

The Study of Thyroid Physiology Using ¹³¹I-Sodium-Iodide Uptake Measurements

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Abstract: The measurement of the radioactive iodine uptake (RAIU) provides the most direct study of thyroid physiology by studying the rate of thyroïdal accumulation, incorporation, and release of radioiodine. A total 69 subjects with a mean age of 34 ± 13 years (range: 8-70 years) that include 70% females and 30% males, referred to the Institute of Nuclear Medicine & Allied Sciences (INMS), Rajshahi for RAIU measurement were evaluated to investigate their thyroid physiology. The uptake study consisted of oral administration of 3.7–7.4 MBq (100–200 μ Ci) of ¹³¹I as sodium-iodide was performed both at 2 hours and 24 hours. The Mean \pm SD of RAIU values for euthyroidism, hypothyroidism and hyperthyroidism were found to be $6.3 \pm 3.4\%$ at 2h and $9.9 \pm 6.8\%$ at 24h, $1.8 \pm 0.8\%$ at 2h and $4.2 \pm 2.6\%$ at 24h, and $36.5 \pm 21.4\%$ at 2h and $54.8 \pm 15.9\%$ at 24h, respectively. The RAIU measured in the present study effectively indicate the status of the respective thyroid.

Keywords: Thyroid gland; Thyroid physiology; Radioactive iodine; Uptake.

1. Introduction

Thyroid [1, 2], one of the ductless endocrine gland produces a variety of amino acids all of which contain iodine. A small amount is released by the thyroid each day for use by the body's tissues but the bulk is stored in the gland. Each day the thyroid gland accumulates from the blood about that amount of iodine required to replace what it releases, incorporated in amino acids (thyroid hormones). These hormones increase the basal metabolic rate (BMR) and body heat production. Extreme excess of thyroid secretion cause the BMR to raise 60-100% above the normal. Complete lack of thyroid secretion can cause BMR to fall 40-50% below the normal [3]. It also influences many bodily functions [4-8], such as physical growth and development, puberty, organ function, fertility and body temperature. The thyroid gland controls how quickly the body uses energy, makes proteins and controls how sensitive the body is to other hormones. Thyroid hormones, and therefore iodine, are essential for mammalian life: they regulate many important biochemical reactions, especially the synthesis of proteins with key functional activities [9].

Iodine is an essential raw material for thyroid hormone synthesis. Its deficiency leads to thyroid disorders. The two most important, although not most common, disorders of the thyroid are associated with either a higher than normal rate of hormone production (hyperthyroidism or thyrotoxicosis) or a lower than normal production (hypothyroidism or myxoedema). According to the latest estimation, about 2.5 billion people worldwide (38% of the world's population) have insufficient iodine intake, of which 313 million are in the South-eastern Asian region that includes Bangladesh. Nearly 69% of Bangladeshi population has biochemical iodine deficiency [10]. Women and children are more affected than men, in terms of both goiter prevalence and urinary iodine excretion (UIE). The widespread severe iodine deficiency in all ecological zones indicates that the country as a whole is an iodine-deficient region. However, the IDD survey in 1999 reported that the biochemical iodine deficiency goiter rate was reduced to about 61% of the population [11]. Iodine deficiency still is the main cause of thyroid morbidity in Bangladesh.

Radioactive iodine uptake (RAIU) is a test of thyroid function. It measures how much radioactive iodine is taken up by the thyroid gland in a certain time period. There are, of course, various other means at the disposal of the physician to make a diagnosis of thyroid malfunction e.g. observation of clinical signs and symptoms, determination of the basal metabolic rate and other tests, but the measurement of RAIU provides the most direct study of thyroid physiology by studying the rate of thyroïdal accumulation, incorporation, and release of radioiodine. A high RAIU taken by the gland is usually found in the hyperthyroidism and a low uptake in the hypothyroidism condition [12]. The uptake is also usually found to be high in the most common thyroid disorder, namely endemic goiter, where the

gland is greatly enlarged without increase in hormone production. Thus, the thyroid RAIU test is now one of the most widely practiced medical applications of radioisotopes.

Since its introduction to clinical studies in the 1940s, ^{131}I has been proven to be very useful radioactive tracer for diagnosing and treating thyroid gland disorders. The radioisotope ^{131}I is rapidly absorbed in the stomach and concentrated in the thyroid. The key reasons for its worldwide used to study the thyroid functions are: ^{131}I is a β -emitting radionuclide with a physical half-life of about 8.04 days; a principal γ -ray of 364 keV; and a principal β -particle with a maximum energy of 0.61 MeV, an average energy of 0.192 MeV, and a range in tissue of 0.8 mm. The patient swallows radioactive ^{131}I in the form of capsule or fluid, and its absorption by the thyroid is studied at various intervals from one to forty-eight hours with the aid of a scintillation counter. In the literature, the normal range of radioactive ^{131}I thyroid uptake [13-15] is as follows: 2 hours 3-12%; 4 hours 6-18%; 24 hours 8-25%. These values, however, are interpreted loosely, because of the variation of equipment, standards, uptake phantoms, and subject individuals from populations with various levels of iodine intake. The objective of the present study was to investigate the thyroid status by evaluating ^{131}I -sodium-iodide uptake absorbed at 2 hours and 24 hours.

2. Materials and Methods

2.1 Physical and Chemical Properties of ^{131}I

^{131}I is produced commercially for medical and industrial uses through nuclear fission. It also is a byproduct of nuclear fission processes in nuclear reactors and weapons testing. In medicine, ^{131}I is supplied as capsules or liquid of a specific activity designed to be swallowed by patients. The physical half-life of ^{131}I is 8.04 days after which it disintegrates into ^{131}Xe through beta and gamma emissions. The average energy of a beta particle is 0.192 MeV (89%), whereas the energy of the emitted gamma ray is 0.364 MeV (81%) [16]. As a product of nuclear fission, it is a dark purple gas that can be inhaled, or absorbed through the skin. ^{131}I in fallout from nuclear weapons or reactor accidents can occur in particle form, which can be ingested in food or water. The radioactive iodine model of ICRP assumes that about 70% of radioactive ^{131}I entered into the human body is excreted in the urine and the remaining 30% settles in the thyroid gland. Furthermore, the biological half-life of radioactive iodine deposited in the thyroid gland tissue varies, depending on the age group. ICRP assumes that it is 80 days for adults, 67 days for 15 years old, 58 days for 10 years old, 23 days for 5 years old, and 15 days for one year old [17].

2.2 Study Subjects

A total 69 subjects with a mean age of 34 ± 13 years (range: 8-70 years) that include 70% females and 30% males, referred to the Institute of Nuclear Medicine & Allied Sciences (INMAS), Rajshahi Medical College Hospital, Rajshahi were evaluated to study their thyroid physiology. The study subjects were chosen from different districts of Rajshahi division. The uptake study was consisted of oral administration of 3.7–7.4 MBq (100–200 μCi) of ^{131}I as sodium-iodide. Prior to oral administration of the isotope, a history to rule out the intake of any iodine containing agents or drugs known to affect thyroid function was asked from all the patients. Patients with deficient records, e.g. incomplete patient records, were excluded.

2.3 Uptake Procedures

The principle of uptake measurement is relatively simple. The amount of gamma-radiation given off by the radio-tracer which has been accumulated by the thyroid at a certain time is compared with the amount of gamma-radiation emitted by the total dose administered to the patient. In the ideal case, both measurements should be done under identical conditions. In the present study the radioactivity counts were taken at 30 cm, using a gamma probe consisting of a collimated sodium-iodide crystal with a cylindrical straight-bore collimator connected to a pulse height analyzer (PHA) and scalar. Fig.1 illustrates the uptake measurement geometry. Neck counts, lower thigh counts (body background), counts of the administered dose and room background counts were obtained at each counting session. A spacer was used so that the same distance was always maintained whenever counting was taken place. Using data from these steps, the following expression was established and the RAIU both at 2 and 24 hours were calculated as the percentage of the administered dose.

$$RAIU (\%) = \frac{\text{neck counts (cpm)} - \text{thigh counts (cpm)}}{\text{admin. counts (cpm)} - \text{background counts (cpm)}} \times 100\% \quad (1)$$

3. Results

The status of the patient's thyroid, on the basis of clinical findings, is classified into euthyroidism, hypothyroidism and hyperthyroidism. The great majority of the patients are female in all groups: female 70% and male 30% in total. The Mean \pm SD of age for these three groups, respectively, are 32 ± 12 years ranging from 8-70 years, 42 ± 13 years with range 20-70 years and 33 ± 12 years with range 20-60 years. It was aimed to study their thyroid physiology by means of ^{131}I -sodium-iodide uptake calculations. The results of RAIU measured at 2h as well as 24h for three clinical groups mentioned above are summarized in Table 1. The uncertainties quoted in the values represent the statistical and systematic errors. The frequency histograms of 2h & 24h RAIU values observed in this study are shown in Fig. 2. As the frequency histograms revealed a non-Gaussian data distribution the mean and standard deviation (\pm SD) values are not presented in these normal distribution curves. The results of the present study for 2h and 24h RAIU are separately furnished in the following sub-sections.

3.1. RAIU at 2h

The mean RAIU of the euthyroid group is 6.3% with an observed range from 2.6 - 16.3% (excluding the nine values of 1.0%, 1.7%, 29.0%, 35.0%, 2.4%, 1.4%, 2.3%, 18.6% and 1.2%) and a standard deviation of 3.4%. The Mean \pm SD RAIU at 2h for hypothyroid group is found to be 1.8 \pm 0.8% with range from 0.6% to 2.9% (excluding the three values of 3.9%, 4.8% and 10.5%) and for hyperthyroid group it is to be 36.5 \pm 21.4% with a range of 15.4-84.4%. The box-plot analysis of 2h RAIU values in Fig. 2(a) shows that about 72% of the euthyroid patients has RAIU values that ranged from 3% to 12%, about 79% of the hypothyroid patients present RAIU values below the normal range and all most 100% of the hyperthyroid patients has RAIU in excess of the normal range.

3.2. RAIU at 24h

In the present study the normal range of RAIU measured at 24h for euthyroid group is found to be 9.3-36.2% with the Mean \pm SD of 19.9 \pm 6.8%. The Mean \pm SD of RAIU for hypothyroid group is 4.2 \pm 2.6% with range 0.3% to 7.7%, and for hyperthyroid group it is 54.8 \pm 15.9% with a range of 37.6-85.6%. The 24h RAIU distribution curve, in Fig. 2(b), shows that about 87% euthyroid patients have uptake values within the normal range of 9-25%.

4. Discussion

The present study shows that the great majority of the patients are female in all groups. The patients who developed hypothyroidism are 64% female and 36% male. In the case of euthyroidism 74% are female and 26% are male and in hyperthyroidism 63% are female and 37% are male. This result provides a clue that female individuals develop thyroid problems easily. On the other hand, the Mean \pm SD age for hypothyroid patients is 42 \pm 13 years, which is significantly higher than that of other two groups. It means that older women are more sufferers from hypothyroidism. Higher frequencies of thyroid problems in females may be attributed to stress, multiple pregnancies and lactation. Due to particular family set-up in Bangladesh, females are more exposed to nutritional deficiencies that cause health problems including thyroid disorders.

The non-Gaussian frequency histogram at 2h RAIU measurement reveals a considerable overlap between the euthyroid and other two groups. 5 euthyroid individuals have RAIU values below the normal range and 3 individuals have above the normal range. 2 hypothyroid patients, on the other hand, draw 2h uptake above the normal range. This was to be expected since they have goiters and might have intact or hyperactive trapping mechanisms although they are unable to produce adequate amounts of thyroid hormone since they have very low levels of circulating thyroxine. However, there is no overlapping found between euthyroid, hypothyroid and hyperthyroid groups in the case of 24h uptake measurements. It may, therefore, be mentioned that uptake measurements at 24h is more reliable than at 2h. The present study gives a good separation of hyperthyroid patients and none of them have uptake value within or below the normal range both at 2h and 24h measurements.

The normal range for euthyroid group observed in the present study is compared with some reported series, which are listed in Table 2. Damle *et al.* [18] reported RAIU normal range as 5-15% at 4h and 15-35% at 24h; Topiwala & Zieve [19] reported as 3-16 at 2h and 8-25 at 24h; Salvatore [13] reported as 3-12 at 2h and 8-25 at 24h; Helena *et al.* [20] reported as 6-18 at 4h and 10-35 at 24h; Williams [21] reported as 5-15 at 2h and 8-35 at 24h; Gonzalez *et al.* [22] reported as 2.3-12.0 at 2h and 6.5-30.1 at 24h *etc.* On comparing the normal range of 2h RAIU measurements in different series, the present study provides an excellent agreement with that of [19, 21], and fairly good agreement with others. On the other hand, 24h RAIU range in this study is in excellent agreement with most of the reported series.

5. Conclusions

In this paper, ¹³¹I-sodium-iodide uptake absorbed at 2 hours as well as at 24 hours in 69 patients: female 70% and male 30% are presented. It was aimed to study their thyroid status by means of RAIU measurements. The Mean \pm SD of RAIU values obtained in this study for euthyroidism, hypothyroidism and hyperthyroidism were, respective, found to be 6.3 \pm 3.4% at 2h and 9.9 \pm 6.8% at 24h, 1.8 \pm 0.8% at 2h and 4.2 \pm 2.6% at 24h, and 36.5 \pm 21.4% at 2h and 54.8 \pm 15.9% at 24h. The present study demonstrates the capability of RAIU measurement to provide useful information regarding the thyroid status. It also shows that 24h uptake measurement is more effective than at 2h. However, the RAIU measurements at 24h in addition 2h RAIU are appreciated to provide effective indications of the functional status of patient's thyroid.

Figure-1. Measurement geometry of thyroid uptake with radioactive iodine

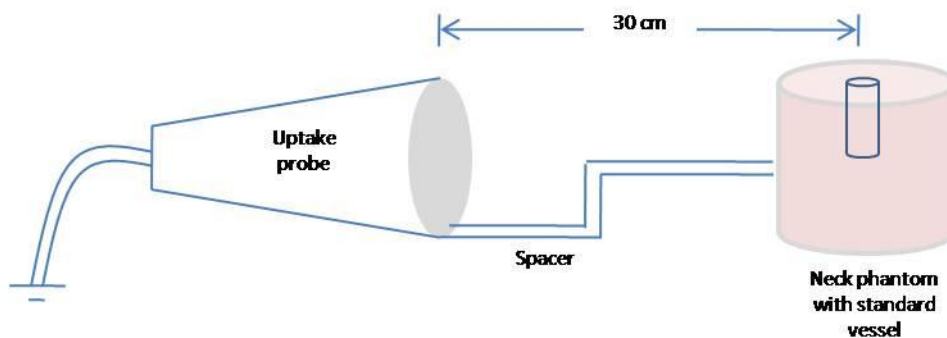


Figure-2. (Color outline) Frequency histogram of RAIU measurement at (a) 2h and (b) 24h. Uptake values for hypothyroidism, euthyroidism and hyperthyroidism are shown, respectively, in red, gray and green boxes.

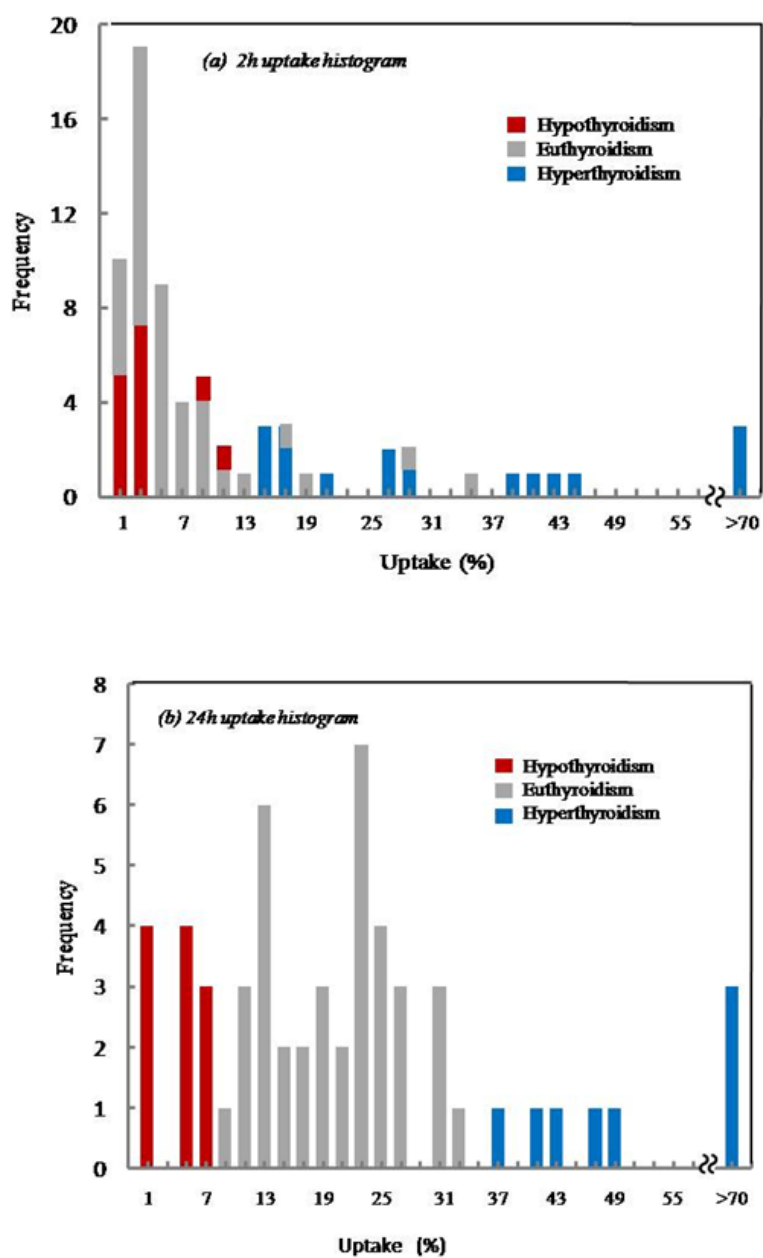


Table-1. Results of 2h and 24h RAIU measurement for three clinical groups.

Thyroid status	2h uptake (%)		24h uptake (%)		Age (year)	
	range	average	range	average	range	average
Hypothyroidism (Male = 36%; Female = 64%)	0.6-2.9	1.8±0.8	0.3-7.7	4.2±2.6	20-70	42±13
Euthyroidism (Male = 26%; Female = 74%)	2.6-16.3	6.3±3.4	9.3-36.2	19.9±6.8	8-70	32±12
Hyperthyroidism (Male = 37%; Female = 67%)	15.4-84.4	36.5±21.4	37.6-85.6	54.8±15.9	20-60	33±12

Table-2. Reported series of RAIU for euthyroid patients

Series	Observed range (%)		Mean uptake (%)	
	at 2h/4h	at 24 h	at 2h	at 24 h
Damle <i>et al.</i> [18]	5-15	15-35	—	—
Topiwala & Zieve [19]	3-16	8-25	—	—
Salvatore [13]	3-12	8-25	—	—
Helena <i>et al.</i> [20]	6-18	10-35	—	—
Williams [21]	5-15	8-35	—	—
Gonzalez <i>et al.</i> [22]	2.3-12.0	6.5-30.1	5.5±1.8	16.2±4.8
Hossain [23]	4-12	12-30	—	—
Islam [24]	2-10	10-30	—	—
Present study	3 - 16	9-36	6±3	20±7

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Reference

- [1] Reza, S., 2011. *Basic human anatomy and physiology*. 4 ed. Dhaka: Mediaplex publisher & Distributor.
- [2] Ganong, W. F. and Barrett, K. E., 1995. *Review of medical physiology*: Appleton & Lange Norwalk, CT.
- [3] Hall, J. E., 2015. *Guyton and Hall textbook of medical physiology*: Elsevier Health Sciences.
- [4] Anderson, G. W., 2008. "Thyroid hormone and cerebellar development." *The Cerebellum*, vol. 7, pp. 60-74.
- [5] Bernal, J., 2002. "Action of thyroid hormone in brain." *Journal of endocrinological investigation*, vol. 25, pp. 268-288.
- [6] Köhrle, J., 2000. "Thyroid hormone metabolism and action in the brain and pituitary." *Acta Medica Austriaca*, vol. 27, pp. 1-7.
- [7] Koibuchi, N. and Chin, W. W., 2000. "Thyroid hormone action and brain development." *Trends in Endocrinology & Metabolism*, vol. 11, pp. 123-128.
- [8] Thompson, C. C. and Potter, G. B., 2000. "Thyroid hormone action in neural development." *Cerebral cortex*, vol. 10, pp. 939-945.
- [9] Rousset, B., 2007. "How iodide reaches its site of utilisation in the thyroid gland—involvement of solute carrier 26A4 (pendrin) and solute carrier 5A8 (apical iodide transporter)." *European Endocrine Disease*, pp. 81-3.
- [10] Yusuf, H. K., Quazi, S., Kahn, M. R., Mohiduzzaman, M., Nahar, B., Rahman, M. M., Islam, M. N., Khan, M. A., Shahidullah, M., *et al.*, 1996. "Iodine deficiency disorders in Bangladesh." *The Indian Journal of Pediatrics*, vol. 63, pp. 105-110.
- [11] Salamatullah, Q. and Yusuf, H., 1997. "Report of the iodine deficiency disorders indicator study in Savar, Bangladesh." *Dhaka: University of Dhaka*,
- [12] Bahn, R. S., Burch, H. B., Cooper, D. S., Garber, J. R., Greenlee, M. C., Klein, I., Laurberg, P., McDougall, I. R., Montori, V. M., *et al.*, 2011. "Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists." *Thyroid*, vol. 21, pp. 593-646.

- [13] Salvatore, D., Davies, T., Schlumberger, M., Hay, I., and Larsen, P., 2011. "Thyroid physiology and diagnostic evaluation of patients with thyroid disorders." *Williams Textbook of Endocrinology*, vol. 12, pp. 327-50.
- [14] Rosenthal, M. S., 2009. *The Thyroid Sourcebook*: McGraw-Hill.
- [15] Balon, H. R., Silberstein, E. B., Charkes, M., Royal, H. D., Sarkar, S. D., and Donohoe, K. J., 2006. "Society of Nuclear Medicine procedure guideline for thyroid uptake measurement." *Thyroid*, vol. 12, p. 0.11.
- [16] ICRP, 1988. *Individual Monitoring for Intakes of Radionuclides by Workers: Design and Interpretation*: International Commission on Radiological Protection: Committee 4.
- [17] ICRP, 1994. *Age-dependent doses to members of the public from intake of radionuclides: part 2 ingestion dose coefficients: a report of a Task group of Committee 2* vol. 2. the International commission on radiological protection: Elsevier Health Sciences.
- [18] Damle, N., Bal, C., Kumar, P., Reddy, R., and Virkar, D., 2012. "The predictive role of 24h RAIU with respect to the outcome of low fixed dose radioiodine therapy in patients with diffuse toxic goiter." *Hormones (Athens)*, vol. 11, pp. 451-457.
- [19] Topiwala, S. and Zieve, D., 2012. "Radioactive iodine uptake." *NIH (US)*. <http://www.nlm.nih.gov/medlineplus/ency/article/003689.htm>,
- [20] Helena, R., Silberstein, E., Meier, D., Charkes, D., Henry, D., Sarkar, S., and Donohoe, K., 2006. "Society of Nuclear Medicine Procedure. ." *Guideline for Thyroid Uptake Measurement. Version 3.*,
- [21] Williams, S., 2012. "Nuclear Imaging Tests-Radioactive Iodine Uptake Test." www.auntminnie.com/index.aspx?sec=ser&sub=def&pag=dis&ItemID=55330,
- [22] González, E., Carmona, C. A., Araya, Q. A., Miranda, F., Massardo, V., Jiménez, R., Jaimovich, F., and Gatica, R., 2008. "[Normal ¹³¹iodine uptake values at 2 and 24 hours]." *Revista medica de Chile*, vol. 136, pp. 1288-1293.
- [23] Hossain, M., 2015. Personal Communication.
- [24] Islam, M., 2015. Personal communication.