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Thyroid function screening and follow-up of children with abdominal distension in Nanjing, China: a cross-sectional study

Hang Xie,[1] Dongmei Chen,[2] Wei Gu,[3] Wei Li ,[3] Xu Wang ,[4] Weibing Tang[1]

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HX and DC contributed equally.

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[1]Department of Neonatal Surgery, Children's Hospital of Nanjing Medical University, Nanjing, China
[2]Department of Emergency, Pediatric intensive care unit, Children's Hospital of Nanjing Medical University, Nanjing, China
[3]Department of Quality Management, Children's Hospital of Nanjing Medical University, Nanjing, China
[4]Department of Endocrinology, Children's Hospital of Nanjing Medical University, Nanjing, China

Correspondence to
Dr Xu Wang;
sepnine@njmu.edu.cn

ABSTRACT

Objective To describe the thyroid function test among children with abdominal distention and to follow up the treatment received by children with abnormal thyroid function.

Design Cross-sectional study.

Setting and participants A total of 1089 children (median age:30 days (IQR=21–60 days) with abdominal distension were included in this single centre study in Nanjing, China.

Result Thyroid dysfunction was found in 43 of 148 Hirschsprung's disease (HSCR) cases, with 3 (2.03%) having hypothyroidism, 3 (2.03%) having subclinical hypothyroidism and 3 (2.03%) having subclinical hyperthyroidism. Thyroid dysfunction was found in 206 of 941 functional abdominal distension cases, with 4 (0.43%) having hypothyroidism, 23 (2.4%) having subclinical hypothyroidism, 28 (2.9%) having subclinical hyperthyroidism and 1 (0.11%) having hyperthyroidism. Among total 65 cases (9 from HSCR, 56 from functional abdominal distension) diagnosed with thyroid diseases, 12 were treated with levothyroxine (LT-4), of which 9 were discontinued treatment at about 2 years old, and 3 were still receiving LT-4. Thirty-two cases received no treatment and thyroid function returned to normal in about 1 month. Twenty-one cases were lost during the follow-up.

Conclusion The paediatrician should be vigilant for hypothyroidism when dealing with children with abdominal distension. Thyroid function should be followed up rather than simply administering a short-term levothyroxine treatment.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This single-centre cross-sectional study included a large sample size of 1089 cases.
⇒ All thyroid disease cases were followed up for treatment and outcome.
⇒ The demographic features, thyroid function and blood biochemical parameters of the included cases were fully described.
⇒ Single-centre studies are less representative.
⇒ The absence of confounding factors may affect the evaluation of children with abnormal thyroid function.

INTRODUCTION

Thyroid hormones (THs) are essential for children's growth and development, untreated hypothyroidism can have serious consequences, such as growth and development restriction and intellectual disability. Congenital hypothyroidism (CH) accounts for the majority of hypothyroidism in children, which can be caused by thyroid dysgenesis as well as dyshormonogenesis.[1] Required hypothyroidism is also an important cause of abnormal growth and development.[2] Subclinical hypothyroidism also deserve attention.[3] In addition, some specific states such as drug interference, non-thyroid disease effects may be associated with altered thyroid function.[4],

The nervous system is one of the critical targets of THs in development and health.[3 5] In addition, THs are important for the digestive system. Abdominal distension, prolonged jaundice, poor feeding and constipation could be manifestations of paediatric thyroid dysfunction.[1 5]

Non-specific digestive symptoms vary greatly between individuals. Among these symptoms, abdominal distension is common in children and can be detected in many disorders, such as Hirschsprung's disease (HSCR). HSCR is a congenital malformation of the digestive tract that occurs in newborns and infants.[6] Abdominal distention in the neonatal period is an early prominent symptom of HSCR, and it can appear suddenly or get gradually worsen.[6 7] For children with abdominal distension, hypothyroidism and subclinical hypothyroidism might be missed diagnosed due to confirmed diagnosis of HSCR or other conditions causing abdominal distension. Furthermore, short-term supplementation of levothyroxine might be provided after confirm thyroid dysfunction, but long-term follow-ups were partially ignored.

Studies on thyroid function test in other childhood digestive disorders such as constipation or jaundice have been conducted.[8–10] Few studies have focused on thyroid function test in children with functional abdominal distension or HSCR. Although newborn screening of thyroid function detected the majority of potential thyroid dysfunction,[11 12] it may still develop later in life in newborns who had normal screening results. The purpose of this study was to describe the current status of thyroid function test among children with abdominal distention in Nanjing and to follow up the treatment received by children with thyroid dysfunction.

METHODS

Study design and population

From January 2016 to September 2021, 1089 children with abdominal distension, including 148 HSCR cases, were enrolled at Children's Hospital of Nanjing Medical University. None of them had a diagnosed history of CH. Thyroid function and blood biochemical parameters were collected, and cases diagnosed with thyroid disease were followed up.

The abdominal distension cases included in the study were retrieved by international classification of diseases 10th revisionICD-10 code. The diagnostic criterion of HSCR was an absence of ganglion cells in the diseased segment through rectal suction biopsy or full-thickness biopsy.[6 7]

Measurements of thyroid function

Serum triiodothyronine (TT3), free triiodothyronine (FT3), thyroxine (TT4), FT4, TSH, thyroid peroxidase antibodies (TPO-Ab) and thyroglobulin antibody (TG-Ab) were determined using Roche Elecsys automated electrochemiluminescence immunoassay. Laboratory reference ranges were shown in online supplemental table 1.

Cases were classified according to the detection of serum TH and TSH concentrations[13]:

1. Overt hyperthyroidism: T3 or T4 above the reference value, while TSH below the reference value.
2. Subclinical hyperthyroidism: normal T3 and T4, while TSH below the reference value.
3. Euthyroid: T3, T4 and TSH maintained normally.
4. Subclinical hypothyroidism: normal T3 and T4, while TSH above the reference value.
5. Overt hypothyroidism: T3 or T4 below the reference value, while TSH above the reference value.
6. High T3 or T4: T3 or T4 above the reference value.
7. Low T3 or T4: T3 or T4 below the reference value.

Measurements of blood biochemical indices and demographic data

Blood biochemical indices of HSCR cases were recorded, which include lipid profile (total cholesterol, high-density lipoprotein and triglycerides), creatinine, blood urea nitrogen, alanine aminotransferase, aspartate aminotransferase, C reactive protein and white cell count. The weight and height of HSCR children had been measured by experienced nurses according to standard protocol. Personal birth history and feeding methods were obtained through a questionnaire.

Follow-up of thyroid diseases

One month after the diagnosis of thyroid disease, regular follow-up via phone or internet was initiated. Content of follow-up:

1. TH levels.
2. Whether on antithyroid drugs.
3. Drug name and dosage.
4. Adverse reactions.

Statistical analysis

SPSS V.20.0 Statistical Program (IBM) was applied for analysis and assessment. Demographic and characteristics were both summarised as medians and IQRs for numerical variables, or numbers and percentages for categorical variables. Laboratory characteristics and thyroid function were documented as percentiles. Comparisons of thyroid dysfunction rate between functional abdominal distension cases and HSCR cases were analysed by the χ^2 test. A subgroup analysis was performed by using χ^2 test for each thyroid disease.

Patient and public involvement

No patients were involved in the design or the recruitment of the study. Some of the patients' parents participated in the study through telephone follow-up. We have sent the latest results of the study to the patients who participated in the study via a web application.

RESULTS

Basic characteristic and thyroid function

Demographic characteristics of 148 HSCR cases are summarised in online supplemental table 2. The median age was 4 months (IQR=3.0–7.0 months) with a male-to-female ratio of 6:1. The results of the blood biochemical examination are shown in online supplemental table 3.

TH levels of 1089 cases are shown in table 1. The median concentrations of FT4 and TSH were 19.62 pmol/L (IQR=17.18–22.33 pmol/L) and 2.96 uIU/mL (IQR=1.66–4.88 uIU/mL), respectively. The thyroid function of 148 HSCR cases is shown in table 2. The median concentration of FT4 and TSH were 19.50 pmol/L (IQR=17.03–22.85 pmol/L) and 3.11 uIU/mL (IQR=1.78–5.55 uIU/mL), respectively. Table 3 shows the thyroid function of 941 non-HSCR abdominal distention children, the median concentration of FT4 and TSH was19.63 pmol/L (IQR=17.20–22.26 pmol/L) and 2.91 uIU/mL (IQR=1.64–4.81 uIU/mL), respectively.

Thyroid dysfunction

Thyroid dysfunction was found in 43 (29.05%) of 148 HSCR cases. Nine (6.08%) cases of thyroid disease were detected and only one female included. Three

Table 1 Thyroid function in 1089 children with abdominal distension

	5th	25th	50th	75th	95th	Range
TT3 (nmol/L)	1.06	1.73	2.16	2.57	3.18	(0.32–7.50)
FT3 (pmol/L)	2.96	4.59	5.56	6.48	7.85	(0.69–20.59)
TT4 (nmol/L)	73.06	102.50	120.30	140.40	173.22	(5.40–237.00)
FT4 (pmol/L)	13.52	17.18	19.62	22.33	28.91	(0.56–45.28)
TSH (uIU/mL)	0.72	1.66	2.96	4.88	9.62	(0.00–100)
*TPO-Ab (IU/mL)	5.00	5.00	7.67	12.43	31.51	(5.00–155.50)
†TG-Ab (IU/mL)	10.00	10.00	10.00	12.74	110.62	(10.00–4000.00)

*A total of 302 cases treated <5 IU/mL as 5 IU/mL.
†A total of 647 cases treated <10 IU/mL as 10 IU/mL, and 1 case treated >4000 IU/mL as 4000 IU/mL.
FT3, free triiodothyronine; FT4, free thyroxine; TG-Ab, thyroglobulin antibody; TPO-Ab, thyroid peroxidase antibody; TSH, thyroid-stimulating hormone; TT3, triiodothyronine; TT4, thyroxine.

(2.03%) of 9 were hypothyroidism, 3 (2.03%) cases had subclinical hypothyroidism and 3 (2.03%) cases were diagnosed with subclinical hyperthyroidism. No hyperthyroidism was found. The remaining 34 cases (22.97%) were found as abnormal thyroid function (high or low T3/T4) (table 4). The minimum FT4 concentration was 4.08 pmol/L, and the maximum TSH concentration was 28.18 uIU/mL, both were detected in a 4-month-old boy with hypothyroidism.

Among 941 functional abdominal distension children, 206 (21.89%) cases had thyroid dysfunction, details are shown in table 5. Fifty-six cases (6.00%) diagnosed with thyroid diseases, and the overall male-to-female ratio was 1:1.07. Four males (0.43%) aged 8–30 days diagnosed with hypothyroidism. Twenty-three cases (2.44%) had subclinical hypothyroidism (11 male, 12 female), and the median age was 24.5 days. Twenty-eight (2.98%) cases had subclinical hyperthyroidism (11 male, 17 female), and the median age was 30 days. The only case (0.11%) of hyperthyroidism was a 2-year-old male. Abnormal thyroid function was observed in 150 cases (15.94%) (high or low T3/T4) (table 5). A 22-day male newborn with delayed diagnosis of CH had a TSH of 100 uIU/mL (maximum) and a FT4 of 0.56 pmol/L (minimum).

There was a marginal statistical difference in the incidence of thyroid dysfunction between HSCR cases (n=43, 29.05%) and functinal abdominal distension cases (n=206, 21.89%) (p=0.05). Subgroup analysis can be found in online supplemental table 4.

Follow-up

A total of 65 cases (9 from HSCR, 56 from functional abdominal distension) with thyroid disease were followed up, and time lines for follow-up are showed in figure 1 and figure 2 (The horizontal axis represents age). In HSCR group, three hypothyroidism cases were treated with levothyroxine (LT–4) and referred to a local hospital for continued treatment. Thyroid function had been kept within a normal limit, and LT–4 was discontinued around 2 years old when thyroid function was remained normal without exogenous thyroxine. Thyroid function of three subclinical hypothyroidism cases and three subclinical hyperthyroidism cases returned normal about 1 month later.

In functional abdominal distension group, three of the four hypothyroidism cases were treated with LT–4 routinely (one case of CH were still receiving LT–4 therapy, one case stopped therapy around 2 years old,

Table 2 Thyroid function in 148 children with Hhirschsprung's disease

	5th	25th	50th	75th	95th	Range
TT3 (nmol/L)	1.11	1.77	2.38	2.87	3.84	(0.71–7.50)
FT3 (pmol/L)	2.72	4.33	5.89	6.99	8.91	(1.33–20.59)
TT4 (nmol/L)	83.41	113.15	130.80	150.70	184.09	(40.80–228.40)
FT4 (pmol/L)	13.64	17.03	19.50	22.85	34.32	(4.08–45.28)
TSH (uIU/ml)	0.73	1.78	3.11	5.55	10.32	(0.22–28.18)
*TPO-Ab (IU/mL)	5.00	5.41	9.25	13.14	26.48	(5.00–73.37)
†TG-Ab (IU/mL)	10.00	10.00	10.00	11.45	34.62	(10.00–4000.00)

*A total of 36 cases treated <5 IU/mL as 5 IU/mL.
†A total of 90 cases treated <10 IU/mL as 10 IU/mL, and 1 case treated >4000 IU/mL as 4000 IU/mL.
FT3, free triiodothyronine; FT4, free thyroxine; TG-Ab, thyroglobulin antibod; TPO-Ab, thyroid peroxidase antibody; TSH, thyroid-stimulating hormone; TT3, triiodothyronine;.

Table 3 Thyroid function in 941 children with functional abdominal distension

	5th	25th	50th	75th	95th	Range
TT3 (nmol/L)	1.04	1.73	2.15	2.53	3.11	(0.328–4.85)
FT3 (pmol/L)	2.96	4.63	5.55	6.41	7.64	(0.69–10.66)
TT4 (nmol/L)	71.73	101.65	118.30	138.35	169.91	(5.40–237.00)
FT4 (pmol/L)	13.51	17.20	19.63	22.26	27.79	(0.56–45.18)
TSH (uIU/mL)	0.71	1.64	2.91	4.81	9.39	(0.00–100.00)
*TPO-Ab (IU/mL)	5.00	5.00	7.53	12.12	32.37	(5.00–155.50)
†TG-Ab (IU/mL)	10.00	10.00	10.00	13.11	110.67	(10.00–2710.90)

*A total of 226 cases treated <5 IU/mL as 5 IU/mL.
†A total of 557 cases treated <10 IU/mL as 10 IU/mL.
FT3, free triiodothyronine; FT4, free thyroxine; TG-Ab, thyroglobulin antibody; TPO-Ab, thyroid peroxidase antibody; TSH, thyroid-stimulating hormone; TT3, triiodothyronine; TT4, thyroxine.

one case was still on medication) and one case were lost during follow-up. Among 23 subclinical hypothyroidism cases, 5 cases were treated with LT–4 until the thyroid function maintained normal around 2 years old, 1 case was still receiving LT–4 therapy, 5 cases turned euthyroid about 1 month later and 12 cases were lost during follow-up. Among 28 subclinical hyperthyroidism, 20 cases turned euthyroid about 1 month later, and 8 cases lost follow-up. One hyperthyroidism turned euthyroid about 1 month later.

DISCUSSION

Abdominal distention is a symptom with a variety of potential aetiology. Causes in adults include coeliac disease, pancreatic insufficiency, gastrointestinal malignancy, etc. Hypothyroidism is also an important cause.[14] Abdominal distension in children requires careful determination of aetiology according to age and signs. Intestinal obstruction, HSCR, appendicitis are common organic causes.[15] Functional abdominal distention is another major cause, and the diagnostic criteria were updated in Rome IV criteria.[16] Before evaluating the features of abdominal distension according to criteria list, organic causes including hypothyroidism better be ruled out.[14]

Thyroid dysfunction in children with abdominal distention needs to be considered seriously, especially hypothyroidism. Hypothyroidism is one of the causes of mental retardation in children and requires early diagnosis and treatment to improve prognosis.[17] Studies have shown that subclinical hypothyroidism also has a certain impact on growth and development, obesity, metabolic abnormalities, as well as cardiovascular disease.[18 19] Newborn screening has become an effective method to diagnose CH in time. However, there are still some undiagnosed CH that develop abdominal distention, vomiting and feeding intolerance in neonatal or even in infancy period.[20 21] Abdominal distention caused by CH usually relieves quickly with thyroxine supplementation, but it may be prolonged when combined with other abdominal disorders.[21] Such possibility should be known to avoid misjudging the condition. For children with normal screening, thyroid disease may still develop later in life due to other risk factors.

THs are necessary for neuronal migration and stratification during brain development.[17 22] Conclusive evidence that THs influence the migration of enteric nerves have not been reported. But cases of HSCR combined with CH be reported from time to time.[23–25] A cross-sectional study

Table 4 Thyroid dysfunction cases in 148 children with Hirschsprung's disease*

	Overt hypothyroidism (n=3;2.03%)	Subclinical hypothyroidism (n=3;2.03%)	Euthyroid (n=105;70.94%)	Subclinical hyperthyroidism (n=3;2.03%)	Overt hyperthyroidism (n=0;0%)	High T3/T4 (n=23; 15.54%)	Low T3/T4 (n=11;7.43%)
TT3 (nmol/L)	1.39, 3.53, 2.91	2.71, 3.20, 2.78	2.44 (1.96–2.87)	1.77, 1.64, 1.60	–	2.17 (1.81–3.09)	1.04 (0.86–1.23)
FT3 (pmol/L)	2.96, 3.10, 1.33	7.19, 7.75, 6.62	6.16 (4.67–6.93)	3.86, 4.73, 3.48	–	5.93 (4.40–9.15)	2.74 (2.43–3.08)
TT4 (nmol/L)	116.80, 143.50, 130.50	135.20, 115.80, 113.00	128.60 (112.55–143.10)	157.80, 131.00, 132.20	–	174.20 (158.25–186.00)	84.03 (51.13–128.70)
FT4 (pmol/L)	22.72, 7.94, 4.08	20.94, 19.96, 17.05	19.06 (16.94–21.35)	24.61, 20.54, 17.73	–	30.26 (29.17–36.41)	15.12 (10.70–19.41)
TSH (uIU/mL)	11.51, 21.06, 28.18	12.77, 9.63, 6.44	2.98 (1.96–4.79)	0.35, 0.61, 0.67	–	3.93 (2.74–8.58)	1.30 (0.52–2.22)

*Data were presented as median (IQR).
FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid-stimulating hormone; TT3, triiodothyronine; TT4, thyroxine.

Table 5 Thyroid dysfunction cases in 941 children with functional abdominal distension*

	Overt hypothyroidism (n=4;0.43%)	Subclinical hypothyroidism (n=23;2.44%)	Euthyroid (n=735;78.11%)	Subclinical hyperthyroidism (n=28;2.97%)	Overt hyperthyroidism (n=1;0.11%)	High T3/T4 (n=53;5.63%)	Low T3/T4 (n=97;10.31%)
TT3 (nmol/L)	2.73, 1.18, 0.78, 0.32	2.26 (1.53–2.84)	2.22 (1.90–2.55)	1.94 (1.75–2.16)	–	2.52 (1.96–3.19)	1.07 (0.90–1.21)
FT3 (pmol/L)	7.24, 3.08, 3.55, 0.69	6.25 (4.56–7.24)	5.73 (4.98–6.44)	4.78 (3.99–5.34)	5.26	6.63 (5.41–8.59)	3.06 (2.60–3.70)
TT4 (nmol/L)	102.30, 63.69, 62.42, 5.40	122.55 (101.83–146.75)	120.30 (105.60–137.45)	110.25 (99.11–123.13)	–	165.00 (149.15–189.88)	75.47 (63.20–93.97)
FT4 (pmol/L)	21.73, 23.83, 8.49, 0.56	20.78 (19.09–23.51)	19.91 (17.71–22.04)	18.20 (15.25–19.45)	39.18	29.23 (28.34–32.66)	14.79 (12.14–17.35)
TSH (uIU/mL)	100.00, 100.00, 15.18, 12.07	13.48 (11.72–20.02)	2.94 (1.85–4.63)	0.57 (0.38–0.66)	0.342	4.16 (3.02–6.10)	1.81 (0.97–4.04)

*Data were presented as median (IQR).
FT3, free triiodothyronine; FT4, free thyroxin; TSH, thyroid-stimulating hormone; TT3, triiodothyronine; TT4, thyroxine.

of the association between CH and congenital defects also identified 2 cases of HSCR in 212 children.[26] In addition, hypothyroidism presenting as pseudo-HSCR has been reported in previous study,[27] Hypothyroidism was detected in time in these cases, whereas another child with misdiagnosis of CH was not so fortunate.[28] The female had surgery when she was 1 month old after being diagnosed with HSCR. She had six more operations after that due to postsurgical complications and persistent symptoms. She was readmitted with bloating, severe neurodevelopmental delays. The previous diagnosis was completely overturned this time, while CH due to thyroid agenesis was diagnose. The female infant developed short bowel syndrome as a result of multiple operations and was unable to speak, walk and had severe mental and motor retardation at 2.5 years old. We may need to remind ourselves that these incidents could occur on our patients. Vigilance must be maintained despite the low incidence.

Another common symptom of hypothyroidism is constipation. Constipation may coexist with functional abdominal distention, and sometimes the two cannot be simply distinguished.[16] The diagnosis of functional constipation is also based on the exclusion of organic causes. However, Rome IV diagnostic criteria recommends that laboratory testing better be scheduled after identification of warning signs. Previous studies have also suggested re-evaluating the need for thyroid function tests in children with isolated constipation.[8] Similar clinical evidence for functional abdominal distention has not been reported.

Hyperthyroidism and subclinical hyperthyroidism were also detected in our study. Although hyperthyroidism is more common with diarrhoea, abdominal distention can also occur.[29] Liver damage due to hyperthyroidism is another possible cause of abdominal distention.[30] Transient hyperthyroidism is also possible.[31] Subclinical hyperthyroidism is a biochemical diagnosis and can be endogenous and exogenous. Exogenous causes are more common, such as overtreatment with levothyroxine (most common cause) or drug-induced thyroiditis. TSH secretion follows a circadian rhythm and is pulse-regulated.[32] Transient fluctuations that happen to be caught by detection might also be defined as a biochemical diagnosis. Hyperthyroidism and subclinical hyperthyroidism cases in our study all turned euthyroid about 1 month after being diagnosed, so the most likely causes were transient.

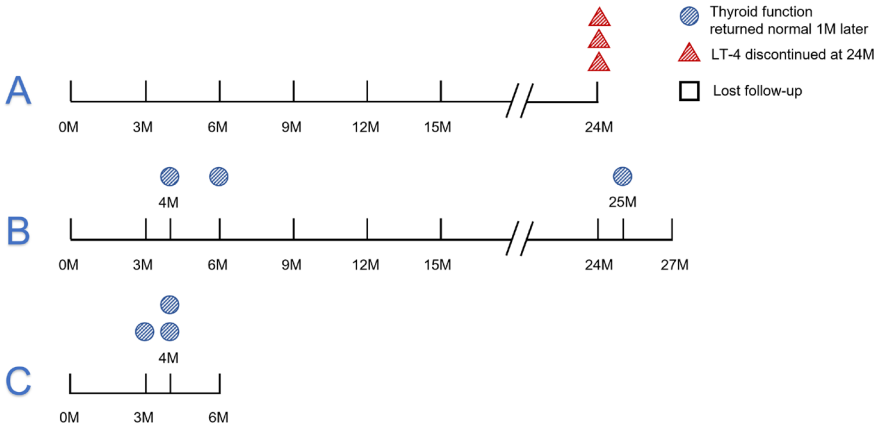

Figure 1 Time line for follow-up in HSCR cases. (A) Three hypothyroidism cases. (B) Three subclinical hypothyroidism cases. (C) Three subclinical hyperthyroidism cases. (The horizontal axis represents age). HSCR, Hirschsprung's disease .

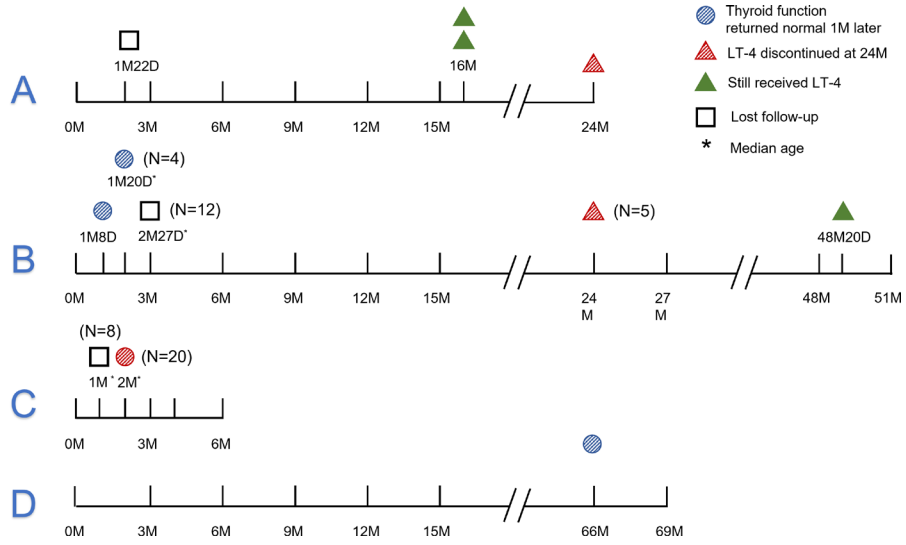

Figure 2 Time line for follow-up in functional abdominal distension cases. (A) Four hypothyroidism cases. (B) Twenty-three subclinical hypothyroidism cases. (C) Twenty-eight subclinical hyperthyroidism cases. (D) One hyperthyroidism case. (The horizontal axis represents age).

Some thyroid dysfunction cases in our study had abnormal thyroid function but could not be diagnosed with thyroid disease. Euthyroid disease syndrome or non-thyroidal disease syndrome (NTIS) needs to be carefully considered in such cases. The THs of NTIS patients follow a general course of change with disease progression: the majority begin with a significant decrease in serum T3, while serum T4 levels increase early and then fall below normal levels.[33] NTIS is a physiological hypothyroid state after cardiac surgery in children and may serve as a marker of disease severity as well as a predictor of prognosis.[34] The development of NTIS after surgery in children with HSCR has not been reported. A total of 34 cases with abnormal thyroid function (23 high T3/T4, 11 low T3/T4) were identified in 148 HSCR cases. However, these results were all preoperative. TH changes like NTIS were not observed in our study due to poor follow-up. For 150 abdominal distension cases with abnormal thyroid function (53 high T3/T4, 97 low T3/T4), the possibility of NTIS cannot be completely excluded given that medical history of acute illness of these children were unclear and that TH recovery can take weeks to months. Test bias or transient physiological changes are other possible explanations.

Timely treatment for both CH or acquired hypothyroidism is necessary. It should be clarified that treatment of hypothyroidism is not simply levothyroxine supplementation; its goal is to restore levels of metabolic parameters, including THs. Poor outcomes result from either overtreatment or undertreatment.[35] Therefore, timely retest, medication adjustment and follow-up treatment are very important. The time lines for follow-up showed that all children not lost to follow-up have recovered in our study, except for two cases of hypothyroidism and one case of hypothyroidism that developed from subclinical hypothyroidism. No growth or developmental abnormalities were found in children being followed up (including cases still on medication). The prognosis for hypothyroidism is desirable, but regular monitoring and treatment are crucial.

Abdominal distention in children requires appropriate laboratory and instrument tests when identifying the aetiology. Most of the common organic causes require surgical intervention (intestinal obstruction, HSCR and appendicitis). Imaging is a good tool to evaluate these children. Thyroid function tests may be somewhat overlooked as non-routine laboratory tests. Hypothyroidism in children is mostly congenital and newborn screening eliminates most of the potential CH, which resulted in fewer overt hypothyroidism cases. The reduced prevalence has caused clinicians to lose their vigilance for hypothyroidism when dealing with abdominal distention children. Therefore, we took this study to emphasise the importance of thyroid function test in children with abdominal distention.

This study is based on actual feedback from clinical activities and has practical implications for front-line clinical work. Long-term follow-up of children with abnormal thyroid function have been conducted, which makes our data more convincing. However, it is a single-centre study, and the sample size limit the power of the data. We lack comprehensive medical history on patients, which has implications for assessing the patient's thyroid functional status, such as NTIS. We also did not follow-up children with abnormal thyroid function but could not be diagnosed with thyroid disease to observe subsequent changes in thyroid function.

CONCLUSION

Thyroid diseases in children with abdominal distention deserve more attention. The paediatrician should be vigilant for hypothyroidism when dealing with children with abdominal distension. Hypothyroidism treatment

needs to be taken seriously. Patients should be referred to an endocrinologist for further treatment and follow-up rather than simply administering a short-term levothyroxine treatment.

Contributors HX collected the data, carried out the initial analyses and drafted the initial manuscript. WG, DC and WL completed the analysis and interpretation of the data and revised it critically. XW and WT designed this study and revised the initial manuscript and XW is responsible for the overall content as guarantor. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Patient consent for publication Not applicable.

Ethics approval The study had been approved by the Medical Ethics Committee of the Children's Hospital of Nanjing Medical University (202101014-1). This study was a retrospective study and does not contain patient privacy information and the requirement for informed consent was therefore waived.

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Data availability statement Data are available on reasonable request. The raw data supporting the conclusions of this article will be made available by the corresponding authors, without undue reservation.

ORCID iDs
Wei Li http://orcid.org/0000-0003-0769-5805
Xu Wang http://orcid.org/0000-0002-1861-5922

REFERENCES

1 Wassner AJ. Congenital hypothyroidism. *Clin Perinatol* 2018;45:1–18.
2 Hanley P, Lord K, Bauer AJ. Thyroid disorders in children and adolescents: a review. *JAMA Pediatr* 2016;170:1008–19.
3 Salerno M, Improda N, Capalbo D. MANAGEMENT of endocrine disease subclinical hypothyroidism in children. *Eur J Endocrinol* 2020;183:R13–28.
4 Koulouri O, Moran C, Halsall D, *et al*. Pitfalls in the measurement and interpretation of thyroid function tests. *Best Pract Res Clin Endocrinol Metab* 2013;27:745–62.
5 Leung AKC, Leung AAC. Evaluation and management of the child with hypothyroidism. *World J Pediatr* 2019;15:124–34.
6 Arshad A, Powell C, Tighe MP. Hirschsprung's disease. *BMJ* 2012;345:bmj.e5521.
7 Kessmann J. Hirschsprung's disease: diagnosis and management. *Am Fam Physician* 2006;74:1319–22.
8 Bennett WE Jr, Heuckeroth RO. Hypothyroidism is a rare cause of isolated constipation. *J Pediatr Gastroenterol Nutr* 2012;54:285–7.
9 Chogle A, Saps M. Yield and cost of performing screening tests for constipation in children. *Can J Gastroenterol* 2013;27:e35–8.
10 Ogundele MO, Waterson M. When should we be conducting thyroid function tests in newborns and young infants? *Arch Dis Child* 2010;95:151–2.
11 American Academy of Pediatrics, Rose SR, Section on Endocrinology and Committee on Genetics, American Thyroid Association, *et al*. Update of newborn screening and therapy for congenital hypothyroidism. *Pediatrics* 2006;117:2290–303.
12 Therrell BL, Padilla CD, Loeber JG, *et al*. Current status of newborn screening worldwide: 2015. *Semin Perinatol* 2015;39:171–87.
13 Zhang Y, Hu X, Hu S, *et al*. Non-invasive imaging methods for brown adipose tissue detection and function evaluation. *Intern Med Open Access* 2018;8:299.
14 Mari A, Abu Backer F, Mahamid M, *et al*. Bloating and abdominal distension: clinical approach and management. *Adv Ther* 2019;36:1075–84.
15 Zhao X-X, Zhang G-Q, Li Z-Y. Clinical features and etiology of abdominal distension in children. *Zhongguo Dang Dai Er Ke Za Zhi* 2019;21:1022–7.
16 Mearin F, Lacy BE, Chang L, *et al*. Bowel disorders. *Gastroenterol* 2016;S0016-5085(16)00222-5.
17 Uchida K, Suzuki M. Congenital hypothyroidism and brain development: association with other psychiatric disorders. *Front Neurosci* 2021;15:772382.
18 Cerbone M, Capalbo D, Wasniewska M, *et al*. Cardiovascular risk factors in children with long-standing untreated idiopathic subclinical hypothyroidism. *J Clin Endocrinol Metab* 2014;99:2697–703.
19 Reinehr T. Thyroid function in the nutritionally obese child and adolescent. *Curr Opin Pediatr* 2011;23:415–20.
20 Smolkin T, Ulanovsky I, Blazer S, *et al*. Rare presentations of congenital hypothyroidism. *Isr Med Assoc J* 2011;13:779–80.
21 Chua C, Gurnurkar S, Rodriguez-Prado Y, *et al*. Prolonged ileus in an infant presenting with primary congenital hypothyroidism. *Case Rep Pediatr* 2015;2015:584735.
22 Ausó E, Lavado-Autric R, Cuevas E, *et al*. A moderate and transient deficiency of maternal thyroid function at the beginning of fetal neocorticogenesis alters neuronal migration. *Endocrinology* 2004;145:4037–47.
23 Eren M, Celik M, Kinik S, *et al*. A case of hirschsprung disease: does thyroid hormone have any effect? *Turk J Pediatr* 2009;51:94–6.
24 Tahan S, Siviero-Miachon AA, de Faria Soares M de F, *et al*. Untreated congenital hypothyroidism mimicking Hirschsprung disease: a puzzling case in a one-year-old child. *Case Rep Pediatr* 2018;2018:9209873.
25 Kota SK, Modi KD, Rao MM. Hirschsprungs disease with congenital hypothyroidism. *Indian Pediatr* 2012;49:245–6.
26 Monroy-Santoyo S, Ibarra-González I, Fernández-Lainez C, *et al*. Higher incidence of thyroid agenesis in Mexican newborns with congenital hypothyroidism associated with birth defects. *Early Hum Dev* 2012;88:61–4.
27 Sharma D, Murki S, Dhanraj G. Congenital hypothyroidism presenting with seizures and pseudo-hirschsprung's disease in newborn. *Indian J Pediatr* 2014;81:837.
28 Buyukyilmaz G, Baltu D, Soyer T, *et al*. Severe hyponatremia and repeated intestinal resections for intestinal dysmotility mimicking congenital aganglionic megacolon due to delay in the diagnosis of congenital hypothyroidism. *Ann Pediatr Endocrinol Metab* 2016;21:230–4.
29 Hsiao F-C, Hung Y-J, Hsieh C-H, *et al*. Abdominal pain and multi-organ dysfunction syndrome in a young woman. *Am J Med Sci* 2007;334:399–401.
30 Burra P. Liver abnormalities and endocrine diseases. *Best Pract Res Clin Gastroenterol* 2013;27:553–63.
31 Lafontaine N, Learoyd D, Farrel S, *et al*. Suppurative thyroiditis: systematic review and clinical guidance. *Clin Endocrinol (Oxf)* 2021;95:253–64.
32 Santos Palacios S, Pascual-Corrales E, Galofre JC. Management of subclinical hyperthyroidism. *Int J Endocrinol Metab* 2012;10:490–6.
33 Lee S, Farwell AP. Euthyroid sick syndrome. *Compr Physiol* 2016;6:1071–80.
34 Ross OC, Petros A. The sick euthyroid syndrome in paediatric cardiac surgery patients. *Intensive Care Med* 2001;27:1124–32.
35 Rodriguez L, Dinauer C, Francis G. Treatment of hypothyroidism in infants, children and adolescents. *Trends Endocrinol Metab* 2022;33:522–32.