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Original Article

Cross-Sectional Comparative study to find out the efficacy of Probiotic in case of children of Acute watery diarrhea(AWD) .

*Ferdoush N[1], Jahan R[2], Islam A[3], Routh T[4], Rashel ATM[5], Ahmed E[6], Tanni TA[7]

Abstract:

Objectives: Diarrhea is a diseases with high fatality rate and having a significant impact on the health and well being of children. In addition to ORS, effectiveness of zinc is already established. Use of probiotic in AWD is a new era of treatment. The aim of this study was to compare the effectiveness of zinc-probiotics combination therapy to zinc monotherapy in reducing the severity of AWD.

Method: This was a cross-sectional compative study which was conducted from july 1,2019 to june 30, 2020 in the department of Pharmacology and Therapeutics at Sylhet M.A.G Osmani medical college Hospital. Total number of 128 patients with acute watery diarrhea ages between 6 months to 5 years were enrolled those who were fulfilled the selection criteria. Participants were subsequently randomized into two group. Group A were treated with Zinc(2mg/kg/day in two divided dose for 14 days), Probiotic(1capsule mixed with 1 tsf of water two times a day for 5 days) and Group B were treated with Zinc(2mg/kg/day in two divided dose for 14 days). Sufficient amount of ORS(Oral rehydration Solution) were supplied to the patients according to their requirement .Patients were followed up for changes of consistency of diarrhea, severity of diarrhea (both frequency and duration),duration of hospital stay for 7 days.

Result: The Study covered, in Group A 57.81% male and 42.19% female where as in Group B 51.56% male and 48.44% female. Stool consistency have improved in Group A then Group B (liquid stool 3.13% versus on day 2 ($p<0.001$).Frequency of stool passing became less than two on third day in Zinc Group A and on fifth day in Group B. Based on the Vesikari severity scoring system, the score became below one on fifth day in Group A and on sixth day in Group B. In Vesikari severity score grading system, all the patients of Zinc + Probiotic Groups became mild on fifth day and of Zinc only Group on sixth day of treatment. Mean duration of hospital stay was significantly ($p = <0.001$) less in Zinc + Probiotic Group (3.36±0.545 days) than Zinc only Group (4.38±0.63 days).

Key words: Acute watery diarrhea, children, probiotic therapy.

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Introduction:

Acute watery diarrohea is characterized by the frequent passing of loose and watery stool, occurring more than three times per day, without the presence of blood, and lasting for a duration of fewer than 14 days.[1]

1. Dr. Nurzahan Ferdoush, Assistant Professor, Department of Pharmacology and Therapeutics, SWMC.
2. Dr. Rifat jahan, Associate Professor (c.c) & Head, Department of Community Medicine, Parkview Medical College.
3. Dr. Arafatul Islam, IMO, Department of Internal Medicine, SOMCH.
4. Dr. Tuli Routh, Assistant Professor, Department of Pharmacology, JRRMC.
5. Dr. Abu Tareq Md Rashel, Assistant professor, Department of Pharmacology and Therapeutics, SWMC.
6. Dr. Estiak Ahmed, Senior Lecturer, Department of Pharmacology and Therapeutics, SWMC.
7. Dr. Tanjina akter Tanni, Senior Lecturer, Department of Pharmacology and Therapeutics, SWMC.

Corresponding author: Dr. Nurzahan Ferdoush
Assistant Professor, Department of Pharmacology and Therapeutics, SWMC. Mirboxtola, Sylhet-3100
Email: nurzahanferdoush1990@gmail.com

The WHO and UNICEF estimated that approximately 2.5 billion instances of diarrhea transpire each year among children under the age of five in under developed nations, with Africa and South Asia accounting for the majority of cases at 46% and 38% respectively.[2] The overall prevalence of occurrence of acute watery diarrhea in children under the age of five is 6.1 in Bangladesh and 2% of death occurs annually due to diarrhea and its related complications.[3] Approximately 70% of instances of acute watery diarrhoea (AWD) are attributed

to viral a etiologies. Of the total cases, 40% of infections occurring within the initial five years of life are attributed to the Rota virus, while the remaining 30% are caused by several other viruses, including but not limited to Cytomegalovirus, Norwalk virus, Hepatitis, and Herpes virus. Approximately 20% of afflicted children can have a bacterial pathogen detected through stool culture, such as C. jejuni, Salmonella, Shigella, E. coli, among others. Parasites are responsible for causing infections in less than 5% of instances.[4] Dehydration, hypokalaemia, and acidosis are the main life-threatening complication of AWD.[5] Many years ago, the World Health Organization (WHO) advised oral rehydration salts (ORS) as part of their recommended treatment approach for AWD in order to prevent and treat dehydration.

The number of children dying each year from diarrhea has decreased over last decade from five to three million in large part due to success of Oral Rehydration Salt (ORS).[6] Use of antibiotics are not indicated in the treatment of AWD due to viral causes. Zinc supplementation has been found to be efficacious in enhancing cellular immunity, facilitating the absorption of water and electrolytes from the colon, promoting epithelization, elevating levels of intestinal enzymes, and augmenting immunological responses, hence leading to the expeditious resolution of diarrhoea.7Probiotic, commonly known as "good bacteria", provide us a good opportunity to overcome the limitations of Zinc and ORS combination therapy in the treatment of AWD in children. Probiotics are live and usually non-pathogenic microbes, which when administered to the host produce a healthy benefit.8 Several available evidences from around the world, like Indonesia, India, Iran etc. showed effectiveness of addition of Probiotic along with Zinc and oral rehydration salt/solution. Improvement observed not only in frequency and duration of diarrhea and stool consistency but also in fever and vomiting and finally duration of hospital stay compared to Zinc and ORS combined therapy without showing any significant adverse effects.[7,9,14,18]

Methodology:

Between July 1, 2019 and June 30, 2020, a cross-sectional comparison research study was conducted in the Department of Pharmacology & Therapeutics at the Sylhet M. A. G. Osmani Medical College Hospital, Sylhet, in partnership with the Department of Pediatrics. A total 128 patients with acute watery diarrhea aged 6 months and 5 years were included. Patients who have received antibiotics or anti-diarrheal within 24 hours of diarrhoea, patient with dysentery, severly malnourished (Assesed by Z score) and persistent diarrhea were excluded. Total 7 patients were dropped out from study due to death of 2 patients and remaining were quited themselves from study.

The participants were subsequently randomly assigned into two groups(Group A and Group B) using a lottery-based procedure at the individual unit level. A total of 64 samples in each group has been enrolled. every odd number of patients was taken in group-A(oral rehydration therapy or cholera saline, Zinc and Probiotic) and even number of patients was taken in group-B (oral rehydration therapy or cholera saline and Zinc). First sample was selected by lottery. Group A received Probiotic in capsule form at the dose of one capsule mixed with one tsf of water twice daily for 5 days and 20 mg zinc syrup daily for 10 days. In group B each patient received 20 mg of zinc syrup daily for 10 days. Zinc syrup daily for 10 days. The diagnosis of AWD of each patient was confirmed by the consultant physicians. Stool consistency was assessed by using "Modified Bristol Stool Chart" (Blake et al., 2016; Koppen et al., 2016; Lane et al., 2011). Vesikari Clinical Severity Scoring system was used to assess the severity of diarrheal condition of the patient on every day at the same time during whole period of study. Frequency and consistency was Monitored at hospital with help of duty doctor through a leaflet ticked by guardian. Every patient was monitored carefully by the researcher and on duty consultant physicians for the development of adverse drug effects and noted in each visit. The duration of hospital stay calculated from the day of admission (or from the day of starting therapy) up to the day when patient's stool became regular in consistency. Patient was allowed to leave the hospital after stopping of passing loose/watery stool. When stool paased <3 times with normal consistency we considered as recovery. Home monitoring

was also done over tele-conversation with parents and/or caregivers.

The research instrument utilized in this study was a pretested semi-structured questionnaire. The data were gathered via in person interviews. The data processing and analysis were conducted utilizing SPSS version 23.0.The quantitative data were presented as the mean and standard deviation. A comparison was conducted between the groups using an unpaired t-test. The qualitative data were represented in terms of frequency and percentage. To compare the data, the chi-square ($\chi 2$) test or Fisher's exact test was employed. A probability value of less than 0.05 was considered as statistically significant. Informed written consent was taken from every patient.

Result:

This comparative observational study was conducted in the Department of Pharmacology & Therapeutics in collaboration with the Department of Pediatrics of Sylhet MAG Osmani Medical College, Sylhet during the period from July 2019 to June 2020. A total of 136 patients who were admitted in the diarrheal unit of Sylhet MAG Osmani Medical College Hospital and fulfilled inclusion criteria were selected for this study. Then they were divided randomly by lottery method into two Groups. The patients of Group A were treated with oral rehydration therapy or cholera saline, Zinc, and Probiotics. The patients of Group B were treated with oral rehydration therapy or cholera saline and Zinc. After randomization 3 patients from Group A and 5 patients from Group B failed to complete follow up were excluded from analysis. So, 64 patients in Group A (Zinc Probiotic and rehydration therapy) and 64 patients in Group B (Zinc and rehydration therapy) were analyzed in this study. Stool consistency was observed by using Vesikari severity scores, which was recorded before initiation of treatment and continued up to 7 days.

Table-I: Baseline characteristics of the respondents (n=128):

Variables	Group A (Zinc + Probiotics) (n=64)	Group B (Zinc) (n=64)
Age		
Month mean ± SD	17.97±0.03	21.61±12.08
Sex		
Male n (%)	37 (57.81%)	33 (51.56%)
Female n (%)	27 (42.19%)	31 (48.44%)
Nutritional status		
Normal nutrition n (%)	42 (65.63%)	35 (54.69%)
Moderately malnourished n (%)	22 (34.37%)	29 (45.31%)
Degree of dehydration		
Some sign dehydration n (%)	51 (79.69%)	57 (89.06%)
Severe dehydration n (%)	13 (20.31%)	7 (10.94%)

The mean age of groups A and B was not similar (17.97±0.03 Vs 21.61±12.08). Male respondents made up the majority in both groups (37% and 33%). Most participants (65.63% and 54.69%) in the two groups had normal nutritional status. In both groups, the majority of participants had some sign of dehydration (79.69% and 89.06%). Data were presented as mean and compared using an unpaired t-test. Here, Group A: Zinc Probiotic and Rehydration therapy (n = 64) and Group B: Zinc and Rehydration therapy (n = 64).At day 1, the mean difference was statistically insignificant (p = 0.0836), (mean ± SD) 10.88±2.15 was in Zinc-Probiotic treated Group and (mean ± SD) 11.28±2.29 in Zinc treated Group. Rapid fall of mean changes was observed in Zinc-Probiotic treated Group on second day (mean ± SD) (3.84±1.01) and third day (mean ± SD) (1.84±0.91). While in Zinc treated Group, changes were gradual. Mean defecation frequency become less than two on third day in Zinc-Probiotic treated Group and on fifth day in Zinc treated Group. The mean differences were statistically significant on day-2 (p = <0.001), day-3 (p = <0.001) and day-4 (<0.001).

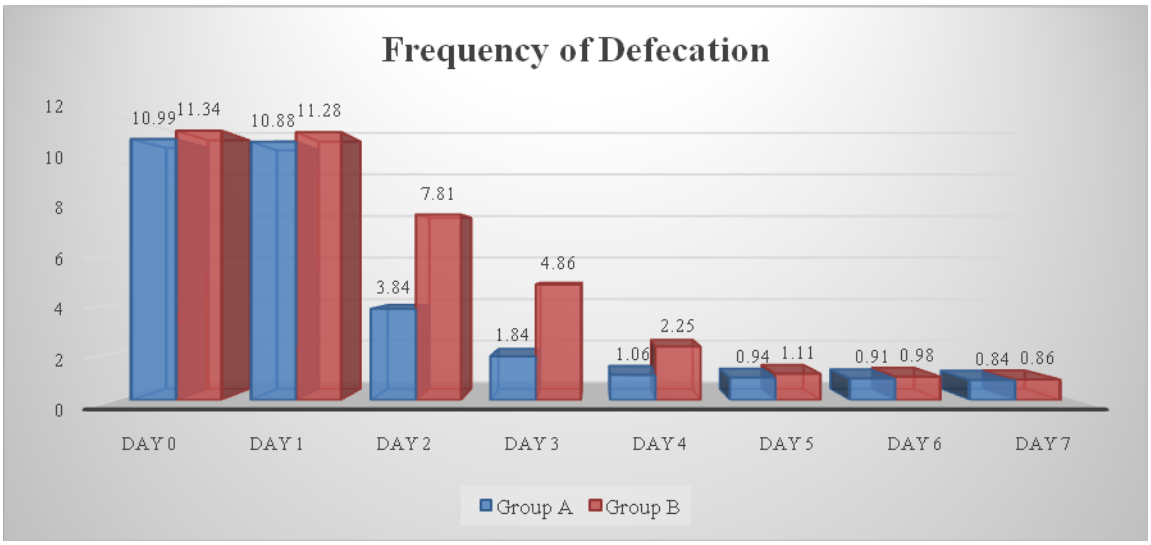

Figure1:Day-to-day mean changes in frequency of defecation

Table-II: Vesikari severity score variation between the study groups

Vesikari severity score	Study groups		p-value*
	Group A (n=64)	Group B (n=64)	
Day 0	9.88±1.33	9.91±1.43	0.45
Day 1	9.48±1.57	9.59±1.59	0.69
Day 2	8.42±1.56	8.94±1.45	0.05
Day 3	5.97±1.82	7.58±0.64	<0.001
Day 4	2.03±2.02	6.03±1.36	<0.001
Day 5	0.11±0.44	2.66±2.38	<0.001
Day 6	0.00±0.00	0.41±0.81	<0.001
Day 7	0.00±0.00	0.00±0.00	1.00

Data were presented as mean standard deviation and compared using an unpaired t-test.
The mean differences were statistically significant on day-3 (p = <0.001), day-4 (p = <0.001), day-5 (<0.001) and day-6 (<0.001).

Table-III: Duration of hospital stay

Hospital stay	Study groups		*p-value
	Group A (n=64)	Group B(n=64)	
Day mean ± SD	3.36±0.545	4.38±0.63	<0.001

An unpaired t-test was used to compare the data, which were shown as mean standard deviation.

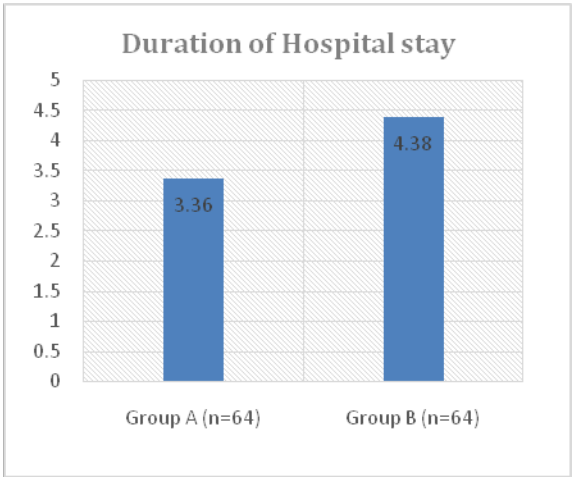

Figure 2: A Simple bar diagram showing Duration of hospital stay

An unpaired t-test was used.

Mean duration of hospital of Group A was 3.36±0.545 days and Group B was 4.38±0.63 days. Patients of the Zinc-Probiotic treated Group stayed in hospital 1.02 day less than Zinc treated Group patients and the difference was statistically significant (t = -9.752, df = 126, p = <0.001).

Discussion:

A total of 128 participants were allocated into two groups: Group A, which received treatment consisting of Zinc, Probiotic, and Rehydration therapy, and Group B, which received treatment

consisting of Zinc and Rehydration therapy. The groups were statistically similar in terms of their sex (p = 0.477), mean age (17.97±10.03 and 21.61±12.08 months in respective groups, p = 0.06), living area (p = 0.392), parental education (p = 0.634 for father's education status and p = 0.551 for mother's education) and their nutritional status (p-0.206). More prevalence in lower age groups reported by Azim et al. (2020) in Chattogram (approximately 11 months; 11.86±6.5 and 11.79±5.98).12Sultana et al. (2017) in Rajshahi, Bangladesh (approximately 14 months; 14.01±6.38 and 13.31±8.02), Ramadas et al. (2016) in Bangalore, India (approximately 13 months; 14±6.38, 11±5.19 and 13±4.91).[2,13] Similar age groups reported by Sobouti et al. (2016) in Iran (approximately 17 months) and slightly higher age group reported by de-Castro et al. (2019) in Philippines (approximately 24 months) and Shaikh et al. (2015) in Hyderabad, India (26.73±12.65 months).[14,15,16]

Nutritional status of this study's patients similarly distributed. The maximum number of participants were normal nutritional status. Sultana et al. (2017) also observed similar result.[2]

We used Bristol Stool Chart for followed up of the changes of consistency of diarrhea. In this research, passing of watery stool stopped on second day and stool consistency of all patients became regular on fourth day in Zinc Probiotic treated group. On the other hand, watery stool passing patient became nil on third day and consistency became regular on fifth day in Zinc only treated group. Bowel frequency was also significantly reduced in Zinc Probiotic combination group compared to Zinc only group. Bowel frequency reduced to less than two on third day in Zinc Probiotic treated group (1.84±0.96) and on fifth day in zinc only treated group (1.11±0.59) and it was started on second day and last up to fourth day; values were 3.84±1.01 vs 7.81±1.67 (p = <0.001) on second day, 1.84±0.91 vs 4.86±1.46 (p = <0.001) on third day and 1.06±0.50 vs 2.25±1.23 (p = <0.001) on fourth day. This study we usedBristol Stool Chartfor followed up of the changes of consistency of diarrhea. [11]

Sharif et al. (2016) also reported similar significant change from third day to fifth day, in Probiotic taking group (3.4±1.3 days) compared to placebo control group (5.5±2.1 days), p = 0.001.[17]

Ramadas et al. (2016) compared multiple Probiotic (lactic acid bacilli acidophilus, Bifidobacteriumlactis and Saccharomyces boulardii) therapy with zinc and ORS, single Probiotic (lactic acid bacilli acidophilus) therapy with zinc ORS and only zinc ORS therapy. Their study showed that the use of more Probiotic was related to less duration of diarrheal episode and early decrease in frequency of passing watery stool. Duration of diarrhea was 3.17±0.37 days, 3.47±0.5 days and 4.5±0.76 days; and frequency of diarrhea on third day was 0.53±0.5, 0.86±0.5 and 1.33±0.47 in respective study groups.[13]

Opposite result is also available. Ahmadipour et al. (2019) made comparison between Probiotic and Zinc separately taking groups on frequency of bowel habit. They found that Zinc alone gives better result than the Probiotic alone in treatment of AWD. Changes in frequency was similar between the groups While, diarrhea persists in 80% cases in Probiotic alone taking group and 47.8% in Zinc only taking group (p = <0.001) until day 4 of admission .Complications of the treatment also present in 35.6% patient in Probiotic group and 2.6% in Zinc group.[7]

Based on the Vesikari severity grading system, all the studied patient became mild diarrhea on sixth day in this study; Probiotic with Zinc taking group on fourth days (100% vs 54.69%, p = <0.001) and Zinc alone taking group on sixth day. The Vesikari score difference also found significant on day 3 (5.97±1.82 vs 7.58±0.64, p = <0.001), day 4 (2.03±2.02 vs 6.03±1.36, p = <0.001) and day 5 (0.11±0.44 vs 2.66±2.38, p = <0.001).[10]

Abraham et al. (2016) examined overall impact of addition of Probiotic with Zinc in AWD and further evaluated effect of counseling of mother. According to their research result, significant change observed in Probiotic taking group then non-Probiotic taking group. They calculated the difference of diarrheal severity based on Vesikari severity grading system between the first day and the last day, did not show day to day variation. At the beginning there was no patient with mild diarrhea, but at the end 81.3% patient taking Probiotic and Zinc became mild

stage diarrhea whereas 22.6% patient taking Zinc only become mild diarrhea.[18]

In this study, mean duration of hospital staying of Zinc-Probiotic taking group was 3.63±0.545 and Zinc only taking group was 4.38±0.63 days. The difference was significant (p = <0.001) and Zinc-Probiotic taking group stayed in hospital cooperatively shorter duration than Zinc only taking group.

Sobouti et al. (2016) compared effectiveness of Probiotic against control Group taking rehydration therapy alone in infant and non-infant patients with Rota virus diarrhea. In their study, Probiotic significantly reduce hospital staying in all study Groups. Probiotic Groups stayed in hospital for 5.07±1.30 days (infant for 5.30±1.70 and non-infant 4.94±1.06 days) and control Group hospitalized for 8.22±2.14 days (infant for 8.15±2.19 and non-infant 8.26±2.16 days). Zinc was not added in their study and the difference was more than three days. This study showed that addition of Zinc with Probiotic further reduce duration of hospital stay both in Probiotic and control Group (less than one day).[14]

Even so, a different recent study carried out in Bangladesh by Azim et al. (2020) reported that there were significant changes in frequency of stool passing, duration of diarrheal period and length of hospital stay. According to their report, mean frequency of stool passing before starting therapy was 10.93±10.27 in Zinc-Probiotic taking group and 12.25±10.35 in Zinc only taking group, which decreased below two by third day in Zinc-Probiotic taking group and by fourth day in Zinc only taking group. The Probiotic receiving group had diarrhea for an average of 56.4±21.36 hours (2.35 days) and had to stay in the hospital for 68.16±23.76 hours (2.84 days). The Zinc receiving group had diarrhea for an average of 70.8±22.8 hours (2.95 days) and had to stay in the hospital for 83.04±26.16 hours (3.46 days). [12]

There were no adverse effects of Probiotics and Zinc observed in this study during the period of hospitalization and also within one week after leaving the hospital. Observing adverse effects of Probiotic in this study were nausea, vomiting, abdominal pain, and sepsis.

Conclusion: In conclusion, Probiotic was found to be safe and effective as add on therapy in AWD in children.There was significant improvement observed in terms of frequency of watery and loose stool passing, duration of diarrhea, severity of diarrhea and duration of hospital staying in Probiotic added Group compared to the control Group.

References:

1. Mollah MAH, Nahar N, editors. Steps on to Paediatrics. 5th ed. Dhaka; 2016.
2. Sultana MM, Islam MS, Akhter S, Hossain MB, Mia MSH. Comparative Study of Zinc and Probiotic versus Zinc Alone Therapy in Children with Acute Watery Diarrhea. J Teachers Assoc. 2017;30(2):32–38.
3. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2011. Dhaka, Bangladesh; 2013.
4. Koletzko S, Osterrieder S. Acute infectious diarrhea in children. DtschArztebl Int. 2009;106(33):539–548.
5. Bhat S, Shreekrishna GN, Savio CD. Efficacy of Probiotic in acute watery diarrhea in children. Int J ContempPediatr. 2018;5(4):1646–1650.
6. Jayanthi N, Ratna Sudha M. Bacillus clausii - The Probiotic of Choice in the Treatment of Diarrhea. J Yoga Phys Ther. 2015;5(4):211–214.
7. Ahmadipour S, Mohsenzadeh A, Alimadadi H, Salehnia M, Fallahi A. Treating Viral Diarrhea in Children by Probiotic and Zinc Supplements. Pediatr Gastroenterol Hepatol Nutr. 2019;22(2):162–170.
8. Mandal A, Sahi PK. Probiotic for Diarrhea in Children. J Med Res Innov. 2017;1(2):05–12.
9. Hatta M, Supriatmo, Ali M, Sinuhaji AB, Hasibuan B, Nasution FL. Comparison of Zinc-Probiotic combination therapy to Zinc therapy alone in reducing the severity of acute watery diarrhea. PaediatrIndones. 2011;51:01–06.
10. Blake MR, Raker JM, Whelan K. Validity and reliability of the Bristol stool form scale in healthy adults and patients with diarrhea-predominant irritable bowel syndrome. Aliment Pharmacol Ther. 2016;44:693–703.

11. Koppen IJN, Velasco-Benitez CA, Benninga MA, di-Lorenzo C, Saps M. Using the Bristol stool scale and parental report of stool consistency as part of the Rome-III criteria for functional constipation in infants and toddlers. J Pediatr. 2016;77:e1:44–48.
12. Azim MA, Doza B, Iqbal S, Chowdhury F, Biswas SK. Comparative evaluation on the effect of Zinc-Probiotic and Zinc therapy in pediatric acute gastroenteritis. Chattogram Maa-O-Shishu Hosp Med Coll J. 2020;19(1):74–77.
13. Ramadas D, Chakraborty A, Chidambaram. A Comparative Study of Probiotic Lactic Acid Bacilli alone and in Combination with Bifidobacterium and Saccharomyces as Adjuvants to ORS and Zinc in the Management of Acute PediatricDiarrhea. Int Arch BioMed Clin Res. 2016;2(3):47–50.
14. Sobouti B, Noorbakhsh S, Ashraf H, Talesh SA. Use of Probiotic for the Treatment of Acute Rotavirus Diarrhea in Children: a Randomized Single-Blind Controlled Trial. Int J Child Adolesc. 2016;2(4):5–9.
15. de-Castro JA, Guno MJVR, Perez MO. Bacillus clausii as adjunctive treatment for acute community-acquired diarrhea among Filipino children: a large-scale, multicenter, open-label study (CODDLE). Trop Dis Travel Med Vaccines. 2019;5(14):01–09.
16. Abraham AA, Amritha SR, Shaji-Selvin CD. A comparative evaluation on the effect of Zinc-Probiotic and Probiotic therapy in pediatric acute watery diarrhea and the impact of counseling of mothers. Int J Pharm Pharm Sci. 2016;8(7):241–243.
17. Shaikh F, Bhand SA, Kumar P, Nizamani MA. Acute watery diarrhea; role of Saccharomyces boulardii in the treatment. Prof Med J. 2015;22(3):281–284.
18. Sharif MR, Kashani HH, Ardakani AT, Kheirkhah D, Tabatabaei F, Sharif A. The effect of a Yeast Probiotic on acute watery diarrhea in children. Probiotic Antimicrob Proteins. 2016;8:211–214.