

Association of Serum Electrolytes, Serum 25-Hydroxycholecalciferol and Serum Thyroid Stimulating Hormone (TSH) in Irritable Bowel Syndrome (IBS)

Nisha Jha¹, Rekha Kumari², Neha Bharti³, Rajeev Kumar⁴, Praveen Kumar⁵, Kumar Pranay⁶

¹Assistant Professor, Department of Biochemistry, NSMCH, Bihta, Patna.

²Professor and Head, Department of Biochemistry, IGIMS, Patna.

³Assistant Professor, Department of Biochemistry, ESIC Medical College and Hospital, Bihta, Patna.

⁴Senior Resident, Department of Biochemistry, IGIMS, Patna.

⁵Additional Professor, Department of General Medicine, IGIMS, Patna.

⁶Scientist – I, Department of Biochemistry, IGIMS, Patna.

Received: 27-09-2023 / Revised: 23-10-2023 / Accepted: 27-11-2023

Corresponding Author: Dr. Rekha Kumari

Conflict of interest: Nil

Abstract:

Introduction: Irritable bowel syndrome (IBS) is one of the most prevalent, that affects up to 1 in 5 people over their lifetime. The Rome III committee defines IBS as a chronic functional disorder characterized by recurrent abdominal pain or discomfort associated with disordered defecation. Approximately 15 to 25% of the world population suffers from irritable bowel syndrome (IBS).1.

Aim: To associate serum electrolytes, serum 25-hydroxy cholecalciferol and Thyroid Stimulating Hormones (TSH) in Irritable Bowel Syndrome (IBS).

Objectives: To measure the serum electrolyte levels in patients with IBS and to compare the same with the serum electrolyte levels of normal healthy adults.

Materials and Methods: A cross sectional study was conducted on 120 individuals 30-60 years age group, divided into 2 groups of 60 IBS cases and 60 apparently healthy control. Under aseptic precautions, 4 ml venous Blood was withdrawn from study participants, who visited to the department of general medicine and gastroenterology with symptoms of IBS on OPD basis and confirmed diagnosis of Irritable Bowel Syndrome (IBS) based on Rome's criteria of IBS for cases and 60 samples collected from apparently healthy controls. S. potassium was estimated by fully automated analyser on DxC 700 AU. Serum TSH and serum 25-hydroxy cholecalciferol were estimated on abott architect i2000 SR that works on the principle of CMIA.

Statistical analysis: All data was evaluated in the form of Mean \pm SD and comparison was done based on pearson correlation coefficient. Then p value was calculated $p < 0.0001$ was considered significant.

Results: Serum chloride was considered to have significant p value when compared among cases and control. Serum TSH, serum sodium, serum potassium and serum 25-hydroxycholecalciferol gave non-significant results in cases of IBS when compared with controls.

Discussion: IBS lacks acceptable bio-markers, and its diagnosis largely depends on the exclusion of underlying organic disease. Hence the diagnosis and management of this disorder can be challenging. maintaining normal serum electrolyte balance is essential for the efficient functioning of living cells. A follow up study would best suggest the efficient role of Vitamin D in IBS.

Conclusion: The present study also tried to provide an insight into the possible changes that can be incorporated in the diet or serum electrolyte supplementation in IBS cases. Since the results were non-specific and statistically nonsignificant, further clinical studies are recommended with larger sample sizes for correlation of dyselectrolytemia.

Keywords : IBS (Irritable bowel syndrome), 25-hydroxy cholecalciferol, TSH (Thyroid Stimulating Hormone).

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Irritable bowel syndrome (IBS) is one of the most prevalent, multifactorial, heterogeneous and complex disorders that affects up to 1 in 5 people

over their lifetime. It has a significant medical and socioeconomic impact that reduces patients' quality of life and it also imposes a significant economic

burden to the healthcare system[1]. The Rome III committee defines IBS as a chronic functional disorder characterized by recurrent abdominal pain or discomfort associated with disordered defecation [either constipation (IBS-C), diarrhoea (IBS-D), or mixed/alternating symptoms of constipation and diarrhea (IBS-M), unidentified (IBS-U)].[2]

Approximately 15 to 25% of the world population suffers from irritable bowel syndrome (IBS) [3]. Patients with hyperthyroidism can experience frequent bowel movements, diarrhea, even malabsorption with steatorrhea[4,5,6]. Chronic dyspeptic symptoms such as epigastric pain and fullness, as well as eructation, nausea and vomiting are also frequently seen in these patients. Less commonly, hyperthyroidism has been reported to cause persistent and intractable vomiting.[7] Individuals diagnosed with IBS have “low-grade intestinal inflammation”, and increased intestinal permeability with changes in the intestinal microbiota.[8] This can create an electrolyte imbalance. It is a well-known fact that maintaining normal serum electrolyte balance is essential for the efficient functioning of cells and organs in the body.

Available studies regarding irritable bowel syndrome suggest controversial reports in the serum electrolyte levels. Some studies have shown that statistically significant improvement in abdominal discomfort or pain is observed when clinical trials with electrolyte supplementation were given.[9] There is a paucity of literature directly linking the levels of the serum electrolytes and IBS, especially in south Indian studies. In addition, studies have suggested that the impact of IBS on health-related quality of life is equally as significant as in congestive heart failure and dialysis-dependent renal failure. Moreover, the association of the electrolyte levels with respect to the severity of the disease is not well established. Hence, the present study was taken up. There has not yet been found any effective cure for IBS; however, some remedies have shown promising effects in the management of it.[10,11] Recently, an analysis of social media (blogs/forums) reported that from 37 patients with IBS, 70% described improvements in their symptoms with Vitamin D supplementation and the majority of these individuals reported being Vitamin D deficient before supplementation.[12] This study suggested a role for Vitamin D in the management of IBS, which was supported by another recent study showing the high prevalence of Vitamin D deficiency in patients with IBS.[13]

Aim: To associate level of serum electrolytes, serum 25-hydroxy cholecalciferol and serum Thyroid Stimulating Hormone (TSH) in patients with Irritable Bowel Syndrome (IBS).

Objectives: To measure the serum electrolyte levels in patients with IBS and to compare it with serum electrolyte levels of apparently healthy individuals.

Materials and Methods: A cross sectional study was conducted on 120 individuals, divided into 2 groups of 60 IBS cases and 60 apparently healthy control. Under aseptic precautions, 4 ml venous Blood was withdrawn from study participants, who visited to the department of General Medicine and Gastroenterology with symptoms of IBS on OPD basis and confirmed diagnosis of Inflammatory Bowel Syndrome (IBS) based on Rome’s criteria of IBS for cases and 60 samples collected from apparently healthy controls. Samples were allowed to stand for 15-20 minutes and centrifuged at 3500 rpm for 15- 20 min. Quality checks were performed from quality control materials on daily basis before processing samples on fully Automated analysers. S. electrolytes were estimated by fully automated analyser on DxC 700 AU that works on the principle of Ion Selective Electrode (ISE) for electrolytes. Serum TSH and serum 25-hydroxy cholecalciferol were estimated on abott architect i2000 SR that works on the principle of CMIA (chemiluminescent microparticle immunoassay). Ethical clearance was taken up as per the guidelines of the research unit of the Institute.

Inclusion criteria:

Cases:1. Patients of age group 30-60 years. 2. Patients with symptoms suggestive of IBS presented to Medicine OPD. 3. Patients with suspected IBS fulfilled the Rome III criteria for IBS based on their responses to a questionnaire administered in the OPD. 4. All participants were examined for serum 25-hydroxy cholecalciferol, serum TSH, serum electrolytes.

Control: Apparently healthy controls coming to General Medicine OPD for routine health check-up and examinations.

Exclusion criteria: 1. Patients with known and established causes of diarrhea other than IBS, Age <30 years and > 60 years, Patients on medications affecting serum electrolytes level, Patients who had diabetes mellitus, hypertension, a salt-restricted diet, steroid therapy, bronchial asthma, previous GI disorders, other systemic disorders.

Procedure: Details were entered in a predesigned proforma that includes personal bio-data, presenting complaint, predominant symptoms, duration of illness and associated history relevant to exclusion criteria. Subjects were requested to fill up a detailed questionnaire (enclosed) related to bowel disorder.

Statistical analysis: Statistical analysis was done using Excel system version 2007 and includes descriptive statistics (mean and standard deviation) and inferential statistics (Chi-square test) to test the significance of difference. When P value is less than

0.05, the difference is considered significant, and the difference is considered highly significant when P-value was less than 0.001.

Results:

Table 1;

Sl. No.	Cases (n=60)	Control (n=60)	p value
1. S. Na	138.21 ± 3.14	139.31 ± 3.77	0.15
2. S. K	4.18 ± 0.23	4.25 ± 0.35	0.20
3. S. Cl	103.40 ± 5.21	101.09 ± 7.89	0.01*
4.S. Vitamin D	1.09±1.41	1.27±2.64	0.76
5. S.TSH	2.85±2.18	2.92±2.16	0.82

Discussion

IBS is a chronic functional symptom-based disorder and is characterized by multifactorial pathophysiological mechanisms including low-grade intestinal inflammation [14], autonomic dysfunction, hypersensitivity to diet and psychological distress. IBS lacks acceptable biomarkers, and its diagnosis largely depends on the exclusion of underlying organic disease. Hence the diagnosis and management of this disorder can be challenging. Maintaining normal serum electrolyte balance is essential for the efficient functioning of living cells. One of the widely accepted views is that existing low-grade intestinal inflammation in IBS can cause increased intestinal permeability, which might possibly create an electrolyte imbalance. Available studies regarding irritable bowel syndrome suggest controversial reports in the serum electrolyte levels. Some studies have shown that statistically significant improvement in abdominal discomfort or pain is observed when clinical trials with electrolyte supplementation were given [15]. This study aimed to estimate the serum electrolyte values in IBS cases and the results suggested a reduction in serum sodium and potassium levels in these cases with non-significant p value, whereas Chapman et al, in their study when compared cases with normal controls they also found the same results. Though there was a statistically significant increase in chloride levels in IBS cases. The possible explanation for this increase could be due to defective chloride transporters on the intestinal mucosa. The values obtained are in accordance with the study done on IBS diarrhoea patients by Vernia et al., which also opines, serum electrolytes and systemic acid-base balance was within the normal range. These data are in agreement with the lack of systemic changes observed in IBS patients even with profuse or longstanding diarrhoea [16]. Although diarrhoea is the predominant bowel dysfunction in as many as one-third of patients with IBS, it is unclear whether there is a specific disorder of intestinal fluid or electrolyte secretion in this syndrome, as there is no published evidence till date (17). Diarrhoea in IBS is generally considered secondary to accelerated colonic transit and reduced volume of the proximal colon [18]. The mucoid

consistency and the small volume of the stools do not significantly affect the levels of serum electrolytes. This might be the probable reason for the lack of significant changes in the serum electrolyte levels in this study.

According to the results of the study conducted by Karas M et al, altered thyroid function was found in patients with suspected IBS. These findings were in disagreement with the findings of Hamm et.al [19,20] who failed to modify the criteria for diagnosis of IBS. The mechanism behind our results was not clear; however, direct hormonal effects or stimulatory actions in the central nervous system have been suggested. Treatment of the thyrotoxicosis with beta blocking agents and anti-thyroid drugs greatly improves these symptoms [21]. The mechanism by which thyroid hormones disturbances affects GIT system is not explained clearly. changes are expected at molecular level with hormone receptors alteration, ANS (autonomic nervous system) dysfunction and myocardial enteric activity as well as changes on a tissue level in the form of myopathy[22]. Hormonal effects seen on gastro-intestinal tract is thought to be the direct effect of thyroid hormones or synergistic effect of catecholamine. Tenore et al, conducted a research work on hypo and hyperthyroid rats and studied the effect of thyroxine (T4) on Intestinal chloride/bicarbonate exchange and found the flux of chloride that leads to mucosal effects of chloride and resultant diarrhoea. these findings were not seen in rat when when thyroxine (T4) was given ex-vivo to the rat Ileum [23]. Examination of Thyroid Function Tests in patients with an established history of IBS revealed an altered function of thyroid comparable to that in the general population; this might be attributed to high Incidence of thyroid problems in older adults.

Although the exact pathophysiology of IBS has not yet been elucidated, it has been shown that alterations in the gut microbiome, intestinal permeability, gut immune function, visceral sensation, brain-gut interactions, and psychosocial status are involved in the development of this syndrome.[24] Furthermore, it has been shown previously that Vitamin D can modulate all of these

probable mechanisms involved in IBS pathogenesis. Bashir et al.[25] have shown that 8-week Vitamin D supplementation changes the human gastrointestinal microflora with a reduction in opportunistic pathogens and an increase in bacterial richness. effects of Vitamin D on the improvement of intestinal barrier function have been demonstrated in in vitro, [26,27] experimental,[28] and human studies.[29] Moreover, it has been shown that Vitamin D regulates immune cell trafficking and differentiation, gut barrier function, and antimicrobial peptide synthesis, all of which, has been shown that play a role in the development of IBS. Vitamin D regulates the innate immune response to the microbiota. Vitamin D is a critical regulator of T-cell function, and the expression of several pattern recognition receptors involved in intestinal inflammation is regulated by Vitamin D.[30] Our results have shown that 6 weeks supplementation with Vitamin D improves the symptoms and QOL in patients with IBS. It seems that Vitamin D supplementation improves the IBS characteristics through improving the factors involved in the development of IBS. Therefore a follow up study would best suggest the efficient role of Vitamin D in IBS [31].

Conclusion:

The prevalence of thyroid dysfunction in IBS patients is high. Therefore, the routine thyroid function tests in the diagnostic evaluation of established IBS patients should be recommended. This study indicates that Vitamin D therapy has some beneficial effects in the management of IBS in women; however, the long-term effects remained to be elucidated. Our study implies that serum electrolyte levels are not greatly altered in IBS cases probably due to the rapid transit in colon, mucoidal consistency and small volume of stools. The present study also tried to provide an insight into the possible changes that can be incorporated in the diet or serum electrolyte supplementation in IBS cases. Since the results were non-specific and statistically nonsignificant, further clinical studies are recommended with larger sample sizes for correlation of dyselectrolytemia with severity for obtaining conclusive evidence of the role of electrolyte supplements in the alleviation of both physical symptoms and psychological distress associated with this poorly understood disease.

References:

1. Lacy BE, Rosemore J, Robertson D, et al. Physicians' attitudes and practices in the evaluation and treatment of irritable bowel syndrome. *Scand J Gastroenterol* 2006; 41:892-902.
2. Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. *Gastroenterology*. 2006; 130:1480-1491

3. Thompson WG: A world view of IBS. In: *Irritable Bowel Syndrome: Diagnosis and Treatment*. 1st edition. Camilleri M and Spiller R (eds). Saunders, New York, NY, pp17-26, 2002.
4. Tinker MB. Discussion of paper by Verbrycke JR. Masked gastrointestinal hyperthyroidism. *JAMA* 1931; 97: 515-516.
5. Karas M, Wienbeck M, Grussendorf M, Erckenbrecht JF, Strohmeier G. Intestinal motor activity in experimental hyperthyroidism in conscious dogs. *Gastroenterology* 1989; 97: 911-919.
7. Hoogendoorn EH, Cools BM. Hyperthyroidism as a cause of persistent vomiting. *Neth J Med* 2004; 62: 293-296.
8. Bassotti G, Pagliacci MC, Nicoletti I, Pelli MA, Morelli A. Intestinal pseudoobstruction secondary to hypothyroidism. Importance of small bowel manometry. *J Clin Gastroenterol*. 1992; 14: 56-58.
9. Ortiz LM, Saz-Peiró P, Sebastián-Domingo JJ. Irritable bowel syndrome immune hypothesis. Part one: the role of lymphocytes and mast cells. *Rev Esp Enferm Dig* 2010;102:637-647.
10. Chapman RW, Stanghellini V, Geraint M, et al. Randomized clinical trial: macrogol/PEG 3350 plus electrolytes for treatment of patients with constipation associated with irritable bowel syndrome. *Am J Gastroenterol* 2013; 108:1508-1515.
11. Chey WD, Kurlander J, Eswaran S. Irritable bowel syndrome: A clinical review. *JAMA* 2015; 313:949-58.
12. Ford AC, Talley NJ. Irritable bowel syndrome. *BMJ (Clinical research ed)* 2012;345:e5836.
13. Sprake EF, Grant VA, Corfe BM. Vitamin D3 as a novel treatment for irritable bowel syndrome: Single case leads to critical analysis of patient-centred data. *BMJ Case Rep* 2012;2012.
14. Khayyat Y, Attar S. Vitamin D deficiency in patients with irritable bowel syndrome: Does it exist? *Oman Med J* 2015;30:115-8.
15. Chapman RW, Stanghellini V, Geraint M, et al. Randomized clinical trial: macrogol/PEG 3350 plus electrolytes for treatment of patients with constipation associated with irritable bowel syndrome. *Am J Gastroenterol* 2013;108:1508-1515.
16. Swathi Kamal, Shubha Jayaram, Sreenivas N, Dharmendra BL, Sudha B Sreenivas. Estimation of serum electrolytes in cases of irritable bowel syndrome and Healthy Adults: A comparative study. *Indian Journal of Medical Biochemistry*, Volume 23 Issue 1 (January-April 2019).
17. Vernia P, Latella G, Magliocca FM, et al. Seeking clues for a positive diagnosis of the irritable bowel syndrome. 1987;17(3):189-193.

18. Field M. Intestinal ion transport and the pathophysiology of diarrhea. *J Clin Invest* 2003;111:931-943.
19. Michael C. Intestinal Secretory Mechanisms in Irritable Bowel Syndrome-Diarrhea. *Clin Gastroenterol Hepatol* 2015;13(6):1051-1057.
20. Hamm LR, Sorrells SC, Harding JP, Northcutt AR, Heath AT, Kapke GF, Hunt CM, Mangel AW. Additional investigations fail to alter the diagnosis of irritable bowel syndrome in subjects fulfilling the Rome criteria. *Am J Gastroenterol.* 1999 May; 94(5):1279-82.
21. Hoogendoorn EH, Cools BM. Hyperthyroidism as a cause of persistent vomiting. *Neth J Med* 2004; 62: 293-296.
22. Karaus M, Wienbeck M, Grussendorf M, Erckenbrecht JF, Strohmeier G. Intestinal motor activity in experimental hyperthyroidism in conscious dogs. *Gastroenterology* 1989; 97: 911-919.
24. 22. Tenore A, Fasano A, Gasparini N, Sandomenico ML, Ferrara A, Di Carlo A, Guandalini S. Thyroxine effect on intestinal Cl⁻/HCO₃⁻ exchange in hypo- and hyperthyroid rats. *J Endocrinol* 1996; 151: 431-437.
25. 23. Thomas FB, Caldwell JH, Greenberger NJ. Steatorrhea in thyrotoxicosis. Relation to hypermotility and excessive dietary fat. *Ann Intern Med* 1973; 78: 669-675.
26. Cashman MD, Martin DK, Dhillon S, Puli SR. Irritable bowel syndrome: A Clinical review. *Curr Rheumatol Rev* 2016;12:13-26.
27. 25. Bashir M, Prietl B, Tauschmann M, Mautner SI, Kump PK, Treiber G, *et al.* Effects of high doses of vitamin D₃ on mucosa-associated gut microbiome vary between regions of the human gastrointestinal tract. *Eur J Nutr* 2016;55:1479-89.
28. 26. Chirayath MV, Gajdzik L, Hulla W, Graf J, Cross HS, Peterlik M, *et al.* Vitamin D increases tight-junction conductance and paracellular Ca²⁺-transport in caco-2 cell cultures. *Am J Physiol* 1998;274:G389-96.
29. 27. Kong J, Zhang Z, Musch MW, Ning G, Sun J, Hart J, *et al.* Novel role of the vitamin D receptor in maintaining the integrity of the intestinal mucosal barrier. *Am J Physiol Gastrointest Liver Physiol* 2008;294:G208-16.
30. 28. Zhu T, Liu TJ, Shi YY, Zhao Q. Vitamin D/VDR signaling pathway ameliorates 2,4,6-trinitrobenzene sulfonic acid-induced colitis by inhibiting intestinal epithelial apoptosis. *Int J Mol Med* 2015; 35:1213-8.
31. Raftery T, Martineau AR, Greiller CL, Ghosh S, McNamara D, Bennett K, *et al.* Effects of vitamin D supplementation on intestinal permeability, cathelicidin and disease markers in crohn's disease: Results from a randomised double-blind placebo-controlled study. *United European Gastroenterol J* 2015; 3:294-302
32. Meeker S, Seamons A, Maggio-Price L, Paik J. Protective links between vitamin D, inflammatory bowel disease and colon cancer. *World J Gastroenterol* 2016; 22:933-48.
33. Jalili, M., Vahedi, H., Poustchi, H., & Hekmatdoost, A. Effects of Vitamin D Supplementation in Patients with Irritable Bowel Syndrome: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial. *International journal of preventive medicine*, 2019;10: 16.