

hepcidin levels in BTM [7,8]. In contrary, higher hepcidin levels in BTM group was observed in few other studies [3-5,9]. Probably several factors influence the production of hepcidin such as time of transfusion, iron chelation, and amount of iron overload [5]. Before transfusion, the active erythropoietic activity suppresses hepcidin. After transfusion, ineffective erythropoiesis partly eases, resulting in increase in hepcidin levels [6,10]. Hepcidin level estimation has been shown to be useful to identify the patients at higher risk of iron toxicity [6,7] and the degree of iron overload [3,4].

The current study showed no significant correlation between hepcidin and ferritin levels in BTM children which is similar to the previous studies [1,7,9]. Hepcidin/ferritin ratio can be used as marker of iron overload and it is an index of appropriateness of hepcidin expression relative to the degree of iron loading and should be approximately one in controls [1,10]. In our study hepcidin/ferritin ratio was significantly decreased in BTM group compared to controls. Similar observations was found in other studies also [1,9].

To conclude, there is no significant correlation between hepcidin and ferritin levels in thalassemia major. Hepcidin/ferritin ratio in thalassemia major is very low, indicating hepcidin levels are not increased proportionately to the degree of iron load.

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#### REFERENCES

1. Chauhan R, Sharma S, Chandra J. What regulates hepcidin in poly-transfused b-Thalassemia Major: Erythroid drive or store drive? *Indian J Pathol Microbiol.* 2014; 57:39-42.
2. Tanno T, Bhanu NV, Oneal PA, Goh SH, Staker P, Lee YT, *et al.* High levels of GDF15 in thalassemia suppress expression of the iron regulatory protein hepcidin. *Nat Med.* 2007;13:1096-101.
3. Assem H, Sharaki O, El-Shennawi M, Gomaa H M. 772 Serum hepcidin in children with beta-thalassemia. *Arch Dis Child.* 2012;97:A222.
4. Kaddah AM, Abdel-Salam A, Farhan MS, Reham R. Serum hepcidin as a diagnostic marker of severe iron overload in beta-thalassemia major. *Indian J Pediatr.* 2017;84:745.
5. Rashidy FH, Abo Elghar HM, Kamal Eldin SM, Taha MZ. Hepcidin and iron regulation in chronic hemolytic anemia. *Menoufia Med J.* 2015;28:463-70.
6. Nemeth E. Hepcidin and  $\alpha$ -thalassemia major. *Blood.* 2013;122:3-4.
7. Jawad M1, Aftab I, Saeed MT, Mumtaz G, Iram S, Mohsin S. Hepcidin levels in multi transfused  $\alpha$  thalassemia major patients. *J Rawalpindi Med Col.* 2016;20:206-8.
8. El Beshlawy A, Alaraby I, Abdel Kader MS, Ahmed DH, Abdelrahman HE. Study of serum hepcidin in hereditary hemolytic anemias. *Hemoglobin.* 2012;36:555-70.
9. Haghpanah S, Esmailzadeh M, Honar N, Hassani F, Dehbozorgian J, Rezaei N, *et al.* Relationship between serum hepcidin and ferritin levels in patients with thalassemia major and intermedia in Southern Iran. *Iran Red Crescent Med J.* 2015;17:e28343.
10. Pasricha SR, Frazer DM, Bowden DK, Anderson GJ. Transfusion suppresses erythropoiesis and increases hepcidin in adult patients with  $\alpha$ -thalassemia major: A longitudinal study. *Blood.* 2013;122:124-32.

## Autism Spectrum Disorders and Celiac Disease: Is there an Association?

We included 150 children aged 2-12 years with Autism Spectrum Disorders and normal serum total IgA levels, and screened them for celiac disease using anti-tissue transglutaminase IgA levels. All the children were screen negative, suggesting lack of positive association between Autism Spectrum Disorders and Celiac disease.

**Keywords:** Etiology, Gluten-free diet, Screening, TTG.

**E**nvironmental factors such as toxin exposure, intrauterine exposure to certain teratogenic drugs, perinatal factors and parental autoimmunity are being proposed as possible contributing factors in the etiology of autism spectrum disorders (ASD) [1,2]. In cognisance with reports of increased gut permeability and high rates of gastrointestinal symptoms noted in children with ASD, celiac disease has also been proposed as a possible etiological factor [3]. Despite inconclusive evidence, many children with ASD are being advised Gluten-free diet. This study was undertaken to elucidate any association between ASD and celiac disease.

This cross-sectional study was conducted at a child development center in Northern India in the year 2016-17. Children aged 2-12 years diagnosed with ASD as per DSM-5 criteria were included. Severity of symptoms of ASD was graded as per Childhood Autism Rating Scale [4], and developmental level was graded as per Developmental Profile-3 Manual [5]. Children on gluten-free diet for <1 month or those diagnosed with autoimmune disorders were excluded. After informed consent, history of gastrointestinal symptoms was elicited and pertinent psychological assessments were done. Blood sample (2 mL) was drawn from all participants for estimation of anti-tissue transglutaminase IgA (Anti-TTG-IgA) levels for screening for celiac disease, and serum total IgA levels to exclude IgA deficiency. Anti TTG-IgA was measured using ELISA (Autostat II, Hycor Biomedical, USA). The Upper limit of Normal (ULN) was 7 IU/mL. Serum total IgA was measured using Nephstar Immunoglobulin A (IgA) kit in which tat principle-Immunonephelometry was applied. Children with low total IgA levels were excluded. Children with raised level of anti TTG-IgA were planned to be tested for HLA-DQ2/DQ8 by PCR and subjected to endoscopic duodenal biopsy. Data were analyzed using SPSS version 23.

A convenience sample of 155 children with ASD was screened. Children with low serum total IgA levels were excluded. The socio-demographic and psychological profile of the study population is shown in **Table I**. Gastrointestinal symptoms were present in 51 (34%) cases. Recurrent abdominal pain was the most frequent complaint (16.6%), followed by constipation (12.6%), chronic/recurrent diarrhoea (8%), abdominal distension (2%), weight loss (1.3%), and anorexia (1.3%). All the children had anti-TTG levels below the ULN; hence, all were screen negative and no further diagnostic testing in form of duodenal biopsy or HLA evaluation was required.

Two studies from Italy have reported prevalence of celiac disease of around 3% in children with ASD as compared to approximately 1% in the general population [6,7]. Majority of other studies have refuted such association. The limitation of present study was inability to perform anti-gliadin antibodies [8,9]. Some researchers consider ASD to be a manifestation of Non-Celiac Gluten Sensitivity (NCGS) [10], which is a poorly defined entity in which neuro-psychiatric symptoms are triggered by gluten ingestion, in the absence of celiac-specific antibodies or classical villous atrophy on duodenal biopsy, with variable presence of first generation IgA Anti-gliadin antibodies (AGA).

To conclude, there does not seem to be any association between ASD and celiac disease, and there is

**TABLE I** SOCIO-DEMOGRAPHIC AND PSYCHOLOGICAL PROFILE OF THE STUDY CHILDREN (N=150)

Characteristics	n (%), N=150
Age (mo)*	65 (25)
Gender; n (%)	117 (78)
<i>Socioeconomic status</i>	
Upper	25 (16.7)
Middle	95 (63.3)
Lower	30 (20.0)
<i>Childhood Autism rating scale severity level</i>	
Minimal or no symptoms (score 15-29)	3 (2)
Mild to moderate autism (30-36)	112 (74.6)
Severe autism(>37)	35 (23.3)
<i>Developmental level<sup>#</sup></i>	
Average (85-115)	8 (5.3)
Below average (70-84)	15 (10.0)
Delayed (<70)	127 (84.6)

<sup>#</sup>Based on Developmental Profile-3 [5]; Values in n (%) except \*mean (SD).

no rationale for routine screening for celiac disease in ASD. Further studies are warranted to evaluate association of NCGS with ASD and any role of gluten-free diet in such patients.

*Contributors:* MJ: conceptualized the study. MJ,AK,SK: were involved in designing the study; AK: collected the data and SK performed the biochemical investigations. AK, RJ: reviewed the literature, analyzed the data and drafted the manuscript. MJ, SK: revised the manuscript for important intellectual content. The final manuscript was approved by all authors. All authors will be accountable for all aspects of the work.

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#### REFERENCES

1. Geschwind DH. Advances in autism. *Annu Rev Med.* 2009;60:367-80.
2. Dalwai S, Ahmed S, Udani V, Mundkur N, Kamath SS, Nair MKC. Consensus statement of the Indian Academy of Pediatrics on evaluation and management of autism spectrum disorders. *Indian Pediatr.* 2017;54:385-93.
3. Ludvigsson JF, Leffler DA, Bai JC, Biagi F, Fasano A, Green PHR, *et al.* The Oslo definitions for coeliac disease and related terms. *Gut.* 2013;62:43-52.
4. Schopler E, Van Bourgondien ME, Wellman GJ, Love SR. *Childhood Autism Rating Scale (2nd ed.)*. Los Angeles, CA: Western Psychological Services; 2010.

5. Alpern GD. Developmental Profile 3, DP-3: Manual. Los Angeles: Western Psychological Services; 2007.
6. Barcia G, Posar A, Santucci M, Parmeggiani A. Autism and coeliac disease. *J Autism Dev Disord.* 2008;38:407-8.
7. Calderoni S, Santocchi E, Del Bianco T, Brunori E, Caponi L, Paolicchi A, *et al.* Serological screening for celiac disease in 382 pre-schoolers with autism spectrum disorder. *Ital J Pediatr.* 2016;42:98
8. Batista IC, Gandolfi L, Nobrega YKM, Almeida RC, Almeida LM, Campos Junior D, *et al.* Autism spectrum disorder and celiac disease: No evidence for a link. *Arq Neuropsiquiatr.* 2012;70:28-33.
9. Lau NM, Green PHR, Taylor AK, Hellberg D, Ajamian M, Tan CZ, *et al.* Markers of celiac disease and gluten sensitivity in children with autism. *PLoS One.* 2013;8:e66155.
10. Ludvigsson JF, Reichenberg A, Hultman CM, Murray JA. A nationwide study of the association between celiac disease and the risk of autistic spectrum disorders. *JAMA Psychiatry.* 2013;70:1224-30.
11. Catassi C, Elli L, Bonaz B, Bouma G, Carroccio A, Castillejo G, *et al.* Diagnosis of non-celiac gluten sensitivity (NCGS): The Salerno Experts' Criteria. *Nutrients.* 2015;7:4966-77.

## Continuous Temperature Monitoring Using Bluetooth-enabled Thermometer in Neonates

We aimed to compare continuous temperature-monitoring using Bluetooth-enabled thermometer (BET) and intermittent monitoring by digital thermometer (DT) in neonates. Continuous monitoring using BET identified 377 episodes of hypo/hyperthermia in 90 baby-days; 316 (83.8%) episodes were confirmed by DT and 61 (16.2%) were false alarms. Five episodes were missed by BET. The agreement between digital thermometer and BET was good. Continuous temperature monitoring helps in early identification of hypo/hyperthermia in neonates.

**Keywords:** *Diagnosis, Hypothermia, Thermometry.*  
**Trial Registration:** CTRI/2016/04/006817

The incidence of neonatal hypothermia continues to be high; 32-88% in hospital-based studies and 11-92% in community-based studies [1]. Temperature monitoring outside the intensive care setting is either not done or done at infrequent intervals. Continuous temperature monitoring using a Bluetooth-enabled thermometer (BET) may aid in early detection of hypo- or hyper-thermia and timely intervention in such infants. We aimed to compare continuous temperature monitoring using BET to intermittent monitoring by digital thermometer (DT) in neonates.

The study was done in the postnatal ward in a tertiary-care hospital in India during June-August 2017. Institutional Ethics Committee approval was obtained and informed written consent was taken from one of the parents.

We used 98.6 Fever Watch (Helyxon Health Care Private Limited) for continuous monitoring. It consists of

an insulated thermistor with Bluetooth connectivity [2]. The thermistor was connected to an iPod (Apple Inc) kept within 30m *via* Bluetooth, which in turn was connected to physician's smartphone *via* Internet.

BET thermistor was attached to baby's skin in right hypochondrium using a transparent film dressing. BET measured baby's temperature every minute, which was displayed in the iPod. When the temperature was abnormal (<36.5 or >37.5°C) the iPod gave an alarm. The nurse would check baby's temperature using DT and take appropriate measures. If hypo/hyper-thermia persisted for 15 minutes, an alert was escalated in the physician's mobile, who would examine the baby and plan further management.

Intermittent monitoring of axillary temperature using DT was done once in 4 hours. Environmental temperature was in the range of 29-38°C during the study period. Kangaroo mother care was given for a minimum of 4 hours per day in low birth weight (LBW) infants during the study. Babies were clothed and wrapped in cotton or woolen clothes, as appropriate. A difference of <0.5°C between the DT and BET measurement was set *a priori* as the acceptable margin.

We recruited 30 term infants with mean (SD) birthweight of 2838 (418) grams and median (IQR) postnatal age of 3 (0.5, 4) days; 15 late preterm infants with birthweight of 2087 (464) grams and postnatal age of 4 (4, 5) days; and 15 preterm infants with mean (SD) gestational age of 31+4 (1+6) weeks, birthweight of 1685 (511) grams and postnatal age of 15 (9, 22) days. Duration of recording was 24 hours for term and 48 hours for preterm infants.

Continuous temperature monitoring using BET identified 377 episodes of hypo/hyperthermia in 90 baby-days, of which 316 (83.8%) episodes were confirmed by DT and 61 (16.2%) did not match with DT measurement and