

Diffuse Enlargement of the Thyroid Gland as a Result of the Impact of Adverse Factors on the Pituitary-thyroid System of Children

Nurlan Bekenov¹, Kanatshan Kemelbekov², Gulmira Bektenova³, Gulmira Datkayeva⁴, Kadyr Ospanov⁵, Elmira Ospanova⁶, Bibigul Doltaeva⁷, Galiya Assanova⁸

ABSTRACT

The problem of diffuse goiter has attracted the attention of many researchers in recent years. The main reason for the formation of endemic goiter is iodine deficiency in the environment. Epidemiological studies conducted in recent years have shown that almost all regions of Kazakhstan are regions of endemic goiter with natural iodine deficiency. Some of them are characterized by an increase in the severity of endemic goiter. The reasons contributing to the progression of goiter endemicity are the cessation of iodine prophylaxis, the deterioration of the environmental situation and the social situation of a significant part of the population.

The purpose of this work was to study the features of thyroid status in children with diffuse goiter.

Material and methods

There were 38 children under our supervision, 20 (main group) had diffuse (endemic) goiter (5 boys and 15 girls), 18 children (control group) - 5 boys and 13 girls, children in the control group were considered healthy.

Results

As a result of comparing indicators of the functional state of the pituitary-thyroid system in patients with diffuse goiter, a relatively increased level of thyroid-stimulating hormone is noted, which indicates the negative impact of diffuse goiter on the thyroid status of children.

Conclusions

As a result of the manifestation of diffuse goiter in children, metabolic disorders of the pituitary-thyroid system occur. Signs of thyroid deficiency are most often observed in children living in iodine-deficient areas.

Keywords

children, status, hormone, control, thyroid gland, hormones, iodine.

INTRODUCTION

Thyroid disease in children is a pressing problem in pediatric endocrinology. This is due to the fact that WHO (World Health Organization) classifies iodine deficiency diseases as the most common non-infectious pathologies. This problem still causes a lot of controversy and discussion in the literature, despite the existing international standards and guidelines for the diagnosis and treatment of thyroid diseases in

1. Candidate of Medical Sciences, teacher of the Department "General Practitioner -1", South Kazakhstan Medical Academy, Shymkent, Kazakhstan, E-mail: 87015262612@mail.ru,
2. Head of the Department of Pediatrics -1, PhD doctor, South Kazakhstan Medical Academy, Shymkent, Kazakhstan,
3. Candidate of Medical Sciences, Head of the Department "Microbiology", South Kazakhstan Medical Academy, Shymkent, Kazakhstan,
4. Head of the Department of "General Practitioner -1", Candidate of Medical Sciences, South Kazakhstan Medical Academy, Shymkent, Kazakhstan,
5. Head of the Department of "General Practitioner-3", Candidate of Medical Sciences, South Kazakhstan Medical Academy, Shymkent, Kazakhstan,
6. Doctor of Medical Sciences, Professor of the Department "Preventive Medicine", Khoja Akhmet Yassawi International Kazakh-Turkish University, Turkestan, Kazakhstan,
7. Candidate of Medical Sciences, Head of the Educational and Methodological Department, South Kazakhstan Medical Academy, Shymkent, Kazakhstan,
8. Candidate of Medical Sciences, Head of the Department of Therapy and Cardiology, South Kazakhstan Medical Academy, Shymkent, Kazakhstan,

Correspondence

Head of the Department of Pediatrics -1, PhD doctor, South Kazakhstan Medical Academy, Shymkent, Kazakhstan,

children^{1,2}. In conditions of children living in areas of iodine deficiency, in addition to an increase in the volume of the thyroid gland, there are delays in the physical, intellectual and sexual development of these children. There is a direct correlation between the degree of delayed puberty and growth in boys and their thyroid status. Iodine deficiency in the environment and the resulting diseases form a wide range of medical and social problems in children. To date, information on the impact of iodine deficiency on the formation of thyroid pathology in children is scarce, especially in adolescents. Prevention programs usually include group prophylaxis in primary school children. The absence of group iodine prophylaxis in children during puberty predetermines a significant increase in the number of cases of diffuse goiter and an increase in the number of patients with nodular thyroid disease during puberty. Translated with DeepL.com (free version) Iodine deficiency diseases are conditions that develop in the population as a result of iodine deficiency and that can be prevented by normal iodine intake^{3,4,5}. According to WHO, 2,5 billion people are at risk of iodine deficiency diseases, which is 1/3 of the world's population! 800 million have enlarged thyroid gland (diffuse goiter)^{6,7,8}. In Kazakhstan, the total area of iodine deficiency is 158 000 square kilometers, which exceeds half of the territory of the republic. Studies conducted by Academician Zeltzer M.E. showed that in Shymkent city there is a moderate degree of iodine deficiency. Iodine deficiency in the environment, in water, air and food products leads to the development of endemic goiter in children. Iodine is involved in the synthesis of thyroid hormones, iodine deficiency in the body leads to the development of iodine deficiency diseases based on insufficient production of thyroid hormones^{9,10}. The most visible manifestation of iodine deficiency is the presence of goiter, and children of pubertal period are most prone to iodine deficiency. The presence of endemic goiter in pregnant women has a pronounced negative impact on the thyroid function of newborns^{11,12,13}.

Endemic goiter is a multifactorial disease of the organism, the defining feature of which is enlargement of the thyroid gland, which is caused by absolute or relative iodine deficiency and is characterized by mass affection of the population in certain geographical

regions^{14,15,16}. The functional status of the thyroid gland in endemic goiter can vary from euthyroid to hypothyroid. It has also been noted that the number of patients diagnosed with diffuse toxic goiter increases in goiter-endemic regions^{17,18}. Thus, the spectrum of diseases of the thyroid gland is wide and, in addition to the most common manifestation of iodine deficiency - diffuse goiter, iodine deficiency can lead to impaired reproductive function, delayed puberty, retardation in physical development, as well as reduced intelligence development up to the formation of severe forms of cretinism and can serve as a background for the growth of somatic diseases. Prevention of iodine deficiency and diffuse goiter allows, without high costs, in a short time, to significantly improve the health of the population and practically eliminate iodine deficiency diseases and their complications.

The interest of researchers in thyroid pathology is explained not so much by its prevalence as by the great importance of thyroid hormones (thyroxine and triiodothyronine) for the formation of the central nervous system, intellectual abilities, physiological course of many metabolic processes, normal growth and skeletal development of children^{19,20,21}.

The aim of the present work was to study the peculiarities of thyroid status in children with diffuse goiter in the region with iodine deficiency and to determine the necessity of iodine prophylaxis in them.

MATERIALS AND METHODS

38 children were under our observation, 20 (main group) were with diffuse goiter (5 boys and 15 girls), 18 children (control group) - 5 boys and 13 girls, children of the control group were considered healthy and were not registered with an endocrinologist with thyroid diseases. Children of both groups were also divided into boys and girls (Table 1). Thyroid status was assessed by thyroid ultrasound. Ultrasound examination of children was performed according to the traditional method on an Alpinion E-CUBE 8 device with a 5-10 MHz transducer. Volumetry results were calculated according to sex and body surface area according to WHO (World Health Organization) standards. Body surface area was calculated by nomogram.

Determination of thyroid hormone levels in children is the most reliable test in the diagnosis of thyroid function and performance disorders. Thyroid hormone parameters were assessed according to the following parameters: thyroid hormone (TTH), free thyroxine (T4) and free triiodothyronine (T3) levels were determined by immunochemiluminescence. Thyroid status was also assessed by thyroid ultrasound. Ultrasound examination of children was performed according to the traditional method on an Alpinion E-CUBE 8 device with a 5-10 MHz transducer. Volumetry results were calculated according to sex and body surface area according to WHO (World Health Organization) standards. Body surface area was calculated according to the nomogram.

Table 1 - groups of studied children by sex difference and the total number of

Group	n	Boys	Girls
Basic	20	5	15
Control	18	5	13

Note: n - number of children

RESULTS

Changes in thyroid size are primarily related to the level of iodine intake, but changes in thyroid volume in response to altered iodine intake can occur over a significant period of time (months to years). In the literature available to us there are few works on the assessment of the structural and functional state of the thyroid gland in children during puberty in the region with iodine deficiency. During puberty, certain changes occur in the child's body associated with adaptation to the rapid rate of growth and development. The development and increase in thyroid gland volume during this period is determined not only by the stimulating effect of thyroid hormone, but also by other indicators - increased formation of free thyroxine and free triiodothyronine, accelerated iodine excretion, increased synthesis of thyroxine-binding globulin. In addition, insufficient iodine intake increases the sensitivity of thyrocytes to the stimulating effect of thyroid hormone. In iodine-deficient areas, the process of puberty is often accompanied by the formation of

diffuse goiter. Among all population groups with diffuse goiter with the highest frequency it is in girls. In our study, diffuse thyroid enlargement was found in 8 girls and 2 boys in the main group. Absence of echographic changes of the thyroid gland was revealed in the majority of examined children of the main group. According to the ultrasound findings, the average thyroid volume in children was 8.2 ± 3.4 ml and practically did not differ between the average volumes of boys (8.4 ± 3.5 ml) and girls (8.1 ± 3.0 ml). Analyses of the results of goiter occurrence in children depending on sex shows that thyroid gland enlargement in girls is 2 times greater than in boys.

A comparative analysis of anthropometric indices in the studied children depending on thyroid volume was also carried out. The values of the comparative analysis showed that girls with goiter have average height (140.1 ± 4.0 cm) and body weight (33.4 ± 5.2) less than girls without goiter (145.2 ± 4.8) and average body weight (38.7 ± 6.5). Boys with goiter also had lower mean height (143.2 ± 4.7) and weight (37.5 ± 3.9) than boys with normal thyroid volume, height (150.2 ± 5.3) and weight (42.8 ± 4.5) respectively.

When assessing the performance indicators of the pituitary-thyroid system, it was found that in patients with diffuse goiter the values of T4 level were identical to those of the control group. The mean value in T4 in the studied group was 15.4 pmol/l, and in the control group 15.1 pmol/l. The value of hormone T3 in the study group was 7.2 pg/ml, and in the control group 6.5 pg/ml. In the study of TTG, it was noted that the mean value of thyroid hormone in the main group was 3.9 mU/L, which was 1.8 mU/L higher than in the control group, where the mean value was 2.1 mU/L (Table 2). Subclinical hypothyroidism was detected in two patients of the main group, as thyroid hormone values were higher than normal.

As a result of comparison of indicators of the functional state of the pituitary-thyroid system in patients with diffuse goiter, a relatively increased level of thyroid hormone is noted, which indicates a negative impact of diffuse (endemic) goiter on the thyroid status of children.

Table 2 - comparisons of functional state indicators pituitary-thyroid system

Group	Average value of free thyroxine (T4)	Average value of free triiodothyronine (T3)	Average value of thyroid hormone (TTG)
Basic Control	15,4 pmol/L	7,2 pg/ml	3,9 IU/L
	15,1 pmol/L	6,5 pg/ml	2,1 IU/L

Assessment of the functional state of the pituitary-thyroid system depending on sex revealed that in boys with diffuse goiter the thyroid hormone values did not differ from the thyroid values of boys in the control group. The mean value of free thyroxine (T4) in the main group was 15.1 pmol/L, and in the control group 15.3 pmol/L. The value of hormone T3 in the study group was 7.1 pg/ml, and in the control group 6.6 pg/ml. The mean values of TTG in boys of the main group were 3.6 mU/d/L, while in the control group 2.2 mU/d/L (Table 3).

Table 3 - comparisons of functional state indicators The pituitary-thyroid system by sex difference in boys

Group	Average free thyroxine (T4) value	Average value of free triiodothyronine (T3)	Average value of thyroid hormone (TTG)
Basic Control	15,1 pmol/L	7.1 pg/ml	3,6 IU/L
	15,3 pmol/L	6.6 pg/ml	2,2 IU/L

In girls with diffuse goiter, the level of free thyroxine (T4) was also not different from the control group girls, where the mean values were 15.2 pmol/l, and in the control group girls - 15.4 pmol/l. And the average value of T3 was 7.2 pg/ml, and in the girls of the control group - 6.8 pg/ml. However, the girls of the main group had a higher level of TTG – 4.1 mU/l, compared to the girls of the control group - 2.5 mU/l (Table 4).

Table 4 - comparisons of functional state indicators The pituitary-thyroid system by sex difference in girls

Group	Average free thyroxine (T4) value	Average value of free triiodothyronine (T3)	Average value of thyroid hormone (TTG)
Basic	15,2 pmol/L	7.2 pg/ml	4,1 IU/L
Control	15,4 pmol/L	6.8 pg/ml	2,5 IU/L

DISCUSSION

When analyzing the indicators of the functional state of the pituitary-thyroid system in the initial period of puberty it was revealed that girls with diffuse (endemic) goiter had worse indicators of the functional activity of the thyroid gland in the form of a relative increase in the level of thyroid hormone and a higher frequency of minimal thyroid insufficiency. These changes are quite understandable and may indicate the tension of adaptation mechanisms in children with diffuse (endemic) goiter during puberty. It is during this period that the requirements to the thyroid gland are increased, and compensatory capabilities are limited due to increased iodine uptake by the thyroid gland, but low iodine concentration in blood plasma.

Thus, when analyzing the functional state of the pituitary-thyroid system depending on sex, it was revealed that girls with diffuse goiter had the worst indicators of the functional activity of the thyroid system in the form of a relatively increased level of thyroid hormone (TTH).

The results of the study showed that the presence of diffuse goiter in children negatively affects the indicators of the functional state of the pituitary-thyroid system. At the same time, it was female patients who had a relatively increased level of thyroid hormone (TTH). Taking into account that girls due to thyroid hormone deficiency more often develop a condition associated with a whole range of pathological disorders, of which the most socially significant are reproductive dysfunction, it is necessary to conduct early diagnosis among children (especially among female patients) for early detection and prophylactic (adequate) therapy.

CONCLUSIONS

1. The presence of diffuse (endemic) goiter in children negatively affects the indicators of the functional state of the pituitary-thyroid system. Every second child with diffuse (endemic) goiter, living in the southern regions of our country in conditions of moderate iodine deficiency in the environment, already has minimal thyroid insufficiency. Insufficient iodine intake by the majority of children in Kazakhstan is directly related to low motivation and poor awareness of the priority role of iodine prevention for children's health. The negative impact of the pituitary-thyroid system due to iodine deficiency is characterized by a delay in the formation of static-motor functions and a decrease in the level of development of intelligence indicators of schoolchildren.
2. To date, the existing iodine deficiency and detected structural disorders of thyroid tissue in children indicate the need for group and also the introduction of individual prophylaxis in the initial period of puberty. In the absence of constant iodine supply of

the population, group iodine prophylaxis should be carried out with the help of preparations containing physiological dose of iodine. Despite significant progress in the elimination of iodine deficiency diseases over the past few decades, dietary iodine deficiency remains a serious public health problem worldwide. Special attention should be paid to continuous monitoring of the effectiveness of preventive measures.

Source of fund: (if any). No funding

Conflict of Interest: The authors have no conflicts of interest to declare.

AUTHORS' CONTRIBUTION

Data gathering and idea owner of this study: Nurlan Bekenov, *Kanatzhan Kemelbekov

Study design: Gulmira Bektenova, Gulmira Datkayeva

Data gathering: Kadyr Ospanov, Elmira Ospanova

Writing and submitting manuscript: Bibigul Doltaeva, Galiya Assanova

Editing and approval of final draft: Kanatzhan Kemelbekov

REFERENCES

- Kurmacheva N.A. The role and tasks of pediatricians in the prevention of iodine deficiency diseases in children // *Pediatrics*. — 2012. — № 2. — P. 11-15. doi.org/10.21518/2079-701X-2014-6-14-21
- Bruno de Benoit, Shvets O.V. Elimination of iodine deficiency is one of the key healthcare objectives // *International Journal of Endocrinology*. — 2011. — № 6 (38). — P. 12-18. doi.org/10.21518/2079-701X-2022-16-5-70-77
- Platonova N. M. Iodine deficiency: the current state of the problem // *Klinicheskaya i eksperimental'naya tireodologiya*. 2015; 1 (11): 12-21. <https://doi.org/10.14341/ket2015112-21>
- Zhang XH, Yuan GP, Chen TL. Clinical effect of methimazole combined with selenium in the treatment of toxic diffuse goiter in children. *World J Clin Cases*. 2022 Feb 6;10(4):1190-1197. [doi: 10.12998/wjcc.v10.i4.1190](https://doi.org/10.12998/wjcc.v10.i4.1190) PMID: 35211552; PMCID: PMC8855191.
- Godovantes OI, Kitsak TS, Vitkovsky OO, Kuzniak LV, Godovantes OS, Chaikovska NM, Fedoniuk LY. The Influence of Diffuse Nontoxic Goiter on the State of Protective Mechanisms of the Oral Cavity in Children. *J Med Life*. 2020 Jan-Mar;13(1):21-25. [doi: 10.25122/jml-2020-0013](https://doi.org/10.25122/jml-2020-0013). PMID: 32341696; PMCID: PMC7175437.
- Dubrovskaya M.I., Polunina V.V., Botkina A.S., Davidenko N.V., Zubova T.V., Lyalikova V.B. Diffuse toxic goiter in an obese teenager, occurring under the guise of anorexia nervosa. *Pediatrics named after G.N. Speransky*. 2019; 98 (3): 290-292. DOI:[10.24110/0031-403X-2019-98-3-290-292](https://doi.org/10.24110/0031-403X-2019-98-3-290-292)
- Nakahata N, Asano M, Abe N, Ejiri H, Ota H, Suzuki S, Sato A, Tazaki R, Nagamine N, Takahashi C, Yamaya Y, Iwadate M, Matsuzuka T, Ohira T, Yasumura S, Suzuki S, Furuya F, Shimura H, Suzuki S, Yokoya S, Ohto H, Kamiya K. Prevalence of thyroid diffuse goiter and its association with body mass index and the presence of cysts and nodules in children and adolescents: the Fukushima Health Management Survey. *Endocr J*. 2024 Feb 16. [doi: 10.1507/endocrj.EJ23-0609](https://doi.org/10.1507/endocrj.EJ23-0609). Epub ahead of print. PMID: 38369332.
- Troshina E.A., Makolina N.P., Kolpakova E.A., Nikiforovich P.A., Isaeva M.P., Abdulkhabirova F.M., Platonova N.M. Structural and morphologic characteristics of nodular goiter in chronic iodine deficiency status. *Clinical and experimental thyroidology*. 2023;19(1):20-28. doi.org/10.14341/ket12748
- Azizi F, Amouzegar A. Management of thyrotoxicosis in children and adolescents: 35 years' experience in 304 patients. *J Pediatr Endocrinol Metab*. 2018 Jan 26;31(2):159-165. [doi: 10.1515/jpem-2017-0394](https://doi.org/10.1515/jpem-2017-0394). PMID: 29306930.
- Yadav K, Pandav C. National Iodine Deficiency Disorders Control Programme: Current status & future strategy. *Indian J Med Res*. 2018;148(5):503 DOI:[10.4103/ijmr.IJMR_1717_18](https://doi.org/10.4103/ijmr.IJMR_1717_18)
- Henrichs J, Ghassabian A., Peeters R.P., Tiemeier H. Maternal hypothyroxinemia and effects on cognitive functioning in childhood: how and why? // *Clin Endocrinol (Oxf)*. 2013. Vol. 79. P. 152–162. DOI:[10.1111/cen.12227](https://doi.org/10.1111/cen.12227)
- Lazarus J.H., Bestwick J.P., Channon S. et al. Antenatal thyroid screening and childhood cognitive function // *N Engl J Med*. 2012. Vol. 366(6). P. 493–501. DOI:[10.1056/NEJMoa1106104](https://doi.org/10.1056/NEJMoa1106104)
- Zimmermann MB, Boelaert K. Iodine deficiency and thyroid disorders. *Lancet Diabetes Endocrinol*. 2015; 3(4):286-95. [doi: 10.1016/S2213-8587\(14\)70225-6](https://doi.org/10.1016/S2213-8587(14)70225-6)
- Moghaddam PA, Virk R, Sakhdari A, Prasad ML, Cosar EF, Khan A. Five Top Stories in Thyroid Pathology. *Arch Pathol Lab Med*. 2016; 140(2):158-70. DOI: [10.5858/arpa.2014-0468-RA](https://doi.org/10.5858/arpa.2014-0468-RA)
- Ayazbekov, A., Nurkhasimova, R., Ibrayeva, D., ...Uteuliye, Y., Kemelbekov, K. Evaluation of women's health with intrauterine fetal death in the city of turkestan for the years of 2013-2017. *Annals of Tropical Medicine and Public Health*, 2018, 17(Special issue), S804.
- Makretskaya N.A., Bezlepkin O.B., Kolodkina A.A., Kiyayev A.V., Vasiliev E.V., Petrov V.M., Chikulaeva O.A., Malievsky O.A., Dedov I. I., Tyulpakov A.N. Molecular genetic basis of thyroid dysgenesis. Clinical and experimental thyroidology. 2018; 14(2): 64–71. [doi: 10.14341/ket9556](https://doi.org/10.14341/ket9556)
- Makretskaya N.A., Kalinchenko N.Yu., Vasiliev E.V., Petrov V.M., Tyulpakov A.N. Clinical case of congenital hypothyroidism caused by a defect in the NKX2-1 gene. *Problems of endocrinology*. 2016; 62(3):21–24. [doi:10.14341/probl201662321-24](https://doi.org/10.14341/probl201662321-24)
- Parnes M, Bashir H, Jankovic J. Is Benign Hereditary Chorea Really Benign? Brain-Lung-Thyroid Syndrome Caused by NKX2-1 Mutations. *Mov. Disord. Clin. Pract*. 2018; 6 (1):34–39. [doi: 10.1002/mdc3.12690](https://doi.org/10.1002/mdc3.12690)
- Kemelbekov, K., Dzhoshibaev, S., Baymagambetov, A., Satymbekova, A., Sheyshenov, Z. Epidemiology and dynamics of congenital heart diseases at the newborns in the Zhambyl region, Kazakhstan. *Research Journal of Medical Sciences*, 2016, 10(3), p.69–75
- Rivkees SA. Controversies in the management of Graves' disease in children. *J. Endocrinol. Invest*. 2016; 39 (11): 1247–1257. DOI: [10.1007/s40618-016-0477-x](https://doi.org/10.1007/s40618-016-0477-x)
- Urmanova Yu.M., Azimova Sh.Sh., Rikhsieva N.T. The frequency and structure of diseases thyroid gland in children and adolescents according to the data of circulation. *International Journal of Endocrinology*. 2018;14(2):163-167. DOI: [10.22141/2224-0721.14.2.2018.130562](https://doi.org/10.22141/2224-0721.14.2.2018.130562)