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CLINICAL PROFILE AND PREDICTORS OF OUTCOME OF PATIENTS WITH SALMONELLA TYPHI AND NON-TYPHOIDAL SALMONELLA BACTEREMIA ADMITTED AT PHILIPPINE CHILDREN'S MEDICAL CENTER

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ABSTRACT

Objectives: **This study aimed to analyze and review the clinical profile and predictors of outcome of *Salmonella* bacteremia specifically the prevalence of *Salmonella* bacteremia at PCMC and to compare the *S. typhi* bacteremia from non-typhoidal *Salmonella* with regards to demographic data of patients, clinical presentation, course of the disease, pattern of antibiotic resistance and outcome.**

Methodology: This is a retrospective study which included chart review of sixty-six subjects with *Salmonella* bacteremia from January 1998-September 2003.

Results/Conclusion: Thirty-seven had *S. typhi* bacteremia and 29 had non-typhoidal *Salmonella*. Results showed that non-typhoidal *Salmonella* bacteremia was more common for ages less than 2 years old. *S. typhi* was seen more in older age groups. Both were more common in males. The most common symptoms was fever for both *Salmonella*. Abdominal tenderness was more common in *S. typhi* while vomiting was more common in non-typhoidal *Salmonella*. Ileitis was a significant complication of *S. typhi*; while meningitis was a significant complication of non-typhoidal *Salmonella*. Non-typhoidal *Salmonella* showed increased resistance to Ampicillin. It also showed resistance to Cotrimoxazole and Chloramphenicol. Chloramphenicol is still a good drug for *S. typhi*. The predictors of outcome of *Salmonella* bacteremia were the duration of fever prior to admission and the duration of illness. These had a linear relationship with the outcome.

INTRODUCTION

Salmonella infection is a major public health problem globally especially in developing countries including the Philippines.[1] This is due to poor environmental sanitation especially in places where water supply is unsafe and sanitation is substandard.

Salmonella is divided into different major subgroups namely: *Salmonella* Group A to *E. Salmonella typhi* belongs to *Salmonella* Group D. However, three other serotypes of *Salmonella* which are non-typhoidal belong to this subgroup namely: *S. enteritidis, S. dublin,* and *S. strasbourg*. The rest of the non-typhoidal *Salmonellae* are the serogroups A, exemplified by *S. paratyphi* A; Group B which is composed of *S. paratyphi B, S. saintpaul, S. typhimurium, S. heidelberg;* Group C, exemplified by *S. paratyphi C, S. cholerasuis*; Group E, composed of *S. newton*, and *S. illinois*[1]. At PCMC, *Salmonella* infections were not reported by specific species but by grouping. Since the infection was comprised of a large group of etiologic agents and may have non-specific manifestations, it was very important that people should be aware of the prevalence of *Salmonella* infection especially here in Manila so as to prevent further increase in the number of cases. Knowledge of this could help us disseminate information on the proper environmental sanitation, water preparation and proper hygiene.

Septicemia caused by *Salmonella typhi* and non-typhoidal *Salmonella spp.* was a serious problem in many countries. It is recognized as a major cause of morbidity globally.

It was estimated that 12.5 million cases with *Salmonella typhi* occurs annually worldwide with an incidence of 365 cases/100,000 persons.[1] On the other hand, about 50,000 cases of non-typhoidal *Salmonella* infections were reported each year in the U.S[1].

Some *Salmonella* serotypes (e.g. *S. typhi, S. choleraesuis, S. paratyphi* A, B and C, *S. heidelberg, S. typhimurium, S. enteritides, S. saint paul, S. newport, S. dublin* and *S. panama*) have a propensity to invade the bloodstream[1]. This can be manifested as fever, chills, diaphoresis, myalgia, anorexia and weight loss that may last for days or weeks.

In a study done by Cheesbrough,et al, in Africa, non-typhoidal *Salmonella* accounted for the majority of isolates in children aged 5 years or less while *Salmonella typhi* predominates among older children and adults. Case fatality rates of up to 20% are reported among children under 5 while death is relatively uncommon among older children.[2] *Salmonella* bacteremia in children up to 60 months of age is an important cause of pyrexia of unknown origin which may lead in the delay of diagnosis and at the same time delay in the administration of specific treatment which

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may contribute to the mortality. It was the aim of this study to analyze and review the clinical profile and predictors of outcome of patients with *Salmonella typhi* and non-typhoidal *Salmonella* bacteremia admitted at Philippine Children's Medical Center. It was also the aim to do a local study since few researches regarding *Salmonella typhi* and non-typhoidal *Salmonella* infections were done. This information may help in the evaluation of factors associated with increase severity of the illness, determination of the appropriate management based on the antibiotic susceptibility and recognition of children at high risk of complications and deaths.

DEFINITION OF TERMS

For purposes of this study, duration of illness was defined as the total number of days from the time the signs and symptoms were first manifested until the first day of defervescence. Treatment failure means shifting of antibiotics after five days due to absence of improvement of signs and symptoms such as better well-being, i.e. if patients are better, able to sit and take some food or even walk, and being afebrile or having low grade fever as compared to high remittant fever. Relapse was defined as the presence of a positive blood culture after having a good clinical response following completion of an appropriate treatment (14 days for Chloramphenicol, Cotrimoxazole and Ampicillin; 5-7 days for Ceftriaxone). Good clinical response was defined as improvement of signs and symptoms such as better well-being and being afebrile of having low grade fever as compared to high remittant fever.

OBJECTIVES

General Objective

To analyze and review the clinical profile and determine the predictors of outcome of *Salmonella* bacteremia among patients admitted at Philippine Children's Medical Center from 1998 to 2003.

Specific Objectives

1. To determine the prevalence of *Salmonella typhi* and non-typhoidal *Salmonella* bacteremia at Philippine Children's Medical Center
2. To compare the demographic data (age, sex distribution, water source and residence), clinical presentation, course of the disease, the species of the causative organisms, complications, outcome and mortality of patients with *Salmonella typhi* and non-typhoidal *Salmonella* bacteremia.
3. To compare the hematological findings of *Salmonella typhi* and non-typhoidal *Salmonella* bacteremia.
4. To compare the antibiotic sensitivity and resistance of *Salmonella typhi* and non-typhoidal *Salmonella* bacteremia.
5. To determine the risk factors associated with mortality of both *Salmonella typhi* and non-typhoidal *Salmonella* bacteremia.
6. To identify the species and the pattern of antibiotic susceptibility of *Salmonella typhi* and non-typhoidal *Salmonella* bacteremia.

METHODOLOGY

Study Design: Retrospective study

SUBJECTS

Inclusion Criteria

All patients admitted at Philippine Children's Medical Center from January 1998 to September 2003 presenting with a final diagnosis of *Salmonella* bacteremia as documented by at least one positive blood culture were included in this study.

Exclusion Criteria

Patients with *Salmonella* infection reported as Group D were excluded in this study

STUDY PROCEDURE

The laboratory records within January 1998 to September 2003 were reviewed and patients who had growth of *Salmonella* in the blood culture were identified. After having identified those patients with *Salmonella* bacteremia, the medical records of the patients with *Salmonella typhi* and non-typhoidal *Salmonella* were retrieved and reviewed. There were 125 patients who had *Salmonella* bacteremia from January 1998 to September 2003 with the following breakdown: fifty eight were *S. typhi isolates*; thirty eight were non-typhoidal isolates and twenty-nine were labeled as Group D isolates. However, only 80 charts were available for review. Only 66 patients were included in this study mainly because 14 patients grew *Salmonella* Group D which was not specified whether it was *Salmonella typhi* or non typhoidal *Salmonella* Group D.

POPULATION CHARACTERISTICS

Pertinent patient data collected included age, sex, address, nutritional status, socioeconomic status and water source.

OUTCOME MEASUREMENTS

The demographic data (age, sex distribution, water source and residence), clinical presentation, course of the disease, the species of the causative organisms, complications, outcome and mortality of patients with *Salmonella typhi* and non-typhoidal *Salmonella* bacteremia were reviewed and compared. The hematological findings, antibiotic sensitivity and resistance of both *Salmonella typhi* and non-typhoidal *Salmonella* were identified and compared. The risk factors associated with the patient's outcome whether improved, treatment failure or mortality were likewise established and compared.

STATISTICAL METHODS

Mean, median, standard deviation, frequency distribution and prevalence were determined. Chi-Square, T-test and Fischer's Exact test were likewise applied. Multiple regression analysis was done to determine the predictors of outcome. All statistical analysis used 95% confidence level with a p value of ≤ 0.05.

RESULTS

From January 1998 to September 2003, 125 cases of *Salmonella* bacteremia by laboratory records were noted. However, only 66 charts were finally included in this study, 37 subjects with *S. typhi* bacteremia and 29 patients with non-typhoidal *Salmonella* bacteremia. A summary of the patients' characteristics was tabulated.

Table 1 shows the number of typhoid cases seen per year from January 1998 to Septempber 2003.

Table 1. Number of *Salmonella* bacteremia per year from 1998-2002

	N=125	%	N=66	%
1998	26	20.8%	15	22.7
1999	14	11.2%	5	7.5
2000	29	23.2%	15	22.7
2001	20	16%	11	16.7
2002	13	10.4%	7	10.6
Sept, 2003	23	18.4%	13	19.8
Total	125	100	66	100

*** subjects included in the study**

Salmonella bacteremia were seen more in males for *S. typhi* with a male to female ratio of 1.3:1 but was almost equal for non typhoidal *Salmonella*.

Table 2 shows the causative organisms of *Salmonella* bacteremia, by age group. It can be seen that *S. typhi* was the causative agent for 56% of the cases, followed by non typhoidal *Salmonella* group D, and then by Group C. The least common was Group A. By age group, the most common causative agents for cases less than 2 years old were group B and group C, comprising 72% of the total. For cases among 2-6 years old, the most common were *S. typhi* which alone comprised 76% of the total, while for those >12 years old; the sole causative organism was *S. typhi*.

Table 2. Causative organisms of *Salmonella* bacteremia by age group

Organism	< 2 years	2-6 years	6-12 years	>12 years	Total
S. typhi	0	7 (38%)	24 (76%)	6 (100%)	37 (56%)
Non-typhoidal Salmonella					
Group A	0	2 (11%)	1 (4%)	0	2 (3%)
Group B	5 (36%)	0	2 (8%)	0	7 (11%)
Group C	5 (36%)	2 (11%)	1 (4%)	0	7 (11%)
Group D	3 (21%)	6 (34%)	1 (4%)	0	10 (15%)
Group E	1 (7%)	1 (6%)	1 (4%)	0	3 (4%)
Total	**14**	**18**	**28**	**6**	**66**

Figure 1 shows that non-typhoidal *Salmonella* bacteremia was more common in younger age group, i.e. < 2 years old while *S. typhi* was more common in older group, i.e. > 12 years old.

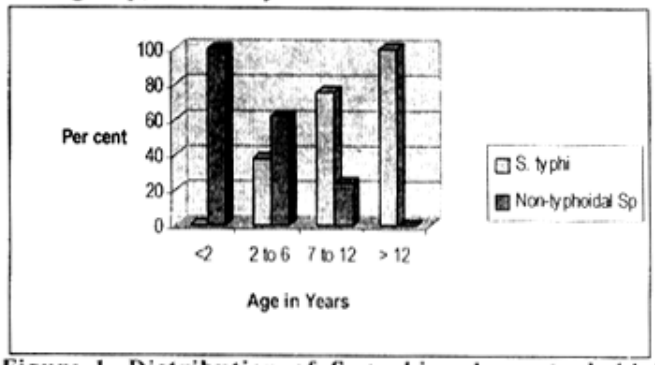

Figure 1. Distribution of *S. typhi* and non-typhoidal *Salmonella*, by age group.

Table 3 shows the distribution of socio-demographic characteristics, by type of causative organism and the results of test of association. It can be seen that age and whether patient was admitted as service or pay patient (surrogate measure for income level) were significantly different between the two groups. Non-typhoidal *Salmonella* bacteremia was seen more in service patients while S. typhi bacteremia was seen more in pay patients.

Table 3. Sociodemographic profile of subjects, by causative organism.

	S. typhi (n=37)	Non-typhoidal species (n=29)	P
Age, in years			**0.000**
< 2	0	14	
> 2	37	15	
Sex			**0.128**
Male	21	11	
Female	16	18	
Residence			**0.565**
Tandang Sora/ Payatas Commonwealth Batasan/Diliman	14	9	
Others	23	20	
Socioeconomic			**0.050**
Service	14	18	
Pay	23	11	

Information regarding the water source of patients with *Salmonella* infection was only reported in 20 (30.3%) patients. Figure 2 shows the source of water in 20 subjects namely: 1. Maynilad (20%) 2. NAWASA (20%) 3. Purified water (25%) 4. Deep well (25%) and 5. Mineral Water (10%).

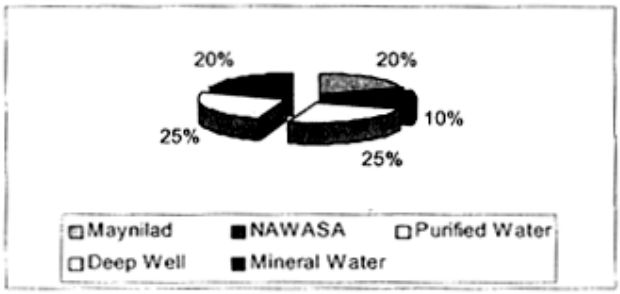

Figure 2. Water source of patients with *Salmonella* infections

The most prominent symptom present in both *Salmonella typhi* and non-typhoidal *Salmonella* bacteremia was fever, *S. typhi* bacteremia presented with anorexia (70%), diarrhea (37.8%) and headache (35.13%) compared to nontyphoidal *Salmonella* bacteremia which presented with anorexia, diarrhea and vomiting (51.7%) as shown in Figure 3.

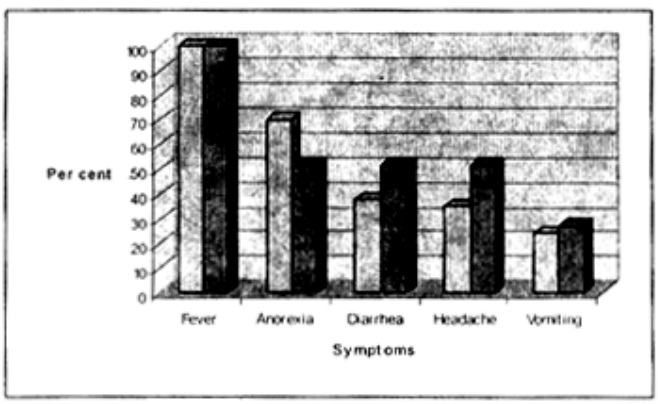

Figure 3. Most common presenting symptoms seen in *Salmonella typhi* and non-typhoidal *Salmonella* bacteremia

Figure 4 shows the presenting signs and symptoms and the clinical course of the disease. Among the presenting signs and symptoms, the parameters that turned out to be statistically different were maximum temperature, abdominal tenderness and vomiting. It can be seen that there was a statistically significant difference in the maximum temperature in *S. typhi* with a mean value of 39.75°C compare to 39.37°C in non-typhoidal *Salmonella* bacteremia. Vomiting was more common in non-typhoidal *Salmonella* bacteremia.

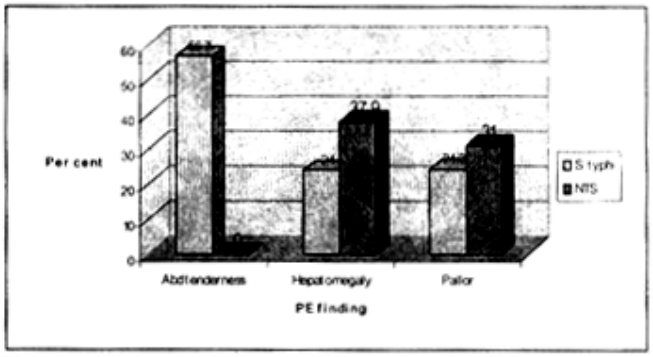

Figure 4. Most common physical examinations findings in *Salmonella typhi* and non-typhoidal *Salmonella* bacteremia

The proportions of subjects without co morbidities was significantly seen in *S. typhi* subjects.

The two groups also differed in terms of the complications. Ileitis was a statistically significant complication noted among patients with *S. typhi* while meningitis was a statistically significant complication of non-typhoidal *Salmonella*.

With regards to treatment, a higher proportion of patients with non-typhoidal *Salmonella* were treated with Ampicillin and Gentamicin. On the other hand, more *S. typhi* bacteremia patients were given Chloramphenicol as the initial treatment.

From among the hematological findings, non-typhoidal *Salmonella* bacteremia patients were more anemic with mean hemoglobin of 112.6. However, this did not reach statistical significance. Mean WBC count was within the normal range (7.3) in patients with *S. typhi* bacteremia as compared to non-typhoidal *Salmonella* bacteremia subjects who showed leukocytosis (12.9). Again, this was not statistically significant. The *S. typhi* bacteremia showed mean neutrophils of 61, while non-typhoidal *Salmonella* showed a mean of 53.3. Only the proportion of lymphocytes was significantly different between the two groups, non-typhoidal cases showing higher mean values than the *S. typhi* group was shown in Table 5.

Table 5. Hematological findings of *Salmonella typhi* and non-typhoidal *Salmonella* bacteremia

	S. typhi	Non-typhoidal	
Hemoglobin			0.095
Mean	112.6	103.6	
SD	23.3	19.7	
WBC count			0.42
Mean	9.7	12.9	
SD	21.1	10.3	
Segmenters			0.056
Mean	61.0	53.3	
SD	13.9	17.3	
Lymphocytes			**0.036**
Mean	37.7	45.9	
SD	13.1	17.0	
Platelet count			0.20
Mean	262	115	
SD	314	188	

With regards to the resistance pattern to antibiotics, it was noted that non-typhoidal *Salmonella* showed a statistically significant difference in the resistance pattern of the antibiotics being more resistant to Ampicillin, Chloramphenicol and Cotrimoxazole. *S. typhi*, however did not show any resistance to Cotrimoxazole and Chlorampenicol. Both groups did not show any resistance to Ciprofloxacin as shown in Table 6.

Table 6. Antibiotic resistance of *Salmonella typhi* and non-typhoidal *Salmonella bacteremia*

Resistant	S. typhi	Non typhi	P Value
Ampicillin	1 (2.7%)	7 (24%)	0.010
Cotrimoxazole	0	4	0.033
Chloramphenicol	0	4	0.033

With regards to the outcome, Table 7 shows that there was a higher proportion of cases in the *S. typhi* group who improved with the initial antibiotic used as compared with the non-typhoidal *Salmonella* group, however, this was not statistically significant. On the other hand, treatment failure was noted to be higher in the non-typhoidal group; again, this did not reach statistic significance. All the deaths were found in the non-typhoidal group, but because of the small number, this did not reach significant level.

Table 7. Outcome of treatment of *S. typhi* and non-typhoidal *Salmonella* bacteremia by causative organism

	S. typhi (n=37)	Non typhoidal (n=29	P
Improved (n=35)	23 (62.1%)	12 (41%)	0.093
Relapsed (n=1)	1 (3%)	0	0.560
Treatment failure (n=27)	13 (35%)	14 (51.8%)	0.281
Expired (n=3)	0	3 (11%)	0.079

PREDICTORS OF OUTCOME

Factors that could influence outcome defined as improvement, treatment failure/relapse and death were analyzed. Only variable that could fit in the regression model were used and these were duration of illness, days of fever prior to consultation, isolate, sex, co-morbidities and complications. Dummy variables were used to assign values to the categorical values, based on presumed relationship with outcome. For example, more severe conditions were given higher values since more adverse outcomes were given higher values (improvement was 1, treatment failure was 2 and death was 3). Other variables that could not be assigned values, such as antibiotics, were not included in the model.

From the regression model, the following variables were found to be significantly correlated with outcome of *Salmonella* bacteremia in general at 95% confidence level.

At 95% confidence level.

1. Days of fever prior to consultation
2. Duration of illness

DISCUSSION

Several studies show that *Salmonella typhi* and *Salmonella* bacteremia remain to be a major health problem worldwide especially in developing countries.

Salmonella typhi bacteremia was estimated to occur in 12 to 33 million cases worldwide each year. On the other hand, non-typhoidal *Salmonella* bacteremia continues to increase markedly. Based on passive laboratory-based surveillance, an estimated 0.8 to 3.7 million cases occur in the United States[3].

In a study done by Yaramis, A in Turkey, the mean age of patients with *Salmonella typhi* infection was 9.6 ranging from 6 months to 16 years old[4]. This study showed that the mean age of *Salmonella typhi* bacteremia was 10.1 years. On the other hand, the mean age of patients with non-typhoidal *Salmonella* bacteremia was 18 months ranging from 6-23 months[1]. This study showed a mean age of 30 months for non-typhoidal *Salmonella* bacteremia.

Based on the distribution of *S. typhi* and non-typhoidal *Salmonella* bacteremia by age group, *S. typhi* was more common in older age group, 12 years old. On the other hand, non-typhoidal *Salmonella* bacteremia was seen to be more prevalent in younger age group <2 years old. This is consistent with the findings of the study done by Cheesebrough including 206 cases of *Salmonella* bacteremia among children in Western Zaire in 1993[2].

There was a greater male to female ratio for both *S. tyhpi* and non-typhoidal *Salmonella* bacteremia which was consistent with other foreign studies which were previously done[2,4,5].

Salmonella infections may cause either acute infections with non-specific signs and symptoms or a chronic asymptomatic infection. The more common symptoms noted with *Salmonella* bacteremia include fever, gastroenteritis, chills, anorexia and weight loss.[1,3]

In a study done by Yaramis, A, et al including 314 children in Turkey, the clinical features of children with *Salmonella typhi* bacteremia were fever (95%), abdominal pain (66%), vomiting and headache (44%). Physical examination showed hepatomegaly (42%) and splenomegaly (20%)[4]. Cayabyab, et al stated in his study at JRMMC, including 117 patients with *S. typhi* bacteremia, that fever was present in 100%. This was followed by anorexia (70%), diarrhea (37.8%) and headache (35.13%). The most notable physical examination findings present in this study were abdominal tenderness, hepatomegaly and pallor. The abdominal tenderness that is usually seen in patients with *S. typhi* bacteremia is attributed to the recruitment of mononuclear cells and lymphocytes resulting to marked enlargement and necrosis of Payer's patches[3].

On the other hand, in a study done by Sai-Cheng L, et al in Taiwan which included 64 cases of patients with non-typhoidal *Salmonella*, the most prominent symptoms present were fever, diarrhea and hepatomegaly[5]. Another study on non-typhoidal *Salmonella* bacteremia involving 7 patients who had sepsis with meningitis showed that the prominent sign and symptoms seen were fever, diarrhea and irritability.[7] The study showed that patients with non-typhoidal *Salmonella* bacteremia presented with fever being seen in 100%. This was followed by anorexia, diarrhea and headache which were seen in 51.7% and vomiting which was seen in 27.5%. Vomiting was more prominent in non-typhoidal *Salmonella* bacteremia than *S. typhi* bacteremia and was statistically significant. Like *S. typhi* bacteremia, this study showed that non-typhoidal *Salmonella* patients also had hepatomegaly and pallor. The characteristics hepatosplenomegaly was related to the replication within the reticuloendothelial cells, the pathologic recruitment of mononuclear cells and the development of cell-mediated immune response.[3]

The complications in the following *Salmonella* infections include pneumonia, meningitis, ileitis, osteomyelitis, cholecystitis, UTI, myocarditis and nephritis.[1,3] In this study, the complications that were noted following *Salmonella* infections include pneumonia, ileitis, meningitis, UTI, ileus and cholecystitis. The complications noted in *S. typhi* bacteremia were noted to differ from the complications following non-typhoidal *Salmonella* bacteremia.

Ileitis was noted to be a statistically significant complication seen in *S. typhi* infection. This can be secondary to the characteristics invasion of *S. typhi* beyond the lamina propia and the local lymphatics as compared with the non-typhoidal *Salmonella species*.[1]

Scragg, et al reported that 45 cases with non-typhoidal *Salmonella* bacteremia with meningitis were seen among 410 children under 6 years old[2]. A retrospective study done by Pongsakdi, et al, reviewed 65 patients below 1 year old who developed meningitis as a complication of non-typhoidal *Salmonella*[8]. This was also observed in this study which showed that meningitis was a statistically significant complication of non-typhoidal *Salmonella*. The tendency of the non-typhoidal *Salmonella species* to develop meningitis as a complication can be secondary to the characteristic invasiveness of non-typhoidal *Salmonella* to rapidly invade the bloodstream.[1] This may lead to hematogenous spread to the meninges resulting to meningitis.

Hematologic abnormalities vary in each group. In a study done by Cheesbrough, the mean hemoglobin was 7.3 g/dl in *S. typhi* bacteremia[2]. This study showed mean hemoglobin of 11.26 g/dl. The study of Yaramis, et al which included 314 patients, the mean white blood cell count was within normal value at 7.3×10^3 / mm^3 with the presence of a left shift in a significantly larger proportion of patients (78%)[4]. This study also showed

a mean WBC count within normal at 9.7 x 10^3 / mm^3; with a mean neutrophils of 61%.

On the other hand, the mean hemoglobin seen in patients with non-typhoidal *Salmonella* bacteremia was noted at 7.2 g/dl as reported by Cheesbrough.[2] This study showed mean hemoglobin of 103.6 g/dl. The study of Sai-Cheng L, et al, showed a WBC count of > 10 x $10x^3$ / mm^3 with lymphocytic predominance in patients with non-typhoidal salmonella bacteremia[5]. This was also seen in this study showing a mean white blood cell count of 12.9 x 10^3 / mm^3.

The worldwide frequency of antibiotic-resistant *S. typhi* has been increasing since the 1960s but remains much lower than that for non-typhoidal *Salmonella*[1]. Drug resistance is a global problem seen in areas like the Middle East, Central and South America and even Asia. This can be secondary to the widespread availability and inappropriate use of antimicrobial agents as over-the-counter drugs[1]. In a study done by Yaramis, resistance rate of *S. typhi* were as follows: Ampicillin (17%), Cotrimoxazole (5%) and Ceftriaxone 94%)[4]. In a study sine by Carlos in the 2001 antimicrobial surveillance data by the Department of Health, resistance rate of *S. typhi* to Ampicillin, Chloramphenicol and Cotrimoxazole remained low at 5%, 1%, and 5% respectively as compared to 4%, 1%, and 4% in 2000[9]. There was no resistance to Quinolones[11] and Chlorampenicol as seen in this study. However, another study including 558 subjects in India showed multi-drug resistance of *S. typhi* to Ampicillin, Chlorampenicol and Cotrimoxazole in 60.8%.[11]

Non-typhoidal *Salmonella* have a tendency to be more resistant than *S. typhi*. *S. typhi* colonize only humans, therefore, disease can be acquired only through close contact with a person with *S. typhi* infections[3]. On the other hand, non-typhoidal *Salmonella species* may infect both humans and animals. The most important factor for development of drug resistance in non-typhoidal *Salmonella* is the overuse and misuse of antibiotics in animals raised for foods. Subtherapeutic concentrations of antibiotics used to enhance growth and prevent infection promote intestinal colonization by antibiotic-resistant bacteria. These organisms may be found in feces and may contaminate meat at the time of slaughter[1]. There was poor susceptibility of non-typhoidal *Salmonella* isolates to Chloramphenicol and Ampicillin as observed in the study done by Cheesbrough[2]. Carlos reported that non-typhoidal *Salmonella* showed higher resistance rates to Chloraphenicol 11%, Ampicillin 15%, Cotrimoxazole 15%, and Ciprofloxacin 5% as observed in 2001[9]. This study also showed resistance of non-typhoidal *Salmonella* isolates to Chloramphenicol, Cotrimoxazole and Ampicillin.

The outcome of *Salmonella* bacteremia maybe one of the following: improved, relapse, treatment failure and death. In this study, more patients with *S. typhi* bacteremia improved compared to non-typhoidal *Salmonella* bacteremia. This can be secondary to the use of Chloramphenicol as an initial drug in patients with suspected *S. typhi* infections in which this study showed that *S. typhi* isolates turned out to be sensitive to Chloramphenicol. The three deaths occurred among patients with non-typhoidal *Salmonella* bacteremia, two of which had isolates resistant to Ampicillin, the drug that was commonly used for empiric treatment. Other factors that could have contributed to the mortality were younger age group of the patients (2 mos, 4 mos and 12 mos) and the presence of malnutrition in two patients. Treatment failure was more common among patients with non-typhoidal *Salmonella* isolates. Again, this could be secondary to the empiric use of Ampicillin in patients with non-typhoidal *Salmonella* when in fact there was an increased in resistance to Ampicillin noted among non-typhoidal *Salmonella* isolates.

The factors that affected the outcome of patients with *Salmonella* bacteremia in general were the days of fever prior to consultation and the duration of illness. Longer duration of fever prior to consultation (delayed consultation) and prolonged duration of illness would be directly related to a poorer outcome. Longer duration of fever prior to consultation led to a delay in the diagnosis and a delay in initiating the proper antibiotic treatment. Prolonged duration of illness also turned out to be a significant predictor of outcome probably because the patients who had prolonged duration of illness were the ones with resistant isolates which warranted a shift in the antibiotic, likewise, these were the patients who had complications, although these factors did not turn out to be significant predictors of outcome by themselves.

CONCLUSION

For the period of January 1998 to September 2003, 125 cases of *Salmonella* septicemia was noted at Philippine Children's Medical Center; 58 were *S. typhi* isolates; 38 were non-typhoidal isolates and 29 were labeled as Group D isolates. Among these, 66 cases were included in the study. 37 subjects had *S. typhi* bacteremia and 29 had non-typhoidal *Salmonella*

bacteremia. This can be seen in children < 2 years old for non-typhoidal *Salmonella* bacteremia and >12 years old for *S. typhi* bacteremia. It is more common in males. Fever is the most common presenting symptom, with a higher maximum temperature for *S. typhi* bacteremia. Other symptoms present were abdominal tenderness which was more common in *S. typhi* bacteremia. Vomiting, on the other hand, was seen in non-typhoidal *Salmonella* bacteremia. Ileitis was a unique and significant complication of *S. typhi* bacteremia , while meningitis was a significant complication of non-typhoidal *Salmonella* bacteremia.

A higher degree of resistance to Ampicillin, Cotrimoxazole and Chloramphenicol was observed in non-typhoidal *Salmonella* isolates. Ciprofloxacin remains to be sensitive for both *Salmonella* infections. Chloramphenicol can still be used for *S. typhi* bacteremia since this study showed no resistance of *S. typhi* isolates to the said antibiotic.

Based on the regression analysis, the factors that could influence the outcome of *Salmonella* bacteremia are the following: the duration of fever prior to admission and the duration of illness. These factors showed a linear/direct relationship with the outcome of patients.

RECOMMENDATIONS

Since this was a retrospective study and was limited by information written in the patient's database, it is therefore recommended that a prospective study be done with a bigger sample size.

It is recommended to use more variables and identify more predictors of outcome under regression analysis and not only use unpreserved or death as outcome measurements.

Since the place of residence was identified in the study, it is recommended that a survey be done, water source be identified and proper environmental sanitation be promoted to decrease the prevalence of *Salmonella* bacteremia.

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