Original Article

Evaluation of thyroid nodules in patients with goitre using nuclear medicine, biopsy and ultrasound in Sudan

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ABSTRACT

Goiter is a common thyroid disorder in Sudan. Most of thyroid nodules are benign, but a small percentage can be cancerous among the other pathology. The aims of this study were to assess the value of scintigraphy, ultrasound (US) and biopsy in the detection of nodules and to determine the prevalence of thyroid nodule among patients with thyroid goiter in Sudan. A total of 100 patients were investigated. 58 patients were investigated with biopsy in addition to the aforementioned techniques. Scintigraphic examination involved the intravenous injection of 2-5 mCi of Tc99m followed in 15 minutes by 300 kC at the neck, US was performed using an instrument with a 7.5 MHz and biopsy was carried out with either Fine Needle Aspiration Biopsy (FNAB) or open operation. The majority of the patients were females (81%). Scintigraphy revealed that 58% of the patients had nodular goiter while the rest had diffuse goiter. The highest incidence of nodules was shown in the age group between 40-60 (23%). US revealed that 48% of the nodules were solitary. Furthermore, 78% the nodules were hypoechoic, 29% were calcified and 28% were hypervascular. The biopsy results showed that 14% of nodular patients were malignant, 88% follicular adenocarcinoma. 36% had nodular goiter with cystic or degenerative changes. The highest percentage of malignancy could be attributed to the fact that patients referred to the hospital in a late stage of the disease. All patients with goiter should undergo US and NM investigation in order to detect the morphology and function of the thyroid.

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Key words: Thyroid, Goitre, Nuclear Medicine, Biopsy, Ultrasound

INTRODUCTION

Thyroid disorders affect a wide spectrum of our population. Numerous imaging modalities, including nuclear medicine, ultrasonography, X-ray fluorescence, computerized tomography (CT) and, more recently, magnetic resonance imaging MRI, have been used in an attempt to provide a pathophysiologically related diagnosis in patients with diseases of the thyroid1

Nuclear medicine imaging of thyroid provides useful information about the shape, size and site of thyroid tissue, the function of thyroid nodule, and functioning thyroid tissue in patients with thyroid carcinoma. Either iodine -123 (I123) or technetium-99m (Tc99m) may be used 2. Iodine deficiency continues to be a significant public health problem in many areas of the world4.
A thyroid nodule is a ‘discrete lesion within the thyroid gland that is palpably and/or ultrasonographically distinct from the surrounding thyroid parenchyma. Thyroid nodules are extremely common, with 7% of adults having palpable nodules and up to 50% of adults having nodules visible on ultrasound around 5% of thyroid nodules are malignant. Thyroid nodules may occur as isolated, often incidental findings, or they may be associated with systemic features of thyrotoxicosis or hypothyroidism. They may be solitary or may present as a dominant nodule in a multinodular goitre. Solitary nodules have a higher likelihood of being malignant although overall the prevalence of cancer is similar between patients with a solitary nodule and patients with multiple nodules. The challenge for the general practitioner is to assess the nodule and determine which patients require referral to a surgeon or endocrinologist for further investigation and management. Referral may be required to exclude or confirm malignancy and is also indicated for patients who are symptomatic from benign thyroid nodules.

Sohaib et al evaluated Correlation of Single Image Tc99m MIBI Scan and Ultrasonography with Fine Needle Aspiration Cytology (FNAC) to assess Neoplasia in Solitary “Cold” Thyroid And reported that Ultrasonography also had a sensitivity of 100% considering solid and cystic lesions as test positive. But specificity of US was found to be only 13%. The sensitivity and specificity of the combined results of Tc99m MIBI scintigraphy and ultrasonography were also not found to be significantly different from those of Tc99m MIBI scan alone (100% and 91% respectively). Hence in patients with solitary cold thyroid nodules on Tc99m Pertechnetate study, a single Tc99m MIBI scan can be used reliably to assess neoplastic nature of the nodule with high degree of sensitivity and specificity. Special emphasis will be put on recent developments in the concept of IDD such as the role of iodine deficiency in the development of brain damage and mental retardation goiter seen as a sign of maladaptation to iodine deficiency rather than as the adaptive process to the deficiency assessment of the iodine status of a population and control of IDD including present achievements; monitoring and side effects. Extensive and recent global reviews of the different aspects of IDD are available elsewhere. The danger of pressure on important structures in the neck is present in any enlarging goitre. This may be brought about by the gradually enlarging thyroid gland compressing the trachea, medinstinal vessels, the recurrent laryngeal nerve and the oesophagus. The sudden enlargement of the gland consequent upon haemorrhage into a cyst. The hazards of surgery are yet another risk that may be encountered in patients undergoing partial thyroidectomy. The aims of this study were to assess the value of scintigraphy, ultrasound (US) and biopsy in the detection of nodules and to determine the prevalence of thyroid nodule among patients with thyroid goiter in Sudan.

**MATERIALS AND METHODS**

This study was done in Nuclear Medicine Department, Radiation and Isotope Center of Khartoum (RICK) in the period from 2007 up to 2010. This part represents the machines used in the experiment and the apparatus used in the laboratories. 100 patients with goiter were recruited for (thyroid scan, ultrasound imaging, thyroid function test and biopsy) for detection of nodular incidence among goiterous patients.

**SPECT MACHINE**

Nuclide gamma camera computer system (planer and duble head whole body SPECT) with general purpose collimators med in Hungary. Generator UltraTechneKow ® FM DRN 4329Mo/ 99mTc Generator Composition (elute) 99Mo content < 25 Bq/MBq 99mTc. Specifications are within the specifications described by monographs of the U.S.A. and the European Pharmacopoeia PH 5.0 – 7.0 Ultrasound system used is General electric (GE) medical system, logic 5 expert. Ultrasound transducer used is Liner probe with a frequency of 6.0 MHz, made by Yokogawa medical system, Ltd. 7-127 Asahigaoka 4-chome Hino-shi Tokyo, Japan. Laboratory Tools ,Biopsy conventional plastic disposable syringe, glass slide.

**RESULTS**

The general characteristics of the sample studied: The majority of patients studied were females (81%), while males present the percent of (19%). The average age of the patients studied was 36 years. The peak incidence was among females between 20-40 years of age presenting the percent of (38%) . So far as the distribution among age groups is concerned, 4 (4%) were below the age of 20, 38 (38%) were in the 20-40 age group,34 (34%) were in the 41-60 age group, and 24 (24%) were above61 years of age. The majority of patients studied were from Khartoum state (36%), Centre (30%), and West (20%), North (8%), South (2.0%) and East (4%). (fig 1)
It has been found that (42%) of the scans were diffuse goitre, forming about 42 patients. 58 among the series patients of 100. (Fig 2)
The study determined the overall of goiter sufferers to be 58 of the population with nodular goiter, 47(81%) were female and 11(19%) were male, . As regards 42 of the population with diffuse goiter, 34 (81%) were female, and 8 (19%) were male. 
In the age groups, there were rather wide variations in the number of patients with nodular and diffuse types of goiter. Among those below 20 years of age, 1(1%) had nodular and 3( 3%) had diffuse goiter, while in the 20-40 age group, 14 (14%) suffered from nodular goiter and 23 (23%) from diffuse goiter. A reversal in the percentages was observed with the higher age groups; in the 41-60 group, 11( 11 %) had nodular while 11( 11 %) had diffuse goiter, and among the patients older than 60, nodular goiter frequency went up to 20 ( 20 %) while diffuse goiter was relatively low 4( 4 %).
The ultrasound imaging findings: Multiplicity Multiple 30(51.7%) Solitary 28 (48.3) echogenicity, echo structure, shape, The echogenicity of each nodule was classified as hypoechoic 34(28.6%), isochoic 19(32.76%), or hyperechoic 5 (8.62%) in comparison with the surrounding tissue of the thyroid gland vascularity well-vascularized 3(5.17%) Medium-vascularized 10 (17.24%)Non-vascularized 45(77.59%),Calcification Calcified 17(29.3%)Non-calcified 41(70.69)Marginal appearance Well-defined 49(84.48%)Poorly-defined 9(15.52%). Echo structure was defined as predominantly solid 16(27.59%), predominantly cystic 8(13.79%), completely solid 16(27.59%), completely cystic or mixed 18(31.03%)Marginal appearance Well-defined 49(84.48%)Poorly-defined 9 (15.52) .

![Figure 1 Geographical Area](image1)

![Figure 2 Thyroid pattern on Tc99m scan](image2)
The biopsy finding, The 58 FNA biopsies performed on thyroid nodules at Khartoum- Sudan a total of 8 procedures (13.8%) histopathological findings that were diagnostic of malignancy, whereas 50 procedures (46.2%) were benign cytologic findings. Among the 8 malignant nodules within the study 7 (87.5%) were follicular adenocarcinoma, and 1 (12.5%) were lymphoma. Histopathological results for the 50 benign nodules included 20 (40%) benign nodular goitre and 18 (36%) were nodular goiter with cystic or degenerative changes and 10 (20%) were colloid nodular goiter, 1 (2%) were found cystic colloid goiter and 1(2%) diagnosed as benign cyst.

Ultrasound findings versus biopsy findings: Hypoechoogenicity was a common sonographic feature in both benign and malignant nodules in this study 29(58%) of benign nodules and 5(62.5%) of malignant nodules. Isoechoogenicity 16(32%) of benign nodules and 3(37.5%) of malignant nodules respectively). Hyperechogenicity, in comparison, was relatively rare within groups, constituting only 5(10%) of benign and nil for malignant nodules. Most of the malignant nodules were mixed 14(28%) or mostly solid with cystic regions 14(28%) and it was the same for completely solid nodules. A solid echo texture, however, was also most common among benign nodules in this study 14 (28%) the same ratio was obtained for predominantly solid and mixed benign nodules. Predominantly cystic nodules appeared to be slightly more associated with benignity than malignancy 8(16% versus 0%).

DISCUSSION
In this study evaluated modalities (ultrasound, biopsy and nuclear medicine) examination incase of thyroid gland goiter and nodules. And found to be (58%) of the patients investigated. The majority of the sample under study were females 81 patients forming the incidence of 81% and male 19 patients forming the incidence of 19%. This is true since Kapur from India found an incidence of thyroid malignancy of 23.2% among males with solitary thyroid nodule compared to 11.4% in females. He concluded that the risk of thyroid cancer in solitary thyroid nodule is nearly double in males. Omran and Ahmed (14) assessed Carcinoma of the thyroid in Khartoum the study included One hundred and twelve patients with thyroid malignancy seen at The Radio-isotope Centre, Khartoum (RICK) during the period 1982-1989 were studied. The female to male ratio was 2.5:1.0 with a high incidence of the disease between the ages of 40 and 70 years.
The average age of the patients studied was 36 years. The peak incidence was among females between 20-40 years of age presenting the percent of (38%). So far as the distribution among age groups is concerned, 4 (4%) were below the age of 20, 38 (38%) were in the 20-40 age group, 34 (34%) were in the 41-60 age group, and 24 (24%) were above 61 years of age. Omran and Ahmed [14] reported that the female to male ratio was 2.5:1.0 with a high incidence of the disease between the ages of 40 and 70 years. Follicular carcinoma was the commonest (42%) followed by papillary (22.3%) and anaplastic (21.4%). Goitre was the main presenting symptom (92.9%). Cervical lymphadenopathy was present almost equally in these three histological types, 26.6%, 32%, and 33% respectively. The majority of patients studied were from Khartoum state (36%), Central Sudan (30%), and Western Sudan (20%), Northern Sudan (8%), Southern Sudan (2.0%) and Eastern Sudan (4%). It has been found that (42%) of the scans were diffuse goitre. Forming about 42 patients, 58 among the series patients of 100. The study determined the overall of goiter sufferers to be 58 of the population with nodular goiter, 47 (81%) were female and 11 (19%) were male, as regards 42 of the population with diffuse goiter, 34 (81%) were female, and 8 (19%) were male. In the age groups, there were rather wide variations in the number of patients with nodular and diffuse types of goiter. Kapur [15] reported an incidence of malignancy of (17.7%) in cold nodules, Kresnik et al. [16] Evaluate thyroid nodules by technetium-99m tetrofosmin dual-phase scintigraphy. The study determined which thyroid nodules retain tetrofosmin and whether preoperative evaluation of malignancy is possible. Tetrofosmin scintigraphy was performed in 57 patients with a cold thyroid nodule on previously performed pertechnetate scintigraphy. All patients had undergone ultrasonography and sonographically guided fine-needle aspiration biopsy.

ULTRASOUND IMAGING FINDINGS
Multiplicity Multipl 30 (51.7%) Solitary 28 (48.3%) echogenicity, echo structure, shape, The echogenicity of each nodule was classified as hypoechoic 34 (28.6%), isoechoic 19 (32.76%), or hyperechoic 5 (8.62%) in comparison with the surrounding tissue of the thyroid gland Vascularity Well-vascularized 3 (5.17%) Medium-vascularized 10 (17.24%) Non-vascularized 45 (77.59%), Calcification Calcified 17 (29.3%) Non-calcified 41 (70.69%) Marginal appearance Well-defined 49 (84.48%) Poorly-defined 9 (15.52%). Echo structure was defined as predominantly solid 16 (27.59%), predominantly cystic 8 (13.79%), completely solid 16 (27.59%), completely cystic or mixed 18 (31.03%) Marginal appearance Well-defined 49 (84.48%) Poorly-defined 9 (15.52%). Kresnik et al. [16] assessed Scintigraphic and ultrasonographic appearance in different tumor stages of thyroid carcinoma. The study was compared the scintigraphic pattern in different tumor stages of thyroid carcinoma.

Popowicz et al. [17] assessed The usefulness of sonographic features in selection of thyroid nodules for biopsy in relation to the nodule's size. The study evaluated the efficacy of selected ultrasound (US) features of thyroid focal lesions useful for establishing indications for fine-needle aspiration biopsy (FNAB) with regard to the lesion's size.

THE BIOPSY FINDING
The 58 FNA biopsies performed on thyroid nodules at Khartoum- Sudan a total of 8 procedures (13.8%) histopathological findings that were diagnostic of malignancy, whereas 50 procedures (46.2%) were benign cytologic findings. Among the 8 malignant nodules within the study 7 (87.5%) were follicular adenocarcinoma, and 1 (12.5%) were lymphoma. Histopathological results for the 50 benign nodules included 20 (40%) benign nodular goitre and 18 (36%) were nodular goiter with cystic or degenerative changes and 10 (20%) were colloid nodular goiter, 1 (2%) were found cystic colloid goiter and 1(2%) diagnosed as benign cyst.

Bashier et al. [18] reported that among 89 patients, 64 had simple goitre (72%), 12 follicular adenoma (13.5%), 12 were malignant nodules (6 follicular, 5 papillary and one anaplastic) (13.5%) and one patient had Hashimoto's thyroiditis. In India, Kapur [15] reported an incidence of (10%) malignancy among a series of 253 patients with solitary thyroid nodule seen at New Delhi. Results of pathologic examination confirmed that, among the 8 malignant nodules 7 (87.5%) were follicular adenocarcinoma, and 1 (12.5%) were lymphoma. Omran and Ahmed [14] reported that Follicular carcinoma had the highest incidence of blood borne metastasis (21 out of 47 patients) being mostly osseous (16 patients). Anaplastic and squamous cell carcinoma showed a locally aggressive behavior to nearby structures resulting in hoarseness of voice.

Hypoechogenicity was a common sonographic feature in both benign and malignant nodules in this study 29 (58%) of benign nodules and 5 (62.5%) of malignant nodules. Isoeohgenicity 16 (32%) of benign nodules and 3 (37.5%) of malignant nodules respectively.)
Hypoechogenicity, in comparison, was relatively rare within groups, constituting only 5(10%) of benign and nil for malignant nodules. Most of the malignant nodules were mixed 14(28%) or mostly solid with cystic regions 14(28%) and it was the same for completely solid nodules. A solid echo texture, however, was also most common among benign nodules in this study 14 (28%) the same ratio was obtained for predominantly solid and mixed benign nodules. Predominantly cystic nodules appeared to be slightly more associated with benignity than malignancy 8(16%) versus 0%. In this study sonographic features among benign and malignant nodules indicates that only the presence of calcification is a predictor of malignancy. Popowicz et al (17) reported that US imaging features of 1141 thyroid nodules (shape, echogenicity, pattern of blood flow, presence of microcalcifications and the presence of other nodules in the thyroid) and their palpability were compared with the post-operative histopathological outcomes. The efficacy of the selected sets of the features was assessed for small nodules (SN)< or =15 mm and large nodules (LN)>15 mm, as well as separately for nodules< or =10 mm In the LN group, the selection criteria based on the shape of lesions and hypoechogenicity were less sensitive than in the SN group, but they allowed further reduction in the number of performed FNABs. Large nodules primarily selected for FNAB should be hypoechogenic, more tall than wide or contain microcalcifications (sensitivity 84%, specificity 72%). The obtained results provide rationale for using features from the US examination in selecting both small and large nodules for FNAB. In the case of LN, the usefulness of sonographic features is less sensitive, but more specific than in the case of SN.

All nodules showing microcalcifications should therefore undergo biopsy. Echogenicity, echo structure, shape, border classification, or grade of intrinsic vascular flow by color Doppler imaging did not show any statistical difference between benign and malignant nodules in this study. Park et al (19) assessed Sonography of thyroid nodules with peripheral calcifications. This study assessed the role of sonography (US) in the differentiation of benign from malignant thyroid nodules with peripheral calcifications. Sixty-four thyroid nodules with peripheral calcifications that were detected on US were included in the study. Nineteen nodules (30%) were benign, and 45 nodules (70%) were malignant and compared the US findings of the benign and malignant nodules, including interruption, thickening (> or =0.5 mm and over more than 50% of the circumference) of calcifications, internal echogenicity, margin, and presence of cystic change, size, and shape. Univariate and multivariate logistic regression analyses were performed. Interruption of peripheral calcifications was more common in malignant nodules (84%) than in benign nodules. Thickening of the peripheral calcification was seen more frequently in malignant nodules (64%) than in benign nodules (11%). For internal echogenicity, malignant nodules (58%) were more often hypoechoic than benign nodules. The mean tumor size was 1.1 cm for malignant nodules and 1.2 cm for benign nodules. There were no significant differences for the presence or absence of cystic change, size, shape, and margin between malignant and benign nodules. Interruption and thickening of peripheral calcifications and decreased internal echogenicity of a thyroid nodule with peripheral calcifications are in favor of malignancy. The use of scintigraphy, biopsy, and ultrasonography to supplement physical examination is beneficial in determining the type of goiter, as well as in monitoring and curing of the disease.

Females in reproductive age group, less than 40 years are affected by different thyroid gland disorders more than males with a female to male ratio of 8:2. Thyroid gland disorders in all its clinical types in the study constitute an incidence of (36%) in Khartoum state, (30%) in Gazira and Central region, (20%) in western region (Kordofan and Darfur States), (8%) in Northern region, (2%) in Southern region, and (4%) in Eastern region. The Goitres detected in the study are diffuse goitres (42%), nodular goitres (58%). U/S image shows the size, shape, and any pathological disorders related to texture of thyroid gland. -N/M shows the functional status of thyroid gland (hot and cold nodule) according to the uptake of the thyroid gland. Thyroid nodules are common and most do not cause significant symptoms. The absence of symptoms however does not reliably exclude malignancy so careful assessment of nodules is required. Nodules that are palpable should be assessed with ultrasound. -FNAB is the single most useful test in the assessment of a thyroid nodule. It is indicated for most nodules that are palpable or show suspicious features on ultrasound and should be considered for nodules >1 cm. The main exception is a nodule in the context of hyperthyroidism, which should be assessed with thyroid scintigraphy and may go on to definitive management without the need for FNAB. A nodule that is not symptomatic and has benign features on ultrasound and FNAB may be safely monitored with clinical and ultrasound review. If FNAB is repeated and is again benign, then the nodule can be dismissed from further review unless symptoms develop.
This study indicates that the presence of intrinsic microcalcification is the only statistically reliable criterion on which to base increased suspicion for malignancy in thyroid nodules. The results of this study indicate the need for biopsy in determining further workup. All nodules that show the presence of intrinsic microcalcification should undergo biopsy, particularly if calcifications resemble a snowstorm (coarse) appearance on sonography. Lastly, it is proper to perform the two image modalities (ultrasound, and nuclear medicine) that because we can obtain accurate diagnosis and detect clearly any anatomical or pathological changes.

REFERENCES