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Brief Communication

Glimpse on shigellosis from endemic Bangladesh: decades of observation with urban-rural differentials

Dipesh Kumar Barua[1], Sumon Kumar Das[2], Abu Syed Golam Faruque[3], Mohammad Habibur Rahman Sarker[4], Jui Das[5], Shahnawaz Ahmed[6], Mohammad Abdul Malek[7], KM Shahunja[8], Mohammod Jobayer Chisti[9]

Abstract

The Diarrhoeal Disease Surveillence System of icddr,b noted increasing proportion of Shigella sonnei and Shigella flexneri at urban Dhaka and rural Matlab from 2000 to 2013. Shigella sonnei appeared as emerging serogroup during 2009-13 compared to 2000-04 among individuals aged ≥ 60 years both in Dhaka and Matlab, while Shigella boydii and Shigella flexneri showed remarkable increase with 400% and 100% respectively in Dhaka, and a moderate increase (55%) both Shigella boydii and Shigella flexneri in Matlab. However, decreased trend of all the Shigella species in both the sites except Shigella dysenteriae in Dhaka was found among under-5 children. Individuals from higher socio-economic status such as those having a monthly family income of >100 USD had protective role against shigellosis in Dhaka during 2009-13. Shigella species and host factors are responsible for changing trend as well as predictors of shigellosis.

Key Words: *Bangladesh, rural, sero-groups, Shigella, urban*

Short communication:

The mortality due to *Shigella* has reduced over the period in epidemic zones due to use of antimicrobials, better sanitation, improved economic status and disappearance of the most virulent species *Shigella dysenteriae* type 1, even though its morbidity is still a great concern.[1] Study also revealed that changing patterns of *Shigella* sero-groups among under-5 children with increasing isolation trend of *Shigella sonnei*, while falling drift for *Shigella dysenteriae* in urban and rural Bangladesh [2]. However, there is scarcity of such information for other age groups such as, adults or elderly. Studies also reported significant decline of *Shigella* cases especially in urban area, but the scenario from rural area is inconsistent with higher prevalence of shigellosis especially among under-5 children.[2,3] Clinical severity, for example, less severe to fatal outcome varied mainly due to virulence properties of the *Shigella* isolates as well as emergence of multidrug resistant strains warned development and introduction of effective vaccination strategies.[4] However, such strategy may be species specific [5], and information on current prevalence of different species of *Shigella* is grossly lacking from endemic countries mostly due to lack of any long term hospital based surveillance system.

The Diarrhoeal Disease Surveillance System (DDSS) of International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) (approved by Research Review Committee and Ethical Review Committee) maintaining a round the clock diarrhoeal disease surveillance in it's urban Dhaka and rural Matlab hospital.[2,4] In Dhaka, it systematically enrols (2% since 1996; every 50th) patients attending the facility irrespective of age and sex; and in Matlab, all patients coming from the Health and Demographic Surveillance System (HDSS) area are enrolled. It records all socio-demographic, clinical informations and collect stool sample for detection of common pathogens (*Shigella* spp., *Vibrio cholerae*, *Salmonella*, and rotavirus) using standard laboratory methods.[2,4] Thus, the present study aimed to demonstrate the changing pattern of *Shigella* sero-groups across different age groups, and also study determinants of such changes at different time periods over last one and half decades (2000-2004 and 2009-2013) in urban and rural areas. Analysis was done for two time periods (5 years apart) of the

1. Dr. Dipesh Kumar Barua, MBBS, Project Research Physician, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b)
2. Dr. Sumon Kumar Das, MBBS, Associate Scientist, icddr,b, School of Public Health, The University of Queensland, Brisbane, Australia
3. Dr. Abu Syed Golam Faruque, MBBS, MPH, Consultant, icddr,b
4. Dr. Mohammad Habibur Rahman Sarker, MPH, Medical Officer, icddr,b
5. Dr. Jui Das, MS, Research Assistant, icddr,b
6. Dr. Shahnawaz Ahmed, MBBS, Assistant Scientist, icddr,b
7. Dr. Mohammad Abdul Malek, MSc (Statistics), Statistician, icddr,b
8. Dr. K.M Shahunja, MBBS, Assistant Scientist, icddr,b
9. Dr.Mohammod Jobayer Chisti, MBBS, MMed, PhD, Scientist, icddr,b

Corresponding Author :

Dr. Sumon Kumar Das
MBBS, PhD student (3rd year)
Associate Scientist
Centre for Nutrition and Food Security (CNFS)
International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b)
68, Shaheed Tajuddin Ahmed Sarani
Mohakhali, Dhaka 1212, Bangladesh &
School of Public Health, The University of Queensland
Brisbane, Australia
Email: sumon@icddrb.org, s.das1@uq.edu.au

14-year observation period which has been considered as an alternative to year-wise analysis to evaluate any potential changes of predictors of shigellosis.

A total of 32,577 and 20,856 patients were enrolled in Dhaka and Matlab respectively during 2000-2013. Of them, 10,069 and 13,286 were enrolled for 1st (2000-2004) and 2nd (2009-2013) observation periods respectively in Dhaka and the corresponding figures for Matlab were 7,582 and 7,019. Individuals with diarrhoea and stool specimens grew *Shigella* 615 (6%) and 361 (3%) for Dhaka in two time periods; 774 (10%) and 524 (8%) for Matlab respectively were considered as cases; conversely, non-*Shigella* cases constituted the comparison group; 9,454 (93%) and 12,925 (97%) for Dhaka in two time periods; 6,808 (90%) and 6,495 (93%) for Matlab respectively. To ascertain the changing patterns of the determinants of shigellosis, analysis was performed at two different time periods (2000-04, and 2009-13) in two sites separately. Percent changes of different sero-groups of *Shigella* (*Shigella flexneri*, *Shigella dysenteriae*, *Shigella sonnei* and *Shigella boydii*) were determined by subtracting the isolation rate from 1st observation period to 2ndobservation period and dividing by 1st observation period and multiplying by 100. Such calculation was also done for different age strata (<5 years, 5-<19 years, 19-59 years, and ≥60 years). Both univariate and multivariate analyses were performed to determine the changes of potential socio-demographic, clinical and stool microscopic examination characteristics between two observation periods in Dhaka and Matlab separately. SPSS (Chicago, IL version 20.0) was used to perform all the analyses with a probability value <0.05 as statistical significant.

In Dhaka, the proportion of *Shigella flexneri* and *Shigella sonnei* increased from 46% and 12% to 52% (13% increase) and 25% (108% increase) respectively between 2000 and 2013. While the proportion of *Shigella dysenteriae* and *Shigella boydii* decreased from 18% to 3% (83% reduction) and 24% to 20% (17% reduction) from 2000 to 2013. During 2000-04, *Shigella sonnei* was not detected in the ≥60 year's age group; however, it represented 5% of total *Shigella* isolates among different age groups in the 2009-13. Moreover, *Shigella boydii* and *Shigella flexneri* also increased significantly with 400% (from 2% to 10%) and 100% (from 5% to 10 %) in the ≥60 year's age group during 2nd observation period (2009-13) in Dhaka. Similarly, in Matlab, the proportion of *Shigella flexneri* increased by 15% (from 59% to 68%) and *Shigella sonnei* by 100% (from 11% to 22%) between 2000 and 2013. However, *Shigella dysenteriae* and *Shigella boydii* were reduced by 83% (from 18% to 3%) and 33% (from 12% to 8%), respectively, over the study period in Matlab. In the ≥60 year's age group, *Shigella sonnei* was not detected during 1st observation period (2000-04); however, it appeared as an emerging serogroup with 5% of total *Shigella* isolates across different age strata during the 2nd time period (2009-13). Furthermore, isolation rates of *Shigella boydii* and *Shigella flexneri* also increased by 55% (rural site) during 2nd time period (2009-13) in this age group.

In Dhaka, shigellosis in under-5 children was commonly observed in 2000-04. Shigellosis was less often observed in individuals aged 19-59 years during 1st [aOR- 0.69, 95% CI: (0.49-0.95)] and 2nd [0.63 (0.41-0.95)] observation periods; however, it was only observed during 2009-13 [0.54 (0.35-0.82)] in Matlab. Elderly (≥60 years) frequently reporting with shigellosis [1.67 (1.06-2.64)] was observed during the 1st time period in Maltab only. As expected, patient population from higher socio-economic context (having a monthly family income of >100 USD) had been found to seek care less often [0.74(0.56-0.98)0.032] for shigellosis during 2nd observation period in Dhaka; although, no such patterns were observed for other time periods irrespective of site. Considering stool microscopic examination findings, presence of red blood cells was significantly associated with *Shigella* in all time periods except 2009-13 in Dhaka; however, for faecal leucocytes it was only most frequently in 2nd observation period in Dhaka [3.77 (2.37-5.95) <0.001]. Other socio-demographic characteristics, clinical features and stool microscopic examining findings were indistinguishable between the sites in two observation periods.

Emergence of *Shigella sonnei* as leading species in our study population is an important observation for the clinicians and essentially demand several explanations: Firstly, *Pleisomonas shigelloides* serotype 017, commonly found in contaminated water, share identical surface antigen with *S. sonnei* [6]. Improvement of water supplies over the period, resulting in decrease in the prevalence of *Pleisomonas shigelloides*; consequently, there was attenuation for cross protection against *Shigella sonnei*. Secondly, *Acanthamoeba castellanii,* an ubiquitous amoeba, act as environmental host for *Shigella sonnei* and allows to withstand chlorination and other adverse environmental conditions [7]. Finally, *Shigella sonnei* acquires and/or maintains a wider array of antimicrobial resistance genes from other enterobacteriace, particularly *Escherichia coli* and *Klebsiella* [8]; whereas, *Shigella flexneri* loses genes faster than any other *Shigella* species [9]. Moreover, increasing isolation rate of *Shigella* species among elderly (≥60 years) population like other global context, could be due to physiological changes such as decreased mucosal immunity, reduced acid production, altered gastrointestinal motility and increased gastrointestinal transit time, poor nutrition and unhygienic practices.

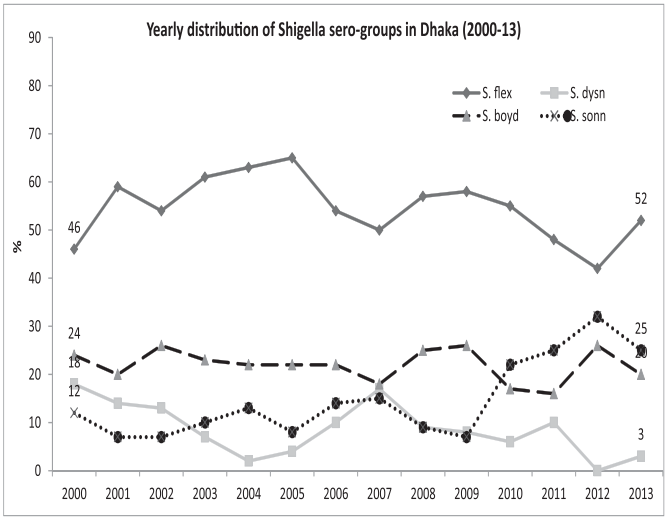
Conversely, downward trend of all the *Shigella* species among under-5 children in both the sites except *Shigella dysenteriae* in Dhaka is one of the markers of improvement of public health in Bangladesh, and might be due to improvement of nutritional status, and improved water and sanitation practices over the period [10]. Interestingly, during 2nd observation period in Dhaka, red blood cells in stool microscopic examination did not show significant increase, and thus may be due to changing sero-groups with emergence of *Shigella sonnei* which is less virulent in producing mucosal ulceration, and because reduced prevalence of highly virulent *Shigella dysenteriae.*

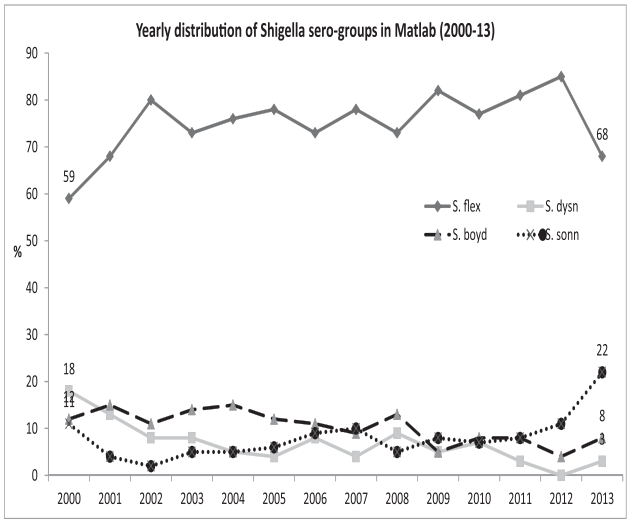
Table: Distribution and association of determinants of *Shigella* at different time periods in Dhaka and Matlab (2000-04 and 2009-13)

Characteristics	Dhaka 2000-04 Adjusted OR (95% CI)	2009-13 Adjusted OR (95% CI)	Matlab 2000-04 Adjusted OR (95% CI)	2009-13 Adjusted OR (95% CI)
Socio-demographic				
Male Sex	1.03 (0.85-1.24)	1.08 (0.85-1.38)	1.06 (0.88-1.27)	1.19 (0.96-1.48)
Age				
<5 years	1.58 (1.13-2.22) *	1.53 (0.97-2.39)	1.18 (0.82-1.69)	1.15 (0.75-1.75)
5-<19 years	1	1	1	1
19-59 years	0.69 (0.49-0.95) *	0.63 (0.41-0.95) *	0.84 (0.57-1.22)	0.54 (0.35-0.82) *
≥ 60 years	1.14 (0.68-1.91)	1.55 (0.88-2.70)	1.67 (1.06-2.64) *	1.06 (0.65-1.70)
Family member (>5)	0.91 (0.75-1.11)	0.91 (0.70-1.18)	1.08 (0.89-1.29)	0.95 (0.76-1.19)
Monthly family income (>100 USD)	1.03 (0.82-1.29)	0.74 (0.56-0.98) *	0.98 (0.79-1.21)	1.08 (0.86-1.36)
Living in the slum	1.02 (0.75-1.40)	1.22 (0.76-1.96)	-	-
Drinking non-tape water	0.90 (0.71-1.14)	0.97 (0.70-1.32)	0.73 (0.17-3.00)	0.89 (0.47-1.71)
Drinking un-boiled water	0.57 (0.84-1.37)	0.97 (0.72-1.29)	0.82 (0.43-1.56)	1.38 (0.54-3.54)
Use of non-sanitary toilet	1.04 (0.84-1.29)	1.05 (0.70-1.44)	1.09 (0.82-1.46)	0.98 (0.73-1.32)
Distance travelled to reach hospital (> 10 Kilometres)	0.80 (0.64-1.01)	0.86 (0.63-1.17)	0.96 (0.78-1.18)	1.14 (0.90-1.43)
Clinical				
Abdominal pain	1.40 (1.14-1.73) *	1.73 (1.33-2.25) *	1.63 (1.344-1.98) *	1.76 (1.35-2.28) *
Fever (temperature 37.8oC)	1.56 (1.12-2.16) *	1.69 (1.13-2.52) *	2.33 (1.89-2.88) *	1.75 (1.35-2.26) *
Duration of diarrhoea (≤24 hours)	1.01 (0.87-1.35)	0.99 (0.75-1.31)	1.18 (0.94-1.48)	0.98 (0.77-1.25)
Non-watery stool	0.58 (0.43-0.81) *	0.54 (0.36-0.79) *	0.41 (0.33-0.51) *	0.46 (0.35-0.59) *
Blood in stool	2.92 (2.06-4.24) *	7.53 (5.40-10.49) *	3.02 (2.42-3.77) *	3.69 (2.84-4.79) *
Number of stools in 24 hours (>10)	1.29 (1.07-1.56) *	1.08 (0.83-1.39)	1.32 (1.10-1.59) *	1.24 (0.98-1.55)
Vomiting in last 24 hours	0.85 (0.67-1.08)	0.64 (0.49-0.84) *	0.69 (0.56-0.86) *	0.88 (0.69-1.22)
Some-to-severe dehydration	0.83 (0.66-1.04)	1.08 (0.78-1.48)	0.82 (0.62-1.07)	0.79 (0.59-1.07)
Hospital stay (≥24 hours)	0.98 (0.81-1.27)	0.91 (0.68-1.20)	1.09 (0.88-1.33)	0.95 (0.75-1.19)
IV used for rehydration	0.65 (0.49-0.84) *	0.46 (0.33-0.65) *	0.53 (0.36-0.79) *	0.39 (0.25-0.62) *
Use of antimicrobials at home	1.19 (0.97-1.45)	0.92 (0.69-1.24)	1.05 (0.86-1.27)	0.88 (0.70-1.12)
Not use of ORS at home	0.85 (0.56-1.28)	1.17 (0.69-1.95)	0.78 (0.77-1.22)	1.06 (0.79-1.41)
Stool microscopic				
Faecal leucocytes >10/HPF	1.28 (0.91-1.80)	3.77 (2.37-5.95) *	1.19 (0.79-1.80)	1.05 (0.51-2.15)
Red blood cell	2.03 (1.54-2.68) *	1.54 (0.85-2.81)	2.04 (1.38-3.01) *	3.01 (1.53-5.92) *
Macrophages	2.87 (2.13-3.87) *	2.16 (1.26-3.67) *	2.85 (2.17-3.75) *	5.47 (4.06-7.38) *

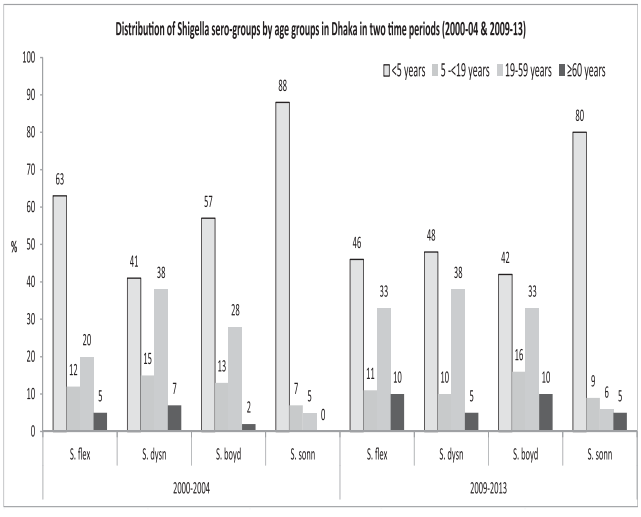
*p< 0.05

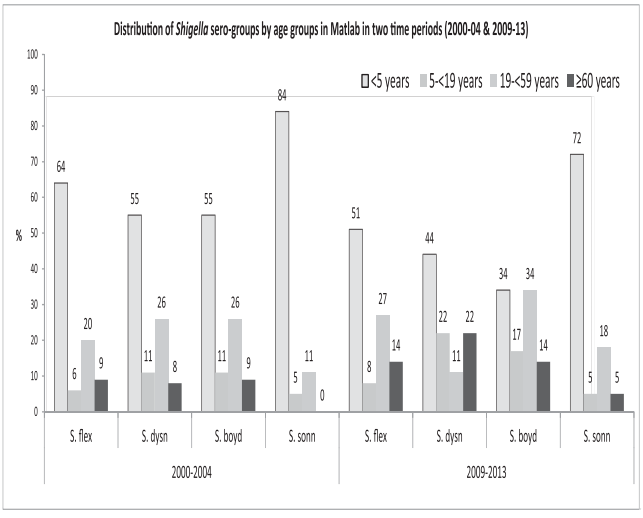
Figure: Overall and age specific changes in sero-groups of *Shigella*in Dhaka and Matlab (2000-13)





Sero-groups	Dhaka	Matlab
S. flexneri	↑13%	↑15%
S. dysenteriae	↓83%	↓86%
S. boydii	↓17%	↓33%
S. sonnei	↑108%	↑100%





Sero-groups	<5 years	5-<19 years	19-59 years	≥60 years
S. flexneri	↓27%	↓8%	↑65%	↑100%
S. dysenteriae	↑17%	↓33%	↑1%	↓28%
S. boydii	↓26%	↑23%	↑18%	↑400%
S. sonnei	↓9%	↑28%	↑20%	*

Sero-groups	<5 years	5-<19 years	19-59 years	≥60 years
S. flexneri	↓20%	↑33%	↑35%	↑55%
S. dysenteriae	↓20%	↑100%	↓58%	↑18%
S. boydii	↓38%	↑55%	↑31%	↑55%
S. sonnei	↓14%	↓9%	↑64%	*

*= no *Shigella sonnei* was found at 1st observation period

In the present study, significant impacts of different socio-demographic and water-sanitation practices were not observed among individuals with shigellosis compared to non-*Shigella* individuals except protective role of higher socio-economic status reflected by monthly family income >100 USD especially in Dhaka at 2nd observation period (2009-13). It could be concluded that such factors are not impacting on changing trend or risks, rather species and host factors are responsible for shigellosis. The present study was conducted only in two hospitals; thus, respondents may not be representative and findings may not be generalizable for the whole country. However, large sample size, unbiased systematic sampling, quality laboratory performance, and longer study period are the strengths of the study.

Conflict of interest:

No conflict of interest.

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