POSSIBILITIES AND LIMITS OF ENDOCRINE IMAGING IN CHILDREN

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Abstract

Ultrasound scanning is non-invasive, widely available, less expensive, and does not use any ionizing radiation. Aim of the paper is to present the most updated information about the use of ultrasound in specific endocrine-related issues, such as thyroid, parathyroid, adrenal gland, and testicle in children and to share interesting cases from our experience. In children it is very important to know the normal US anatomy of the screened gland and the changing that occurs during pediatric life. US in the pediatric population is important in order to establish a complete diagnosis and subsequent monitoring. In cases of complex anomalies when US findings are incomplete or inconclusive, MRI provides precise demonstration of anatomic features in multiple planes.

Keywords: ultrasound, children, endocrine disease

Introduction

Ultrasound (US) is very useful in infants and children because of its innocuousness, simplicity, and reliability. Its value is being more and more recognized by many clinical specialists in assessing the anatomy of different anatomic parts. The endocrine system is made up of the pituitary gland, thyroid gland, parathyroid glands, adrenal glands, pancreas, ovaries (in females) and testicles (in males). Excepting the pituitary gland, all the others endocrine glands can be scan by US. Morphology and size can be evaluated by US and also the presence of lesions within these organs can be detected.

Aim of the paper is to present the most updated information about the use of ultrasound in specific endocrine-related issues, such as thyroid, parathyroid, adrenal gland, and testicle in children and to share interesting cases from our experience.

In children it is very important to know the normal US anatomy of the screened gland and the changing that occurs during pediatric life. In the following each endocrine organ will be described in terms of ultrasound imaging.

Normal US Anatomy of Genital Organs in Infants and Children:

- *The Uterus*

Uterine anatomy changes during pediatric life:

The neonatal uterus is prominent under the influence of maternal and placental hormones:

The cervix is larger than the fundus (fundus-to-cervix ratio = 1/2)

The uterine length is approximately 3.5 cm, and the maximum thickness is approximately 1.4 cm;

The endometrial lining is often echogenic

Some fluid can also be seen within the endometrial cavity (Fig.1 a.) [1,2].

The prepubertal uterus has a tubular configuration

Anteroposterior cervix equal to anteroposterior fundus or sometimes a spade shape (anteroposterior cervix larger than anteroposterior fundus)

The endometrium is normally not apparent; however, high-frequency transducers can demonstrate the central lining in some cases

The length is 2.5–4 cm; the thickness does not exceed 10 mm (Fig.1.b) [3,4].

The pubertal uterus has the adult pear configuration (fundus larger than cervix)

(fundus-to-cervix ratio = 2/1 to 3/1)

5–8 cm long, 3 cm wide, and 1.5 cm thick.

The endometrial lining is seen and varies with the phases of the menstrual cycle (Fig.1.c) [5,6].

- *Ovaries:*

Ovarian size : V = ½ length × width × depth

In infants, measurements are greater than previously reported, with an average of slightly greater than 1 cm3 for the first year of life and 0.67 cm3 for the second year

The mean ovarian volume in girls less than 6 years of age is less than or equal to 1 cm3.

The increase in ovarian volume begins after 6 years of age. (Tabel 1)

In prepubertal girls (6–10 years old), ovarian volumes range from 1.2 to 2.3 cm3. In premenarchal girls (11–12 years old), ovarian volumes range from 2 to 4 cm3.

In postmenarchal girls, the ovarian volume averages 8 cm3 (range, 2.5–20 cm3). [7]

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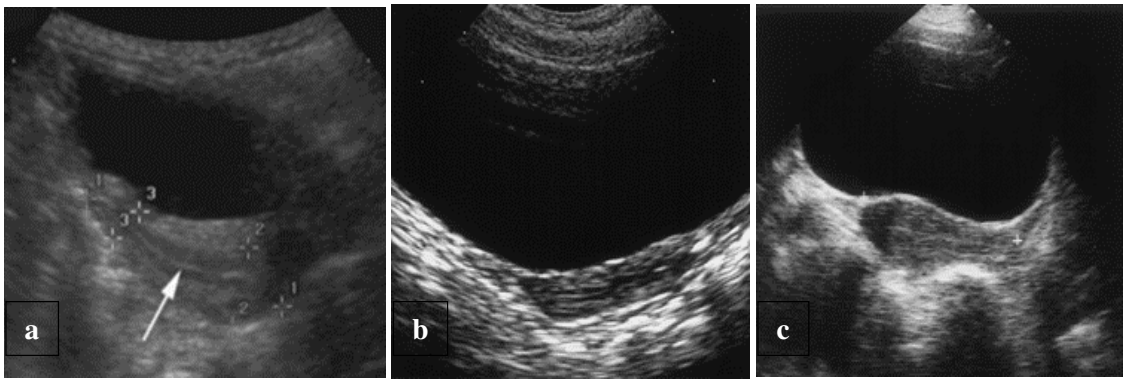


Fig 1. a. Neonatal Uterus; b. Prepubertal uterus; c. Pubertal uterus.

Table 1. Mean volume and standard deviation-ovary [7].

Age (y)	Mean Volume (cm^3)	Standard Deviation
1	1.05	0.7
2	0.67	0.35
3	0.7	0.2
4	0.8	0.4
5	0.9	0.02
6	1.2	0.4
7	1.3	0.6
8	1.1	0.5
9	2.0	0.8
10	2.2	0.7
11	2.5	1.3
12	3.8	1.4
13	4.2	2.3

Neonatal ovarian cysts (NOC) are the most common type of benign tumors found in female newborns [8]. The routine use of ultrasound allows the detection of NOC during the neonatal period. NOC with a diameter exceeding 2 cm are considered pathological. The incidence of ovarian cysts has been estimated at more than 30%. [9]. The correlation of the diameter with the clinical symptoms and ultrasound appearance allows an optimal therapeutic approach [10].

The etiology of NOC remains unknown, but hormonal stimulation, advanced gestational age and increasing placental chorionic gonadotropin levels in complicated pregnancies with large placenta such as in diabetes, pre-eclampsia and Rh incompatibility are the most frequently mentioned assumptions [11-13]. Additionally, fetal hypothyroidism and congenital adrenal hyperplasia due to 21-hydroxylase deficiency or 11 beta-hydroxylase deficiency have also been reported to cause NOC [14]. NOC are classified according to their ultrasonographic features as “simple” or “complex”, and according to their size as “small” or “large” cysts [15,16]. Most cysts are functional in origin and histologically simple and benign (Figure 2) [17]. Complications that can occur include intracystic hemorrhage, rupture with possible intraabdominal hemorrhage, gastrointestinal or urinary tract obstruction, ovarian torsion and necrosis, incarcerated inguinal hernia, dystocia by excess of fetal abdominal part, and respiratory distress at birth from a mass effect on the diaphragm [18].

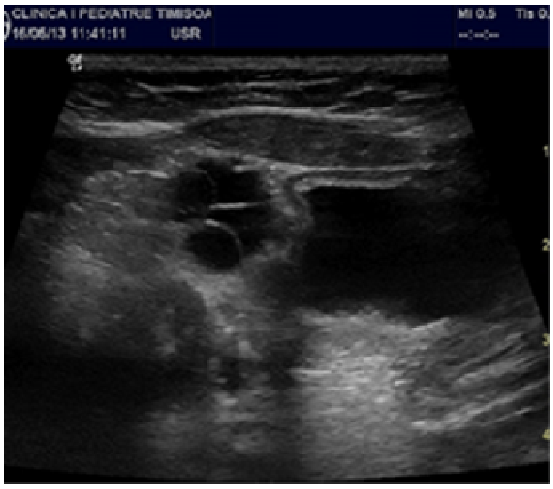


Fig. 2 Ovarian cysts in 2 months old girl.

Mnemonic:

Upper values for prepubertal girls:

Uterine length = 4.5 cm, uterine thickness = 1 cm (the single most useful criterion), ovarian volume = 4–5 cm^3.

- Testis:

Volume of the testis (table 2) can be calculated using the formula:

Testicular size : V = ½ length × width × depth

Table 2. Normal values for right and left testis by age [19].

Age group (years)	Mean±SD							
	Right testis				Left testis			
	Length (cm)	Antero-posterior diameter (cm)	Width (cm)	Volume (cm^3)	Length (cm)	Antero-posterior diameter (cm)	Width (cm)	Volume (cm^3)
0-1	1.48±0.35	0.76±0.13	0.90±0.17	0.78±0.38	1.46±0.29	0.75±0.14	0.89±0.18	0.76±0.38
1.1-2	1.41±0.21	0.74±0.14	0.83±0.14	0.65±0.18	1.40±0.28	0.72±0.11	0.84±0.10	0.65±0.23
2.1-3	1.43±0.23	0.76±0.14	0.87±0.10	0.70±0.21	1.40±0.22	0.74±0.12	0.87±0.12	0.68±0.18
3.1-4	1.50±0.23	0.77±0.11	0.89±0.09	0.73±0.18	1.52±0.28	0.73±0.11	0.91±0.13	0.75±0.25
4.1-5	1.51±0.30	0.68±0.11	0.89±0.13	0.67±0.21	1.50±0.32	0.70±0.12	0.88±0.15	0.71±0.38
5.1-6	1.61±0.19	0.75±0.16	0.92±0.11	0.82±0.21	1.55±0.20	0.76±0.11	0.92±0.08	0.83±0.21
6.1-7	1.56±0.25	0.74±0.08	0.91±0.12	0.80±0.19	1.54±0.26	0.74±0.10	0.89±0.11	0.77±0.16
7.1-8	1.59±0.44	0.81±0.29	0.91±0.17	0.99±0.81	1.46±0.35	0.83±0.26	0.90±0.16	0.86±0.57
8.1-9	1.61±0.32	0.81±0.17	0.96±0.15	0.98±0.57	1.61±0.34	0.79±0.15	0.93±0.15	0.98±0.55
9.1-10	1.82±0.41	0.82±0.19	1.00±0.27	1.24±1.02	1.74±0.34	0.82±0.17	0.96±0.23	1.16±0.88
10.1-11	1.95±0.91	0.88±0.14	1.16±0.42	1.74±2.17	1.90±0.75	0.88±0.16	1.10±0.37	1.59±0.83
11.1-12	2.20±0.38	0.98±0.16	1.20±0.22	1.89±0.55	2.31±0.37	1.01±0.19	1.22±0.22	1.95±0.49
12.1-13	2.81±0.84	1.10±0.24	1.71±0.53	3.95±2.94	2.79±0.83	1.17±0.24	1.71±0.63	3.99±3.00
13.1-14	3.62±1.05	1.26±0.20	2.00±0.74	6.60±4.02	3.65±1.02	1.29±0.20	2.02±0.71	6.72±3.25
14.1-15	3.68±1.10	1.37±0.22	2.45±0.78	8.92±3.76	3.73±0.97	1.36±0.30	2.49±1.09	9.01±4.90

SD = Standard deviation

US investigation of genital disorders is useful in evaluating precocious puberty: central due to hamartomas causing increased testis volume (Figure 3 a. and b.) and peripheral, gonadotropin-independent due to autonomous ovarian follicular cysts. US demonstrates a stimulated uterus and an unilateral follicular ovarian cyst which is characterized by the daughter cyst sign. Spontaneous regression of the symptoms at clinical examination and the ovarian cyst at US alternates with variable recurrences (Fig. 4) [20,21]. High estradiol level, low levels of follicle-stimulating hormone and luteinizing hormone, and no response to stimulation with luteinizing hormone–releasing hormone are seen in peripheral precocious puberty [22].

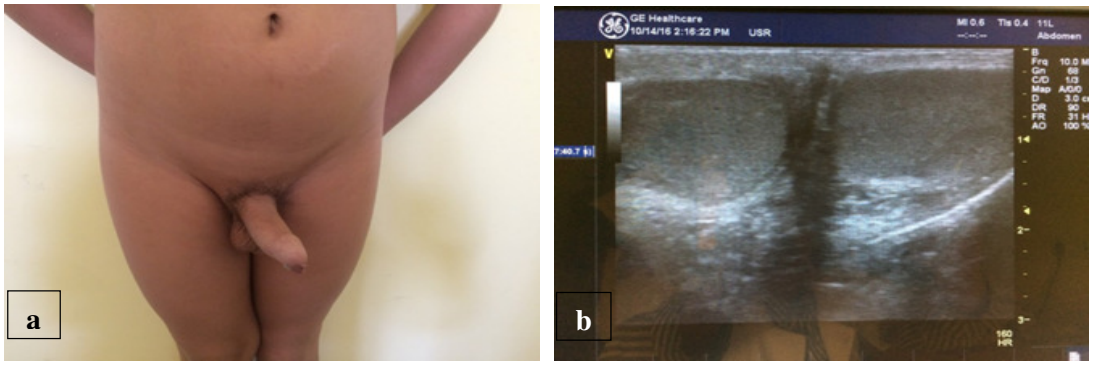


Fig. 3 a. Macropenia in a 5 year old boy with central precocious puberty; b. Increased testis volume.

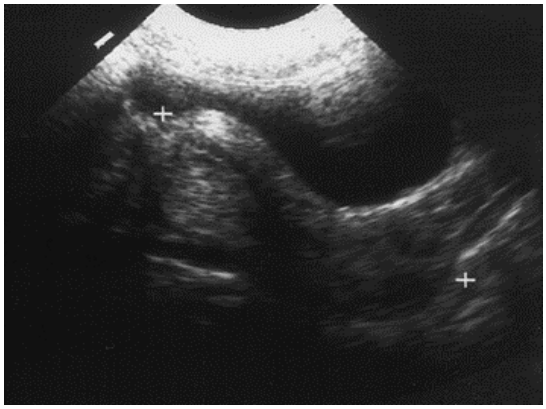


Fig. 4 A pubertal uterus in a 5 old girl with peripheral precocious puberty.

• Contribution of US in Patients with Ambiguous Genitalia:

In the male fetus, sexual differentiation is hormonally mediated by means of production of antimüllerian hormone and testosterone by the fetal testes [23]. Conversely, in the female fetus, sexual differentiation is basically an autonomous process [24].

US is very effective in demonstrating the presence or absence of a uterus in newborns with ambiguous genitalia.

Most cases of ambiguous genitalia consist of female pseudohermaphroditism due to congenital adrenal hyperplasia; in these cases, US shows a normal uterus and ovaries. Increased size of the adrenal glands has been reported in newborns and infants with congenital adrenal hyperplasia (Fig. 5 a) [25].

In the rare cases of male pseudohermaphroditism or true hermaphroditism, high-frequency transducers can also demonstrate testicular parenchyma (Fig. 5 b) [26].

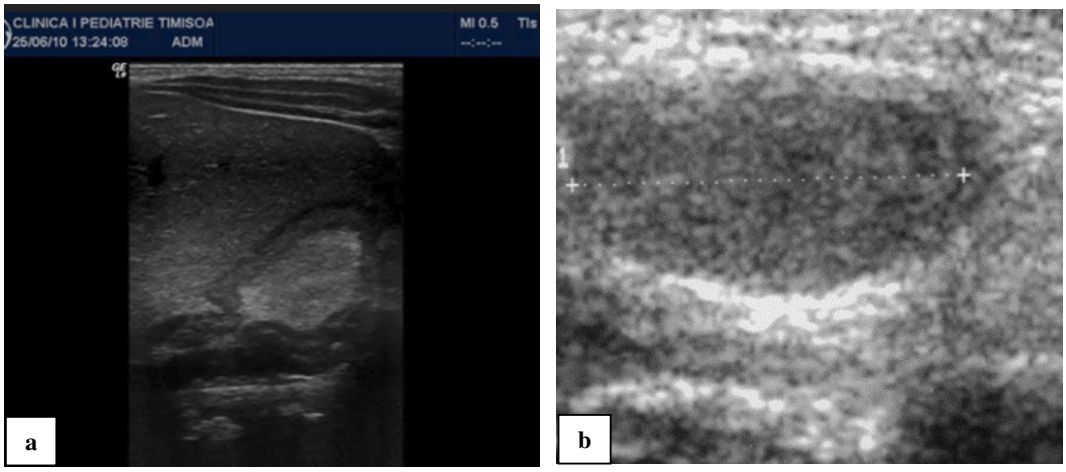


Fig. 5 a Female pseudohermaphroditism due to congenital adrenal hyperplasia;
b. Male pseudohermaphroditism or true hermaphroditism, high-frequency transducers.

• Contribution of US in genetic disorders:

Patients with the 45XO karyotype, the ovaries are not visible, consistent with the classic description of absent or fibrous streak ovaries (Fig.6). US is helpful in Rokitanski syndrome, where absence of uteruls and presence of normal ovaries is seen (Fig. 7a ,b) [27].

McKusick-Kaufman syndrome is an autosomal recessive disorder characterized by genitourinary malformations, especially hydrometrocolpos, polydactyly, and, more rarely, heart or gastrointestinal malformations (Fig. 8a,b) [28].

US can be very helpful in newborns with ambiguous genitalia. In the case below uterus and scrotal testis were found in the same patient. Karyotype was 46 XY and the diagnosis of persistent Mullerian duct syndrome were established (Fig.9 a,b).

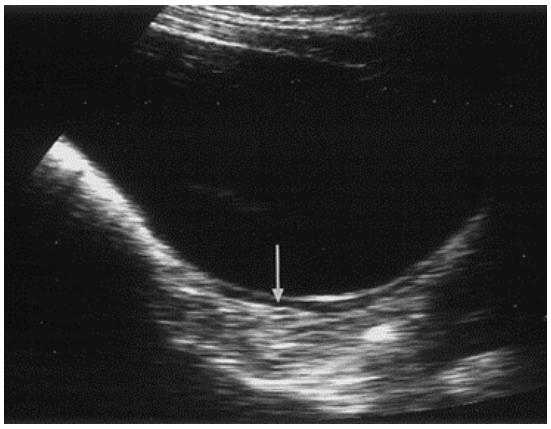
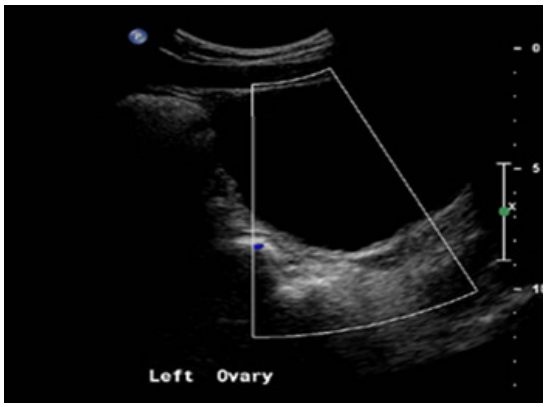


Fig. 6 Turner syndrome- prepubertal uterus and nonvisualized or streaky ovaries.



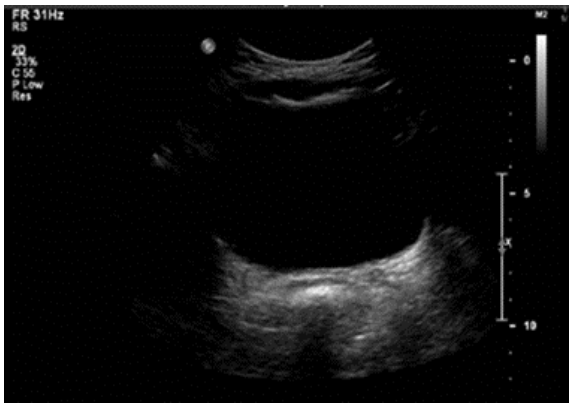
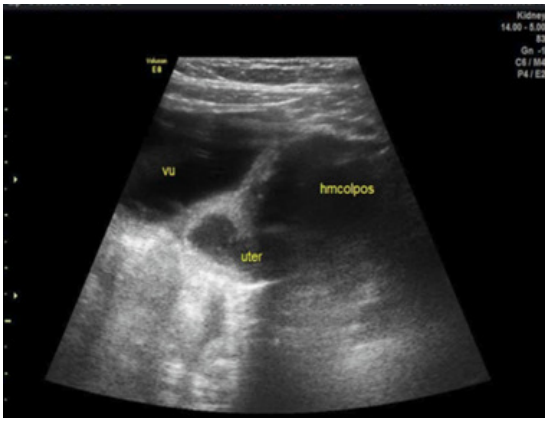


Fig. 7 Rokitanski syndrome. a. Presence; b. Absence of uterus and of normal ovaries.



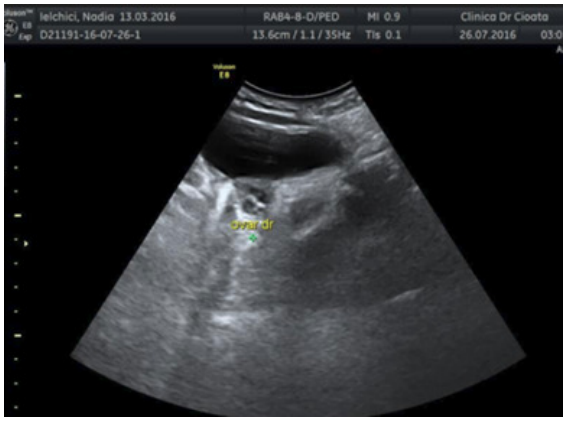


Fig. 8 a. Hydrometrocolpos in a 1 year old girl; b. Presence of the ovary with McKusick-Kaufman syndrome.

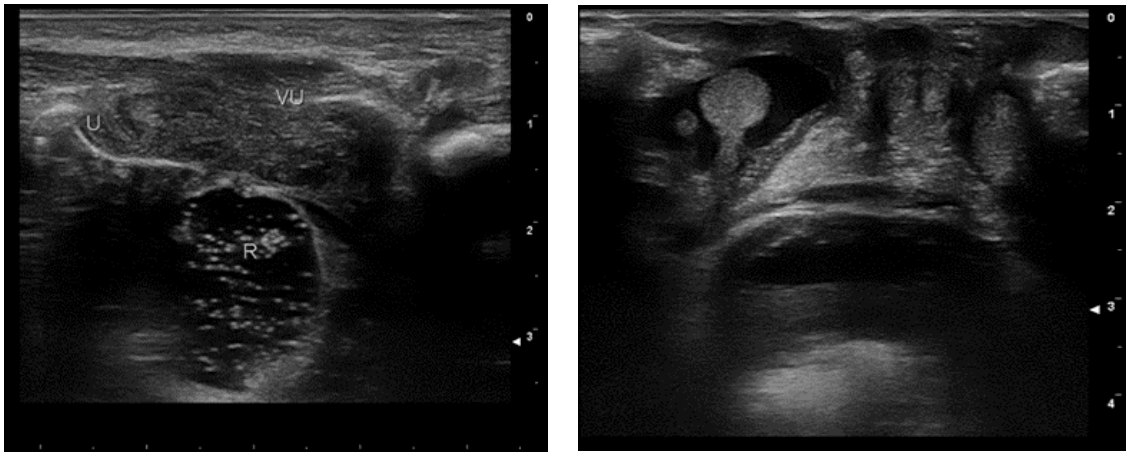


Fig. 9 a. Presence of uterus and b. testis in the scrotum in a newborn with ambiguous genitalia.

• Adrenal gland

The sonographic appearance of the normal adrenal gland in children varies with age. In newborns, the cortex is large and hypoechoic, whereas the medulla is relatively small and hyperechoic [29]. With increasing age, the cortex becomes smaller and the medulla relatively larger [30]. The cortex remains hypoechoic and the medulla hyperechoic until age 5-6 months, by which time the gland has become hyperechoic and smaller, with poor or absent sonographic differentiation between cortex and medulla. After 1 year of age, the appearance of the gland is similar to that of the adult gland, with straight or concave borders and a hypoechoic character [31].

Normal size [30]:

- Neonates: 9–36 mm, mean 15 mm, thick 2–5 mm;
- Adults: <10 mm thick, 40-60 mm length.

Ultrasound can reveal suprarenalian hemorrhage in newborns with severe hypoxia (Fig. 10) or tumours in the adrenal gland region, neuroblastoma (Fig 11).

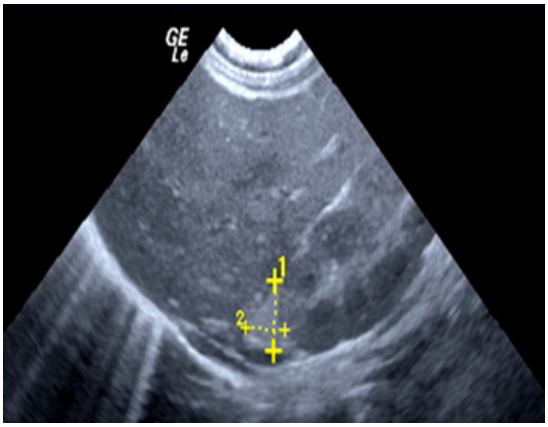


Fig. 10. Suprarenalian hemorrhage in a newborn.

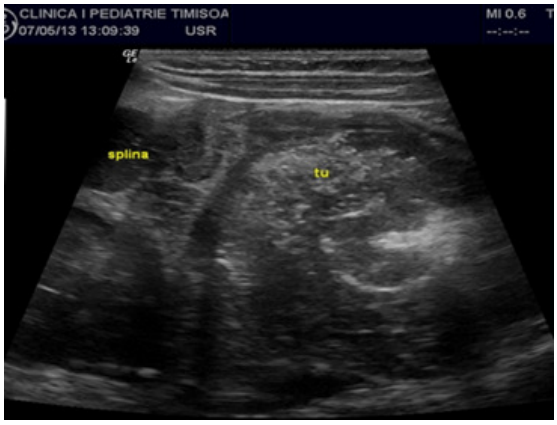


Fig. 11. Neuroblastoma in 4 year old girl.

• Thyroid gland

The normal thyroid gland consists of two lobes and a bridging isthmus. Thyroid size, shape and volume varies with age and sex. There are nomograms according to age and to body surface in children(Table 3,4) [32]. Normal thyroid lobe dimensions are: 18-20 mm longitudinal and 8-9 mm antero-posterior (AP) diameter in newborn; 25 mm longitudinal and 12-15 mm AP diameter at one year age; and 40-60 mm longitudinal and 13-18 mm AP diameter in adult population [33]. The limits of normal thyroid volume (excluding isthmus, unless its thickness is >3 mm) are 10-15 ml for females and 12-18 ml for males [34].

Indications for thyroid gland US scan are congenital hypothyroidism, absence or thyroid hypoplasia (Fig. 12).

In Graves disease thyroid Ultrasound show a diffuse swelling of the lobe, which has a rather hypo-echoic appearance and a slightly lobulated contour (Fig. 13) [35].

Table 3. Median thyroid volume normal values by age [32].

Age (years)	Median thyroid volume (cm^3)			
	Boys		Girls	
	Benin	WHO/NHD	Benin	WHO/NHD
6	1.73	1.60	1.69	1.57
7	1.54	1.80	1.54	1.81
8	1.62	2.03	1.77	2.08
9	1.61	2.30	1.94	2.40
10	1.85	2.59	1.99	2.76
11	2.58	2.92	2.51	3.17
12	2.75	3.30	2.79	3.65
13	2.92	3.07		
14	3.71	3.67		
15	4.64	4.41		
16	4.54	4.89		

Boys = $P > 0.05$; df = 16; t = 0.661 (no significant difference between present study boys and WHO/NHD boys for age). Girls = $P > 0.05$; df = 16; t = 0.531 (no significant difference between present study girls and WHO/NHD girls for age). Thyroid volume is slightly larger in girls than boys in both studies; however, this differences is statistically insignificant ($P > 0.05$).

Table 4. Normal thyroid volume values by body surface [32].

BSA	Thyroid volume (cm^3)							
	Boys				Girls			
	Range	Mean	Median	SD	Range	Mean	Median	SD
0.8	1.24–2.09	1.55	1.43	0.36	1.17–1.90	1.47	1.39	0.29
0.9	1.15–2.46	1.65	1.64	0.35	1.03–2.37	1.62	1.61	0.33
1.0	1.00–2.11	1.51	1.53	0.30	0.90–2.56	1.59	1.54	0.44
1.1	1.24–3.24	2.05	1.90	0.55	1.03–2.58	2.11	2.25	0.47
1.2	1.20–3.49	2.39	2.42	0.66	1.67–3.44	2.53	2.52	0.42
1.3	2.42–5.12	3.09	2.68	0.89	1.63–4.52	2.89	2.77	0.88
1.4	1.65–6.87	3.29	3.17	1.18	3.48–7.19	4.72	3.48	2.14
1.5	2.58–6.90	4.04	3.64	1.23	3.07–5.95	3.89	3.70	0.99
1.6	2.46–5.69	3.51	3.39	0.86	2.61–6.72	4.23	3.66	1.33
1.7	3.24–6.41	4.43	4.02	1.18	2.01–4.77	3.89	4.34	0.93
1.8	3.57–4.66	4.14	4.37	0.51	5.02–5.48	5.25	5.25	0.33
1.9	-	-	-	-	3.70–7.04	4.90	4.58	1.25

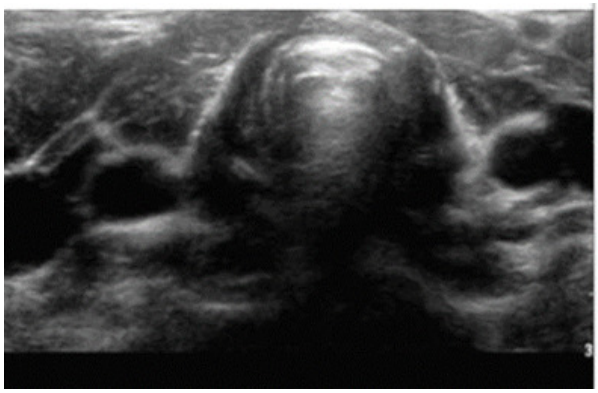


Fig. 12. Absence of the thyroid gland.

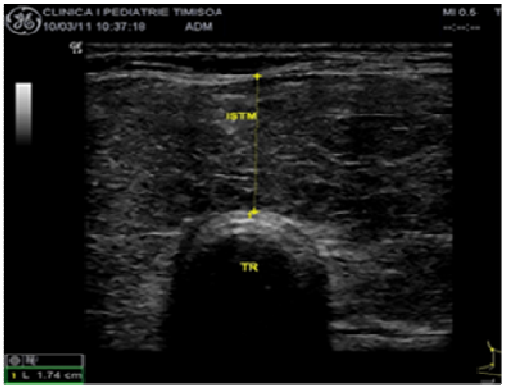


Fig. 13. Thyroid US in Graves disease.

In Hashimoto the thyroid gland is seen enlarged with lobulated outline and heterogenous parenchyma showing a myriad of tiny hypoechoic nodules, separated by fibrous echogenic septa. The gland shows increased vascularity on Doppler interrogation. No otherwise sizable solid or cystic mass lesion (Fig. 14) [36].

US is recommended as one of the first diagnostic tests in all children with thyroid nodules;

It can easily differentiate between a solid or cystic lesion. A solid nodule is being more likely susceptible to malignancy, although most solid lesions are benign, and the presence of a cystic lesion does not exclude malignancy.

A number of other US characteristics are associated with a higher risk of malignancy:

-> solitary solid lesion,

-> multifocal lesions within an otherwise clinically solitary nodule,

-> nodule with hypoechogenic echostructure, subcapsular localization, increased intranodular vascularity (high intranodular flow by Doppler), irregular infiltrative margins, microcalcifications, and suspicious regional lymph nodes accompanying nodule (Fig.15) [37,38].

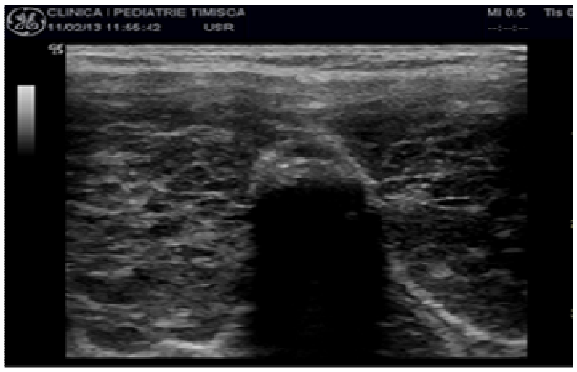


Fig. 14. Thyroid US in Hashimoto.

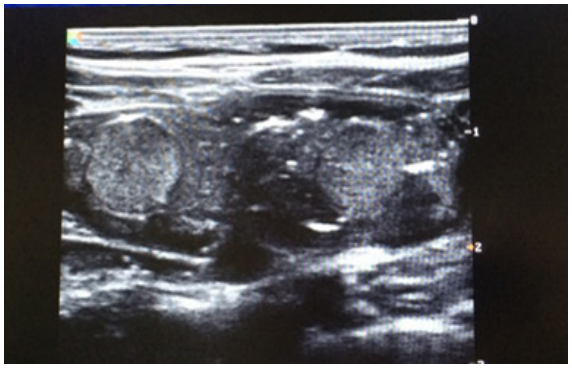


Fig. 15. Malign nodules in a 14 years old boy.

Conclusions

Ultrasound scanning is non-invasive, widely available, less expensive, and does not use any ionizing radiation. Further, real time ultrasound imaging helps to guide diagnostic and therapeutic interventional procedures. In endocrine diseases, US helps giving information about size and structure of the gland.

US in the pediatric population is important in order to establish a complete diagnosis and subsequent monitoring.

In cases of complex anomalies when US findings are incomplete or inconclusive, MRI provides precise demonstration of anatomic features in multiple planes.

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