ORIGINAL ARTICLE

Characteristics and Blood Pressure Profile of Goitre Patients in A Tertiary Hospital in South-West Nigeria

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ABSTRACT

Background: Goitre remains endemic in iodine deficient areas of the world despite widespread introduction of iodine fortified food. In Nigeria, it is the second most common condition in endocrinology clinic. There is a therefore a need to document the blood pressure profile and clinical characteristics of this condition.

Objective: This study assessed the clinical characteristics, biochemical and blood pressure profile of patients with goitre in the study area and assessed their knowledge and practice of preventive measures against goitre.

Methodology: A comparative study of 103 adults with goitres and 103 healthy controls. An interviewer administered questionnaire was used and venous blood samples were obtained for analyses. Variables of interest included socio-demographic, anthropometric, thyroid function, and blood pressure.

Results: The mean age of the goitre group was 46.92 ± 13.85 years with 86.4% carrying the swelling for up to 5 years. Anthropometric parameters, social habits, knowledge, and practice of the preventive role of iodized salt were similar between the goitre and control groups.

Forty-six percent of the goitrous subjects were hyperthyroid. Weight and BMI were significantly higher among the hypothyroid subgroup (p<0.001), with subjects in the hyperthyroid subgroup having significantly higher pulse rate and systolic blood pressure (p<0.001). The hypothyroid subgroup had significantly higher diastolic blood pressure and lower pulse pressure (p< 0.001).

Conclusion: This study concluded that patients with hyperthyroidism and hypothyroidism were more likely to have elevated systolic and diastolic blood pressure, respectively. Routine cardiovascular status check is therefore important in goitrous patients.

Key words: *Goitre, Thyroid Disease, Euthyroidism, Hyperthyroidism, Hypothyroidism*

INTRODUCTION

Goitre refers to any enlargement of the thyroid gland whether visible or palpable.[1] It is also defined as a thyroid gland that is larger than the upper limit of normal for the patient's age and sex.[2] The World Health Organisation (WHO) reported a worldwide prevalence of 7%, and it is common in endemic areas of developing countries especially among people living around hilly and mountainous terrains.[3] The topsoil of these areas is leached by erosion and thus the iodine content of the food crops grown is significantly low.[1] Inland area like the Alps, Himalayas, and the Andes are also prone to iodine deficiency due to similar reasons.[4] In endocrinology clinics in Nigeria, thyroid disorders are the second most common endocrine disorders seen.[5]

In a survey done by Isichei *et al*. in Jos, Plateau State in northern Nigeria, prevalence ranged from 1–23% of the population and iodine deficiency was common in the study population.[6] The Colorado prevalence study done by Canaris *et al* suggested that thyroid disease affects as many as 9% to 15% of the American adult female population and a smaller percentage of adult males.[7] However, in contrast to the survey in Jos, autoimmune mechanism was responsible for the common forms of thyroid disease in Americans.[8]

Iodine deficiency is a public health challenge in Africa. It's reported to be the most common cause of thyroid disorders in the continent.[9] Sidibe in a review of thyroid disease in sub-Saharan Africa also documented thyroid disease to be predominantly due to iodine deficiency and other goitrogens, but noted the increasing emergence of hyperthyroidism due to autoimmune conditions most especially Graves' disease, atrophic auto-immune hypothyroidism, and thyroid cancer.[10]

The thyroid gland absorbs ingested iodine from the blood and uses it to produce thyroid hormones, thyroxine (T4) and triiodothyronine (T3).[11] Synthesis and release of T3 and T4 are stimulated by the release of thyroid-stimulating hormone (TSH or thyrotropin) from the anterior pituitary gland. When T3 and T4 concentrations are low, TSH production is increased and vice versa via a negative feedback loop between the hypothalamus-pituitary-thyroid axis.[12]

Goitre may manifest as low levels of thyroid hormones in the blood (hypothyroidism), high levels of thyroid hormones (hyperthyroidism) and normal levels of thyroid hormone (euthyroidism) and its manifestation may be limited to the area of enlargement in the neck (pressure symptoms) or systemic which will include symptoms of overproduction or underproduction of thyroid hormones.[13,14] These systemic symptoms overtly or covertly affect the cardiovascular system and blood pressure changes (systolic and diastolic hypertension) have been seen in some goitre patients.[15] Cardiac decompensation, arrhythmias and heart failure have also been seen with thyroid dysfunctional states.[15,16]

Food iodization (fortification of food with iodine) is one of the main means of increasing a population's iodine intake and reducing the risk of Iodine Deficiency Diseases (IDD) including goitre.[14] Universal iodization of salt is the preferred strategy for the control of IDD in most countries. Salt is the vehicle of choice because of general consumption in most localities.[14] Despite these efforts, the prevalence of goitre is still high in many populations especially the agrarian communities of the developing world.[17] This may indicate interplay of multiple aetiological factors which may

include other goitrogens and autoimmune thyroid disease.[13,18]

There are sparse reports of cardiovascular and blood pressure abnormalities in goitre patients in our locality.[5,19] Therefore the aim of this study was to document the clinical characteristics, thyroid function and blood pressure profile of patients with goitre in an endemic region of South-West Nigeria and also assess the knowledge and practice of the subjects on ingestion of iodine fortified salt as a means of prevention.

METHODOLOGY

This was a comparative study of consecutive consenting adult patients presenting at the Surgery and Endocrinology Clinics of Obafemi Awolowo University Teaching Hospital(OAUTH) Ile-Ife, a tertiary health facility in South-West Nigeria. One hundred and three patients with goitre were consecutively recruited into the study and an equal number of age and sex matched healthy subjects were also recruited consecutively among staff, students and hospital visitors to serve as control. Written informed consents were obtained from all participants after explaining the purpose of the study to them. The study period was from March 2014 to February 2016. All patients with previous treatment with antithyroid drugs or thyroxine and those who were post thyroidectomy were excluded. Ethical approval was obtained from our institutional ethics and research committee before the commencement of the study.

Data were obtained from each participant with the aid of an interviewer administered questionnaire; each participant also had a complete physical examination, and 5ml of venous blood was collected for biochemical and haematological analysis. The body mass index (BMI) was calculated for each subject. Knowledge and practice of intake of iodized salt, alcohol consumption and cigarette smoking were recorded in the questionnaires.

Blood pressure was measured using standard protocols according to the 7th report of the Joint national committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC VII).[20]

Enzyme immunoassay test kits from Cusabio Biotech Company Limited, USA was used to measure the serum concentrations of free thyroxine (FT4), free triiodothyronine (FT3) and sensitive thyroid stimulating hormone (sTSH).

The normal reference ranges for FT3, FT4 and sTSH are 1.4-4.2pg/ml, 0.8-2.0ng/dl, and 0.5-5.6IU/ml respectively. All participants had thyroid function test done which helped to classify them into 4 groups viz: hypothyroid, hyperthyroid, euthyroid goitre and the control groups.

Patients who have goitre and symptoms suggestive of hypothyroidism and supporting biochemical findings of low FT3, low FT4 and elevated sTSH were classified as hypothyroid, those who have goitre and symptoms suggestive of thyrotoxicosis and supporting biochemical findings of elevated FT4 and/or elevated FT3 and low sTSH were classified as hyperthyroid. Those who have goitre with no symptoms suggestive of hypothyroidism nor thyrotoxicosis and normal FT3, FT4 and sTSH were classified as euthyroid. The healthy control group had no goitre and had normal thyroid function test. Control subjects with subclinical hypo- or hyper- thyroidism were excluded.

The data were analysed using the Statistical Product and Service Solution (SPSS) 20.0 version software (SPSS Inc, Chicago, IL). Descriptive statistics were computed for continuous variables while frequency tables were generated for categorical variables. The

continuous variables were expressed as means ± standard deviation while categorical data were expressed as percentages. Differences between two continuous variables were determined with the independent Students t-test and one-way analysis of variance (ANOVA) with Duncan post hoc test for differences among 3 or more continuous data. The differences between categorical data were done by the Chi-square (X2) test. The Pearson coefficient test was used to test the correlation between relevant variables. Level of statistical significance was defined as a p value ≤ 0.05 and a confidence interval of 95%.

RESULTS

A total of two hundred and six subjects made up of 103 subjects with goitre and an equal number of age- and sex-matched healthy controls completed the study. There were 15 males and 88 females in each group.

The socio-demographic characteristics of the study population are as summarized in table 1. The mean ages of both groups was similar (goitre group 46.92 ±3.85 years vs control group 46.58± 11.62 years; p = 0.8510). The least age for both groups was 18 years, while the oldest ages were 83 and 71 years for the goitre and control groups, respectively.

Table 1. Socio-demographic characteristics of the study population.

Parameters	Goitre (N=103)	Control (N=103)	*P* value
Age (Years)	46.92 ± 13.85	46.58 ± 11.62	0.8510
Sex; Male	15 (14.6%)	15 (14.6%)	1.0000
Female	88 (85.4%)	88 (85.4%)	
Diagnosis; Hyperthyroid	47 (45.6%)		
Euthyroid	45 (43.7%)	103 (100)	
Hypothyroid	11 (10.7%)		
Cigarette Smoking	8 (7.8%)	6 (5.8%)	0.5790
Alcohol Ingestion	9 (8.7%)	10 (9.7%)	0.5160
Ingestion of Iodide Salt	51 (49.5%)	60 (58.3%)	0.1240
DONS; 1-5 years	89 (86.4%)	0	
6-10 years	9 (8.7%)	0	
>10 years	5 (4.9%)	0	

Key: DONS=Duration of Neck swelling

Table 2. Physical and Blood pressure profile of the study population

Parameters	Hyperthyroid Mean ± SD N = 47	Euthyroid Mean ± SD N = 45	Hypothyroid Mean ± SD N = 11	Control Mean ± SD N = 103	*P* value
Weight (Kg)	63.58±7.08a	77.41±8.66	93.00±4.85 f	70.61±11.21	<0.0001
Height (M)	1.70±0.04e	1.67±0.04	1.67±0.05	168.34±4.17	0.0154
BMI(Kg/M2)	22.17±1.62	27.60±3.18	33.30±2.17f	24.94±4.20	<0.0001
BSA(M2)	1.73±0.11	1.89±0.11	2.01±0.07f	1.81±0.15	<0.0001
PR (B/M)	105.51±5.75e	77.96±8.5	59.11±2.03	74.78±10.88	<0.0001
SBP (mmHg)	144.46±10.59e	116.82±11.16	112.22±15.64	123.20±14.63	<0.0001
DBP (mmHg)	66.38±9.42	72.50±7.19	84.44±18.11f	72.80±11.98	<0.0001
PP (mmHg)	78.94±11.08e	43.86±9.21	24.44±5.27	49.50±11.32	<0.0001
MABP(mmHg)	92.41±7.89a	87.27±7.20	93.70±16.70	89.60±11.51	0.0725

KEY: a=p<0.05 for hyperthyroid vs euthyroid and control; b=p<0.05 for hyperthyroid vs hypothyroid; c=p<0.05 for hypothyroid vs euthyroid and control; d=p<0.05 for euthyroid vs control; e=p<0.05 for hyperthyroid vs euthyroid, control and hypothyroid; f=p<0.05 for hypothyroid vs euthyroid, control and hyperthyroid; SD = standard deviation; BMI= Body mass index; BSA= Body surface area; PR=Pulse rate; SBP= Systolic blood pressure; DBP= Diastolic blood pressure; PP= Pulse Pressure; MABP=Mean arterial Blood Pressure.

Table 3. Selected Laboratory parameters

Parameters	Hyperthyroid Mean ± SD N = 47	Euthyroid Mean ± SD N = 45	Hypothyroid Mean ± SD N = 11	Control Mean ± SD N = 103	*P* value
sTSH(IU/ml)	0.30±0.10	1.44±0.85	11.62±5.03f	1.22±0.72	<0.0001
FT3(pg/ml)	10.31±4.15e	3.11±0.73	0.88±0.21	3.15±0.77	<0.0001
FT4 (ng/dl)	4.25±1.34e	1.34±0.26	0.43±0.07	1.33±0.30	<0.0001
Serum Na(mmol/L)	140.87±2.21	140.61±2.25	142.22±1.48	139.89±2.47	0.3000
Serum K(mmol/L)	3.80±0.27	3.87±0.21	3.93±0.27	3.87±0.22	0.2297
Serum Cl(mmol/L)	101.26±3.10	101.84±3.75	102.55±3.28	100.00±4.90	0.0525
Serum urea(mmol/L)	4.1±0.88	4.0±0.90	4.2±0.98	4.1+0±0.92	0.3134
Serum creatinine (Umol/L)	102±5.62	100±6.67	99±8.45	101±7.92	0.4329
PCV (%)	38.17±3.70	38.11±3.11	37.22±4.24	38.96±4.13	0.3597

KEY: a=p<0.05 for hyperthyroid vs euthyroid and control; b=p<0.05 for hyperthyroid vs hypothyroid; c=p<0.05 for hypothyroid vs euthyroid and control; d=p<0.05 for euthyroid vs control; e=p<0.05 for hyperthyroid vs euthyroid, control and hypothyroid; f=p<0.05 for hypothyroid vs euthyroid, control and hyperthyroid; sTSH= sensitive Thyroid stimulating hormone; FT3=Free triiodothyronine; FT4=free thyroxine; Na=Sodium; K=Potassium; Cl=Chloride; PCV= Packed cell volume

Forty-seven (45.6%) subjects of the goitre group were hyperthyroid, 45 (43.7%) were euthyroid, while 11 of them (10.7%) were hypothyroid. All the apparently healthy subjects in the control group were euthyroid.

Eight per cent of the goitre population smoked significant pack years of cigarettes as compared to 6% of the control group. This, however, was not statistically significant (p = 0.5790). Furthermore, 9% and 10% of the goitre and control groups, respectively, ingested significant amount of alcohol (p = 0.5160). Knowledge and practice of intake of iodized salt in both groups were not statistically significant (p = 0.1240).

The duration of anterior neck swelling ranged from less than one year to 12 years with 86.4%% of the cases having their goitre for less than 5 years.

The physical and blood pressure profile of the goitre and the control group is as summarized in Table 2. There was no significant difference in the height of all the groups. However, the hypothyroid group had a significantly higher body weight, body mass index, and body surface area (p <0.001) compared to the other groups. There was no statistically significant difference between the pulse rate of the control and the euthyroid group, however, the pulse rate of the hyperthyroid group was significantly higher. The systolic blood pressure of the hyperthyroid group was significantly higher than the other groups (p<0.001), so also was the pulse pressure. There was a significantly higher diastolic blood pressure in the hypothyroid group with a resultant lower pulse pressure (p<0.001).

The mean arterial blood pressure was however not statistically significantly different among the 4 groups (p = 0.0725).

Figures 1-3 shows the clinical features of the hyperthyroid, hypothyroid, and euthyroid subgroups, respectively.

Figure 1. Clinical features in subjects with hyperthyroid goitre

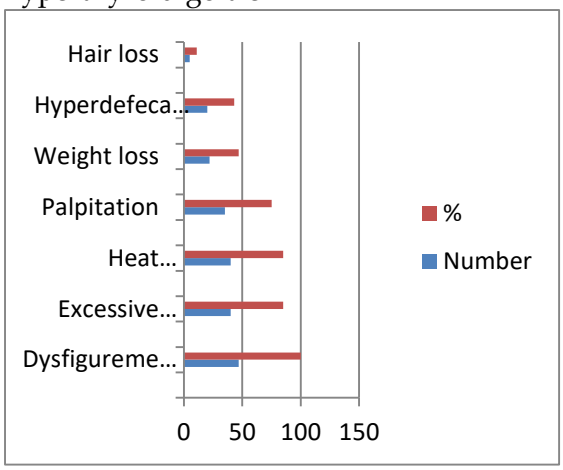


Figure 2. Clinical features of patients with Hypothyroid goitre

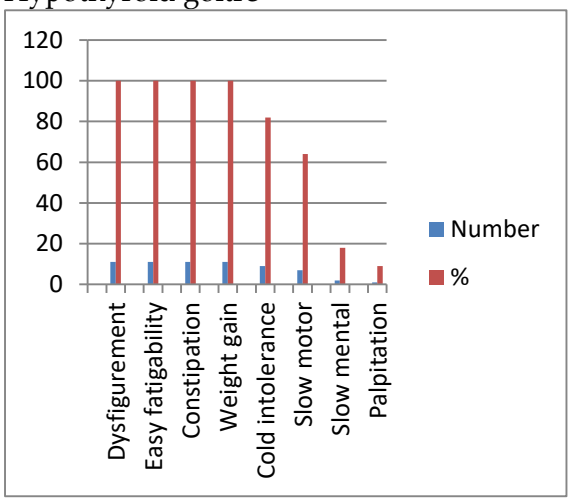
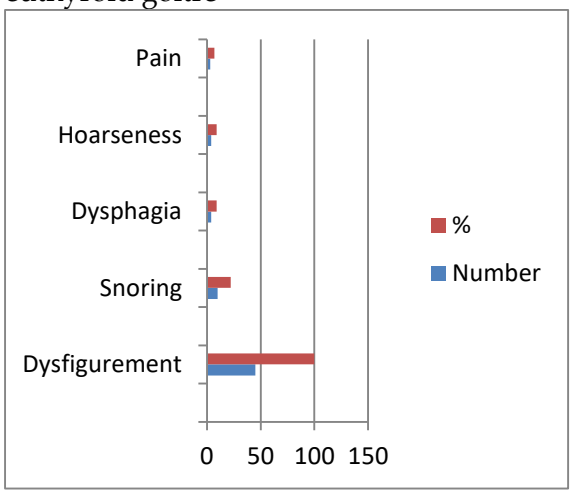


Figure 3. Clinical features of patients with euthyroid goitre



DISCUSSION

This study showed a female preponderance of goitre (F:M ratio of 6:1) which is consistent with previous studies. The high female preponderance is independent of the thyroid function. The mean age of occurrence of goitre in this study was 46.92 ± 13.85 years and this compared favourably with previous studies. Famuyiwa *et al.*[19] in Ibadan found a mean age of 41.4±16.5 years, Ogbera *et al.*[5] got a mean age of 40±12.4 years in Lagos while Ojo[18] in Ile Ife and Chehade[21] in America found a mean age of 44.6±13.8 and 47.8±14.9 years respectively. In this study, as in other reports from other parts of Africa the peak age of incidence of thyroid diseases was around the fourth and fifth decade of life. [22,23,24,25]

Commonest biochemical presentation of goitre was hyperthyroidism. This was closely followed by those patients who presented in euthyroid state. The rarity of hypothyroid subjects was also seen in the studies of Ojo *et al.* and Ogbera *et al.* who got hypothyroid cases in 2% and 7% of their goitre subjects respectively.[5,18] There appears to be an increase in the proportion of hyperthyroid patients, this may be a reflection of an emerging change in the aetiology of goitre from iodine deficiency to conditions like autoimmune diseases. Assay of thyroid-stimulating antibodies in future studies may give better insight into this observation.

The fact that our hospital is a regional referral centre may also account for the observed high proportion of hyperthyroid patients as severe and potentially complicated patients are more likely to be referred from secondary hospitals where less challenging cases would have been treated. Further study involving multiple centres is needed to determine the exact distribution of the goitre subtypes in our environment. A high case of

hyperthyroidism was also noted by Ogbera who found hyperthyroidism in 84% of goitre patients in a study conducted in Lagos State University Teaching Hospital. Therefore, the documented increasing prevalence of hyperthyroidism further strengthens the need towards routine perioperative thyroid hormonal assays as inadvertent surgery on a hyperthyroid patient may be catastrophic.

Of the goitrous patients, 86.4% of them have had their neck swelling for about 5 years. This duration is slightly higher than that of Ojo *et al.* in whose patient had a mean duration of neck swelling of 34.0±20.9 months.[18] Late presentations on account of slowly progressive thyroid enlargement in an endemic area has also been reported in goitre patients as well as other chronic illnesses, which may have been aided by economic hardships.[25,26, 27, 28, 29]

All the goitre patients in this study complained of disfigurement as a result of anterior neck swelling as the most common reason for seeking medical help. This was also reported by Kebede *et al.* who reported disfigurement in 99% of his goitre series.[25]

Aside this, the most common symptoms of hyperthyroidism were excessive sweating, heat intolerance, palpitations, weight loss, and hyper-defecation, while that of hypothyroid subjects was easy fatigability, weight gain and constipation. These had also been noted in other studies, at home and abroad.[5,18,19,25] The most common symptoms of hyperthyroidism observed by Ojo *et al.* were excessive sweating and weight loss. Ogbera *et al*. reported weight loss, excessive sweating, palpitations, and heat intolerance among the first five symptoms. In a study of 44 Nigerians with thyrotoxicosis, Famuyiwa *et al*. also observed similar features but weight loss and palpitations appeared to be the two most frequent symptoms.[19] The common symptoms of the euthyroid groups were snoring, dysphagia, hoarseness of voice, and pain. Hegedus *et al.* documented mechanical compression of the trachea and/or oesophagus in 30% to 85% of the patients in a surgical case series studied.[30]

The hyperthyroid group had a significantly lower body weight, body mass index, and body surface area compared to the other groups, probably from increased metabolic rates. This compared favourably with previous studies.[15,16,29,31] The increased weight in the hypothyroid group may be as a result of the associated myxoedema which was worsened by the fluid retention and reduced metabolism.[32]

The difference in the packed cell volume (PCV) across the groups in this study was not statistically significant. Although, some previous studies had documented increased erythropoiesis in hyperthyroid patients, however, Biondi *et al*. noted a parallel increase in blood volume with an increase in erythropoiesis and therefore PCV value remains normal in thyroid diseases.[31] Famuyiwa *et al*. found no significant difference in the PCV between thyrotoxic patients and apparently normal control group.[33]

The pulse rate and the systolic blood pressure of the hyperthyroid group were significantly higher and so was the pulse pressure. These findings had previously been documented.[15,16,31] In the study by Famuyiwa *et al*., 94% of the thyrotoxic subjects had a pulse rate greater than 90 beats per minutes while 75% had a pulse rate greater than 100 beats/min.[19] The pulse rate of the subjects reported by Famuyiwa *et al*. ranged between 68 and 144 beats/ minute which compared with the pulse rate in this study (96 and 128 beats per minutes). The average pulse rate in the hypothyroid subjects was 59.11±2.03 which compares

favourably with the study of Coppola *et al.* and Tielens *et al*. [32,34]

The prevalence of hypertension in both hyperthyroid and hypothyroid goitre had also been documented in previous studies. In this study, 85.1% of the hyperthyroid group were hypertensive (predominantly systolic) while 44.5% of hypothyroid were found to be hypertensive (predominantly diastolic). Ojo found more than 60% of her thyrotoxic subjects to be hypertensive.[18] Cardozo *et al*. reported that one-third of patients with diffuse toxic goitre had systolic hypertension which is less than the findings in this study, probably because our subjects were more advanced in age and the duration of symptoms was longer in this study than theirs (less than 18months).[22] The presence of cardiovascular morbidities in our goitre patients can delay surgery and can potentially lead to perioperative morbidities and mortalities. These patients are often unaware of their cardiovascular morbidity until their index presentation. Clinicians managing goitres should be aware of this and specifically be on the lookout for such occult cardiovascular disease in goitrous patients.

There was a high knowledge and practice of ingestion of iodine fortified food among the goitre group as well as the control group. The global fortification of food and salt with iodine and the lack of statistical significance among the healthy control group and the goitre group about practice of ingestion of iodized salt may point to the fact that iodine deficiency may not be majorly responsible for the high prevalence of goitre in our patients. Isichei *et al.* suggested that the aetiology of endemic goitre may not only be associated with iodine deficiency.[6] There may be interplay of multiple aetiological factors. Ojo *et al*. also suggested rising autoimmune prevalence among Africans while Ogbera *et al*. noted that goitrogens like selenium deficiency and thiocyanate toxicity may be likely culprits in the aetiology of goitre.[5,18] Studies to identify these emerging aetiologies in our environment are desirable.

CONCLUSION

Goitre is still prevalent among females and the commonest reason for presentation remains cosmetic while late presentation is more likely.

Patients with hyperthyroidism and hypothyroidism were more likely to have elevated systolic and diastolic blood pressure, respectively. Therefore, routine cardiovascular status check is important in patients with goitre.

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