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Urinary iodine percentile ranges in the United States

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Abstract

Background—The status of iodine nutrition of a population can be determined by measurement of urinary iodine concentrations since it is thought to indicate dietary iodine intake. Normally, these results are compared to population-based criteria, since there are no reference ranges for urinary iodine.

Objective—To determine the percentile ranges for urinary iodide (UI) concentrations in normal individuals in the United States.

Materials and methods—The third National Health and Nutrition Examination Survey (NHANES III) (1988–1994) database of the civilian, non-institutionalized, iodine-sufficient US population was used. The 2.5th to 97.5th percentile ranges for urinary iodine and for urinary iodine per gram creatinine ratio (UI/Cr) (μg/g) were calculated for females and males, 6–89 years of age, each stratified by age groups.

Results and conclusions—We calculated the percentile ranges for urinary iodine. After exclusions of subjects with goiter or thyroid disease, the study sample included 21,530 subjects; 10,439 males and 11,091 females. For women of childbearing age (14–44 years), urinary iodine concentration 2.5th to 97.5th percentiles are 1.8–65 μg/dl or 36–539 μg/g creatinine. For pregnant women, the ranges are 4.2–55 μg/dl or 33–535 μg/g creatinine.

Keywords

Iodine deficiency; diagnosis; epidemiology; environmental; prevention and control; Human; Nutrition surveys; Pregnancy; Public health

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1. Introduction

Iodine is an essential micronutrient and an integral component of thyroid hormones. Normal concentrations of thyroid hormones are required for normal metabolism and optimal brain development, especially during gestation and the first 3 years of life. Iodine deficiency during pregnancy may result in neurodevelopmental deficits and in extreme cases in cretinism.

The status of iodine nutrition of a population is determined by measurements of iodine as urinary iodide (UI) concentrations since it is considered an indicator of the adequacy of the iodine intake of that population, when carried out with appropriate technology and sampling [1,2]. UI/Cr is considered a more reliable measure of iodine excretion than random spot concentration measurement since it corrects for hydration status and for body mass. The choice among methods depends on the intended application, reliability and complexity of instrumentation, number of samples, technical capability, safety and cost. Epidemiological field studies are large by default and therefore demand simple, reliable, rapid and cost-effective methods for determining the iodine status of the population.

The criteria for iodine deficiency in a population has been established by the World Health Organization (WHO) stating that the median UI concentration in a population should be >10 μg/dl, and ≤20% of the population should have UI concentrations of < 5 μg/dl [2]. If the UI per gram creatinine ratio is used for iodine evaluation, the ratio should be >50 μg I/g Cr [2].

However, these parameters apply to populations and not to individuals. We used the third National Health and Nutrition Examination Survey (NHANES III) database of the civilian, non-institutionalized, iodine-sufficient US population to calculate the age-related normal urinary iodine concentration ranges (2.5th to 97.5th percentiles) for females and for males, 6–89 years of age, stratified by age groups. Percentile ranges are important to identify the at-risk population. In the case of urinary iodine globally, the lower 2.5% cut-off is of greater clinical relevance. As we were dealing with a normal population, we were able to use the percentile approach to calculate these percentile ranges [3].

2. Methods

NHANES III, a stratified, multistage probability study was conducted between 1988–1994 and represented all the states in the US and the District of Columbia [4]. Urinary iodine testing was performed on children >6 years on carefully selected, non-institutionalized population representing all races across the US. The age ranges were separated as pre-pubertal, reproductive age and post-reproductive age. Up to 13 years, the data was grouped in age ranges consisting of 2–4 years to assess changes in iodine exposure during growth and development. Adequate iodine availability is critical during the reproductive years (as defined by CDC) for fetal development, thus, the large group of ages 14–44 years.

2.1. Study sample

The present study included all subjects 6–89 years of age whose urinary iodide and urinary creatinine concentration measurements were available. Of the 22,088 subjects with both urinary iodine and creatinine concentration measurements, 459 cases of thyroid disease and 99 cases of goiter were excluded (17 subjects reported having both). The present study includes 21,530 subjects including 290 pregnant women (14–44 years) (Table 1).

2.2. Laboratory methods

2.2.1. Urinary iodine—UI concentrations were determined using the Sandell–Koltoff reaction [5]. The limit of detection (LOD) was 0.2 μg/dl. The UI concentrations were determined at the Iodine Research Laboratory, the University of Massachusetts Medical Center, Worcester, MA. Iodine standards were prepared from analytical grade potassium iodate (KIO_3) and consisted of four concentrations of KIO_3 ranging from 0 to 0.3 μg/ml iodine. The samples were analyzed in duplicate with every 10 urine samples. UI concentrations were calculated from the slope of the *y*-intercept of the standard curve. A quality control sample was digested and analyzed with every 10 urine samples. Samples were repeated for values < 0.1 μg/ml by using a larger sample size and for those above the highest standard by diluting the sample. The coefficient of variance for UI determination ranged from 2.7% to 7.0%.

2.2.2. Urinary creatinine

NHANES III creatinine was measured by the Jaffé alkaline picrate method. The LOD was 1 mg/dl. Creatinine concentration standards (50–300 mg/dl) were analyzed in duplicates with every 60 urine samples. Urinary creatinine concentrations were calculated from the slope *y*-intercept of the standard curve. Quality control sample was analyzed with every 20 urine samples. Samples were repeated for values < 10 and >300 mg/dl. The coefficient of variance for urinary creatinine determination ranged from 1.5% to 7.7% [4].

2.2.3. Statistical analysis

Statistical analysis was performed using SPSS, version 10, from SPSS, Chicago, IL, 2001. In all analyses, sampling weights were used to adjust for unequal probabilities of selection and to account for non-response. Variance estimates that account for the complex survey design were calculated. The data was divided to males and female subjects and stratified by age. Urinary iodide geometric means and S.E.M. were calculated (Table 2). The 2.5th to 97.5th percentile ranges for females and for males were stratified by age groups (Table 3).

3. Results

After exclusions of subjects with goiter or any thyroid disease, the study sample included 21,530 subjects (Table 1), ranging from 6 to 89 years of age representing over 220 million US children and adults. Females comprised 51.5% of the total sample survey and 2.61% of the females were pregnant.

The female and male populations were stratified by age. All females of childbearing age were calculated together (14–44 years), with and without the group of pregnant women (n = 290). In Table 2, the geometric means, standard error of the means and confidence intervals, medians and other percentiles have been calculated for urinary iodine concentrations of each of the age groups, together with the UI/Cr ratios. The 2.5th to 97.5th percentile ranges for each of the age groups are presented in Table 3.

3.1. Demographic characteristics

After exclusions of subjects who had goiter and/or thyroid disease, the study sample included 21,530 subjects; 10,439 males and 11,091 females of ages ranging from 6 years of age to their 90th birthday. NHANES III urinary iodine testing was performed on children 6 years and older. Females comprised 51.5% of the total sample survey and 2.61% of the females were pregnant.

4. Discussion

Dietary iodine is ingested in a variety of forms and most of it is reduced in the gut to iodide, and is rapidly absorbed [6]. Most of the iodide is transported into the thyroid and incorporated into thyroid hormones. The extrathyroidal inorganic iodine pool consists of iodide derived from the diet and from peripheral catabolism of thyroid hormones and iodothyronines by deiodination and is in dynamic equilibrium with the thyroid gland and with the kidneys. Urinary iodine concentration is currently the most practical biochemical marker for determining the iodine nutrition of populations at the time of measurement [2]. The NHANES data represents casual spot urine samples, reflecting the findings of a population at a point in time, known to include wide variations both in regional and in individual UI concentrations [7]. Some of the variation was overcome by measurements of urinary creatinine to correct for urinary dilution that could affect urinary iodine concentrations.

The Total Diet Study of the Food and Drug Administration (FDA), a yearly program that measures the amounts of minerals in foods and estimates their intakes in representative diets of specific age–sex categories, indicated that the average intake of iodine in the US was adequate (1982–1991) [8]. The NHANES III survey also reported that the US population is iodine sufficient according to WHO criteria [9]. NHANES III database of the civilian, non-institutionalized, iodine-sufficient US population was used here to calculate the percentile ranges for urinary iodine concentrations for individuals for females and males stratified by age groups.

NHANES III indicates that UI concentrations were higher for males of all ages than for females of the same age group (beside the group of pregnant women) probably because of a higher iodine intake (Table 2). UI concentrations were highest in the 6–9-year age group (GM = 20.32 μg/dl) for females, and in the 10–11-year age group (GM = 26.45 μg/dl) for males. Iodine values were lowest in the 45–59-year age group for both females (GM = 9.72 μg/dl) and males (GM = 13.44 μg/dl). The geometric means for UI/Cr were higher for males up to age 14 years than for females of the same age group. However, from age 14 years, the UI/Cr ratios were higher for the females. The UI/Cr concentrations were highest at the 6–9-year age group for both females (GM = 258 μg/g) and males (GM = 290 μg/g). They were lowest at the 14–44-year age group for both females (GM = 120 μg/g) and males (GM =104 μg/g).

The Total Diet Study of iodine intake survey indicated that during 1982–1991, the iodine intake for 2-year-olds was higher than the Recommended Dietary Allowances (RDA) suggested by the National Research Council (NRC) and National Academy of Sciences. The higher iodine intake of the younger age groups relative to the intake of the older >age groups may explain in part the higher UI concentrations of the younger age groups in the NHANES III data.

Pregnancy is accompanied by alterations in the requirements for iodine. Because of the susceptibility of the developing fetus to iodine deficiency, women of childbearing age are at a particularly sensitive stage and need to make sure their iodine intake is sufficient. Of the 5522 females of childbearing age (ages ranging from 14 to 44.99 years), 290 women were pregnant. UI geometric means for the pregnant women were higher (15.4 F0.66 μg/dl) than those of non-pregnant women of childbearing age (12.06 F 0.15 μg/dl). Renal iodide clearance depends principally on glomerular filtration rate (GFR) [10]. It is normal for the GFR to be higher (as much as 50% higher) during pregnancy, leading to a higher renal iodide loss beginning in the early weeks of gestation through the pregnancy, and to a wide variability in plasma and UI concentrations [11]. UI concentrations increased during pregnancy in iodine-replete areas [12–14] and in borderline-sufficient areas [12,15] increasing during the course of pregnancy. [12,16].

It is reported that iodine intake from food of healthy adults in the United States is within the daily requirements for both women and men (1991–1997) [17]. When maternal iodine consumption during early pregnancy and during the second trimester is insufficient, low nutritional iodine status may lead to spontaneous abortion, stillbirth and neurodevelopmental consequences. The transfer of iodide from the maternal circulation to the developing fetus for fetal thyroid hormone production during the second half of gestation further compromises the mother when she is iodine deficient. UI concentrations are higher in pregnant women in comparison to non-pregnant women (this is not due to an increase in dietary I intake) indicating they may not be a true reflection of their iodine status during pregnancy, which may in fact be lower.

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Table 1

Demographics for urinary iodine concentrations (μg/dl) and urinary iodine/creatinine ratio (UI/Cr)(μg/g) data from NHANES III, females and males age 6–89 years[a,b]

Age groups	*n*		
Female	**Sample size**	**% of females**	**% of total patients**
6–9 years	950	8.56	4.41
10–11 years	520	4.69	2.41
12–13 years	429	3.87	1.99
14–44 years	5522	49.79	25.65
45–59 years	1411	12.72	6.55
60–89 years	2259	20.37	10.49
Total females	11,091	100	51.50
Pregnant women[c]	290	2.61	1.35

Male	Sample size	% of males	% of total patients
6–9 years	1025	9.82	4.76
10–11 years	553	5.31	2.57
12–13 years	390	3.73	1.81
14–44 years	4782	45.8	22.21
45–59 years	1312	12.57	6.09
60–89 years	2377	22.77	11.04
Total males	10,439	100	48.50
Total individuals	21,530		100

[a]Based on NHANES III (1988–1994) laboratory sample.

[b]Excluding patients with goiter and thyroid disease.

[c]Pregnant women are already included in the group of 14–44-year-old females.

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Table 2

Means and percentiles for urinary iodine concentrations (μg/dl) and UI/Cr (μg/g) ratios for females and males 6–89 years[a,b] and for pregnant women

Subgroup	*N*	GM[c] ± S.E.M. (95% confidence intervals)	Percentile				
		Urinary iodine (μg/dl) UI/creatinine ratio (UI/Cr)	10th	25th	50th	75th	90th
Female	*11,091*						
6–9 years	950	20.32 ±0.52 (19.30–21.39)	7.4	13	22	32.8	48.8
		258 ±6 (247–270)	113	168	263	393	540
10–11 years	520	17.83 ±0.55 (16.75–18.97)	7.2	11.5	18.5	26	42.5
		187 ±6 (176–198)	84	122	171	304	483
12–13 years	429	16.66 ±0.59 (15.51–17.89)	6.6	10.5	17	26	40.5
		140 ±4 (132–149)	67	88	144	207	295
14–44 years	5522	12.20 ±0.14 (11.91–12.50)	3.8	7	13	21.2	33.5
		120 ±1 (117–122)	53	74	113	177	292
45–59 years	1411	9.72 ±0.25 (9.24–10.23)	2.9	5	10	17.8	30.2
		143 ±3 (138–149)	61	89	134	221	355
60–89 years	2259	11.62 ±0.22 (11.19–12.07)	4	6.4	11.8	19.2	32.8
		173 ±3 (168–180)	72	106	161	270	414
Childbearing age (14– 44 years)							
Pregnant	290	15.40 ±0.66 (14.14–16.77)	6.2	9.2	14.8	25.3	41
		155 ±6 (143–169)	69	97	145	286	390
Not pregnant	5232	12.06 ±0.15 (11.77–12.38)	3.7	6.9	13	21	33.3
		118 ±1 (116–121)	53	73	112	174	285
All female	5522	12.20 ±0.14 (11.91–12.50)	3.8	7	13	21.2	33.5
		120 ±1 (117–122)	53	74	113	177	292
Male	*10,439*						
6–9 years	1025	25.20 ±0.56 (24.10–26.34)	10.8	16.2	26.8	39.5	58
		290 ±5.7 (279–302)	133	203	282	435	629
10–11 years	553	26.45 ±0.83 (24.85–28.16)	10.5	16.5	28.7	42.5	62
		249 ±7.2 (235–264)	112	158	259	360	575
12–13 years	390	20.28 ±0.93 (18.50–22.24)	8.5	12.5	19.3	29.2	46.5
		177 ±8.2 (161–194)	68	106	157	266	453

Subgroup	*N*	GM[c] ± S.E.M. (95% confidence intervals)	Percentile				
		Urinary iodine (μg/dl) UI/creatinine ratio (UI/Cr)	10th	25th	50th	75th	90th
14–44 years	4782	14.72 ±0.17 (14.39–15.07)	5.5	9.5	15.5	24	37.5
		104 ±1 (102–106)	46	65	99	157	245
45–59 years	1312	13.44 ±0.32 (12.81–14.09)	4.2	7.9	13.8	22	38.5
		120 ±2.3 (115–125)	52	76	113	179	289
60–89 years	2377	15.46 ±0.28 (14.91–16.02)	5.5	9.2	15.2	25.8	41.5
		148 ±2.4 (144–153)	63	90	136	224	365

[a] Based on NHANES III (1988–1994) laboratory sample, weighted to national population.

[b] Excluding patients with thyroid disease and goiter.

[c] GM—Geometric means. Weighted geometric mean ± standard error of the mean (S.E.M.) and 95% confidence interval.

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Table 3

2.5th to 97.5th Percentile ranges for urinary iodine concentrations (μg/dl)[a] and urinary iodine per gram creatinine (UI/Cr) (μg/g) ratios for males, females (6–89 years)[a,b,c] and pregnant women

Subgroup	*N*	2.5th to 97.5th percentiles	
		Urinary iodine concentration (μg/dl)	UI/creatinine ratio (UI/Cr) (μg/g)
Female	*11,091*		
6–9 years	950	3.6–74.0	68–947
10–11 years	520	4.1–80.0	57–744
12–13 years	429	3.6–75.0	42–564
14–44 years	5522	1.8–65.0	36–539
45–59 years	1411	1.7–67.0	39–743
60–89 years	2259	2.2–62.0	47–723
Childbearing age (14– 44 years)			
Pregnant	290	4.2–55.0	33–535
Not pregnant	5232	1.8–65.0	36–541
All female	5522	1.8–65.0	36–539
Male	*10,439*		
6–9 years	1025	5.4–85.0	80–940
10–11 years	553	6.0–98.0	62–820
12–13 years	390	4.5–74.0	51–840
14–44 years	4782	2.4–66.0	34–420
45–59 years	1312	2.6–70.0	39–527
60–89 years	2377	2.6–86.0	41–769

[a]UI conversion factor from μg/l to nmol/l = × 7.90.

[b]Based on NHANES III (1988–1994) laboratory sample, weighted to national population.

[c]Excluding patients with thyroid disease and goiter.