IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 12 Ver. 1 (December. 2018), PP 50-55
www.iosrjournals.org

"Risk factors of typhoid fever in children: A study in several private clinics, Jamalpur, Bangladesh"

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***Abstract**: We conducted a case-control type of descriptive study during October 2017 to April 2018 in several private clinics, Jamalpur, Bangladesh. Our aim was to find out risk factors of Typhoid fever in children. The sample was drawn from the selected clinics, were 200 (100 cases and 100 controls). Out of 100 participants in each group 70% cases and 69% controls respondents were mother of the children. Most of the study subjects were under 5 years. Mean ± SD of age were (4.9042 ± 3.35575) for cases and (3.4951 ± 2.49218) for controls. Age distribution of the children was statistically significant where p -value was 0.0001 for t-test and 0.01151045 for chi-square ($p<0.05$). Most of the children were urban dwellers 90% cases and 96% controls. The difference was statistically significant ($\chi^2 = 4.134$, $p = 0.04202989$) and 35% of cases drunk supply water in comparison with 14% of controls. There was positive association of drinking supply water and typhoid fever (RR=2.6316 and OR=3.5101 and $\chi^2 = 12.85$; p-value = 0.000337). Crowded habitat was reported by 38% of Cases and 11% of Controls. There is a strong association of crowded condition of habitat and typhoid fever (RR = 3.5463; OR = 5.1269 and $\chi^2 = 20.41$; p =0.0001). There was no positive association of different blood group but when each group was individually considered, blood group 'B' indicated there may be some positive association (RR = 1.4505, OR = 1.8713 and $\chi^2 = 4.66$, p = 0.030873). Only 3% children in case group and 4% in control group had Rh negative blood group. Widal test result was positive in 83% of cases; the remaining 17% were found to be Widal negative. Typhoid fever has a strong relation with socio-economic and demographic conditions.**

Key words: *Risk factors, Typhoid fever, Socio-economic conditions, Socio-demographic conditions*

Date of Submission: 25-11-2018 Date of acceptance: 07-12-2018

I. Introduction

Typhoid fever is a type of enteric fever, along with paratyphoid fever. The cause is the bacterium Salmonella Typhi, also known as Salmonella enterica serotype Typhi, growing in the intestines and blood. Typhoid is spread by eating or drinking food or water contaminated with the feces of an infected person. Typhoid fever is an important cause of morbidity and mortality in many developing countries. In 2000, it was estimated that over 2.16 million episodes of typhoid occurred worldwide, resulting in 216 000 deaths, and that more than 90% of this morbidity and mortality occurred in Asia.[1] Typhoid fever is endemic in all parts of Bangladesh and still constitutes a significant health hazard. The resistance of *Salmonella enterica* subspecies *enterica* serovar typhi (*S.* Typhi) to chloramphenicol was first reported in India from Kerala, where a substantial outbreak took place in 1972. Since then multidrug-resistant strains of *S. typhi* have escalated into a worldwide problem. The steadily increasing multidrug resistance in *S. typhi* strains is a cause of grave concern in Bangladesh, where such strains are endemic in many parts.[2] Typhoid fever may occur at any age, but it is considered to be a disease mainly of children and young adults. In endemic areas, the highest rate occurs in children aged 8-13 years. In a recent study from slums of Delhi, it was found that contrary to popular belief, the disease affects even children aged one to five years. About 20-30% of typhoid fever cases are children below ten years.[3] According to Indonesia Demographic and Health Survey (2002 – 03) report prevalence of typhoid fever in children under five years of age was

26%.[4] Human ABO blood group have been associated withsusceptibility to certain infection.[5,6] It has been observed that some historical pandemics have influenced the current distribution of the ABO gene frequencies in different part of the world.[7] Various adaptations of people with different phenotypes of ABO blood group are considered to be the result of screening mutagens. Immunologists explain this by the presence of some pathogens of antigens similar to antigens of human blood.[8] During long-term observations it is found that the holders of blood groups O, A, B, and AB have different predisposition to diseases. Statistical studies confirm that holders of blood group A get sick of viral hepatitis more often, and O-type people are less resistant to influenza virus.[12] According on the blood group, children under 7 years old usually get sick with diseases such as paratyphoid fever, rubella, scarlet fever, colibacillosis, and among children with blood group A it fails to develop immunity against smallpox even at re-vaccination.[8] Purification of supply water, improvement of basic sanitation and promotion of food hygiene are essential measures to interrupt transmission of typhoid fever.[9] So, there is a great need for the people to be aware of all the consequences of typhoid fever and it is the most important area where the health personnel should take serious measures to create an understanding and awareness among the public regarding typhoid fever and its risk factors. Typhoid fever continues to be a major health problem in Bangladesh. In the topical areas however, it is endemic in many places, due to the low standard of living, unprotected water supply and unhygienic methods in the preparation and handling of food. Many children with Typhoid fever are admitted in the hospital with various complications. Few studies have been performed worldwide about these particular topics of Typhoid fever. But in Bangladesh such studies is practically absent. If these can be done then probably we will be able to increase the awareness about Typhoid fever so they may enjoy a good quality of life .

II. Objectives

General objective:

- To assess the risk factors of typhoid fever in children.

Specific objectives:

- To find out the socio-economic status of children with typhoid fever.
- To find out the socio-demographic status of children with typhoid fever

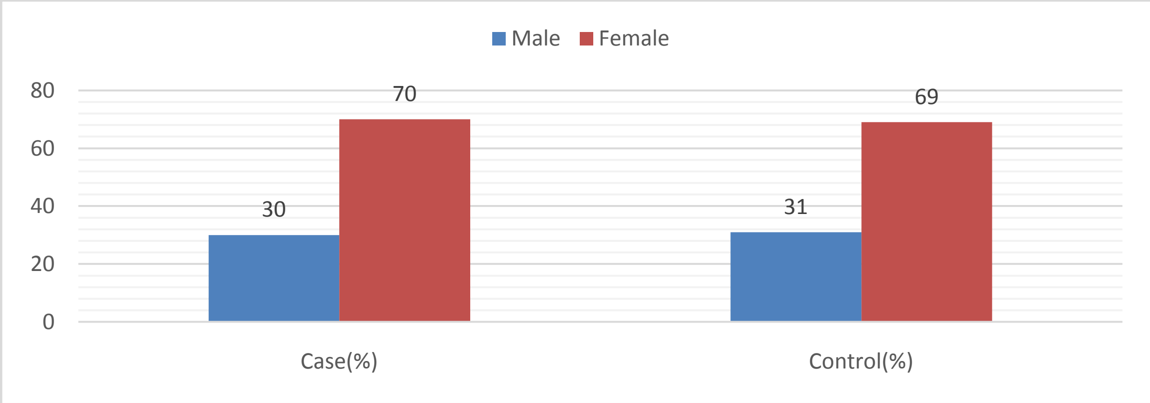
III. Materials and Methods

We conducted a case-control type of study during October 2017 to April 2018 in several private clinics, Jamalpur, Bangladesh. Our aim was to find out risk factors of Typhoid fever among children. The sample size was drawn from the selected clinics, was 200 (100 cases and 100 controls)The study included children of paediatric age group both male and female. For each baby detailed history of age, sex, socio-economic information, and blood group were recorded. Subjects were grouped on the basis of age, sex, blood phenotypes, ABO and Rh into the case (Typhoid positive) and controls (Typhoid negative).Two hundred(200) samples were purposively selected for the study which was divided into 100 cases and 100 controls. 1 to 15 years old children and toddlers were included in the study who were suffering from typhoid confirmed by Widal test and or culture positive as case and suffering from any febrile illness, other than typhoid fever as control group. Participants suffered from meningitis, febrile convulsion, immune-compromised children, unwillingness to participate were excluded from the study. Prior to data collection, a questionnaire was designed for this study by reviewing all the available questionnaire of previous studies. The questionnaire was finalized following pretesting. Prior to answering the semi-structured questionnaire, every respondent had to undersign an informed written consent. All the data were collected and recorded systematically in a questionnaire and was analyzed using computer software SPSS -17 (Statistical Package for Social Sciences).

IV. Results

This study was undertaken with the objective to find out risk factors of typhoid fever among children. A total of 200 children, out of whom 100 were suffering from typhoid fever (cases) and 100 were non-typhoid (controls), were included in this study.

Figure: 1 Distribution of the respondents (n=200)



$\chi2$ =-3.069 ,P-value=0.07979854

Figure shows that Females are dominating in the distribution. Average seventy (70%) percent in cases and sixty nine (69%) percent in control.Malesare thirty (30%)percent and thirty one (31%)percent in case group and control group respectively. No positive association between the groups as p-value is greater than 0.05.

Table: 1 Demographic characteristics of the study participants (n=200)

Characteristics'	Case (%)	Control (%)	$\chi2$	P-value
Distribution of the children by Gender			4.284	0.0384727
Male	69	55		
Female	31	45		
Distribution of the children by age group			4.009(t-test)	0.0001
≤ 5	62	81		
5-10	26	16		
10>	12	3		
Distribution of the children by Religion			1.709	0.42549589
Muslim	96	91		
Hindu	4	9		
Others	0	0		
Educational status of the respondents			48.024	0. 0001
Illiterate	4	1		
Primary	30	8		
Secondary	22	28		
Higher secondary	15	51		
Graduate	20	12		
University	9	0		
Occupation of the respondents			10.676	0.00480547
Job	57	65		
Business	30	34		
Others	13	1		

The most of the children were male, 69% in cases and 55% in controls. $\chi2$ =4.284, df = 1, p-value = 0.038; which means there are an association between different gender groups. By age distributions of both groups were in the '≤ 5 years' age group; 62% of Cases group and 81% of Controls group were in the age group. The p-value was 0.0001 for t-test and 0.01151045 for chi-square, which means there was an association in age distribution between the groups. ($p<0.05$) . Male and Female ratio was about 1: 2.22in cases and 1:1.22 in controls. The difference between age groups was statistically significant ($\chi2$ = 4.284, df = 1; p-value = 0.03847271) ($p<0.05$). Education of the respondents were mostly(57%) below SSC and the association were statistically positive. In the occupational category, most of them were job holders (57%) and the relation was positive statistically.

Table-2: Risk factors of the respondents (n=200)

Respondents	Case (%), n= 100	Control(%), n=100	Statistical Analysis	χ2	P-value
Area of Residence					
Urban	90	96		4.134	0.04
Rural	10	4			
Water consumption					
Boiled water	61	77	RR=0.8044; 95% CI: 0.6663-0.9713 OR=0.4894; 95% CI: 0.2647-0.9047	5.28	0.02
Tube well	4	9	RR=0.33; 95% CI: 0.0981-1.11 OR=0.3071; 95% CI: 0.0857-1.1013	3.62	0.05
Supply water	35	14	RR=2.6316; 95% CI: 1.4923-4.6405 OR=3.5101; 95% CI: 1.7283-7.1291	12.85	0.0003
Habitat					
Neat	62	89	RR=3.5463; 95% CI: 1.9158-6.5645 OR=5.1269; 95% CI: 2.4237-10.8452	20.41	0.0001
Crowded	38	11			
Sanitation					
Sanitary	95	98		4.186	0.04
Hanging	4	1			
Open	1	1			
Food Habits					
Raw food	18	6	RR=3.1552; 95% CI: 1.2933-7.6977 OR=3.6379; 95% CI: 1.3656-9.6914	7.37	0.006
No raw food	82	94			

Above table shows that most of the children were urban dwellers (90% in cases and 96% in controls); the difference was statistically significant ($\chi2 = 4.134$, $p = 0.04202989$). 35% of cases drink supply water in comparison with only 14% of controls. There was a positive association of drinking supply water and typhoid fever (RR=2.6316 and OR=3.5101 and $\chi2$ =12.85; p-value = 0.000337). Crowded habitat was reported by 38% of Cases and 11% of Controls. There may be strong association of crowded condition of habitat and typhoid fever (RR = 3.5463; OR = 5.1269 and $\chi2 = 20.41$; $p < 0.0001$). Out of total 200 participants 5 cases used non-sanitary latrine in cases and 2 in controls ($\chi2 = 4.186$, $p = 0.04075916$). 18% of cases and 6% of controls were found to have the practice of 'Eating raw or under cooked food' and was a positive association.

Table-3: Laboratory findings of all study participants (n=200)

Blood Group	Cases (n=100) Percent	Controls(n=100) Percent	Statistical calculations
O	16	27	RR=0.6073; 95% CI: 0.3535-1.0433 OR=0.5285; 95% CI: 0.2665-1.0482 $\chi^2 = 3.39$; p-value = 0.065593
A	26	24	RR=1.0; 95% CI: 0.5272-1.6162 OR=1.0; 95% CI: 0.6187-1.8967 $\chi^2 = 0.0$; p-value = 1.0
B	48	33	RR=1.4505; 95% CI: 1.0287-2.0452 OR=1.8713; 95% CI: 1.0565-3.3144 $\chi^2 = 4.66$; p-value = 0.030873
`AB	10	16	RR=0.7042; 95% CI: 0.3293-1.5061 OR=0.6714; 95% CI: 0.2837-1.5889 $\chi^2 =0.83$; p-value = 0.362273

Above table shows that most of the children having blood group B, 48% in case and 33% in control respectively. It is illustrates that in a gross calculation, there was no statistically difference in distribution of ABO blood group of the children between cases and controls ($\chi2 = 6.125$ df = 3; p-value = 0.10568457). However, when each group was individually considered, blood group 'B' indicated there may be some positive association with typhoid fever [RR = 1.4505 (95% CI: 1.0287-2.0452) and OR = 1.8713 (95% CI: 1.0565-3.3144)]. The difference was statistically significant χ2 = 4.66, df = 1; p-value = 0.030873. ($p < 0.05$)

Table-4: Laboratory findings of all study participants (n=200)

Blood group	Cases (n=100) Percent	Controls (n=100) Percent	Statistical calculations
Rh typing of Blood			
Positive	97	96	RR=0.7857; 95% CI: 0.1909-3.2341
Negative	3	4	OR=0.7784; 95% CI: 0.1791-3.3828
			χ^2=0.112 df=1; p-value = 0.73787855
Widal Test			
Positive	83	0	
Negative	17	100	

Above Table shows that only 3% children in case group and 4% in control group had Rh negative blood group. There was no positive association [RR = 0.7857 (95% CI: 0.1909-3.2341) and OR = 0.7784 (95% CI: 0.1791-3.3828. Widal test result was positive in 83% of cases; the remaining 17% negative in case group and all (100.0%) of the controls were found to be Widal negative in control group. Participants were included on the basis of their Widal test and or blood culture findings; patients who had already done the tests were considered for this study.

V. Discussion

This study was aimed to find out risk factors of Typhoid fever among children. A total of 100 cases (typhoid fever) and 100 controls (non-typhoid) were included in this study. In both groups most of the study participants were in under 5 years’ age group , Mean ± SD of age was, (*4.9042 ± 3.35575*) for cases and for controls (*3.4951 ± 2.49218*), p-value was 0.0001 for t-test and 0.01151045 for chi-square, which means there was statistically deference in age distribution between the groups ($p<0.05$). A study in Dhaka Metropolitan Area found, the age-specific incidence rate was highest for the 0–4 years age group (277 cases). In our study, Valenzuela CY and Herrera P found a mild susceptibility to males. The male-female ratio of typhoid cases was found to be 1.36 by Dewan AM, Comer R, Hashizume M and Ongee ET, suggesting that in this population males are either more susceptible to typhoid, or more likely to present for hospital treatment, than females. Statistical differences of educational status of the respondent is significant χ2 = 48.024, df = 5, p-value = 0.0001. There was a statistically significant difference between the groups (χ2 = 4.134, df = 2, p-value = 0.04202989) of occupational differences. In a study conducted in Dhaka Metropolitan Area (DMA) of Bangladesh, the Student's t test revealed that there is no significant difference on the occurrence of typhoid between urban and rural environments ($p>0.05$) but there was a positive association of drinking supply water with typhoid fever [RR=2.6316 (95% CI: 1.4923-4.6405); OR=3.5101 (95% CI: 1.7283-7.1291) and χ2 =12.85; p-value = 0.000337]. There statistically significant difference between the groups in the source of drinking water (χ2 = 14.75 df = 2; p-value = 0.00062673). In Kamalapur, Dhaka, Bangladesh, cases were 7·6 times more likely than controls to report drinking any unboiled water at home during the 14-day exposure period (mOR 7·6, 95% CI 2·2–26·5, P=0·002). There may be strong association of crowdie condition of habitat with typhoid fever [RR = 3.5463 (95% CI: 1.9158-6.5645) and OR = 5.1269 (95% CI: 2.4237-10.8452)]. χ2 = 20.41; p-value < 0.0001. The difference was statistically significant between the two groups (χ2 = 4.186 and p-value = 0.04075916). Ram PK, et.al. found that, cases were less likely than controls to use a latrine for defecation (mOR 0·3, 95% CI 0·1–1·0, P=0·053). Out of 120 participants in each groups 18.3% of cases and 5.8% of controls were found to have the practice of ‘Eating raw or under cooked food’ statistically strong positive association of eating raw or under cooked food and typhoid fever [RR = 3.1552 (95% CI: 1.2933-7.6977) and OR = 3.6379 (95% CI: 1.3656-9.6914)] χ2 = 7.37 df = 1; p-value = 0.006632). In Kamalapur, cases were 3·6 times (95% CI 1·1–11·2, P=0·03) more likely to report eating food from a restaurant or street stall during the 14-day exposure period than their matched controls. On gross calculation, there was no statistically difference in distribution of ABO blood group of the children between cases and controls (χ2 = 6.125 df = 3; p-value = 0.10568457). However, when each group was individually considered, blood group ‘B’ indicated there may be some positive association with typhoid fever [RR = 1.4505 (95% CI: 1.0287-2.0452) and OR = 1.8713 (95% CI: 1.0565-3.3144)]. The difference was statistically significant χ2 = 4.66, df = 1; p-value = 0.030873. Valenzuela CY and Herrera P found that, the B allele conferred protection to females. Herrera P et.ai. Tested a hypothesis that blood phenotype B is associated to typhoid fever either directly or interacting with other phenotypes of the Rh or MNSs blood systems.38 Only 3% children in case group and 4% in control group had Rh negative blood group. There was no positive association [RR = 0.7857 (95% CI: 0.1909-3.2341) and OR = 0.7784 (95% CI: 0.1791-3.3828)]; nor any statistically difference in distribution of the blood group of the children between cases and controls ($\chi2$=0.112 df=1; p-value = 0.73787855). Valenzuela CY and Herrera P reported the CDe haplotype (or the RH3 phenotype, mostly CDe/CDe) was associated with protection against Salmonella in both sexes, while cDE (or RH7, mostly cDE/cDE, and RH8, mostly cDE/cde) was associated with susceptibility to typhoid fever. Widal test result was positive in 83.0% of cases; the remaining 17% was negative in case group and all (100.0%) of the controls were found to be Widal negative. The difference of Widal test result between the groups was statistically significant $\chi2$ = 18.22, df = 1; p-value <.0001.

VI. Limitations of the study

This study was conducted in several private clinics, Jamalpur, Bangladesh. So the study findings may not reflect the exact scenario of all around the country regarding typhoid fever. The current study was conducted among 200febrile children, not a large study to draw a definite conclusion about typhoid fever. Very limited study so far found regarding fever associated with environmental conditions, not only in Bangladesh but also in the whole world. So, difficulty was faced to compare the findings to other research findings

VII. Conclusion and Recommendations

Risk of typhoid fever is higher in children aged ≤ 5 years. Male are more susceptible to develop Typhoid fever has positive association with the risk factors, such as, drinking supply water, eating raw or under cooked food, crowdie habitat and, use non-sanitary latrine. So, our recommendations are to Improvements of water-supply infrastructure or promotions of household disinfection of water represent important measures to reducing the burden of typhoid fever in endemic areas. This was a small-scale study done at a single centre over a brief period of time. A large scale, multi-centre study over long duration will give a complete picture on association of typhoid fever with various factors

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Dr. Md. Tazul Islam. , "".“Risk factors of typhoid fever in children: A study in several private clinics, Jamalpur, Bangladesh"". " IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 12, 2018, pp 50-55.