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Original Article

A Comparative Evaluation on the Effect of Zinc-Probiotic Combination and Probiotic Therapy Alone in Paediatric Acute Diarrhoea

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ABSTRACT

Introduction: *Diarrhea is one of the main causes of childhood disability and death worldwide, resulting in 5-10 million deaths annually. It is a major public health problem in developing countries like Bangladesh. It was observed that probiotics alleviated diarrhea in 3-4 days.* ***Methods and materials:*** *This study examined the effects of zinc and probiotics in combination for the management of acute diarrhea in children. 50 children were divided into two groups, where Group I received a combination of zinc and probiotics and Group II received probiotics alone.* ***Result:*** *Group I had a mean age of 18.22±11.78 months and 60.0% of patients were male, with a mean weight of 10.92±3.6 kg. 26.0% had mild malnutrition and 28.0% had fever. 64.0% had a volume of stool/purging 7-13, and the mean hospital stay was 3.46±1.02. Group II had a mean age of 12.66±7.87 months and 44.0% were male, with a mean weight of 9.26±2 kg. 24.0% had mild malnutrition and 24.0% had fever. 72.0% had a volume of stool/purging 7-13, and the mean hospital stay was 3.99±1.13. Overall, 44.0% of patients had a number of vomitus <5 and 90.0% had liquid consistency of stool.* ***Conclusion:*** *Zinc and probiotic therapy together is more effective in treating diarrhoea and vomiting in children than probiotic*

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therapy alone. Clinical pharmacist interventions can reduce the emergence and severity of this disease, and education and counseling of mothers is essential for effective management.

Keywords: *Diarrhea, childhood disability, probiotics, zinc supplementation, diarrheal episodes in children.*

INTRODUCTION

Diarrhoeal diseases are the leading causes of mortality and morbidity worldwide, particularly in developing countries [1,2]. They kill more children worldwide, compared to tuberculosis, malaria, and AIDS combined. Dehydration, acidosis, impairment of renal function and secondary infections are some of the important factors closely associated with deaths due to diarrhoeal disease [3]. According to the WHO definition, Diarrhoea is defined as the passage of three or more loose stools in 24 hours. Diarrhea can be classified as Acute watery diarrhea (diarrhea that lasts for less than 14 days including cholera), Dysentery or invasive diarrhea (blood in the stool), Persistant diarrhoea (diarrhea that lasts for 14 days or more) [4]. The organisms that cause Acute watery diarrhea are Rotavirus, Enterotoxigenic E. coli, Salmonella species, Vibrio cholera, Giardia lamblia, Cryptosporidium, Clostridium perfinges, etc. Food intolerances are also an important cause of diarrhea in children. Administration of antibiotics and antacids containing magnesium may also lead to diarrhea [3]. The breakthrough in the treatment of acute gastroenteritis in children was the introduction of oral rehydration solution (ORS) in the early stages of illness [5,6]. Latter research demonstrated that rice-water and rice-based ORS are superior to ORS alone in reducing the frequency and stool volume in acute gastroenteritis [7,8]. However, nutritional intervention does not usually reduce the duration of diarrhea. In developing countries, younger children with malnutrition and impaired immune status are more likely to have severe and prolonged diarrhea. Zinc supplementation can help these children recover more quickly [9,10]. Studies evaluating the effect of zinc supplementation on diarrheal diseases found a preventive and long-lasting impact. These showed that 10 mg to 20 mg of zinc per day, for 10-14 days, reduced the number of episodes of diarrhea in 2 - 3 months after the supplementation [11]. The WHO and UNICEF recommend zinc supplements for children with acute diarrhea. Zinc can help shorten the duration of diarrhea and prevent future episodes. Probiotics are also being studied for their potential to treat diarrhea. Probiotics are live bacteria that can be beneficial for health. Some common probiotics include Lactobacillus, Bifidobacterium, and Saccharomyces boulardii [12,13]. They are used in the prevention and treatment of diarrhea based on the assumption that they modify the microflora composition of the colon and act against enteric pathogens [12]. Meta-analyses have demonstrated a therapeutic effect of probiotics, mainly Lactobacillus GG, on acute diarrhea caused by the Rotavirus. This treatment usually reduces the duration of diarrhea by a few hours [14,15]. Possible explanations for the observed effects of probiotics include inhibition of pathogen adhesions,

enhanced mucosal integrity, beneficial effects on the dysregulated immune response, production of antimicrobial substances, and modification of intestinal receptors. The recommended doses of probiotics are as follows: for children under 2 years, 1 cap (containing Lactobacillus acidophilus 2 billion, Lactobacillus bulgaricus 1 billion, Bifidobacterium bifidum 1 billion, Fructooligosaccharides 100 mg) every 12 hours for 10 days; and for children over 2 years, 2 caps every 12 hours for 10 days [16]. In addition to probiotics, intervention trials have demonstrated that the addition of oral zinc can faster reduce diarrhea and the severity of acute diarrhea in children [9,15,17]. Probiotics have been used to treat acute diarrhea for a long time, but their effectiveness is still being debated. Probiotics may work by competing with harmful bacteria for nutrients, preventing them from attaching to the lining of the intestine, producing antimicrobial substances, or boosting the immune system [15,18,19].

OBJECTIVES

General Objective

- To compare the efficacy of zinc-probiotic combination therapy and probiotic therapy alone in the treatment of acute pediatric diarrhea.

Specific Objectives

- To see the combined effect of zinc-probiotics in reducing the frequency and volume of stool.
- To determine the synergistic effect of zinc probiotics in shortening the duration of diarrhea, and
- To observe whether zinc-probiotics together help minimize the severity of diarrhea.

METHODS AND MATERIALS

The current study is a randomized control trial, carried out in the department of Paediatrics, Uttara Adhunik Medical College Hospital Dhaka, during six (6) months period. The study aimed to determine the combined role of zinc probiotics in the management of acute diarrhea in children. A total of 100 children (6 months to under 5 years of age) with acute diarrhea who were admitted to the Department of Paediatrics, Uttara Adhunik Medical College Hospital, were included in this study. All the study patients were divided into two equal groups (group-I and group II) each comprising 50 children. Group-I represents the study group that received the zinc-probiotic combination and group II is the control group that received probiotics alone for the management of diarrhea in the study patients. A convenient and purposive sampling technique was employed to include the required number of children. The demographic data, details of socioeconomic status, severity, duration, and frequency of diarrhea, and the presence of other associated symptoms were recorded using predesigned proforma.

Inclusion Criteria

- Patients with age between 6-59 months
- Patients having the passage of three or more loose stools in 24 hours for up to 14 days

Exclusion Criteria

- Children with severe dehydration
- Children with metabolic acidosis and acute renal failure
- Children receiving antibiotics, zinc, probiotics, or any other anti-diarrhoeal medication in the last 24 hours
- Patients who had the presence of blood in the stool (clinical dysentery),
- Immuno-suppressed children, children with severe malnutrition &other chronic diseases
- Parents of the patient not willing to participate in the study

RESULTS

In Group I, 22%, 50%, and 28% of the patients were below 10 months, between 10-20 months, and above 20 months, respectively. The corresponding percentages for Group II were 38%, 56%, and 6%. The mean age in Group I was 18.22 months (SD=11.78) and 12.66 months (SD=7.87) in Group II. The sex distribution showed 60% males and 40% females in Group I, compared to 44% males and 56% females in Group II. The p-value for sex distribution was 0.109 (marginally significant). The distribution of nutritional status revealed 8% normal and 26% mild malnutrition in Group I, whereas Group II had 2% normal and 24% mild malnutrition. The p-value for nutritional status was not statistically significant (**Table I**).

Table I: **Distribution of the study patients according to baseline characteristics (N=100)**.

Baseline characteristics	Group I (n =50)		Group II (n =50)		p-value
	n	%	n	%	
Age (in a month)					
<10	11	22	19	38	
10-20'	25	50	28	56	
>20	14	28	3	6	
Mean ±SD	18.22±11.78		12.66±7.87		[a]0.683[ns]
Range(min-max)	6-50		5-48		
Sex					
Male	30	60	22	44	[b]0.109[ms]
Female	20	40	28	56	
Nutritional Status					
Normal	4	8	1	2	[b]0.247[ms]
mild malnutrition	13	26	12	24	

s=significant | ns = not significant | p-value reached from unpaired t-test | bp value reached from the Chi-square test

The analysis reveals that there were no significant differences between the groups in terms of dehydration (p=0.826), number of stools (p=0.260), number of vomitus episodes (p=0.324), consistency of stool (p=0.749), presence of fever (p=0.648), volume of stool per purging (p=0.157), and total stool volume per day (p=0.806). The descriptive statistics indicate that the mean age in Group I was 9.76 (SD=4.74) and 10.76 (SD=4.06) in Group II, while the mean number of vomitus episodes was 4.17 (SD=1.89) in Group I and 3.85 (SD=1.28) in Group II. The majority of patients in both groups had liquid stools (90% in Group I, 88% in Group II) and exhibited no signs of dehydration (12% in Group I, 16% in Group II) (**Table II**).

Table II: **Distribution of the study patients according to clinical characteristics on admission day (N=100).**

Clinical characteristics on day0	Group I		Group II		p-value
	n	%	n	%	
Dehydration					
No sign of dehydration	6	12	8	16	[a]0.826[ns]
Some dehydration	13	26	15	30	
Number of stools					
≤10	34	68	29	58	
>10	16	32.0	21	42	
Mean ±SD	9.76±4.74		10.76±4.06		[b]0.260[ns]
Range(min-max)	4-22		5-20		
Number of vomitus					
<5	22	44	22	44	
≥5	13	26	11	22	
Mean ±SD	4.17±1.89		3.85±1.28		[b]0.324[ns]
Range(min-max)	1-9		1-6		
Consistency of stool					
Liquid	45	90	44	88	[a]0.749[ns]
Semi-solid	5	10	6	12	
Fever					
Yes	14	28	12	24	[a]0.648[ns]
No	36	72	38	76	

Volume of stool(ml)/purging					
7-13	32	64	36	72	
14-24	18	36	14	28	
Mean ±SD	13.24±4.45		12.06±3.8		[b]0.157[ns]
Range(min-max)	7-24		7-22		
Total stool volume(ml)/day					
<50	3	6	3	6	
50-100	27	54	21	42	
>100	20	40	26	52	
Mean ±SD	115.12±54.82		112.76±40.18		[b]0.806[ns]
Range(min-max)	22-300		40-200		

ns=not significant | [a]p value reached from the Chi-square test | [b]p value reached from unpaired t-test

In Group I, 80% had less than 10 stools compared to 68% in Group II. Group I had a mean stool count of 6.54 (SD=3.59), slightly lower than Group II with a mean of 7.92 (SD=2.89). There were no significant differences in the number of vomitus episodes or stool consistency between the two groups. Fever occurrence was 20% in both groups. Regarding stool volume, 40% of Group I had volumes greater than 10 ml per purging episode, while it was 28% in Group II. The mean volume of stool per purging episode was 10.64 ml (SD=3.8) in Group I, significantly lower than the mean of 105 ml (SD=2.5) in Group II. Finally, the total stool volume per day was significantly lower in Group I (mean=58.82 ml, SD=33.87) compared to Group II (mean=73.68 ml, SD=33.47) (**Table III)**.

Table III: Distribution of the study patients according to clinical characteristics on 1st day(N=100).

Clinical characteristics on day 1	Group I		Group II		p-value
	(n=50)		(n=50)		
	n	%	n	%	
Number of stool					
<10	40	80	34	68	
≥10	10	20	16	32	

Mean ±SD	6.54±3.59		7.92±2.89		[a]0.036[s]
Range(min-max)	2-18		3-15		
Number of vomitus					
<2	6	12	4	8	
≥2	3	6	4	8	
Mean ±SD	1.11±1.26		1.5±1.19		[a]0.114[ns]
Range(min-max)	0-3		0-3		
Consistency of stool					
Liquid	44	88	41	82	[b]0.400[ns]
Semi-solid	6	12	9	18	
Fever					
Yes	10	20	10	20	[b]1.00[ns]
No	40	80	40	80	
Volume of stool(ml)/purging					
>10	20	40	14	28	
10-20	28	56	36	72	
>20	2	4	0	0	
Mean ±SD	10.64±3.8		105±2.5		[a]0.828[ns]
Range(min-max)	6-21		5-16		
Total stool volume(ml)/day					
<50	19	38	11	22	
50-100	27	54	34	68	
>100	4	8	5	10	
Mean ±SD	58.82±33.87		73,68±33.47		[a]0.029[s]
Range(min-max)	6-145		10-160		

s=significant | ns = not significant | "p-value reached from unpaired t-test | p-value reached from the Chi-square test

Table IV presents the distribution of study patients (n=89) based on their clinical characteristics on the second day. Group I had a higher percentage of patients with 5 or fewer stools (78.6% vs. 57.4% in Group II). There was a significant difference in stool consistency, with Group I having 19% of patients with liquid stool compared to 38.3% in Group II. Group II had a higher mean volume of stool per purging episode (7.57 ml) compared to Group I (6.84 ml), and this difference was statistically significant. Additionally, the total stool volume per day was significantly higher in Group II (37.27 ml) compared to Group I (27.2 ml) (**Table IV)**.

Table IV: Distribution of the study patients according to clinical characteristics on the 2nd day(n=89).

Clinical characteristics on day 2	Group I (n=42)		Group II (n=47)		p-value
	n	%	n	%	
Number of stool					
≤5	33	78.6	27	57.4	
>5	9	21.4	20	42.6	
Mean ±SD	4.47±2.33		5.17±2		[a]0.110[ns]
Range(min-max)	2-12		1-10		
Consistency of stool					
Liquid	8	19	18	38.3	[b]0.046[s]
Semi-solid	34	81	29	61.7	
Volume of stool(ml)/purging					
<10	39	92.9	39	83	
≥10	3	7.1	8	17	
Mean ±SD	6.84±1.26		7.57±2.02		[a]0.032[s]
Range(min-max)	5-10		5-12		
Total stool volume(ml)/day					
<50	39	92.9	35	74.5	
≥50	3	7.1	12	25.5	
Meant ±SD	27.2±14.85		37.27±17.60		[a]0.002[s]
Range(min-max)	9-80		5-72		

s=significant | ns = not significant | [a]p value reached from unpaired t-test | [b]p value reached from the Chi-square test

70% of patients in Group I and 80% in Group II had fewer than 5 stools, with mean numbers of stools of 3.27 (SD=1.54) and 3.02 (SD=1.67), respectively (p=0.438). Regarding stool consistency, 85% of patients in Group I and 80% in Group II had semi-solid stools, while 15% and 20%, respectively, had liquid stools (p=0.663). In terms of volume of stool per purging, 85% in Group I and 88% in Group II had a volume of 5 ml or more, with mean volumes of 5.41 ml (SD=0.91) and 5.97 ml (SD=1.32), respectively (p=0.015). For total stool volume per day, 55% in Group I and 48% in Group II had a volume of 10-20 ml/day, with mean volumes of 15.41 ml (SD=7.46) and 18.14 ml (SD=10.87), respectively (p=0.146) (**Table V**).

Table V: **Distribution of the study patients according to clinical characteristics on the 3rd day(n=45)**

Clinical characteristics on day 3	Group I (n=20)		Group II (n=25)		p-value
	n	%	n	%	
Number of stool					
<5	14	70	20	80	
≥5	6	30	5	20	
Mean ±SD	3.27±1.54		3.02±1.67		[a]0.438[ns]
Range(min-max)	1-6		0-7		
Consistency of stool					
Liquid	3	15	5	20	[b]0.663[ns]
Semi-solid	17	85	20	80	
Volume of stool(ml)/purging					
<5	3	15	3	12	
≥5	17	85	22	88	
Mean ±SD	5.41±0.91		5.97±1.32		[a]0.015[s]
Range(min-max)	4-8		4-10		
Total stool volume(ml)/day					
<10	4	20	5	20	
10-20	11	55	12	48	
>20	5	25	8	32	
Mean±SD	15.41±7.46		18.14±10.87		[a]0.146[ns]
Range(min-max)	5-28		5-46		

s=significant | ns=not significant | [a]p value reached from unpaired t-test | [b]p value reached from the Chi-square test

100% of patients in Group I and 69.2% in Group II had fewer than 5 stools, with mean numbers of stools of 2.8 (SD=0.78) and 3.3 (SD=1.18), respectively (p=0.077). Regarding stool consistency, 90.9% of patients in Group I and 61.5% in Group II had semi-solid stools, while 9.1% and 38.5%, respectively, had liquid stools (p=0.121). In terms of volume of stool per purging, 72.7% in Group I and 30.8% in Group II had a volume of 5 ml or more, with mean volumes of 4.7 ml (SD=0.48) and 4.14 ml (SD=1.06), respectively (p=0.001). For total stool volume per day, 63.6% in Group I and 46.2% in Group II had a volume of 10-20 ml/day, with mean volumes of 12.8 ml (SD=6.52) and 18.66 ml (SD=12.84), respectively (p=0.004) (**Table VI**).

Table VI: **Distribution of the study patients according to clinical characteristics on the 4th day(n=24).**

Clinical characteristics on day 4	Group I (n=50)		Group II (n=50)		P value
	n	%	n	%	
Number of stool					
<5	11	100	9	69.2	
≥5	0	0	4	30.8	
Mean ±SD	2.8±0.78		3.3±1.18		[a]0.077[ns]
Range(min-max)	2-4'		1-7;		
Consistency of stool					
Liquid	1	9.1	5	38.5	[b]0121n[s]
Semi-solid	10	90.9	8	61.5	
Volume of stool(ml)/purging					
<5	3	27.3	9	69.2	
≥5	8	72.7	4	30.8	
Mean ±SD	4.7±0.48		4.14±1.06		[a]0.001[s]
Range(min-max)	4-5'		3-6'		
Total stool volume(ml)/day					
<10	3	27.3	3	23.1	
10-20'	7	63.6	6	46.2	
>20	1	9.1	4	30.8	
Mean ±SD	12.8±6.52		18.66±12.84		[a]0.004[s]
Range(min-max)	5-28		7-50		

s=significant | ns=not significant | [a]p value reached from unpaired t-test | [b]p value reached from the Chi-square test

At the fifth day with 12 participants, clinical characteristics revealed all patients in Group I had no stool output (0%) compared to 66.7% of patients in Group II who had 2 stools, while the remaining 33.3% had 4 stools. The consistency of stool was exclusively semi-solid for all patients in Group II (100%). In terms of volume of stool per purging, all patients in Group I had no output (0%), while 66.7% of patients in Group II had a volume of less than 5 ml/purging, and the remaining 33.3% had a volume of 5 ml or more. Additionally, all patients in Group II had a total stool volume of 12 ml/day (**Table VII**).

Table VII: **Distribution of the study patients according to clinical characteristics on the 5th day**(n=12).

Clinical characteristics on day5	Group I (n=50)		Group II (n=50)		P value
	n	%	n	%	
Number of stool					
2	0	0	8	66.7	
4	0	0	4	33.3	
Mean ±SD			2.66±1.15 2-4		
Consistency of stool					
Semi-solid	0	0	12	100	
Volume of stool(ml)/purging					
<5	0	0	8	66.7	
≥5	0	0	4	33.3	
Mean ±SD			4.3±0.57 4-5		
Total stool volume(ml)/day					
12	0	0	12	100	
Mean ±SD			12±0		
Range(min-max)			12±12		

78% of patients in Group I and 52% in Group II experienced diarrhea for 5 days or less, while 22% in Group I and 48% in Group II had diarrhea for more than 5 days. The p-value for the duration of diarrhea was 0.006, indicating a statistically significant difference between the two groups (**Table VIII**).

Table VIII: **Duration of diarrhea of the studied patients(N=100).**

Time to the cessation of diarrhea (days)	Group I (n=50)		Group II (n=50)		P value
	n	%	n	%	
≤5	39	78	26	52	
>5	11	22	24	48	0.006[s]

s=significant | p-value reached from the Chi-square test

In Group I, 16% of patients had a hospital stay of 2 days, 44% stayed for 3 days, 18% stayed for 4 days, and 22% stayed for 5 days. There were no patients in Group I with a hospital stay longer than 5 days. In Group II, the distribution of hospital stay was as follows: 6% stayed for 2 days, 44% for 3 days, 24% for 4 days, 2% for 5 days, 8% for 6 days, and 16% for 7 days. The mean hospital stay was 3.46 days (SD=1.02) in Group I and 3.99 days (SD=1.13) in Group II. The p-value for the duration of hospital stay was 0.016, indicating a statistically significant difference between the two groups (**Table IX**).

Table IX: **Distribution of the study patients according to hospital stay(N=100)**

Hospital Stay (in days)	Group I (n=50)		Group II (n=50)		P value
	n	%	n	%	
2	8	16	3	6	
3	22	44	22	44	
4	9	18	12	24	
5	11	22	1	2	
6	0	0	4	8	
7	0	0	8	16	
Mean ±SD	3.46±1.02		3.99±1.13		0.016[s]
Range(min-max)	2-5		2-7		

s=significant | p-value reached from the Chi-square test

DISCUSSION

The baseline characteristics of the study patients revealed that in Group I, 50.0% of patients were aged 10-20 months, with a mean age of 18.22±11.78 months, while in Group II, 56.0% were in the same age range, with a mean age of 12.66±7.87 months. In terms of gender, 60.0% of patients in Group I were male, compared to 44.0% in Group II. Mild malnutrition was present in 26.0% of patients in Group I and 24.0% in Group II. These findings are consistent with the results reported by the authors [20]. In this study, the clinical characteristics on the admission day of the study patients showed that approximately one-fourth had signs of dehydration in both groups. The majority of patients had several stools ≤10, and the mean numbers of stools were similar between the groups. Nearly half of the patients had several vomitus <5, with slightly higher mean numbers in Group I. The majority of patients had liquid consistency of stool,

and fever was present in a notable proportion of patients in both groups. The volume of stool per purging was similar between the groups, with a slight difference in mean volumes. More than half of the patients had a total stool volume per day of 50-100 ml, and the mean volumes were comparable between the groups. The differences in these clinical characteristics were not statistically significant between the two groups. These findings were similar to that of another study. In that study, in Group II, the majority (86.6%) were outpatients, while 13.3% were inpatients. Abdominal pain was present in 97.3% of patients, fever in 71.3%, vomiting in 82%, and severe dehydration in 24.6%. These findings align with our study [21]. In this study, on the 5th day, clinical characteristics in Group II showed that 66.7% of patients had several stools with a mean number of 2.66±1.15. All patients had semi-solid consistency of stool, and 66.7% had a volume of stool per purging of <5 with a mean volume of 4.33±0.57. All patients had a total stool volume per day of 12 ml, and the mean total stool volume per day was 12±0. Additionally, 66.7% of patients had a frequency of purging per day. In terms of the time to the cessation of diarrhea, 78.0% of patients in Group I and 52.0% in Group II had diarrhea cease within 5 days, and the difference between the two groups was statistically significant ($p<0.05$). In this study, weight at discharge showed that 60.0% of patients in Group I and 34.0% in Group II had a weight at discharge of 10-20kg, with mean weights of 10.76±3.04 in Group I and 9.54±2.06 in Group II. Regarding hospital stay, 44.0% of patients in both groups stayed for 3 days, with mean hospital stays of 3.46±1.02 in Group I and 3.99±1.13 in Group II. The difference in hospital stay between the two groups was statistically significant ($p<0.05$). In a randomized controlled trial involving infants with acute watery diarrhea, a combination therapy of zinc and probiotics was found to improve stool frequency, consistency, and reduce the duration of illness, which is consistent with the findings of our study.

Limitations of the Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

This study concluded that diarrhea is a common problem in our country, especially in children. There are many treatment options for acute watery diarrhea in addition to oral rehydration saline. It can be inferred that a combination of zinc and probiotic therapy is more effective than probiotic therapy alone in the treatment of acute diarrhea in under 5 years old children.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. *Rehan HS, Gautam K, Gurung K. Mothers needs to know more regarding management of childhood acute diarrhea. Indian J PrevSoc Med. 2003;34(1):40-5.*
2. *Mukhtar A, Izham MI, Pathiyil RS. A survey of mothers' knowledge about childhood diarrhoea and its management among a marginalised community of*

Morang, Nepal. The Australasian medical journal.2011;4(9):474.

3. *Mwambete KD, Joseph R. Knowledge and perception of mothers and caregivers on childhood diarrhoea and its management in Temeke municipality, Tanzania. Tanzania journal of health research.2010;12(1):47-54.*
4. *Mayhew M, Ickx P, Newbrander W, Stanekzai H, Alawi SA. Long and short Integrated Management of Childhood Illness (IMCI) training courses in Afghanistan: a cross-sectional cohort comparison of post-course knowledge and performance. International journal of health policy and management.2015 Mar;4(3):143.*
5. *Gorelick MH, Shaw KN, Murphy KO. Validity and reliability of clinical signs in the diagnosis of dehydration in children. Pediatrics. 1997 May 1;99(5): e6-.*
6. *Walker-Smith JA, Sandhu BK, Isolauri E, Banchini G, van Caillie-Bertrand M, Dias JA, Fasano A, Guandalini S, Hoekstra JH, Juntunen M, Kolacek S. Guidelines prepared by the ESPGAN Working Group on Acute Diarrhoea: Recommendations for feeding in childhood gastroenteritis. Journal of pediatric gastroenterology and nutrition.1997 May 1;24(5):619-20.*
7. *Wall CR, Swanson CE, Cleghorn GJ. A controlled trial comparing the efficacy of rice - based and hypotonic glucose oral rehydration solutions in infants and young children with gastroenteritis. Journal of gastroenterology and hepatology.1997 Jan;12(1):24-8.*
8. *Mazumder S, Taneja S, Bhandari N, Dube B, Agarwal RC, Mahalanabis D, Fontaine O, Black RE. Effectiveness of zine supplementation plus oral rehydration salts for diarrhoea in infants aged less than 6 months in Haryana state, India. Bulletin of the World Health Organization.2010;88:754-60.*
9. *Sazawal S, Black RE, Ramsan M, Chwaya HM, Stoltzfus RJ, Dutta A, Dhingra U, Kabole 1, Deb S, Othman MK, Kabole FM. Effects of routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in a high malaria transmission setting: community-based, randomised, placebo-controlled trial. The Lancet.2006 Jan 14;367(9505):133-43.*
10. *Black R. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries. Am.J.Clin ,Nutr.2000;72:1516-22.*
11. *Scrimgeour AG, Lukaski HC. Zinc and diarrheal disease: current status and future perspectives. Current Opinion in Clinical Nutrition & Metabolic Care.2008 Nov 1;11(6):711-7.*
12. *Szajewska H, Setty M, Mrukowicz J, Guandalini S. Probiotics in gastrointestinal diseases in children: hard and not-so-hard evidence of efficacy. Journal of pediatric gastroenterology and nutrition. 2006 May 1;42(5):454-75.*
13. *Guandalini S. Probiotics for prevention and treatment of diarrhea. Journal of Clinical Gastroenterology.2011 Nov 1;45: S149-53.*
14. *Markowitz J, Stig B. Probiotics in health and disease. Pediatric Clinics of North America,2002;49.*
15. *Szajewska H, Mrukowicz JZ. Probiotics in the treatment and prevention of acute infectious diarrhea in infants and children: a systematic review of published randomized, double-blind, placebo-controlled trials. Journal of pediatric gastroenterology and nutrition. 2001 Oct 1;33: S17-25.*
16. *Kligler B, Cohrssen A. Probiotics, American family physician.2008 Nov 1;78(9).*
17. *Strand TA, Chandyo RK, Bahl R, Sharma PR, Adhikari RK, Bhandari N, Ulvik RJ, Mølbak K, Bhan MK, Sommerfelt H. Effectiveness and efficacy of zinc for the treatment of acute diarrhea in young children. Pediatrics. 2002 May 1;109(5):898-903.*
18. *Guandalini S, Pensabene L, Zikri MA, Dias JA, Casali LG, Hoekstra H, Kolacek S,Massar K, Micetic-Turk'D, Papadopoulou A, de Sousa JS. Lactobacillus GG administered in oral rehydration solution to children with acute diarrhea: a multicenter European trial. Journal of pediatric*

gastroenterology and nutrition. 2000 Jan 1;30(1):54-60.

19. *Shornikova AV, Isolauri E, Burkanova L, Lukovnikova S, Vesikari T. A trialin the Karelian Republic of oral rehydration and Lactobacillus GG for treatment of acute diarrhoea. Acta Paediatrica.1997 May;86(5):460-5.*
20. *Abraham AA, Amritha SR, Selvin CD.A comparative evaluation on the effect of zinc-probiotic and probiotic therapy in paediatric acute diarrhoea and the impact of counselling of mothers. Int J Pharm Pharm Sci. 2016; 8:241-3.*
21. *Sultana MM, Islam MS, Akhter S, Hossain MB, Mia MS. Comparative Study of Zinc and Probiotics versus Zinc Alone Therapy in Children with Acute Watery Diarrhea. TAJ: Journal of Teachers Association. 2017;30(2):32-8.*