

FREQUENCY OF HYPOTHYROIDISM IN CHILDREN WITH CELIAC DISEASE AT A TERTIARY CARE HOSPITAL

DR. MUHAMMAD ZEESHAN, MBBS

Department of Pediatric Medicine,
Nishtar Hospital, Multan, Pakistan.

DR. ABEEHA MALIK, MBBS

Department of Pediatric Medicine,
Nishtar Hospital, Multan, Pakistan.

DR. MUHAMMAD HAMZA BASHIR, MBBS

Department of Pediatric Medicine,
Nishtar Hospital, Multan, Pakistan.

ABSTRACT;

Background; The prevalence of thyroid disease is likely increased among children with celiac disease (CD). In addition, exposure to gluten-free treatment may be associated with a risk of thyroid disease, but this association remains controversial. This study was conducted to determine frequency of hypothyroidism in these children as there is no such study done in our local population of Southern Punjab. **Objective;** The objective of this study is to determine the frequency of hypothyroidism in children with celiac disease at a tertiary care hospital. **Material and methods;** A total of 115 children with celiac disease were registered in this cross - sectional study which was conducted at department of pediatric medicine, Nishtar Hospital Multan from June 2015 to December 2016. These children were screened for their thyroid hormone levels to diagnose hypothyroidism. **Results;** Of these 115 study cases, 49 (42.6%) were male patients and 66 (57.4%) were female patients. Mean age of our study cases was 6.31 ± 2.05 years. Of these 115 study cases, 59 (51.3%) belonged to rural areas while 56 (48.7%) from urban areas, 45 (39.1%) were from poor families while 70 (60.9%) were from middle income families. Of these 115 study cases, 31 (27 %) were from urdu speaking families, 38.3 % Punjabi, 30 (26.1%) Saraikis and 10 (8.7%) were Baloch. Of these 115 study cases, mothers were illiterate in 75 (65.2%) and literate in 40 (34.8%). Mean disease duration was 5.27 ± 2.11 months and 69 (60%) had disease duration up to 6 months and 46 (40%) had more than 6 months. Mean T_3 level was 86.43 ± 26.25 ng/dl, mean T_4 level was 5.02 ± 1.69 μ g/dl and mean TSH level was 3.80 ± 1.21 IU/ml and hypothyroidism was present in 44 (38.3%). **Conclusion;** High Frequency of hypothyroidism was noted in children with celiac disease in our study. Hypothyroidism was significantly associated with age, ethnicity and prolonged disease duration. Clinicians treating children having celiac disease should monitor thyroid hormone levels so as to decrease disease morbidity which will save them future hardships and improve quality of life of such patients.

Keywords; Celiac disease, hypothyroidism, thyroid dysfunction.

INTRODUCTION;

Celiac disease (CD) is one of the most common chronic diseases in childhood, affecting approximately 0.5–3% of the population in the Western world.¹⁻² It is characterized by an autoimmune response triggered by gluten and possibly other environmental cofactors, leading to small-intestinal mucosal injury³. This in turn leads to malabsorption with a variable clinical expression ranging from no symptoms to severe malnutrition. The disease can have its onset at any age throughout life⁴.

CD is a well-established T-cell-mediated autoimmune enteropathy with a strong genetic component and variable clinical manifestations (ranging from asymptomatic to global malabsorption). Human leukocyte antigen (HLA) haplotypes DR3-DQ2.5, DR5-DQ7/DR7-DQ2.2, and DR4-DQ8 are the main genetic risk factors associated with CD and the absence of their respective alleles practically excluded the condition^{5,6}. Autoimmune conditions including thyroid diseases such as Hashimoto thyroiditis and Grave's disease are associated with celiac disease with a reported prevalence up to 10 times that in the general population.⁷

An association between CD and other autoimmune disorders-such as insulin-dependent diabetes, Addison's disease, systemic lupus erythematosus, rheumatoid arthritis, alopecia areata and autoimmune endocrine diseases-has been described. Of these, thyroid dysfunction is commonly seen in CD^{2,4}. Forchielli et al⁸ and Kowalska et al⁹ reported that incidences of hypothyroidism disease associated with CD in 37.6%, and 41.1%, respectively while another study by Ansaldi et al¹⁰ reported 8.1% hypothyroidism in children with CD. This study was planned to document frequency of hypothyroidism in children with celiac disease in our local population.

MATERIAL AND METHODS;

Children with celiac disease of either gender with their ages ranging from 2-12 years were taken in this study. Children with mental disorders, malignancies and with growth retardation, poor oral intake were excluded from our study. All the patients who meet inclusion as well as exclusion criteria of this study were registered from Department of Pediatrics, Nishtar Hospital, Multan. Children with celiac disease were enrolled and venous blood sample (3 ml) was drawn and sent to be Hospital pathology laboratory for serum TSH, T₃ and T₄ levels analysis. The findings were noted in the study proforma by researcher. All the data was entered and analyzed using SPSS-18.

RESULTS;

Our study comprised of a total of 115 study cases with celiac disease who met inclusion criteria of our study. Of these 115 study cases, 49 (42.6%) were male patients and 66 (57.4%) were female patients. Mean age of our study cases was 6.31 ± 2.05 years (with minimum age of our study cases was 4 years while maximum age was 11 years). Mean age of the male patients was 5.57 ± 2.01 years while that of female patients was 6.86 ± 1.92 years ($p=0.001$). Our study results have indicated that majority of our study cases i.e. 78 (67.7%) were aged up to 7 years. Of these 115 study cases, 59 (51.3%) belonged to rural areas while 56 (48.7%) from urban areas, 45 (39.1%) were from poor families while 70 (60.9%) were from middle income families. Of these 115 study cases, 31 (27 %) were from urdu speaking families, 38.3 % Punjabi, 30 (26.1%) Saraikis and 10 (8.7%) were Baloch. Of these 115 study cases, mothers were illiterate in 75 (65.2%) and literate in 40 (34.8%). Mean disease duration was 5.27 ± 2.11 months and 69 (60%) had disease duration up to 6 months and 46 (40%) had more than 6 months. Mean T₃ level was 86.43 ± 26.25 ng/dl, mean T₄ level was 5.02 ± 1.69 µg/dl and mean TSH level was 3.80 ± 1.21 IU/ml. Hypothyroidism was present in 44 (38.3%) of our study cases.

DISCUSSION;

An increased prevalence of thyroid dysfunction has been reported in patients with CD. In a study from Sweden where the prevalence of CD was 95.5 per 10,000, Midhagen et al found that thyrotoxicosis occurred in 5.0% and spontaneous hypothyroidism in 5.8% of the celiac patients. These thyroid disorders were sometimes diagnosed before, and sometimes after, the diagnosis of CD and instigation of the gluten-free diet. The duration of the gluten-free diet in relation to the diagnosis of thyroid disease was not stated. In a cohort of 70 celiac patients, Volta et al noted four with hypothyroidism and one with thyrotoxicosis¹¹.

Our study comprised of a total of 115 study cases with celiac disease who met inclusion criteria of our study. Of these 115 study cases, 49 (42.6%) were male patients and 66 (57.4%) were female patients. Babar et al¹² from Raheem Yar Khan also reported 60 % female gender predominance which is close to our study results. Alvi et al¹³ from Lahore also reported 1:1.2 male to female ratio in children with celiac disease which is in compliance with our study results. A study conducted in Sukkur by Jamro et al¹⁴ has also documented high female gender preponderance with 71 % which is in compliance with our study results. Soomro et al¹⁵ from Karachi also documented male to female ratio was 1:1.4 which is in compliance with our study results. Mean age of our study cases was 6.31 ± 2.05 years (with minimum age of our study cases was 4 years while maximum age was 11 years). Mean age of the male patients was 5.57 ± 2.01 years while that of female patients was 6.86 ± 1.92 years ($p=0.001$). Our study results have indicated that majority of our study cases i.e. 78 (67.7%) were aged up to 7 years. Babar et al¹² from Raheem Yar Khan also reported 6.35 ± 2.83 years mean age of the children with celiac disease which is close to our study results. Butt et al¹⁶ from Faisalabad reported 7.26 years mean age of the children with celiac disease which is close to our study results. Alvi et al¹³ from Lahore also reported 6.7 years mean age which is close to our study results. . A study conducted in Sukkur by Jamro et al¹⁴ has also documented similar findings. Hashmi et al¹⁷ from Lahore reported 6.67 ± 3.35 years mean age which is close to our study results.

Of these 115 study cases, 59 (51.3%) belonged to rural areas while 56 (48.7%) from urban areas, 45 (39.1%) were from poor families while 70 (60.9%) were from middle income families. Of these 115 study cases, 31 (27 %) were from urdu speaking families, 38.3 % Punjabi, 30 (26.1%) Saraikis and 10 (8.7%) were Baloch. Of these 115 study cases, mothers were illiterate in 75 (65.2%) and literate in 40 (34.8%). Mean disease duration was 5.27 ± 2.11 months and 69 (60%) had disease duration up to 6 months and 46 (40%) had more than 6 months.

Mean T_3 level was 86.43 ± 26.25 ng/dl, mean T_4 level was 5.02 ± 1.69 μ g/dl and mean TSH level was 3.80 ± 1.21 IU/ml. Hypothyroidism was present in 44 (38.3%) of our study cases. Forchielli et al⁸ reported 37.6 % hypothyroidism in children with celiac disease which is hypothyroidism disease in children with celiac disease was 41.1% which is close to our study results. Ansaldi et al¹⁰ reported 8.1% hypothyroidism in children with celiac disease which is quite lower than that being reported in our study.

CONCLUSION;

High Frequency of hypothyroidism was noted in children with celiac disease in our study. Hypothyroidism was significantly associated with age, ethnicity and prolonged disease duration. Clinicians treating children having celiac disease should monitor thyroid hormone levels so as to decrease disease morbidity which will save them future hardships and improve quality of life of such patients.

REFERENCES

1. Mustalahti K, Catassi C, Reunanen A, Fabiani E, Heier M, McMillan S, et al. The prevalence of celiac disease in Europe: results of a centralized, international mass screening project. *Annals Med*. 2010;42(8):587-95.
2. van der Pals M, Ivarsson A, Norström F, Högberg L, Svensson J, Carlsson A. Prevalence of Thyroid Autoimmunity in Children with Celiac Disease Compared to Healthy 12-Year Olds. *Autoimmune Dis*. 2014;2014: Article ID 417356. <http://dx.doi.org/10.1155/2014/417356>.
3. Butt T, Mumtaz A, Qasim A, Hameed N, Ibrahim M, Azhar K. Assessment of thyroid dysfunction in children with celiac disease. *Biomedica*. 2011;27:123-7.
4. Lionetti E, and Catassi C. New clues in celiac disease epidemiology, pathogenesis, clinical manifestations, and treatment. *Int Rev Immunol*. 2011;30(4):219-31.
5. Kaukinen K, Lindfors K, Collin P, Koskinen O, Mäki M. Coeliac disease--a diagnostic and therapeutic challenge. *Clin Chem Lab Med*. 2010;48(9):1205-16.
6. Ontiveros N, Hardy MY, Cabrera-Chavez F. Assessing of Celiac Disease and Nonceliac Gluten Sensitivity. *Gastroenterol Res Pract*. 2015;2015:723954.doi: 10.1155/2015/723954
7. Norstrom F, Sandstrom O, Lindholm L, Ivarsson A. A gluten-free diet effectively reduces symptoms and health care consumption in a Swedish celiac disease population. *BMC Gastroenterol*. 2012;12:125.

8. Forchielli M, Collina A, Zannarini L. Celiac disease and thyroid abnormalities: another possible association. *J Pediatr Gastroenterol Nutr.* 2000;31:S63.
9. Kowalska E, Wasowska-Krolikowska K Toporowska-Kowalska E. Estimation of antithyroid antibodies occurrence in children with coeliac disease. *Med Sci Monit.* 2000;6:719-21.
10. Ansaldi N, Palmas T, Corrias A, Barbato M, Altiglia MR, Campanozzi A, et al. Autoimmune thyroid disease and celiac disease in children. *J Pediatr Gastroenterol Nutr.* 2003;37:63-6.
11. Ch'ng CL¹, Jones MK, Kingham JG. Celiac disease and autoimmune thyroid disease. *Clin Med Res.* 2007 Oct;5(3):184-92.
12. Babar MI, Ahmad I, Rao MS, Iqbal R, Asghar S, Saleem M. Celiac disease and celiac crisis in children. *J Coll Physicians Surg Pak.* 2011;21(8):487-90.
13. Alvi MY, Abbas M, Ahmed M, Farooq A, Kazi MY. Clinical presentation of celiac disease in children. *Pak J Med Health Sci.* 2010;4(4):552-4.
14. Jamro BU, Chana SM, Sankarlal SL, Jamro S. An experience of celiac disease in children at tertiary care hospital Sukkur. *Rawal Med J.* 2012;37(3):235-8.
15. Soomro S, Baig S, Sharafat S, Mirza T. Prevalence of Tissue Transglutamase Antibodies in cases of Celiac Disease. *J Dow Uni Health Sci.* 2015;9(1):9-13.
16. Butt MA, Hameed S, Bashir T, Ashraf A, Ansari Z. Clinical presentations of Coeliac disease: A prospective study. *Pak J Pathol.* 1998;9(3):115-20.
17. Hashmi MA, Hussain T, Masood N, Asghar RM. Diarrheal Versus Non-diarrheal Presentations of Paediatric Celiac Disease. *J Coll Physicians Surg Pak.* 2016;26(8):662-6.