ORIGINAL ARTICLE

Effect of X-ray on serum thyroxin hormone level in patients undergoing brain computed tomography in Port Harcourt

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ABSTRACT

Background: Thyroxin hormone (T4) is produced by the thyroid glands which lies antero-lateral to the trachea. Computed tomography (CT) scan is one of the commonly used imaging modality in the brain investigation. It uses X-ray which could induce biological effect on the thyroid gland that is highly radiosensitive. The study aimed to determine the effect of X-ray on Serum thyroxin hormone level in patients undergoing brain CT in Port Harcourt.

Methods: A prospective longitudinal study was carried out in Rivers State University Teaching Hospital in Port Harcourt with 60 participants sent for brain CT that fulfilled the study criteria. A 64 slice helical GE Optima CT machine was used. Patient venous blood was collected to measure serum thyroxin levels before, immediately, after and 7-day post exposure using Total Thyroxin Enzyme Immunoassay Test Kit. The thyroxin level of each participant was also recorded. The data collected was analyzed using SPSS windows version 22.0 statistical software. Pearson correlation and linear regression analysis models were used to evaluate correlation between the variables.

Results: The mean (±SD) serum thyroxin hormone levels in Pre-exposure, Immediate post-exposure, and 7-day post CT were 7.46 ± 1.30 µg/dl, 6.62 ± 1.78 µg/dl, and 7.89 ± 1.13µg/dl, respectively. There was no correlation between the pre exposure, immediate post exposure, and 7-day post exposure serum thyroxin levels.

Conclusion: There was no effect of X-radiation on Serum thyroxin hormone level in patients undergoing brain CT in Port-Harcourt. Although the serum thyroxin level is not adversely affected, there is a great need to protect the thyroid gland.

Keywords: Thyroxin hormone, computed tomography, X-ray, Port Harcourt.

INTRODUCTION

External radiation in the treatment of tumor is the most significant source of ionizing radiation exposure to the thyroid gland [1]. Diagnostic medical radiation exposure now represents the largest source of man-made exposure to ionizing radiation [1].

Computed tomography (CT) traditionally uses X-ray, therefore, significant exposure to X-rays following its use is increasing exponentially [1], and more than a third of all CT scans investigations involve the head and neck region [2].

The radiation dose involved in CT is much larger than that used in conventional X-ray imaging procedures [1]. The 2009 Ionizing radiation exposure of the population of the United States; Report no. 160, states that between 1980 and 2006, there was five times increase in the average exposure to medical X-rays, from an estimated 0.4 to 2.2 mSv, while the fraction of man-made sources in 2006 (3 mSv) due to CT imaging increased dramatically to 48% (1.5 mSv), whereas the fraction from nuclear medicine, mostly for cardiac imaging, rose to 24% (0.74 mSv) [1].

The research about the effects of ionizing radiation on living tissues has been in progress for about a century and these research studies have amassed more than any other physical or chemical agent [3]. Many factors have been found to influence the biologic response of a cell, tissue or organ to radiation exposure, and these factors involve variables associated with the source and type of radiation as well as the organ or tissue being irradiated [3]. The type of response from a given exposure to ionizing radiation depends on the radiosensitivity and complexity of the biologic tissue or organ thus complex organs or organisms will also exhibit a resultant complex reaction. In the same vein, some responses to radiation exposure appear instantaneously, while others may take weeks, years, or even decades [3]. Exposure to ionizing radiation could cause injury to a few cells or even a single cell which could result in production of the disease because the stochastic effect of ionizing radiation does not have a dose threshold. "The benefits derived from a properly conducted CT procedure will continue to outweigh the small risks associated with it; nonetheless, it is important to be able to specifically quantify the risks" [4]. Therefore, even minor exposures may carry some, albeit small, increased risk.

The biologic changes seen during radiation interactions with biologic tissues could be classified as either a direct or indirect effect. The direct effect takes place by direct action on

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the macromolecule of the tissue such as DNA, RNA, or protein which becomes ionized or excited by an ionizing particle or photon passing through or near it, whereas the indirect effect occurs within the medium (e.g., cytoplasm) which create reactive molecules that in turn interact with the target molecule. A small quantity of energy from exposure to ionizing radiation like X-ray could lead to non-uniform deposition of energy and through biochemical processes that amplify damage [5].

X-ray as a form of ionizing radiation can induce detrimental biological effects in organs, especially the thyroid gland which is highly radiosensitive. This could alter the thyroid gland hormone production (thyroxin levels) and function thereby altering the thyroxin hormone levels. Due to the increase in CT scan of the brain in Port Harcourt [6], there is a need to evaluate the changes in serum thyroxin hormone levels in these patients after undergoing brain CT.

Thyroid hormones are produced by the thyroid gland following its stimulation by thyroid-stimulating hormone which is produced in the pituitary gland located in the brain [7,8]. The hypothalamus controls the pituitary gland in the brain which monitors the amount of circulating thyroid hormone [8]. The thyroid gland is a small butterfly-shaped endocrine organ located anterolateral to the trachea [9]. Two hormones are produced by the thyroid gland; thyroxin (T4) and triiodothyronine (T3) of which 95% is thyroxin and 5% is triiodothyronine. Triiodothyronine is the active form of thyroid hormone that is produced when an iodinemolecule is being cleaved from thyroxin [8]. With the fact that thyroxin is inactive, implies that the majority of thyroid hormone produced is inactive [10].

According to Laway et al. [11], there is an increased prevalence of hypothyroidism in radiotherapy patients; however, the effect of diagnostic dose from CT scan needs to be further evaluated. A non-randomized prospective study conducted by Laway et al. [11], to evaluate the response of the thyroid gland before and after exposure to radiation showed low thyroid hormone levels (hypothyroidism). There are few pieces of literature regarding the index study in our environment; this makes it imperative to evaluate the effect X-ray on serum thyroxin levels among patients undergoing CT scan in the Nigerian population.

In a study, to evaluate the effect of age on the radiosensitivity of the thyroid gland of rats by Preston et al. [12] revealed a decrease in the radiosensitivity of the thyroid gland with ageing. It is documented that after irradiation, the number of proliferating cells in the thyroid gland of the younger age group reduces more when compared with that of the adult age group Mutsumi et al. [13]. Therefore, there is a need to determine the relationship between changes in serum thyroxin level after exposure to X-ray with age and other anthropometric variables like weight and height.

METHODS

A prospective study design was adopted over duration of 6 months (March to September 2018) in the CT suite of Radiology Department in Rivers State University Teaching Hospital Port Harcourt, Rivers State, Nigeria. Patients referred for brain CT scan for indication not related to thyroid diseases that also met the inclusion criteria participated in the study. All the participants provided informed consent, whereas ethical approval for the study to be carried out was obtained from the ethical committee of the Rivers State Health research ethics committee in line with the Helsinki declaration.

The sample size was calculated using the sample population of 70 being the number of brain CT examination from January to June the previous year. The sample size was derived from the Yamane formula [14] as follows:

$$n = \frac{N}{1 + N(e)^2}$$

where: n = sample size, N = Population size (70), and e =level of precision (0.05).

Having a pre-exposure normal thyroxin level as well as accessibility of patient address of residence was also considered.

A 64 slice helical GE Optima CT machine having current quality control measurements and calibration with Pump injector was used. The procedure was explained to the participants in detail, followed by obtaining informed consent. The participants were requested to change to a gown. Then the age, height, and weight of the patients and blood sample for the pre-exposure serum thyroxin level measurement were collected prior to Brain CT Scan. The examination was done with the patient in supine position on the CT table, according to standard protocols for brain CT.

The Dose Length product (DLP) values were obtained by default from the CT machine at the end of the examination. A tissue-weighting factor of 0.0023 for the brain was used to convert the DLP to effective dose in Sievert (Sv) as recommended by the International Commission on Radiological Protection.

The patients were monitored for few minutes before they are allowed to leave the CT suite.

The standard assay procedure documented by Total Thyroxin (T4) Enzyme Immunoassay Test KIT catalog number BC -1007 is the adopted method used by the chemical pathology unit of the hospital. The quantitative measurement of the serum thyroxin level was assayed by ELISA—Enzyme Immunoassay using Total Thyroxin (T4) Enzyme Immunoassay Test kit. The test kit provides sheep anti-T4 coated microliter plate with 96 wells, Zero buffer, enzyme conjugate concentrate, enzyme conjugate diluent, tetramethylbenzidine (TMB) reagent, stop solution and a T4 reference standard containing 0, 2, 5, 10, 15, and 25ug/dl. The kit also contains an enzyme conjugate concentrate, enzyme conjugate dilute, TMB reagent, a stop solution and a timer for accurate timing of the procedure.

Using aseptic technique, the blood specimen was collected by venipuncture into a plain sample bottle that does not contain anticoagulant. The blood samples were collected immediately before, after and 7 days post brain CT scan for each patient. The seventh day sample was collected at the patient home and taken immediately to the Chemical Pathology Department

enveloped with a black cellophane bag to avoid contamination.

The blood samples were allowed to clot and the serum was separated by centrifugation. Serum sample was then carefully pipetted into a pre-labeled tube with proper patients' identification. The sample was analyzed according to standard ELISA protocols for thyroxin hormone. The reaction leads to a color change and the T4 level is read out as the T4 level directly proportional to the color intensity of the test sample.

All variables obtained were collated and documented into tabulated data sheet and analyzed in accordance with the study objective. The data was studied and analyzed using Statistical Package for Social Sciences (SPSS) windows version 22.0 statistical software (SPSS Inc, Chicago, IL), and the results obtained were presented in tables, charts and graphs.

A descriptive statistical tool was used to determine central tendencies while a paired-sample t-test was used to obtain significance between means. Pearson correlation coefficient and linear regression analysis model were also used to evaluate correlation between variables.

RESULTS

Anthropo-technical parameters of the participants studied showed that 32 participants were males and 28 were females. The mean age (±standard deviation) of the subjects is 60.80 + 7.60 years with a range of 38–74 years, while the mean weight, height and BMI are 76.53 + 9.28 kg, 1.73 + 0.07 m, and 25.55 + 3.20, respectively (Table 1). The male participant had a higher BMI compared to females (Table 1).

The KVp used in the studies range from 80 to 120 and mean mA of 110 ± 7.48 as shown in Table 1. The mean DLP and resultant brain effective dose were 662.451 + 230.782 and 1.667 ± 0.603 mSv (mean ± standard deviation), respectively (Table 2). Table 2 also shows that the DLP (mean ± standard deviation) of the obsessed group was 737.95 + 275.55(mGy-CM) and 1.83 + 0.662 mSv and higher than that of normal body weight group.

The mean serum thyroxin hormone (±standard deviation) level in the Pre-exposure, Immediate post-exposure, and 7-day post CT scan examination were 7.46 ± 1.30 µg/dl, 6.62 ± 1.78 µg/dl, and 7.89 ± 1.13 µg/dl, respectively (Table 3).

Table 3 does also summarize the Pre-exposure, Immediate post-exposure, and 7-day post-exposure serum thyroxin hormone levels in male as 7.65 ± 1.40 µg/dl, 6.93 ± 2.20 µg/dl, and 8.13 ± 1.07 µg/dl, whereas that of females as 7.24 ± 1.16 µg/dl, 6.28 ± 1.06 µg/dl, and 7.61 ± 1.16 µg/dl, respectively. Overweight participants had the highest pre-exposure and 7 days post exposure thyroxin hormone levels while normal weight participants has the highest level of immediate post exposure thyroxin level (Table 3).

No significant positive correlation was seen between brain effective dose and thyroxin hormone levels (pre, post, and

Table 1. Anthropo-techinical parameters of participants.

Parameter	Anthropometric		
	Range (Mean ± SD)		Range (Mean ± SD)
	Male (*n* = 32)	Female (*n* = 28)	Both gender (*n* = 60)
Age (years)	58–74 (65.28 ± 3.90)	38–69 (55.68 ± 7.59)	38–74 (60.80 ± 7.60)
Weight (kg)	65–102 (77.91 ± 8.24)	58–100 (74.96 ± 10.27)	58–102 (76.53 ± 9.28)
Height (m)	1.58–1.85 (1.74 ± 0.06)	1.58–1.85 (1.73 ± 0.07)	1.58–1.85 (1.73 ± 0.07)
BMI (kg/m2)	20.32–34.08 (25.86 ± 2.94)	20.45–33.80 (25.19 ± 3.49)	20–37 (25.55 ± 3.20)
Technical			
	Range	**Mode**	**Mean**
KVp	80–120	80	86.67 ± 10.84
mA	100–120	110	110 ± 7.48

KVp = kiloVoltage peak, mA = miliAmpare and BMI = Body Mass Index.

Table 2. DLP and brain effective dose characteristic of participants.

Variables	*N*	DLP (mGy-CM) Mean ± SD	ED Brain (mSv) Mean ± SD
Age group (years)			
38–47	4	706.33 + 221.73	1.74 + 0.55
48–57	15	708.97 + 293.86	1.80 + 0.78
58–67	31	633.67 + 206.73	1.60 + 0.54
68–77	10	637.34 + 182.04	1.60 + 0.49
BMI			
Normal	28	587.130 + 238.399	1.476 + 0.607
Overweight	26	726.144 + 192.840	1.832 + 0.544
Obese	6	737.95 + 275.55	1.83 + 0.662
Sex			
Male	32	587.130 + 238.399	1.476 + 0.6069
Female	28	726.144 + 192.840	1.832 +0.544
Composite	60	662.451 + 230.782	1.667 + 0.603

DLP = Dose length product, ED = Effective dose.

7-day post exposure) as shown in Table 4. This was also revealed by the non-uniform distribution of the scatter plot in Figures 1–3 (for the pre exposure, immediate post exposure, and 7-day post-exposure thyroxin hormone levels, respectively.

There was a weak correlation between post exposure serum thyroxin level with age yielding a Pearson's correlation coefficient (r) of 0.123 and 0.279, respectively for immediate post exposure and 7-day post exposure serum thyroxin levels (Table 5). No correlation was seen between serum thyroxin levels and BMI (Table 5).

DISCUSSION

Thyroxin hormone (T4) is produced by the thyroid glands which lies anterolateral to the trachea, extending from the thyroid cartilage of the trachea superiorly to the sixth tracheal ring inferiorly. Since the advent of CT scan, it has become one of the most commonly used imaging modality in the investigation of brain lesions. CT uses an X-ray to produce cross-sectional images of internal organs [3] and could also induce biological effects on organs like the thyroid gland that is highly and exquisitely radiosensitive.

The normal serum thyroxin hormone reference level of the hospital ranges from 5 to 13 µg/dl. In the present study the mean serum thyroxin hormone levels in the Pre-exposure, Immediate post-exposure, and 7-day post brain CT scan examination were 7.46 ± 1.30 µg/dl, 6.62 ± 1.78 µg/dl, and 7.89 ± 1.13 µg/dl, respectively. This shows that the serum thyroxin levels obtained were within normal limits, although a marginal reduction in the mean immediate post-exposure thyroxin level was observed. The values obtained in this study were euthyroid; therefore, contrary to a low thyroid hormone levels (hypothyroidism) in the non-randomized prospective study conducted by Laway et al. [11], to evaluate the response of the thyroid gland before and after exposure to radiation. The low thyroxin hormone levels recorded in the study by Laway et al. [11] can be attributed to the fact that radiation energy intensity was of therapeutic range and not diagnostic energy levels as it was in the present study. In the present study the Pre-exposure, Immediate post-exposure, and 7-day post-exposure serum thyroxin hormone levels obtained were within normal limits which were also contrary to the study conducted by Abdulah [15], at Kirkuk General Hospital in Kirkuk city in the north of Iraq, with 30 patients which showed a reduction in the serum thyroxin level. The study by Abdulah [15] also revealed that the reduction in serum thyroxin level increases with an increase in the exposure time or X-ray dose using 0.02 to 0.136 Gy (20 to 136 mGy). This is in accordance with that documented by Laway et al. [11] as well as Amis and Butler [16] but contrary to the findings in the present study. The variation in result may be due to the fact that the primary radiation was directed to the thyroid gland while in the index study the biological effect is assessed from the effect of scatter radiation reaching the thyroid gland. Therefore, this may explain the high radiation dose

Table 3. Serum thyroxin hormone level characteristic of participants.

Variable	*N*	Pre-exposure T4 level (µg/dl)	Immediate post-exposure T4 level (µg/dl)	7 days post-exposure T4 level (µg/dl)
Age group (years)				
38–47	4	7.45 + 1.32	6.45 + 0.77	7.45 + 1.31
48-57	15	7.16 + 0.94	5.79 + 0.79	7.41 + 1.23
58–67	31	7.72 + 1.45	7.12 + 2.17	8.01 + 1.10
68–77	10	7.00 + 1.27	6.31 + 1.39	8.28 + 1.04
BMI				
Normal	28	7.42 + 1.67	6.65 + 1.87	7.73 + 1.13
Overweight	26	7.58 + 1.48	6.64 + 1.76	8.25 + 1.10
Obese	6	7.12 + 1.15	6.47 + 1.65	7.12 + 0.80
Sex				
Male	32	7.65 + 1.40	6.93 + 2.20	8.13 + 1.07
Female	28	7.24 + 1.16	6.28 + 1.06	7.61 + 1.16
Composite	60	7.46 + 1.30	6.62 + 1.78	7.89 + 1.13

Table 4. Pearson's correlation between Brain ED and thyroxin hormone levels.

Variable	Brain ED	Pre exposure T4	Immediate post exposure T4	7 days post exposure T4
Brain ED				
Pearson correlation	1	0.110	−0.153	0.010
Sig. (2-tailed) *N*	60	60	60	60
Pre Exposure T4				
Pearson correlation	0.110	1	0.478**	0.652**
Sig. (2-tailed) *N*	60	60	60	60
Immediate Post Exposure T4				
Pearson correlation	−0.153	0.478**	1	0.266*
Sig. (2-tailed) *N*	60	60	60	60
7 days Post Exposure T4				
Pearson correlation	0.010	0.652**	0.266*	1
Sig. (2-tailed) *N*	60	60	60	60

**Correlation is significant at the 0.01(2-tailed). ED = Effective, T4 = Thyroxin hormone.

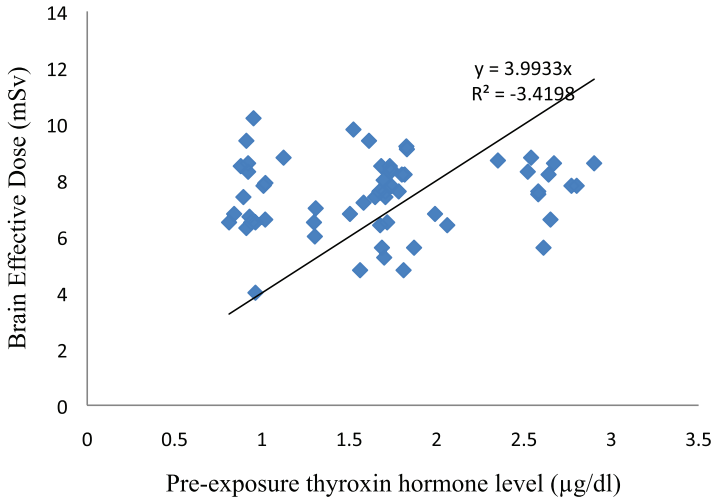

Figure 1. Scatter plot of the distribution of Brain effective dose and thyroxin level (pre-exposure thyroxin hormone level).

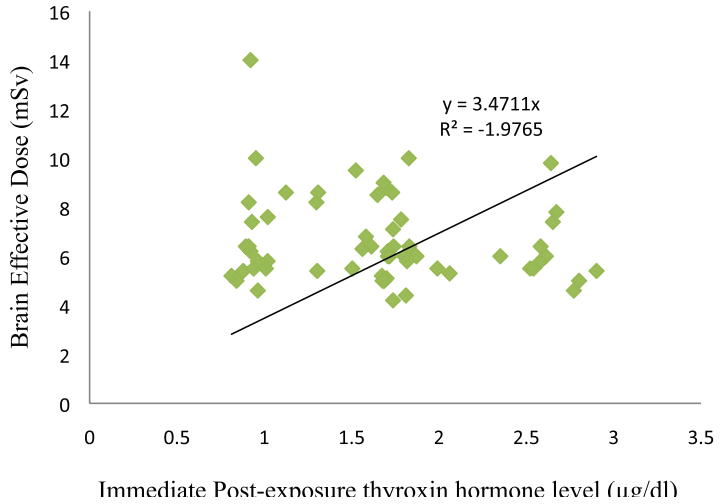

Figure 2. Scatter plot of the distribution of brain effective dose and thyroxin level (immediate post-exposure thyroxin level).

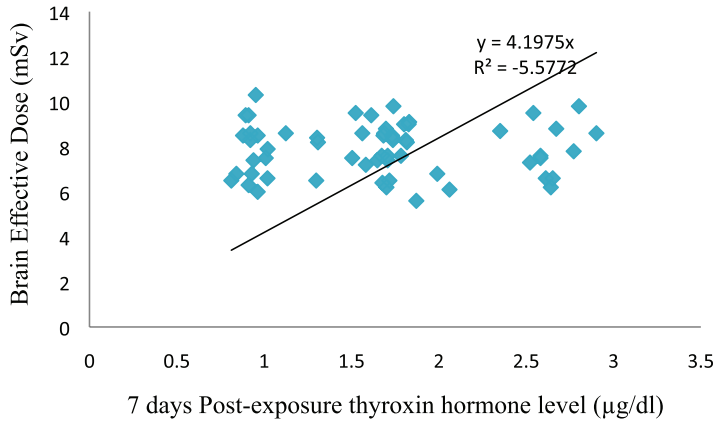

Figure 3. Scatter plot of the distribution of brain effective dose and thyroxin level (7 days post-exposure thyroxin level).

reaching the thyroid gland in the study by Abdulah [15] and Laway et al. [11] when compared with the present study.

The result obtained in this study was also in consonance with that documented by Philip [17] in a review in 1966 with twenty patients having laryngeal cancer being treated with large doses of X-rays. Their result showed no effect on the serum thyroxin level after 11 to 12 years duration of treatment. A close evaluation of the present study findings with that observed in experimental rats by Bertók and Nagy [18] in Japan to evaluate serum thyroxin (T4) level and the response of the thyroid gland to X-ray of 8 Gy (8,000 mGy) gave an antipode result. The irradiated rats were studied on the 7th-day post-irradiation revealing that the irradiation reduced the thyroid function significantly. The significant reduction could be due to the high absorbed dose in the rats, their small body mass, low circulating total thyroxin levels when compared with human subjects with higher metabolic activity, greater body mass and higher amount of circulating serum thyroxin, as well as variation in the transport system.

The present study revealed that the thyroid effective dose correlation with age while BMI revealed no correlation. Although there is paucity of literature on the relationship between changes in serum thyroxin levels and age, weight, height, and BMI, a closely related study by Mutsumi et al. [13] documented that after irradiation the number of proliferating cells in the thyroid gland of the younger age group reduces more when compared with that of the adult age group which suggests that radiation effect on the thyroid gland reduces with increasing age. Another study by Preston et al. [12] to evaluate the effect of age on the radiosensitivity of the thyroid glands of rat revealed a decrease in radiosensitivity with an increase in age. This was contrary to the index study which revealed a week relationship between age and 7 days post-exposure thyroxin level in the index study. No correlation was seen between BMI and serum thyroxin levels. The variation in findings with the index study may be due to the radiation dose or the study population employed.

Table 5. Pearson's correlation between pre and post exposure T4 levels with age and BMI.

Variable	Age	BMI	Pre-exposure T4	Immediate post exposure T4	7 days post-exposure T4
Age					
Pearson correlation	1	0.171	0.082	0.123	0.279*
Sig. (2-tailed)		0.191	0.533	0.349	0.031
N	60	60	60	60	60
BMI					
Pearson correlation	0.171	1	−0.132	−0.045	−0.087
Sig. (2-tailed)	0.191		0.317	0.732	0.510
N	60	60	60	60	60
Pre-exposure T4					
Pearson correlation	0.082	0.132	1	0.478**	0.652**
Sig. (2-tailed)	0.533	0.317		0.000	.000
N	60	60	60	60	60
Immediate post exposure T4					
Pearson correlation	0.123	0.045	0.478**	1	0.266*
Sig. (2-tailed)	0.349	0.732	0.000		0.040
N	60	60	60	60	60
7 days post exposure T4					
Pearson correlation	0.279*	−0.087	0.652**	0.266*	1
Sig. (2-tailed)	0.031	0.510	0.000	0.040	
N	60	60	60	60	60

**Correlation is significant at the 0.01(2-tailed). ED = Effective.

There is paucity of literature on the effect of X-ray on serum thyroxin levels in patients undergoing brain CT scan in our environment. With the increasing use of CT scan in the evaluation of brain lesions, there is a need to further assess the biologic effect of the X-ray on thyroid function on a larger group of patients notwithstanding the result obtained from the index study.

CONCLUSION

The mean serum thyroxin hormone levels in the Pre-exposure, Immediate post-exposure, and 7-day post brain CT scan examination were within normal limits. There is no significant effect of X-ray on serum thyroxin levels in patients undergoing brain CT scan as evident by the euthyroid result obtained. However, following the marginal reduction in the immediate post exposure mean thyroxin level obtained, a sustained exposure and (or) increase in exposure factors could plunge the thyroxin level to hypothyroidism. Therefore, it is pertinent to protect the thyroid gland during brain CT scan examination.

Recommendation

Although the serum thyroxin levels were not altered by the examination, the quantity of radiation dose absorbed by the thyroid gland is well significant. It is, therefore, recommended that thyroid shielding be used routinely during brain CT scan.

List of Abbreviations

BMI	Body mass index
CT	Computed tomography
DLP	Dose length product
ED	Effective dose
ELISA	Enzyme linked Immunoassay
KVp	kiloVoltage peak
mA	miliAmpare
mSv	miliSievert
SPSS	Statistical Package for Social Sciences
Sv	Sievert
T3	triiodothyronine
T4	Thyroxin
TMB	Tetramethylbenzidine

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent for publication

Written informed consent was taken from all the participants.

Ethical approval

Ethical approval was granted by the Rivers State Health Research Ethics Committee through a letter dated 28th March 2017.

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