Causes of goiter in children attending Assiut University Children Hospital

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Introduction
Goiter accompanies almost all thyroid diseases in children. It may be of congenital or acquired causes. Neck ultrasound (US) combined with color Doppler US on thyroid vasculature is useful in adjunct to clinical assessment and assessment of thyroid function in the diagnosis of goiter and its cause. In this study, we aimed to assess the causes of goiter in children attending Assiut University Children Hospital.

Patients and methods
This cross-sectional observational study included 28 patients with goiter. Each child was subjected to full clinical history and systemic examination and thyroid gland examination. The following investigations were done: neck US, thyroid-stimulating hormone and free T4, and thyroid autoantibodies in the indicated cases.

Results
Goiter in children is more prevalent in females by about three-fold than males. Acquired goiter is more prevalent than congenital goiter, constituting 82% of the studied cases of goiter. Family history of thyroid disorders was positive in all patients with congenital goiter and in six out of 23 patients with acquired goiter. Goiter with hyperthyroidism (mostly Grave's disease) is the most common cause of acquired goiter in children, followed by goiter with hypothyroidism (mostly Hashimoto's disease), then goiter with euthyroidism (mostly simple goiter). Neck US on thyroid gland with color Doppler US on thyroid vasculature is useful in cases with goiter for the diagnosis of goiter and its cause.

Conclusion
Acquired goiter is more prevalent than congenital goiter. Goiter with hyperthyroidism is the most common cause of acquired goiter in children. Neck US on thyroid gland with color Doppler US on thyroid vasculature is useful for the diagnosis of goiter and its cause.

Keywords:
goiter, thyroid, neck ultrasound, thyroid-stimulating hormone, FT4, children

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Introduction

Thyroid gland disorders are one of the most common endocrine problems in pediatrics [1]. Goiter is a common reason for referral of children and adolescents to pediatric endocrine centers.

Clinically, goiter is defined as enlargement of the lobes greater than the terminal phalanx of the patient's thumb.

Goiter may be congenital or acquired, endemic, or sporadic. Persons with goiter can have hyperthyroidism, hypothyroidism, or euthyroidism. Detection of a goiter should prompt an investigation of its cause. Goiter most often results from the increased pituitary secretion of thyroid-stimulating hormone (TSH) in response to decreased levels of thyroid hormones. Activation of the TSH receptor from thyrotropin receptor-stimulating antibodies, inappropriate TSH secretion (as TSH-secreting adenomas), and infiltrative processes that may be inflammatory or neoplastic can also cause thyromegaly [2]. No reported data are found as regards the causes of goiter in children in our locality, so we accomplished this study to highlight this problem.

Aim

The aim of this work is to assess the causes of goiter in children attending Assiut University Children Hospital.

Patients and methods

This study included all children aged since birth up to 18 years old presented with goiter who attended Assiut

University Children Hospital during the period from the first of January 2018 to the 30th of June 2019.

Each child was subjected to full clinical history and history of manifestations suggesting congenital hypothyroidism or acquired hypothyroidism or hyperthyroidism. All cases were subjected to full clinical general and systemic examinations, as well as thyroid gland examination.

Grading of goiter was assessed according to WHO classification/grading [3]:
(1) 0: no goiter.
(2) 1a: palpable lobe.
(3) 1b: noticeable gland on neck hyperextension.
(4) 2: gland noticeable with neck in normal position.
(5) 3: visible gland at a distance of 10 m.

The investigations done included neck US, TSH, and free T4, thyroid autoantibodies in the indicated cases. The levels of TSH were considered normal at 0.5–4.8 μIU/ml and FT4 level at 0.8–2.2 ng/dl [4].

Exclusion criteria

(1) Patients with neck swelling other than goiter.
(2) Refusal of participation in the study.

Statistical analysis

Data collected were transferred to computer software using Microsoft Excel 2010 software. Numerical data were expressed in the form of mean ± SD (range), while categorical data were expressed in the form of numbers and frequency (percentage).

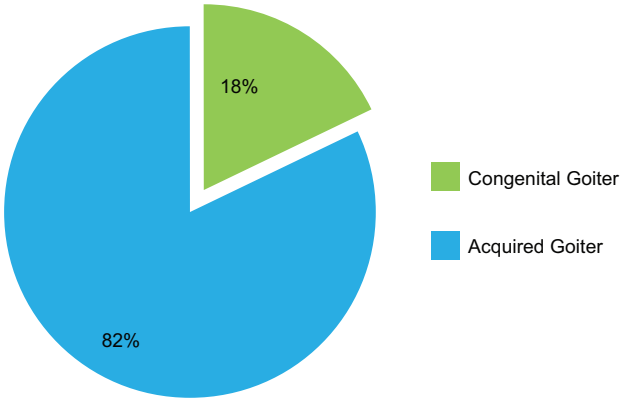
Ethical consideration

Assiut University Faculty of Medicine Ethical Committee approved that study (IRB: 17100044). Confidentiality of the entire data was secured. Written informed consent was obtained from patients for participation in the study and for publishing their photographs.

Results

This cross-sectional observational study included 28 patients aged from 2 days up to 17 years old. They were seven males and 21 females. According to the clinical presentation, five (18%) patients had congenital goiter and 23 (82%) patients had acquired goiter (Fig. 1).

Figure 1



Distribution of the studied cases according to the type of goiter.

Congenital goiter

Congenital goiter including five patients: three females and two males. All of them had hypothyroid goiter.

The first patient was female (Fig. 2a), presented at the age of 2 days by goiter and respiratory distress since birth with a history of her brother who had goiter and receiving thyroxine. Thyroid function showed hypothyroidism. She was suggested to have dyshormonogenesis. Genetic testing and enzymatic assay are not available in our locality to determine the exact type of enzymatic defect.

The second was a male patient, whose mother is on antithyroid drug (propylthiouracil). The mother noticed the goiter after birth. Thyroid profile showed hypothyroid state. On follow-up, thyroid function and the size of goiter regained normalcy, suggesting transient hypothyroidism.

Three patients were suggested to have Pendred syndrome: one male and two females, with mean age of 3.16 years at the time of examination. Two sisters (4.5 and 3.5 years) (Fig. 2b) were presented with neck swelling and hearing aids. The hearing impairment (sensorineural) was diagnosed first at the age of 2 years. At the age of 4.5 and 3.5 years, they developed goiter and the investigations showed hypothyroidism.

The other male patient who is 18 months old was presented with neck swelling and hearing impairment in addition to poor growth. His brother had Pendred syndrome. Investigations showed sensorineural deafness and hypothyroidism.

In all of those patients with congenital goiter, US revealed an enlarged, orthotropic thyroid gland, with a homogeneous decrease in echogenicity. Color Doppler showed normal vascularity of thyroid gland.

Acquired goiter

Including 23 patients, they were grouped according to thyroid function into.

Acquired goiter with hyperthyroidism

There were 11 patients: two males and nine females, their mean age was 9.23 ± 5.19 years. Thyroid examination showed goiter (grade 1–2), characterized by diffuse enlargement that is smooth, firm, and nontender, and a bruit and thrill were elicited in six cases. Thyroid function showed depressed TSH level 0.072 ± 0.097 μIU/ml, while FT4 level was 13.31 ± 11.62 ng/dl. Patients who had acquired goiter with hyperthyroidism included in our study showed that the most frequent presenting manifestations were heat intolerance, palpitation, tachycardia, fatigue, appetite, thirst, and nervousness. Six out of those 11 patients presented with proptosis (Fig. 3a) in addition to thyrotoxic manifestations. Low TSH and high FT4 were found on investigations.

Transverse-neck ultrasonography (US) scan of these cases showed moderate enlargement of thyroid gland and inhomogeneous decreased echogenicity, color Doppler image showed hypervascularity of the gland in most of them, thyroid inferno (Fig. 3b).

Acquired goiter with hypothyroidism

There were eight patients (Fig. 4a): two males and six females. Their mean age was 9.23 ± 5.19 years. Thyroid examination showed goiter (grade 1–2), the gland was diffusely enlarged, nontender, and firm, with a rubbery consistency and a pebbly surface. Thyroid function showed raised TSH levels than the normal reference (34.86 ± 20.79), while FT4 level was lower than the normal reference (0.66 ± 0.40). Seven out of these patients were positive for antithyroid peroxidase and antithyroglobulin antibodies suggestive of Hashimoto's thyroiditis (HT).

US imaging of patients with goiter and hypothyroidism showed moderately enlarged thyroid gland with a diffusely heterogeneous, coarse echotexture and multiple discrete hypoechoic micronodules. Color Doppler showed hypovascularity in most of the cases (Fig. 4b).

Acquired goiter with euthyroidism

There were four patients: one male and three females. Their mean age was 12.7 ± 2.7 years. One patient was presented by goiter and the other three patients were incidentally discovered. For all of them, no clinical manifestations of either hypothyroidism or hyperthyroidism were detected. Family history was negative for thyroid disorders. Thyroid examination of all of them showed: goiter (grade 1 in three out of the four cases), the gland was diffusely enlarged, firm, smooth surface, and nontender. Their thyroid profiles were within normal ranges. Neck US findings in those patients with goiter and euthyroidism: Thyroid size showed mild-to-moderate enlargement, with its echostructure remaining homogeneous and isoechoic with unchanged vascularity of the thyroid according to color-coded Doppler imaging in all cases. These four patients were suggested to have simple goiter.

Discussion

Goiter is often the first sign of thyroid disease, so the diagnostic considerations can be approached from the perspective of the goiter [2]. Clinical examination fails to assess the thyroid volume correctly in about 35% of cases, so thyroid gland-size measurement by US is preferable [5]. Neck US with color Doppler US on thyroid vasculature are useful adjuncts to clinical examination in evaluating thyroid size, anatomy, and detecting nodules, also in the diagnosis of the cause of goiter [6].

This study included 28 patients aged from 2 days up to 17 years old, there were seven (25%) males and 21 (75%) females, with female:male ratio 3:1. This is agreeing with the results of a study conducted by Onyiriuka *et al.* [7], who revealed that female-to-male ratio was 4:1 in children with thyroid disorders in Nigeria.

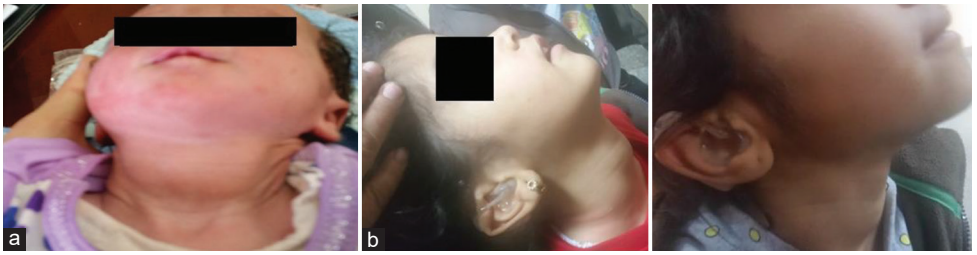
Out of the included 28 cases, we found that children with a family history of goiter were 11 (39.3%) patients. Dessie *et al.*[8] found that children who have a family history of goiter have double the chance to develop goiter in Ethiopia.

Five (18%) patients had congenital goiter in our study, while 23 (82%) patients had acquired goiter. Huang and laFranchi [2] reported that congenital goiter occurs usually in sporadic cases.

All patients with congenital goiter had hypothyroidism and 80% of them were suggested to have defects in thyroxin synthesis (dyshormonogenesis). Calabria [9] reported that about 15% of cases of congenital hypothyroidism have goiter. There are a number of gene abnormalities that cause dyshormonogenesis; they commonly have an autosomal recessive form of inheritance, and many of them are single-gene defects [9].

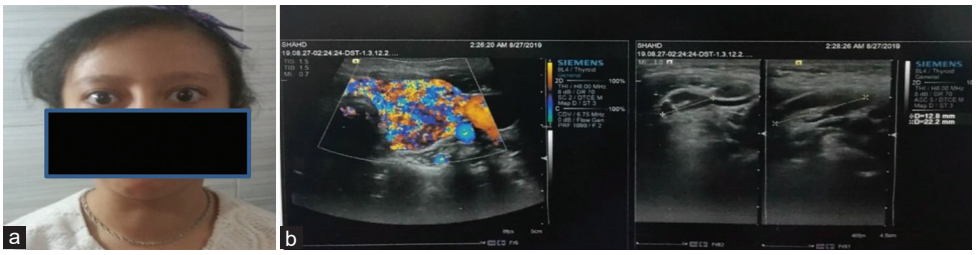
Out of these four patients, three cases (one male and two females) were suggested to have Pendred syndrome as they were presented with goiter, hearing impairment, and their siblings had the same problem. Huang and laFranchi [2] reported that dyshormonogenesis and Pendred syndrome presented as autosomal recessive

Figure 2



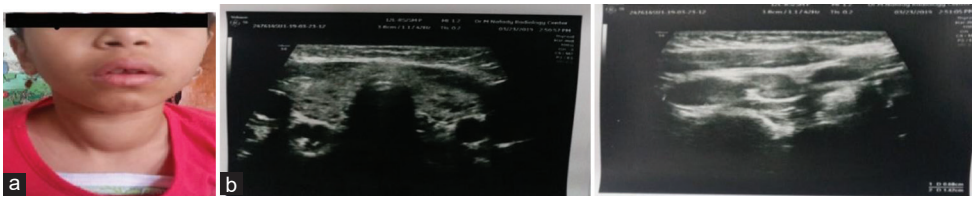
(a) A 2-day-old baby presented with goiter and hypothyroidism suggestive of dyshormonogenesis. (b) Two sisters having sensorineural hearing impairment with hearing aids, presented with goiter and hypothyroidism suggestive of Pendred□s syndrome.

Figure 3



(a) A 14-year-old girl with hyperthyroidism, mild proptosis, and grade 2 goiter. (b) Neck US showing enlarged thyroid gland with heterogeneous echopattern, color Doppler examination shows marked increased vascularity (thyroid inferno). US, ultrasound.

Figure 4



(a) A type 1 diabetic girl with goiter and hypothyroidism with positive antithyroid antibodies suggestive of Hashimoto's thyroiditis. (b) Neck US showing average-sized thyroid gland with a heterogeneous diffuse echopattern showing multiple tiny innumerable hypoechoic nodules, color Doppler shows normal vascularity. US, ultrasound.

disorders, so there is positive family history and no sex predilection.

Patients suggested to have Pendred syndrome were presented at mean age of 3.1 years. This agrees with Bizhanova and Kopp [10] who reported that Pendred syndrome is mostly presented with goiter and sensorineural hearing loss later in life. Family history of thyroid disorder was positive in all of the studied patients with congenital goiter suggested to have dyshormonogenesis, this converges with Huang and laFranchi [2] who reported that dyshormonogenesis is caused by recessive mutations, so its inheritance runs in families. Also, they reported that Pendred syndrome is characterized by familial goiter and neurosensory hearing loss.

The last case of congenital goiter was suggested to be a result of maternal intake of antithyroid drug (propylthiouracil) during pregnancy, and his thyroid profile showed hypothyroidism. Goitrogens, such as amiodarone or antithyroid drugs (e.g., propylthiouracil, methimazole), taken by the mother during pregnancy, can cross the placenta, sometimes causing hypothyroidism and rarely causing goiter for the baby [9].

In all patients with congenital goiter, US revealed an enlarged, orthotropic thyroid gland, with homogeneous decreased echogenicity. Color Doppler on the gland showed normal vascularity. This agrees with Hong *et al.* [11], who reported that US in patients with dyshormonogenesis reveals an enlarged, orthotropic thyroid gland, with homogeneous decrease in echogenicity and normal vascularity of the gland.

Out of the studied cases, 23 (82%) patients had acquired goiter. Of these, 11 (47.8%) patients, had goiter with hyperthyroidism. This result converges with the results of a study conducted by Onyiriuka *et al.*[7]

in Nigeria, who reported that the most common form of thyroid disorders observed in childhood and adolescence was hyperthyroidism. Kehar [3] reported that hyperthyroidism in children is mainly caused by Graves' disease. The mean age of those 11 patients was 9.23 ± 5.19 years, while Onyiriuka *et al.*[7] reported that mean age of patients with hyperthyroidism at presentation was 12.8 years, slightly older than our cases. This could be explained by different sample size.

In those patients with goiter and hyperthyroidism: Transverse-neck US scan showed moderate enlargement of thyroid gland and inhomogeneous decrease in echogenicity. Color Doppler image showed hypervascularity of the gland 'thyroid inferno in cases suspected to have Graves' disease,' this agrees with Hong *et al.* [11], who reported that US characteristics in Grave's disease reveal diffuse heterogeneous and hypoechoic enlargement of the thyroid with hypervascularity in the thyroid referred to as a 'thyroid inferno.'

Patients who had acquired goiter with hypothyroidism were eight (34.7%) patients. Their mean age was 9.23 ± 5.19 years. Five of those eight (21.7%) patients were suggested to have HT [Fig. 4a]. This is agreeing with Kehar [3] and Hanley *et al.* [12], who reported that HT is the most common cause of acquired hypothyroidism. Not all patients with HT are presented with goiter, and the manifestation of hypothyroidism may be subtle, leading to late presentation as mentioned by Kehar [3], who reported that 3–35% of patients with autoimmune thyroid disease (AITD) have compensated or subclinical hypothyroidism in which there is raised TSH level with normal FT4 level. The most frequent presenting manifestations of acquired goiter with hypothyroidism were decreased energy, poor appetite, constipation, and somnolence.

Family history of thyroid disorder was positive in six of those 11 patients who were suggested to have AITDs (Grave's disease and Hashimoto's disease). This agrees with Tomer [13], who reported that several studies of young people with AITD showed a definite genetic propensity for thyroid autoimmunity to have familial pattern of inheritance. Also, Kehar [3] mentioned that a family history is present in 30% of affected children with AITD.

In those patients with goiter and hypothyroidism: US imaging showed moderately enlarged thyroid gland with a diffusely heterogeneous, coarse echotexture and multiple discrete hypoechoic micronodules. Color Doppler on the gland showed hypovascularity mainly. Yamashiro *et al.*[14] reported that at the initial phase of Hashimoto's disease, US shows hypoechogenic areas with irregular poorly defined margins, especially in the subcapsular zones, followed by pseudonodule formation in the central region of the thyroid gland, Doppler examination in the early phases of Hashimoto's disease may show diffuse hypervascularization similar to Graves' disease. But later on, it shows a reduction in size of the thyroid gland with diffuse heterogeneity due the intense fibrosis and avascularity.

Four (17.4%) patients of the included cases with acquired goiter had goiter with euthyroidism, their mean age was 12.7 years, there were one male and three females, this was different than the results of a study conducted by Onyiriuka *et al.* [7], who reported that 11.1% of children with thyroid disorders in Nigeria had goiter with euthyroidism. This is attributed to the absence of symptoms in these patients and the accidental discovery of goiter.

All of those four patients were suggested to have simple goiter as they were presented at and before pubertal age and according to clinical presentation; there was goiter with no manifestations of hypothyroidism or hyperthyroidism, normal TSH, FT4, and neck US on thyroid gland showed the presence of goiter with unchanged echogenicity and normal vascularity of the gland. Those four patients' ages ranged from 10 up to 16 years old. This agrees with Kehar [3], who report that simple goiter is the most common cause of euthyroid goiter in childhood, also he reported that it predominates in girls and has a peak incidence before and during the pubertal years. Family history of thyroid disorder in all of cases that had goiter with euthyroidism was negative. Muirhead [1] reported that family history of chronic lymphocytic thyroiditis is positive in 50% of all patients with simple goiter.

Our limitations

Genetic testing and enzymatic assay for patients with congenital goiter due to dyshormonogenesis are not available in our locality, as well as other investigations were needed, such as thyroid scintigraphy and fine-needle biopsy for the final diagnosis of the cause of acquired goiter.

We recommend further studies on goiter in children on a larger number of cases and with other investigations for detection of the final diagnosis of the cause of goiter in children in our locality.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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