of independence between inadequate iodine an anthropometric status, whatever the combination considered (P-value for chi-square tests ranging from 0.29 to 0.74).

Association of the double burden with socio-demographic factors

The reported results are relative only to the study of the iodine intake above requirements (UIC ≥ 200) – overweight double burden due to the low rate of the other forms (Table 2).

Table 2
Multinomial regression: crude or adjusted associations between the categories of the “iodine above requirements (UIC ≥ 200 µg/L) and overweight” double bu
and socio-demographic factors among 6–12 y. Tunisian school children.

		UIC ≥ 200 µg/L & not overweight					UIC < 200 µg/L & overweight					UIC ≥ 200 µg/L & overweight				
		Crude			Adjusted		Crude			Adjusted		Crude			Adjusted	
	n	%[a]	RPR[b]	C.I. [c]	RPR[b]	C.I. [c]	% [a]	RPR[d]	C.I. [c]	RPR[d]	C.I. [c]	% [a]	RPR[e]	C.I. [c]	RPR[e]	C.
Sex			**P[f]=0.001**		**P[f]=0.0011**			P[g]=0.12		**P[g]=0.0.046**			P[h]=0.73		P[h]=0.60	
Boy	780	52.8	1	-	1	-	6.5	1	-	1	-	9.1	1	-	1	-
girl	780	39.6	**0.6**	**0.4–0.8**	**0.6**	**0.4–0.8**	11.0	1.4	0.3-2.0	1.5	1.0-2.2	10.4	0.9	0.5–1.5	0.9	0. 1.
Age (years)			P = 0.41		P = 0.39			P = 0.42		P = 0.21			P = 0.23		P = 0.21	
6–7	441	51.2	1	-	1	-	7.0	1	-	1	-	7.1	1	-	1	-
8–9	537	44.9	0.8	0.6–1.1	0.8	0.6–1.1	9.6	1.3	0.9-2.0	1.5	0.9–2.5	9.3	1.2	0.6–2.4	1.4	0. 2.
10–12	582	44.4	0.9	0.6–1.2	0.8	0.6–1.1	9.0	1.3	0.6–2.7	1.5	0.7–3.1	12.2	1.7	0.8–3.7	1.9	0. 4.
Milieu			P = 0.66		P = 0.96			**P = 0.009**		P = 0.71			**P = 0.007**		P = 0.16	
Urban	858	45.4	1	-	1	-	10.4	1	-	1	-	11.7	1	-	1	-
Rural	702	48.4	0.9	0.4–1.7	1.0	0.6–1.6	5.5	0.4	0.2–0.8	0.9	0.6–1.5	6.2	**0.4**	**0.2–0.8**	0.7	0. 1.
Region			**P < 0.0001**		**P < 0.0001**			**P = 0.026**		P = 0.24			**P < 0.0001**		**P < 0.0001**	
Greater Tunis	240	50.6	1	-	1	-	11.4	1	-	1	-	11.4	1	-	1	-
North East	180	24.3	0.2	0.1–0.6	0.2	0.1–0.6	18.1	0.8	0.5–1.2	1.0	0.6–1.6	5.2	0.2	0.1–0.9	0.3	0. 1.
North West	360	46.8	0.6	0.3–1.3	0.6	0.3–1.4	6.1	0.3	0.2–0.7	0.5	0.2–1.2	7.1	0.4	0.2–0.7	0.6	0. 1.
Centre East	240	40.6	0.5	0.2–1.3	0.5	0.2–1.4	8.5	0.5	0.2–0.9	0.5	0.2–1.2	9.9	0.6	0.2–1.4	0.7	0. 1.
Centre West	180	52.5	0.8	0.3–2.2	0.8	0.3–2.2	3.0	0.2	0.1–0.5	**0.3**	**0.1–0.8**	8.2	0.5	0.2–1.3	0.9	0. 2.
South East	180	67.2	2.5	1.2–5.3	2.7	1.2-6.0	3.0	0.5	0.3–0.8	0.6	0.3–1.2	15.9	2.6	1.8–3.9	**3.6**	**2. 5.**
South West	180	60.5	1.7	0.7–3.7	1.7	0.7–3.8	6.9	0.8	0.3–2.7	0.9	0.3–2.3	13.7	1.7	0.4–7.5	1.9	0. 5.
Education of the father																
			P = 0.88		P = 0.55			**P < 0.0001**		P = 0.31			P = 0.29		P = 0.06	
No formal schooling	92	52.7	1.1	0.5–2.2	1.4	0.7–2.7	1.3	0.1	0.02–0.5	0.3	0.1–1.5	9.9	0.8	0.3–2.3	3.1	1. 8.
Primary schooling	648	47.8	0.9	0.6–1.4	1.1	0.7–1.8	6.0	0.4	0.02–0.5	0.9	0.5–1.5	8.2	0.6	0.3–1.3	1.2	0. 2.
Secondary and more	820	44.9	1	-	1	-	11.4	1	-	1	-	10.9	1	-	1	-
Education of the mother																
			P = 0.17		P = 0.42			**P < 0.0001**		**P = 0.0002**			**P = 0.0002**		**P = 0.0021**	
No formal schooling	236	54.2	1.0	0.6–1.8	1.0	0.7–1.5	3.9	0.2	0.1–0.5	0.5	0.2–1.1	4.6	0.3	0.1–0.5	0.2	0. 0.
Primary schooling	648	47.3	0.8	0.6–1.1	0.8	0.6–1.1	5.1	0.3	0.2–0.4	0.4	0.3–0.6	7.4	0.4	0.3–0.7	0.4	0. 0.
Secondary and more	676	43.6	1	-	1	-	13.0	1	-	1	-	13.1	1	-	1	-
Occupation of the father																

		UIC ≥ 200 µg/L & not overweight					UIC < 200 µg/L & overweight					UIC ≥ 200 µg/L & overweight				
			P = 0.44		P = 0.82			P < 0.0001		P = 0.12			P = 0.31		P = 0.90	
Not working	93	44.9	0.9	0.3–3.3	0.8	0.4-2.0	13.9	0.9	0.3–3.2	1.8	0.5–6.9	7.7	0.6	0.2-2.0	0.9	0. 1.
Worker/employee	1104	46.9	0.8	0.6–1.1	0.9	0.6–1.3	6.8	0.4	0.3–0.6	0.7	0.5–1.1	9.1	0.6	0.3–1.2	0.7	0. 2.
Upper executive employee	363	40.7	0.4	-	1	-	15.6	1	-	1	-	12.5	1	-	1	-
Occupation of the mother																
			P = 0.71		P = 0.63			**P = 0.0007**		P = 0.32			**P = 0.0001**		P = 0.09	
Not working	1234	47.6	0.8	0.5–1.4	0.9	0.6–1.3	7.1	0.3	0.2–0.5	0.9	0.6–1.3	8.9	0.5	0.3–0.7	0.8	0. 1.
Worker/employee	181	43.8	0.9	0.5–1.3	1.1	0.7–1.7	10.3	0.5	0.2–1.1	1.1	0.7–1.7	13.7	0.8	0.4–1.9	1.4	0. 3.
Upper executive employee	145	36.2	1	-	1	-	19.7	1	-	1	-	13.4	1	-	1	-

[a]Weighted percentage (accounting for sampling design, including unequal probabilities of selection).

[b] RPR: for category of cofactor vs. reference category (for which RPR = 1), crude or adjusted Relative Prevalence Ratio of having the double burden of $IAR\&$(vs. $\overline{IAR}\&\overline{Ow}$category (base response category).

[c] Confidence interval at 95% for crude or adjusted RPR.

[d] RPR: for category of cofactor vs. reference category (for which RPR = 1), crude or adjusted Relative Prevalence Ratio of having the double burden of $IAR\&$(vs. $\overline{IAR}\&\overline{Ow}$category (base response category).

[e] RPR: for category of cofactor vs. reference category (for which RPR = 1), crude or adjusted Relative Prevalence Ratio of having the double burden of $\overline{IAR}\&$(vs. $\overline{IAR}\&\overline{Ow}$category (base response category).

[f] Crude or adjusted P-value for association of $IAR\&\overline{Ow}$ with co-factor.

[g] Crude or adjusted P-value for association of $\overline{IAR}\&Ow$ with co-factor.

[h] Crude or adjusted P-value for association of $IAR\&Ow$ with co-factor.

Being a girl (adjusted RPR = 0.6; 95% CI: [0.4–0.8]) or living in the North-East region (adjusted RPR = 0.2; 95% CI: [0.1–0.6]) appears to be a protective factor as regard the occurrence of $IAR_{200}\&\overline{Ow}$ while living in the South-East region (adjusted RPR = 2.7; 95% CI: [1.2-6.0]) appears to be a risk factor. Also, few associations were depicted for the single burden of $\overline{IAR_{200}}\&Ow$: girls were more prone *vs.* boys (adjusted RPR = 1.5; 95% CI: [1.0-2.2]) while subjects in the Centre-West region were less at risk (RPR = 0.3; 95% CI: [0.1–0.8]). No association was found between the co-occurrence of $IAR_{200}\&Ow$, and age or gender. In crude analyses, children living in rural areas, the North-East and the North-West were less prone to $IAR_{200}\&Ow$, however, these association did not stand after adjustment. Children living in the South-Eastern part of the country were more at risk (adjusted RPR = 3.6; 95% CI: [2.5–5.2]). A father with a low level of education increased the risk (adjusted RPR = 3.1; 95% CI: [1.1–8.5]) while the same educational level among mothers appears to be a protective factor (adjusted RPR = 0.2: 95% CI: [0.1–0.5]).

Discussion

In a nutrition transition context, where excess adiposity but also inadequate iodine intake is of concern among children, our original study assessed the prevalence and the associated factors of the different forms of the within-subject double burden of excess of adiposity and inadequate iodine status among Tunisian 6–12 y. children. We showed that the most prevalent form of such a double burden was the co-occurrence of IAR (UIC ≥ 200) with overweight, which concerned one child out of ten. We also underlined that excess adiposity and the different types of inadequate iodine (ID, IAR and IE) status co-occurred independently.

As this study is to our knowledge the first to tackle that issue, comparisons are difficult. This prevalence is coherent with the observed significant prevalences of both iodine intake above requirements (one child out of two) and overweight (two children out of ten). Nevertheless, how the prevalence of the double burden derives from the prevalences of each single burden depends on whether their co-occurrence is synergistic (e.g. the probability of iodine intake above requirements increases if the child is overweight or vice versa), antagonistic (e.g. the probability of iodine intake above requirements decreases if the child is overweight and vice versa) or independent. In the present study, whatever the type of iodine inadequate status (i.e. deficiency or excess), our data were in accordance with the hypothesis of its independent co-existence with overweight. Beyond the observed prevalences, this also is consistent with the observed associations of the excess iodine and overweight double burden with the area of residence and socio-demographic characteristics: indeed in the case of probabilistic independence it can be shown that the measure of associations (RPR) of the double burden $IAR_{200}\&Ow$ with the co-factors should be identical (or at least close) to the product of the RPR for the single burden categories $IAR_{200}\&\overline{Ow}$ and $\overline{IAR_{200}}\&Ow$ [15]. Nevertheless, there are several hypotheses that could be in favour of a non-independent co-occurrence of inadequate iodine status and overweight either at the physiological and environmental level.

As for the physiological level, several epidemiologic and clinical studies have examined links between thyroid function and obesity [11, 27–34]. A conceptual framework was elaborated in order to depict the different factors that could modulate the association between both tissues (in Additional file 1: Figure S1.) [11, 13, 16, 35–49]. Thyroid is deeply involved in the regulation of energy expenditure, basal metabolism, regulate food intake and thermogenesis. Theoretically, the slowdown of thyroid activity (hypothyroidism) is believed to cause low metabolic rate, reduced gluconeogenesis, reduced liposis and hence promoting weight gain [50, 51]. This hypothesis was consistent with the reported negative association between body mass index and thyroid hormones level [28, 30–32, 52].

More than adequate iodine intake may increase subclinical hypothyroidism [53]. In fact, a recent research conducted by Shan and al. [54] reported that subclinical hypothyroidism prevalence was significantly higher among population having more than adequate iodine (22.6% vs. 12.7% for adequate iodine intake, $P < 0.01$). A meta-analysis reported a significant risk of hypothyroidism pertaining to iodine excess [55]. In the other hand, it is thought that hypothyroidism could be a consequence of obesity [56, 57]. In fact, low chronic inflammation grade, typically observed in obese subjects, has been proposed to depress thyroid function [11, 32, 58]. The link seems to be ensured by the leptin and pro-inflammatory cytokines [59]. There are clear association between thyroid hypofunction and hyperleptinemia [33, 60]. This raise of hyperleptinemia is showing to increase the secretion of the pro-inflammatory cytokines. The different links between thyroid function, leptin and obesity have been extensively reviewed by Duntas and colleagues [33]. Iodine appeared to be an important link in a loop configuration characterizing the association between thyroid gland and fat tissue accumulation.

Beyond the physiological pathways discussed above, in the context of the nutrition transition that countries of the MENA region are experiencing, there are also external factors e.g. linked to the food environment that could increase the risk of both inadequate iodine status and excess adiposity at subject level. Generally, the nutrition transition is characterized by an increased intake of foods with a high sugar, fat and salt content, and Tunisia is no exception [10, 17, 61]. Indeed, several studies reported a very high salt consumption, from 11 to 14 g/day vs. the 5 g/day recommended. [62, 63]. Also, as part of a worldwide strategy to tackle iodine deficiency disorders [16], Tunisia has implemented a USI program since 1995 [18]. Failure in the program monitoring and control has resulted in inadequately iodized salt (as a quarter of the commercialized salt is excessively iodized) [22]. In a such a context subjects with diets with high sugar, fat and salt content which would make them more prone to excess adiposity, would also be more at risk of excess iodine (as a cumulative effect of high salt intake and inadequate salt iodization). So that would be in favour of a synergetic rather than independent co-occurrence. There could be also interactions with the metabolic pathways above, e.g. in relation with the interactions between thyroid function and adipose tissue.

Compared with all the elements in favour of a synergistic co-occurrence explained above, our observations (which are in accordance with the independence hypothesis) may be due to methodological limitations. As for measurements, urine spot measurements have known limitations for the assessment of iodine status at individual level and especially long-term high iodine intake [64]. Also, no data was available about thyroid function biomarkers (free thyroxin and thyroid stimulating hormone). We did not either estimate iodine intake e.g. by measuring dietary intake. More importantly, it could be that the metabolic pathways pertaining to the non-independent co-occurrence of iodine excess and excess adiposity (and/or their interactions with environmental factors) get fully activated only in the long term. So that they would not manifest themselves fully in this population of 6–12 y. children. Testing that hypothesis would require the same kind of data on the same subjects when they reach adulthood or at a least on a comparable sample of adults. So that the 6–12 y. age-class is a limitation of our study. Nevertheless, this is by recommendation of the WHO, as school age children are the target age class for assessment of iodine status [25].

Beyond assessing the nature of the co-occurrence of iodine status and excess adiposity (i.e. synergistic, antagonistic or independent), the study population of school-age children also has limitations regarding the assessment of the magnitude of the double burden in the whole population. Nevertheless, WHO also considers that iodine status of school-age children can be used as an approximative estimate of iodine status of the whole population [16]. Based on the assumption that iodine status and excess adiposity are co-occurring independently, one can then infer a rough estimate of the double burden by the product of our observed prevalence of iodine intake above requirements (about a half) and that of overweight among Tunisian adults (about two thirds) [61, 65]: so that about a third of Tunisian adults would be at risk of both iodine intake above requirements and overweight (and all the more for adult women which are much more prone to excess adiposity in this context). From the same reasoning one can infer that about one woman out of ten would also be affected by the co-occurrence of overweight and iodine deficiency. These estimates would be a lower bound if one takes into account that the co-occurrence of inadequate iodine status and excess adiposity is likely more synergistic than independent in older subjects (vs. our studied age-class for which our data was compatible with the independence hypothesis). But this estimated prevalence of subject-level co-occurrence of overweight and inadequate iodine intake are nevertheless significant from a public health point of view, especially with regards to intergenerational effects on risk of both chronic diseases and mental development [66] as we underlined they are higher among women which are much more prone to excess adiposity in the context.

Conclusion

In the MENA region, lifestyles which underly the increase in excess adiposity and associated NCDs include diets with possibly increased salt content. This may result in excess iodine intake, which may cluster with excess adiposity both due to these shared environmental factors and synergistic metabolic pathways. In this study of Tunisian children, this hypothesis was not shown to be true. While obesity and excess iodine intake were documented, little overlap was detected.

As the nutritional transition proceeds in the MENA region it would be useful to monitor the prevalent double burden of excess iodine intake and excess adiposity.

List Of Abbreviations

95% CI: : 95% confidence interval; IAR: Intake Above Requirements; ID: Iodine Deficiency; IE: Iodine Excess; LMICs: Low- and Middle-Income Countries; MENA: Middle East and North Africa; NCDs : Non Communicable Diseases; RPR : Relative Prevalence Ratios ; UIC : Urinary Iodine Concentration; USI: universal salt iodization; WHO: World Health Organization.

Declarations

Ethical Approval and Consent to participate

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the Ethics Committee on Human Research of the National Institute of Nutrition and Food Technology, and the Tunisian National Council of Statistics (visa n∘ 8/2012). Written informed consent was obtained from the parents of all the children included in the study.

Consent for publication: Not applicable.

Availability of supporting data: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Additional File

Figure S1. Conceptual framework of factors influencing the co-occurrence of inadequate iodine status and excess of adiposity

Supplementary Files

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