

PHYSICIANS' KNOWLEDGE AND ATTITUDE CONCERNING THE CLINICAL USE OF PROBIOTICS FOR THE TREATMENT OF INFANTILE DIARRHEA IN SINDH, PAKISTAN

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ABSTRACT

Since last few years in Pakistan, use of probiotics is emerging for the treatment of infantile diarrhea. In general, several nutritional and pharmaceutical companies are encouraging healthcare professionals (HCPs) for the recommendation of probiotics in pediatric community. It was speculated that knowledge and clinical use of probiotics were varied among General Physicians and Pediatricians. The objective of the present study was to investigate the knowledge of General Physicians and Pediatricians and their approach for the recommendation of probiotics in infants to treat diarrheal illnesses. A

cross-sectional quantitative study was carried out coordinated 1000 physicians, including 580 Pediatricians and 420 General Physicians from 9 suburban districts of Sindh, Pakistan. Survey results revealed that 99.3% Pediatricians (Pds) and 76.2% General Physicians (GPs) were familiar with probiotics followed by 0.7% Pds and 23.8% GPs were unfamiliar. 90.8% Pds and 13.8% GPs were aware about the contributing factors needed for the required benefits of probiotics in diarrhea. It is concluded that Pediatricians were more knowledgeable and aware about the advancement of probiotics compared to General Physicians. It is needed that knowledgeable healthcare professionals and health department should make opportunities in order to educate the medical community on the effective application of probiotics in infants and children.

KEYWORDS: Probiotics, diarrhea, infants, pediatricians, general physicians.

INTRODUCTION

Probiotic is a word which comes out from the Latin and Greek vocabulary “Pro” means “for” and “biotic” means “life”.

The most all-around acknowledged definition of a probiotic is “a live microorganism when ingested provide the beneficial effects to the host by improving its intestinal microbial balance” (FAO/WHO, 2001).

Probiotics are being frequently recommended in developed and developing countries for the prevention and treatment of gastrointestinal disorders, including diarrheal illnesses in infants and children. Since last few years, many nutritional companies have supplemented probiotics in their powder milk formulae and complementary foods. Moreover, certain pharmaceuticals companies are marketing several probiotics formulations in different dosage forms such as drops, capsule, and powder. However, more exploration is needed about the effective dose and strain-specific benefits of the particular probiotic.

The prerequisites of probiotics regarded as effective should provide beneficial effects to the host, nonpathogenic and hazardless, capable to survive and proliferate in the intestine. Lactobacilli and Bifidobacteria are frequently used probiotics in children aged below 5 years for the prevention and management of infectious diarrhea. (Rijkers et al, 2010).

Probiotics by lowering of intestinal pH, reducing the gut permeability, productions of short-chain fatty acids and bacteriostatic and bactericidal substances, regulation of Gut associated lymphoid tissues and regulation of gut motility hence strengthen the immune system and protect from diarrhea and other infectious diseases. (de Vrese et al, 2007).

Diarrhea is derived from the Greek word means “dia and rhein” meaning “through and to flow”. The universal accepted definition of diarrhea is “loose or watery stools at least three times in a day or more frequent passage than is normal for the individual”

“Consistency of stool is more important, frequent passing of formed stools is not considered as diarrhea, nor passing of pasty stools by breastfed infants”. (de Vrese et al, 2007).

Diarrhea on the basis of duration is classified into acute and persistent or chronic diarrhea associated with different pathological and physiological causes.

Worldwide, particularly in developing countries, acute infectious diarrhea induced by enteric pathogens is one of the most important cause of morbidity and mortality among infants and children under 5 years of age. It is usually related to a wide range of bacteria, viruses, and parasites. The prevalence of viral-induced diarrhea has been observed in infants aged from 6-12 months, parasites infectious in infants older than 1 year, whereas bacteria were found equally prevalent in all ages of infants and children. (Nitiema et al. 2011).

Diarrheal is the second top listed infectious diseases with a morbidity of 1.7 billion cases and mortality of 846,000 annually worldwide in children aged under 5 years. (UNICEF/WHO, 2016).

Infectious diarrhea induced by viral, bacterial and parasitic organisms are the major source of diarrheal mortality in children under 5 years of age (Walker et al. 2012, Liu et al. 2012, Rudan et al. 2013). Estimated 2,195 children under 5 years of age die daily due to moderate to severe diarrhea in Pakistan, India, Bangladesh and some regions of Africa. (Kotloff et al, 2013).

Every year in Pakistan around 100 million infants and children are being consulted with acute infectious diarrhea among them 250,000 die due to not receiving the care or prefer to manage diarrhea at home. (Aslam et al, 2010).

MATERIAL AND METHODS

Study Design

Cross-sectional, quantitative study was conducted to identify the physicians' knowledge and attitude about the clinical use of probiotics in the treatment and management of infantile diarrhea.

Ethical consideration

The researcher mentioned the disclaimer on the questionnaire for confidentiality of acquired information to be used for research purpose only and on the same oral approval was obtained from each respondent.

Study Period

Data was collected during the period of six month from 1st January 2017 to 1st June 2017.

Study Instrument

The instrument used in this study was a Paper-and-Pencil Interviewing (PAPI) structured questionnaire in English language, developed as per research objectives. The Survey was composed of 17 questions divided into three categories which were further divided into 3 to 5 different variables. A questionnaire designed to close-ended multiple choice with subsequent other option space, in a case when the respondents want to give additional information or suggestions. The objective of the questionnaire was to get the insight of respondents' demographic information such as gender, age, clinical experience, and specialty. Secondly, to investigate the age at which diarrhea is prevalent in infants and children, diarrheal pathogenesis, knowledge about the probiotic concept, their safety and efficacy, recommendation and finally level of satisfaction about the use of probiotics in the management of infantile diarrhea.

A pilot study was conducted with 30 Pediatricians and 20 General Physicians of Karachi, over the period of one month, i.e. December 2016 in order to evaluate its validity and reliability. After the pilot study made necessary amendments such as modified the confusing words, addition of some probing words and consent disclaimer, then finally approved from the Department of Pharmaceutics, University of Karachi for subsequent study.

Sample and Data Collection

A random sampling technique was used all over the survey. Since infants and children are more often consulted with Pediatricians compared to General Physician, it is therefore, collected the data from 580 Pediatricians and 420 General Physicians at their consultation clinics which belong to 9 suburban districts of Sindh including Karachi, Thatta, Hyderabad, Sukkur, Larkana, Mirpur Khas, Dadu, Badin, and Nawabshah.

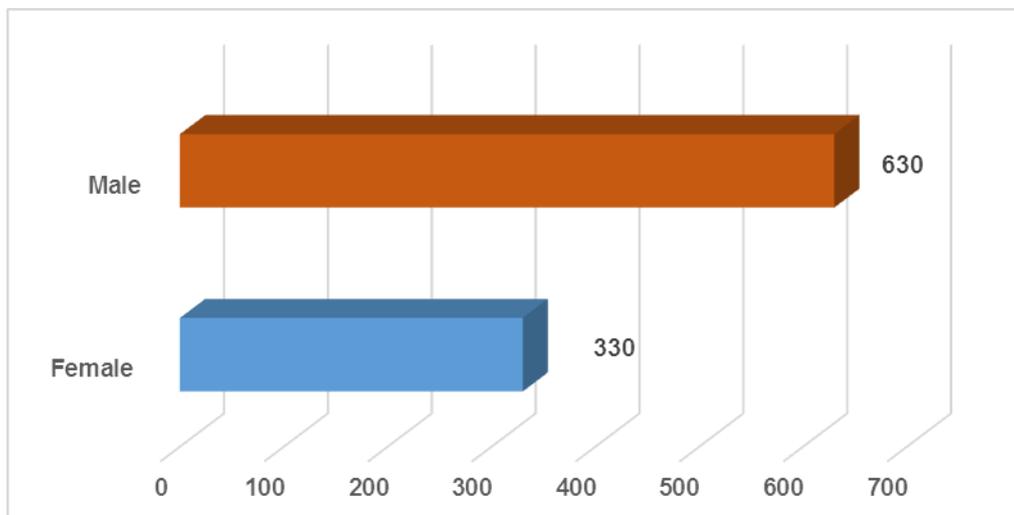
METHODOLOGY

Collected data initially was recorded into Microsoft Office Excel software program. The statistical data analysis was carried out with IBM SPSS Statistics (SPSS 24.0 V) and Minitab 1.8. Performed cross tabulation, correlation and Chi-square statistical analysis with the significant threshold value was set at p -value < .001

RESULTS AND DATA ANALYSIS

Demographic Characteristics

Physicians in terms of gender, there were 630 males and 370 females participated in the survey as mentioned in below graph.



Graph 1: Gender.

Table 1: Participants' Age.

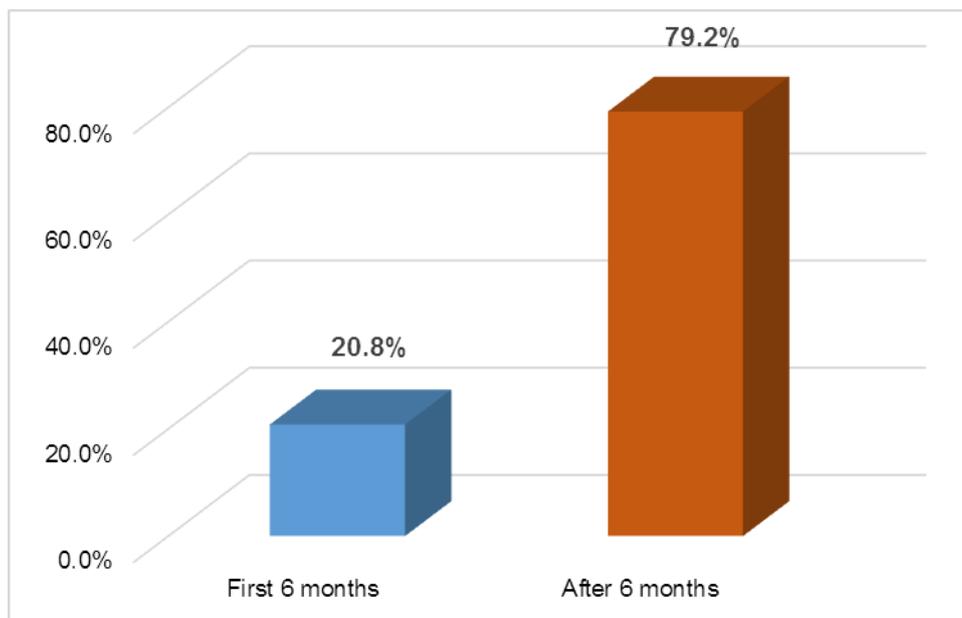
Age	NO.	%
Below 35 Years	70	7.0%
36 - 50 Years	558	55.8%
Above 50 Years	372	37.2%
Total	1000	100.0%

Respondents were categorized in three age groups who frequencies can be seen from the above table, 70 respondents were below 35 years of age, 558 in between 36-50 years, and 372 were above 50 years.

Table 2: Relation of Specialty with Clinical Experience.

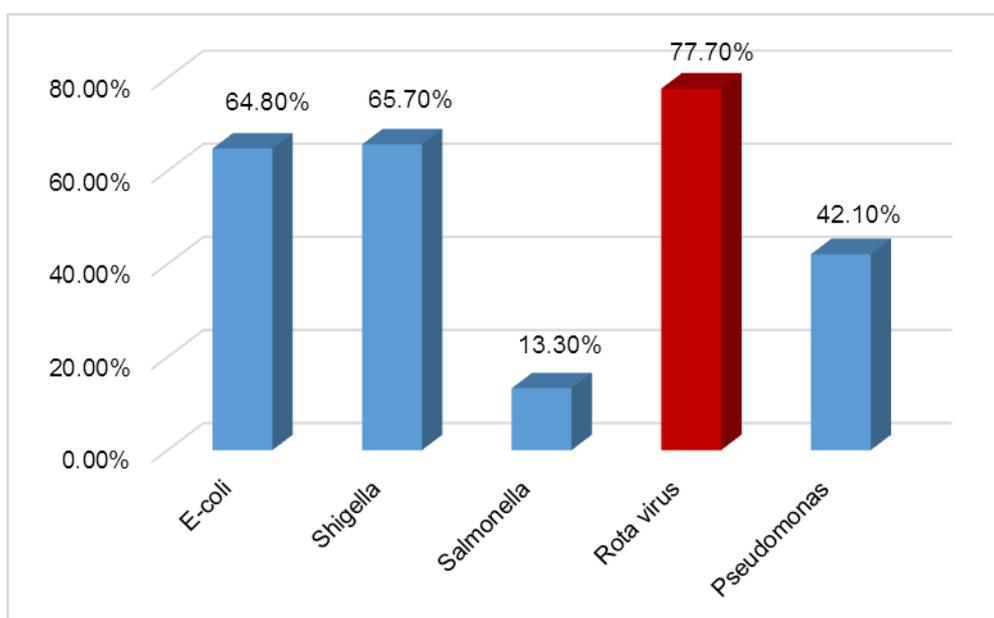
<i>Experience * Specialty Cross tabulation</i>					
			Specialty		Total
			Pediatrician	General Physician	
Experience	Less than 10 Years	No.	134	76	210
		%	23.1%	18.1%	21%
	11-20 Years	No.	244	226	470
		%	42%	53.8%	47%
	More than 20 Years	No.	202	118	320
		%	34.9%	28.1%	32%
Total		No.	580	420	1000
		%	58.0%	42.0%	100.0%

Concerning the clinical experience, It can be depicted from the above table that out of 1000 physicians, 470 (47%) had clinical experience of more than 11 years and 320 (32%) with more than 20 years of experience.



Graph 3: Critical Age of Diarrhea in Infants.

Graph 3 indicated participants’ observations about the prevalence of diarrhea in infants that was (79.2%) after 6 months of age and only (20.8%) during the first 6 months. So it can be said that after 6 months of age infants are more prone to get diarrhea.



Graph 4: Pathogenesis of diarrhea.

The pathogenesis of viral induced diarrhea was (77.7%) followed by Shigella (65.7%), E-Coli (64.8%), Pseudomonas (42.1%), and then least infected with Salmonella (13.3%).

Table 3: Beliefs about Probiotics.

			Level of HCPs familiarity with Probiotics				Total
			Extremely Familiar	Very Familiar	Familiar	Unfamiliar	
specialty	Pediatrician	No.	239	287	50	4	580
		Expected No.	149.6	190.8	179.2	60.3	580.0
		%	41.2%	49.5%	8.6%	0.7%	100.0%
	General Physician	No.	19	42	259	100	420
		Expected No.	108.4	138.2	129.8	43.7	420.0
		%	4.5%	10.0%	61.7%	23.8%	100.0%
Total	No.	258	329	309	104	1000	
	Expected No.	258.0	329.0	309.0	104.0	1000.0	
	%	25.8%	32.9%	30.9%	10.4%	100.0%	

<i>Chi-Square Tests</i>			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	589.513 ^a	3	.000
Likelihood Ratio	666.122	3	.000
Linear-by-Linear Association	491.207	1	.000
N of Valid Cases	1000		

Apart from the demographic characteristics, respondents were also evaluated in term of their level of familiarity with probiotics. There were significant number of Pds 239 (41.2%) highly familiar with probiotics compared to GPs 19 (4.5%). Moreover, only 4 (0.7%) Pds had limited knowledge of probiotics whereas 100 (23.8%) GPs were found unfamiliar with probiotics. The relationship was statistically significant $p < .001$. that the GPs were less aware compared to Pds on probiotics concept and their clinical role in infants and children.

Table 4: HCPs Perception Regarding Probiotics Safety and Efficacy.

		Specialty			
		Pediatrician		General Physician	
		No.	%	No.	%
Do you think probiotics are safe to be used in infants	Yes	571	98.4%	343	82%
	No	9	1.6%	77	18%
Do you think benefits of probiotics are strain and dose dependent	Yes	527	90.8%	58	13.8%
	No	53	9.2%	362	86.2%

Closer examination of table 4 further compared the understating of GPs and Pds in terms of probiotic safety and benefits. Both groups were satisfied with the safety of probiotics in infants and children. 58 (13.8%) GPs out of 420 and 527 Pds (90.8%) out of 580 were responded that benefits of probiotics are strain and dose.

Table 5: Recommendation of Probiotics in Diarrhea.

Acute Diarrhea

	Observed N	Expected N
No	128	500.0
Yes	872	500.0
Total	1000	

Antibiotic-associated Diarrhea

	Observed N	Expected N
No	536	500.0
Yes	464	500.0
Total	1000	

Test Statistics	
Chi-Square	553.536
df	1
Asymp. Sig.	.000
$p < .001$	

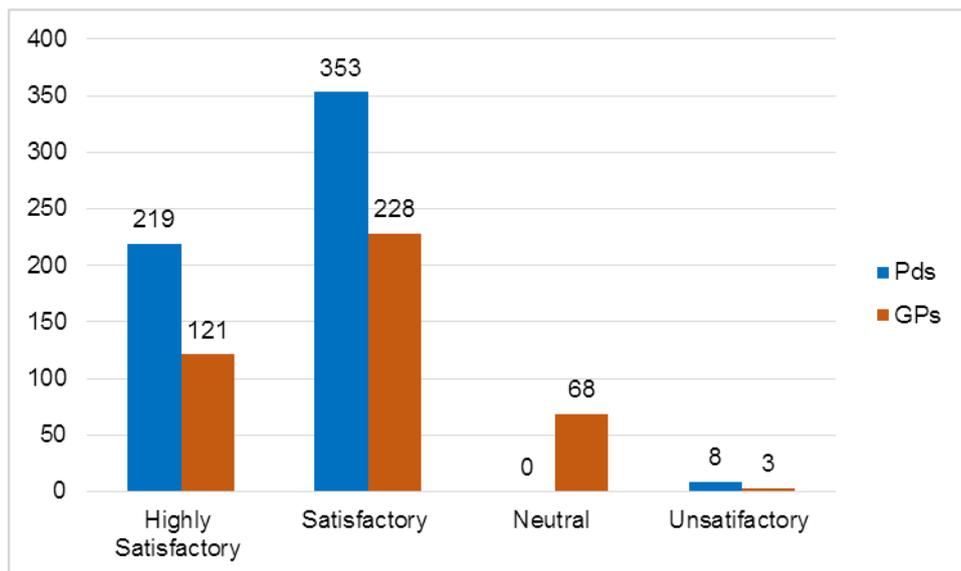
Test Statistics	
Chi-Square	5.184
df	1
Asymp. Sig.	.023
$p > .001$. (NS)	

There was a significant relationship of probiotics in acute diarrhea as out of 1000 physicians 872 were recommending probiotics in the treatment of acute diarrhea. On the other hand only 464 physicians were using the probiotics for the prevention of antibiotic-associated diarrhea.

Table 6: Responses Regarding Effective Probiotic Strains in Diarrhea.

		Specialty			
		Pediatrician		General Physician	
		No	%	No	%
S.Bularidi	No	426	42.6%	341	34.1%
	Yes	154	15.4%	79	7.9%
Lactobacillus	No	159	15.9%	93	9.3%
	Yes	421	42.1%	327	32.7%
Bifidobacterium	No	217	21.7%	193	19.3%
	Yes	363	36.3%	227	22.7%
Multiple Probiotic	No	283	28.3%	217	21.7%
	Yes	297	29.7%	203	20.3%
S.Bularidi+Probiotics	No	528	52.8%	386	38.6%
	Yes	52	5.2%	34	3.4%

It was also evaluated that which probiotics strains preferred by the Pds and GPs in the treatment of infantile diarrhea. Lactobacillus strains preference was highly recognized by both specialty such as Pds 421 (42.1%) and GPs 327 (32.7%) then with Bifidobacterium strains, Pds 363 (36.3%), GPs 227 (22.7%), and to a lesser extent convinced with the the use of multi strain probiotics and *S.Bularidi*.



Graph 5: Satisfaction level of Recommending Probiotics.

It can be depicted from the above graph that confidence of Pds was high with respect to GPs. Only 8 Pds were unsatisfactory and no one had a neutral opinion, whereas 3 GPs were unsatisfactory and 68 had a neutral point of view.

DISCUSSION

The study was performed with an ambition to evaluate the overall clinical experience of those physicians who are mostly approached by the parents for their infants and children's well-being, including the treatment of diarrheal diseases. Hence, Pediatricians and General Physicians were selected, in general, they are usually involved in providing the health care to the pediatric population, however, it has been observed in some district, flow of pediatric patients were high at GPs clinics compared to other districts where infants and children were mostly referred to the Pediatricians.

Majority 99.3% Pds were updated with the probiotics, including 41.2% were highly familiar and only 0.7% were unfamiliar. On the other hand 76.2% GPs were familiar including 4.5% were highly familiar and 100 out of 420 were unfamiliar.

Besides to investigate the knowledge level of Pds and GPs for the general concept of probiotic and their practical application, this study also identified other factors such as critical age of diarrhea, diarrheal pathogenesis, safety, effectiveness, recommended probiotic species and level of confidence to use probiotics in infants and children.

The Study revealed the prevalence of diarrhea in infants 79.2% were higher after 6 months of age, the time when infants are progressively shifting to the semi-solid diet and more likely to expose with pathogenic bacteria. Despite the fact that globally diarrheal mortality is being controlled to a certain level, but it remains a second leading cause of mortality in infants and children. Since, a prevalence of viral, bacterial and parasitic gut infections are highest in developing countries.

Global enteric multicenter study (GEMS) which was conducted in South Asia, including Pakistan observed the causative pathogens includes, rotavirus, Cryptosporidium, Shigella, and Enterotoxigenic E. coli, Involved in moderate to severe diarrhea in infants and children aged below 5 years of age. (Kotloff et al. 2012).

Researcher identified the physicians point of view about the pathogens frequently involved in diarrheal diseases. Physicians as per intensity and clinical experience responded to the Rotavirus then Shigella, E-Coli, Pseudomonas and finally Salmonella.

Since in Pakistan several studies have been done to investigate the causative diarrheagenic pathogens usually involved in children aged below 5 years. (Irfan et al. 2017, Saeed et al. 2015, Guhar et al. 2015, Alam et al. 2013, Vikram et al. 2008, Zafar et al. 2005, Ali et al. 2003, Bari et al. 1998).

It has been found that most of the physicians do recommend diarrheal treatment without lab test because of multiple factors such as a financial burden, parents required fast recovery, less follow up, unawareness, and still the trend is not common in our society, however, some leading institutes are doing stool tests for better diagnosis and effective treatment.

Overall Pds were more confident compared to GPs that probiotics are safe and effective to be used in infants and children, but still there is a need to know that all probiotics are not safe and their benefits depend upon the strain and their effective dose. Many of the physicians were confused in between the species and strains of probiotics as all species are not equally effective.

There is a need that physicians should investigate a strain which is being used has FDA GRAS status and the amount of probiotics contain in a single dose.

Multiple studies have been done on the clinical safety and efficacy (Hanna et al. 2014, Thomas et al. 2010, Indrio et al, 2009, Rautava et al. 2009, Vlieger et al. 2009, Arine et al. 2009, Chouraqui et al. 2008).

A positive trend has been observed for the recommendation of probiotics in acute diarrhea in order to reduce the duration and frequency of diarrheal episodes and it has been established with multiple studies (Wilkins et al. 2017, Cruchet et al. 2015, Lee et al. 2015, Braegger et al. 2011, Neveen et al. 2015, Dinleyici et al. 2015).

Since the use of antibiotics is very common in Pakistan for the treatment and as a preventive therapy against secondary bacterial infections. Moreover, there is a need to use probiotics along with antibiotic treatment as several studies suggested their role in the prevention of antibiotic-associated diarrhea (Stuart et al. 2012, Sharp et al. 2009, Marchand, 2015).

Bifidobacterium and *Lactobacillus* strains are the widely used probiotics also endorsed by the physicians during the survey. Neither Pediatricians nor General Physicians remained unsatisfied with the effective role of probiotics in diarrhea, however, knowledge and recommendation were varied among Pds and GPs.

CONCLUSION

It has been concluded that Pediatricians are more updated compared to GPs with regard to the conceptual understanding of probiotics and their clinical use in infants and children. Moreover, there were substantial differences in beliefs and barriers about the use of probiotics which is needed for further exploration.

There is a need of time to work on the present study outcomes. Leading and knowledgeable healthcare professionals and health department may play a vital role in the awareness of the medical community in order to make sure the correct use of probiotics, not only for the treatment but for the preventive purpose as well.

The finding may motivate the future researcher to conduct more research on probiotics in Pakistan which will contribute in advancement of healthcare, especially in pediatric community.

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