

## **EXTRAIESTINAL FOCAL INFECTIONS IN ADULTS WITH NON-TYPHOID SALMONELLA BACTEREMIA: RISK FACTORS AND CLINICAL PRESENTATIONS**

**BACKGROUND:** Non-typhoid *Salmonella* (NTS) isolates can lead to not only self-limited, acute gastrointestinal infections, but also bacteremia with or without extraintestinal focal infections (EFIs). The risk factors associated with EFIs in adults with NTS bacteremia are not clearly elucidated.

**SUBJECTS AND METHODS:** In a medical center in southern Taiwan, patients aged  $\geq 18$  years old with NTS bacteremia from January 1999 and June 2005, were included in the analysis.

**RESULTS:** Among 129 patients, 51 (39.5 %) were complicated with EFIs. The most common EFIs were mycotic aneurysm, followed by lung or pleura, and spinal osteomyelitis. Univariate analysis showed that diabetes mellitus ( $P=0.018$ ), hypertension ( $P=0.021$ ) and chronic lung disease ( $P=0.006$ ) were associated with occurrence of EFIs, while malignancy ( $P=0.014$ ) and immunosuppressive therapy ( $P=0.025$ ) were negatively associated with EFIs. After multivariate analysis, age was found to be an independent risk factor for EFIs (OR: 1.045; 95% C.I.: 1.020-1.070;  $P<0.0001$ ), however malignancy was a negative predictor (OR: 0.160; 95% C.I.: 0.142-0.780;  $P=0.011$ ). EFIs were associated with high mortality, severe septic manifestations, longer hospital stays and antimicrobial therapy.

**CONCLUSION:** NTS bacteremia should be considered as a severe and potentially life-threatening infectious diseases in the aged. Recognition of specific host factors in patients with NTS bacteremia with localized symptoms/signs is helpful for early identification of EFIs.

**Key words:** Non-typhoid salmonella bacteremia, extraintestinal focal infection, outcome

Table 1. Clinical characteristics of 129 adults with non-typhoid *Salmonella* bacteremia.

Characteristics	No. (%) of cases
Age, years	56.5±18.2
Gender, male	83 (64.3)
Underlying diseases	121 (93.7)
Malignancy	47 (36.4)
Diabetes mellitus	38 (29.5)
Immunosuppressive therapy	37 (28.7)
Renal insufficiency	37 (28.7)
Hypertension	36 (27.9)
HIV infection	9/47 (19.1)
Connective tissue disorders	20 (15.5)
Liver cirrhosis	18 (14.0)
Coronary heart disease	13 (10.1)
Congestive heart failure	12 (9.3)
Chronic lung disease	7 (5.4)
Extraintestinal focal infections	51 (39.5)
Mycotic aneurysm	19 (14.7)
Pneumonia/Empyema	13 (10.1)
Spinal osteomyelitis	7 (5.4)
Spontaneous bacterial peritonitis	3 (2.3)
Liver abscess	2 (1.6)
Splenic abscess	2 (1.6)
Septic arthritis	2 (1.6)
Others*	3 (2.3)

Note: A case may have more than one underlying diseases or extraintestinal focal infections.

HIV= human immunodeficiency virus.

\*Includes infective endocarditis (1 case), Port-A catheter-related infection (1), and soft-tissue infection (1).

Table 2. Comparisons of clinical categorical variables in cases of non-typhoid *Salmonella* bacteremia with or without extraintestinal focal infections.

Variables	Extraintestinal focal infections		<i>P</i> values
	Yes (n=51)	No (n=78)	
Gender, male	36 (70.6)	48 (61.5)	0.292
Underlying diseases	48 (92.3)	77 (92.2)	1.000
Diabetes mellitus	21 (41.2)	17 (21.8)	0.018
Hypertension	20 (39.2)	16 (20.5)	0.021
Renal insufficiency	16 (31.4)	22 (28.2)	0.700
Malignancy	12 (23.5)	35 (44.9)	0.014
Immunosuppressive therapy	9 (17.6)	28 (35.9)	0.025
Chronic lung diseases	7 (13.7)	1 (1.3)	0.006
Liver cirrhosis	5 (9.8)	13 (16.7)	0.271
Connective tissue disorder	4 (7.8)	17 (21.8)	0.050
HIV infection*	1/19 (5.3)	8/29 (27.6)	0.068
Clinical signs			
Fever	35 (70)	62 (80.5)	0.173
Tachycardia	32 (64)	45 (58.4)	0.531
Altered consciousness	7 (13.7)	12 (15.6)	0.772
Shock	25 (49.0)	16 (20.5)	0.001
Severe sepsis	39 (76.5)	39 (50.0)	0.003
Pittsburgh's bacteremic score $\geq$ 4	7 (13.5)	3 (3.9)	0.089
Persistent bacteremia	8 (15.7)	6 (7.7)	0.154
Infections caused by <i>S. enterica</i> serotype Choleraesuis	20 (39.2)	21 (26.9)	0.143
Appropriate antimicrobial therapy within 72 hours	43 (84.3)	51 (67.1)	0.003
Mortality at 90 days after the onset of bacteremia	23 (45.1)	19 (24.5)	0.014

Note: Data is presented as the case numbers with their proportions in parentheses, unless indicated otherwise.

\*Only 47 patients were tested for human immunodeficiency virus (HIV) infection.

Table 3. Comparisons of continuous and discrete clinical variables in cases of non-typhoid *Salmonella* bacteremia with or without extraintestinal focal infections.

Continuous variables	Extraintestinal focal infections		P values
	Yes (n=51)	No (n=77)	
Means ± standard deviations			
Age, years	63.8±16.0	51.2±17.7	<0.0001
C-reactive protein (mg/L)	168.3±138.5	83.5±88.3	<0.0001
Leukocyte (cells/mm <sup>3</sup> )	13829.4±116	9136.4±6401.	0.004
	42.8	9	
Hemoglobin (g/dL)	11.4±2.6	10.7±2.4	0.129
Platelet (x 1,000 cells/mm <sup>3</sup> )	192.5±111.0	190.6±130.8	0.928
Serum creatinine (mg/dL)	1.62±1.55	1.86±2.16	0.495
Aspartate aminotransferase (U/L)	99.9±221.2	132.1±295.9	0.515
Alanine aminotransferase (U/L)	78.9±119.8	73.7±129.4	0.821
Glucose (mg/dL)	205.1±199.1	169.8±134.7	0.379
Duration, median (interquartile range) (days)			
Clinical symptoms before admission	2.0 (1.0-7.0)	2.0 (1.0-7.0)	0.436
Antimicrobial therapy	20 (9-42.5)	14 (10-21)	0.045
Hospitalization	22 (10-49)	11 (7-22)	0.001

Note: Data is presented as the case numbers with their proportions in parentheses, unless indicated otherwise.

Table 4. Multivariate analysis of host factors for extraintestinal focal infections in cases of non-typhoid *Salmonella* bacteremia.

Variables	Odds ratio	95% confidence interval	P values
Age*	1.045	1.020-1.070	<0.0001
Malignancy*	0.160	0.142-0.780	0.011
Connective tissue disorders	0.139	0.018-1.439	0.160
Chronic lung diseases	0.153	0.017-1.399	0.096
Diabetes mellitus	0.565	0.238-1.345	0.197
Immunosuppressive therapy	1.051	0.340-3.250	0.932
Hypertension	1.040	0.387-2.796	0.938

\*: statistically significant.

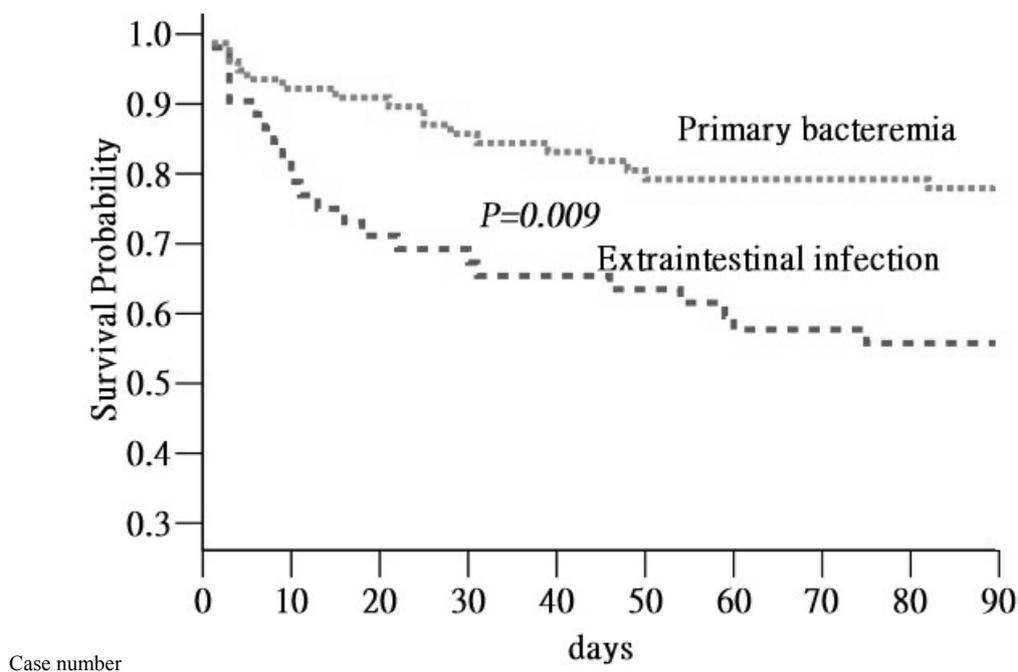


Figure Legends

Figure 1. Kaplan-Meier survival analysis of cases of non-typhoid *Salmonella* bacteremia with or without extraintestinal focal infections (the latter were referred to be “primary bacteremia”) until 90 days after the onset of bacteremia.