higher T4 values, with higher levels of TSH also. Values of T3 in our tested DS group did not significantly differ from the results of the control group, which is consistent with the research of Stoll and associates (3) and Toledo and associates (5). However, in the researches of Lejeune and associates (14) and Hestnes and associates (15), values of T3 in the DS groups were lower comparing to the values in the control groups. Even though the values of TSH were elevated in DS children, they were never as high as the values observed in the cases of congenital hypothyreodism (3). However, together with the values of T3 and T4 in the range of referent levels they indicate compensated insufficiency of thyroid gland (16). As a cause of increase in TSH values in DS, Zergollern (17) suggests agenesio or ectopio of thyroid gland in children with DS. We did not find either agenesio or ectopio of the thyroid gland, although 45,62% of our tested people with DS had somewhat ultrasound visible structure changes of thyroid gland. Our studies also did not confirm lower values of rT3 in cases of DS, which were noticed by other researchers (3, 5, 14). Also, negative correlation between the values of rT3 and TSH in our DS patients also could be confirmed (as a consequence of possible autoregulation of these two hormones), because the values of TSH were high followed by normal values of rT3. The rT3/TSH ratio in the tested with DS was lower, mainly because of the rising value of TSH and not because of the lower values of rT3, as other authors suggested (3, 4, 5). Comparing to the control group, in our research on DS patients, highest average values of TSH were noticed in the age group of 0-6 year and in the group of 7-14 years-olds. Lower values of were highly noticeable in the age of 7-14 years while the difference in rT3/TSH ratio peaked in the age of 0-6 years, Lower rT3 value was highly apparent in the age >14 years. When comparing the age groups, we found no differences between values of T3 in the tested with DS and the control group, which is consistent with the results of other authors (3, 4, 5, 7, 14). In 35 cases (60,35%) of 58 tested DS people we identified elevated values of TSH in all the age groups and 16 (27,58%) of them received medical treatment. Most of them were 0-6 years years of age (63,23%). In the research of Noble and associates (18) it is stated that frequency of dysfunction of thyroid gland within the group of 204 children with DS in the age of 5-17 years was 7,3%. Most of the cases were of the age 7-14 (66,6%), while in the group of 7 year-olds and younger the frequency was only 6,6%. Mitchell and associates (9) stated that frequency of compensated hypothyroidism among children with DS was 19% with 2,5% of them less than 10 months old. In both tested groups with DS, which were formed considering referent levels of TSH (Chart 1), values of this parameter were significantly higher than the ones in the relevant control groups. Therefore, the issue is compensated insufficiency of thyroid gland, with level of TSH being raised, while T3 and T4 are maintained still in the referent range. As the results of the research of the function of thyroid gland could not clearly indicate hypothyroidism, a question follows: do the results have clinical implications? According to the results of other author's researches (19), children with low level of T4, even if just temporary, have increased risk of early or late complications in their future psychomotoric development. Also, children with high level of TSH when younger than 4 years, lag behind in growth and development comparing to the children with normal TSH level (13, 20). It is explained that with increased stimulation of the gland, despite glandular hypoplasia, secretion of hormones in the first months or years of life in children with DS may be sufficient for the need of the organism. Later in life, when the needs of organism increase and the secretion of the hormones gets insufficient, real biochemical and clinical image of hypofunction of the thyroid gland can be observed (16). As increase in TSH is considered a goitrous factor, it is recommended that a supstitutional treatment be introduced (3, 4, 5, 16) in all cases with increased level of TSH or low levels of T4 and/or T3, without waiting for clinical hypothyroidism to develop. Contribution to this is information that generally in population, prevalence of subclinical hypothyroidism, clinically manifested only with cognitive problems or attitude issues (21), is high and that use of L-thyroxin can help with these kinds of conditions (16, 22). However, other authors do not confirm the necessity of the treatment when it comes to patients with DS who have elevated TSH level, because of belief that treatment is necessary only in cases with clear biochemical and clinical signs of hypothyroidism, anomalies in thyroid structure (17) and appearance of antithyroid antibodies (23).

Conclusion

Our studies confirmed significantly higher frequency of thyroid dysfunction in people with DS comparing with the control group. Even though the values of TSH were significantly higher in the tested with DS comparing to the results of the control group, serum values of T3 and T4 were still within referent range. That contributes to higher incidence of compensated insufficiency of thyroid gland in cases of DS comparing to general population (24). The results of our research on increased levels of serum TSH in the tested group with DS at the age under 6 years are consistent with the results of Mitchell et al.(9). They point at the necessity of correction of early attitudes on thyroid function testing in cases of children with DS, because tests once a year during childhood and once in 2 years after puberty have proven to be insufficient (25, 26, 27, 28). There are no references for systematic monitoring of patients with DS in Bosnia and Herzegovina. Since thyroid dysfunction is common and easily overlooked, periodic thyroid function examinations should be performed. We consider that it is necessary to accept the recommendations of The First Congress of European Association on Down Syndrome (29), that besides neonatal TSH screening, thyroid function in cases of DS should be controlled during the first three months, and at the 6th, 12th, 18th and 24th month of child's life, and also at least once a year up to the time of puberty; every six months or once a year during puberty; once a year up to 20th year of life and later on once in two to three years.

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