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Clinical Presentation of Extraintestinal Infections Caused by Non-typhoid Salmonella Serotypes Among Patients at the University Hospital in Cracow During an 7-year Period

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Abstract

The most characteristic finding in non-typhoid salmonella (NTS) infection is acute food related outbreaks of gastroenteritis, which is usually benign and self-limiting. However, more serious extraintestinal findings, such as bacteraemia and focal infections localized to any organ may appear. The objective of this paper is to describe the most important characteristic of the extraintestinal infections due to NTS serotypes observed in University Hospital, in Cracow between January 2000 and December 2006. To do so, we reviewed the clinical presentations, risk groups, complications and outcomes of in-patients, in which extraintestinal non-typhoid *Salmonella* serotypes were isolated, applying a clinomicrobiological protocol. Out of 30 patients with either bacteraemias (n = 22) or focal salmonella infections (n = 8), 12 had malignancies, 17 had immune dysfunction state, 9 had gastrointestinal disorders and 8 had chronic heart, pulmonary or kidney disease. Four of these patients (13%) who had hematological malignancies (2), renal transplantation (1) and pulmonary disease (1) died. Regarding the clinical picture, primary bacteraemia and focal infections occurred with similar frequency (33.3% and 26.7%, respectively); the remaining were bacteraemias secondary to gastroenteritis. The incidence rate (mean 0.30/1000 hospital admission/year) increased steadily from 0.19/1000 to 0.32/1000 hospital admission during the study period. From 30 *Salmonella* isolates from extraintestinal samples collected, only four isolates were resistant to ampicillin, ciprofloxacin or trimethoprim-sulfamethoxazole. This finding indicate that multidrug resistance does not represent a serious problem among NTS serotypes collected from the our medical center as monitored over a period of 7 years. Given this presentation, clinicians need to have a high index of suspicion and to consider preemptive therapy, especially in elderly patients who are likely to develop severe immunosuppression following interventions.

Key words: *Salmonella* serotypes, salmonella infections, risk factors, bacteraemia, immunosuppression

Introduction

Salmonella spp. are Gram-negative, facultative anaerobic, motile, non-lactose-fermenting, non-spore-forming bacilli. All *Salmonella* serotypes share the ability to invade the host by inducing their own uptake into cells of the intestinal epithelium and establishing systemic infection through their ability to survive and replicate in mononuclear phagocytes (Ohl and Miller, 2001). Recent years have seen a dramatic rise in the incidence and severity of cases of human salmonellosis (Gradel *et al.*, 2006; Jean *et al.*, 2006). Non-typhoid salmonella is widely dispersed in nature, and presents as sporadic food related outbreaks of gastroenteritis with or without extraintestinal manifestations, especially in immunocompromised patients (Glaser *et al.*, 1985; Pagano *et al.*, 1997; Hohmann, 2001). These manifestations are varied and if unrecognized can be important causes of morbidity and mortality (Gordon *et al.*, 2001; Habib, 2004). Extraintestinal non-typhoid salmonella infections make up 1.8% of all salmonellosis and most of them occur in childhood or in the elderly (Ruiz *et al.*, 2000).

Host conditions associated with increased risk of salmonellosis include gastric hypoacidity, extremes of age, alteration of the endogenous bowel flora,

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malignancy, diabetes mellitus, rheumatological disorders, reticuloendothelial blockade (sickle cell disease, malaria or bartonellosis), and therapeutic immunosuppression (Hsu *et al.*, 2003; Hsu and Lin, 2005). In certain conditions, non-typhoid salmonella can get into the bloodstream, and cause bacteraemia or localized infections in different organ systems (Pagano *et al.*, 1997; Day *et al.*, 2002; Habib, 2004; Gönen *et al.*, 2004; Minami *et al.*, 2004; Gagnon *et al.*, 2007). Therefore it is important to identify high-risk patients and treat them as early as possible.

The aim of our study was to determine the incidence of salmonella infections with extraintestinal manifestations among patients hospitalized at the University Hospital in Cracow during 2000–2006. Here we report a clinical audit of salmonella septicaemic patients seen over a 7-year period in order to describe the risk groups, complications and hospital outcome of non-typhoid salmonella infections. Moreover, we assessed the antimicrobial susceptibility profile of *Salmonella* clinical isolates collected from patients with extraintestinal infections seen during the study period. The present analysis confirmed the work of others that the greatest risk of acquiring focal infections is associated with the existence of underlying illness or immunodepression.

Experimental

Materials and Methods

Patients. Patients were recruited from a retrospective analysis of the clinical, and bacteriological data for adult patients with non-typhoid salmonella from January 2000 through December 2006. Patients were included if they had at least one culture positive for NTS. A total of thirty patients with extraintestinal manifestations of salmonella infections were included in the study. The isolates of *Salmonella* were recovered from specimens collected from: (a) venous blood (VB; n = 21); (b) blood from central venous catheter (CVC; n = 1); (c) urine (U; n = 4); (d) pus (P; n = 3), and (e) bronchial washings (BW; n = 1).

Data collection. Details for all patients whose blood cultures tested positive for *Salmonella* were drawn from the our Department of Microbiology, and medical records of University Hospital in Cracow, in the study period. Clinical and laboratory data were obtained from patient's records and analyzed retrospectively. The medical records of patients with NTS salmonellosis were reviewed, and data were recorded for demographic (age and gender), underlying medical diseases (diabetes mellitus, liver cirrhosis, systemic lupus erythematosus, hypertension, pneumonia, bronchitis, previous isochaemic stroke, chronic obstructive pulmonary disease, organ abscesses, human immunodeficiency virus infection, hematological malignancy or solid organ malignancy), bacteriology (Serogroups A, B, C, D, E, G and H) and hospital outcome (death). We defined immunodeficiency as having acquired human immunodeficiency virus (HIV) infection, use of corticosteroid and chemotherapeutic agents for malignancy or autoimmune diseases, or use of immunosuppressive agents for organ transplantation (Hsu *et al.*, 2003).

Qualitative evaluation of bacteria. The study material was based on taking venous blood samples (95.2%), and from CVC (4.8%). Microbiological blood examination were performed in constant monitoring system of collected specimens. Automatic BacT/Alert (bioMerieux) system was used, what allowed for early bacterial blood samples identification. For aerobic bacteria cultures standard media was used – BacT/Alert^{TM} SA *Culture Bottle*, and BacT/Alert^{TM} FA *Culture Bottle*. Additionally, all tested samples were placed directly onto nonselective Columbia agar plates supplemented with 5% of blood sheep, and onto selective McConkey'a agar plates (bioMerieux). Stool samples, and rectum swabs were placed additionally onto selective routine media Wilson-Blair (Difco), *Salmonella-Shigella* (Difco), and selenito F (Difco). The plates were then incubated at 37°C for 18–24 h, and the colonies suspected for salmonella bacilli were isolated. Isolates of *Salmonella* were initially identified by biochemical tests. Additionally, cultured microorganisms were identified with usage of commercial ID 32E system (bioMerieux) for *Enterobacteriaceae* family according to the manufacture's guidelines. Serogruping was determined by agglutination testing with use of antisera specific to O antigen: AO, BO, CO, DO, and EO (Biomed, Cracow). All *Salmonella* isolates, excluding *Salmonella enterica* subsp. *enterica* serovar Enteritidis (*S*. Enteritidis), were further sent to Reference Laboratory in Cracow for serological types confirmation.

Antibiotic susceptibility testing. The agar disc-diffusion method was performed according to Clinical and Laboratory Standards Institute (CLSI/NCCLS – National Committee for Clinical Laboratory Standards (NCCLS, 2003a; CLSI, 2007). Single colonies were selected and suspended in sterile 0.9% NaCl solution to prepare the inoculum. Bacterial suspension was inoculated with a sterile swab dipped into the inoculum adjusted to the density 0.5 McFarland turbidity standard. Inoculated Mueller-Hinton agar plates (bioMerieux) were left to dry before application of antibiotic discs. The plates were then inverted and incubated at 35°C for 16–18 h. Analysis was also conducted with the use of antibiogram cards VITEK and VITEK®2 compact (bioMerieux) for Gram-negative rods. The tests are in the form of small, waterproof cards with 64 wells containing antibacterial drugs (anti-

biogram tests) in different dilutions suitable for testing microorganism according to the CLSI recommendations. Tests were performed according to the manufacture's instruction. The following antimicrobials were included in the study: ampicillin (10 μg), cefotaxime (30 μg), ceftazidime (30 μg), ciprofloxacin (5 μg), and trimethoprim-sulfamethoxazole (1.25/23.75 μg). The antibiotic discs were obtained from Oxoid.

ESBL detection. Extended-spectrum β-lactamase activity was detected in *Salmonella* isolates by the double disc synergy (DDS) test (Jarlier *et al.*, 1988) with discs containing cefotaxime, ceftazidime and amoxicillin/clavulanate.

Results

Over a seven-year period (2000–2006), 438 isolates belonging to *Salmonella* were isolated from clinical samples of patients (n = 9 418) of University Hospital in Cracow. Among them, there were 405 intestinal salmonella infections (92.5%), 22 bloodstream infections (5.0%), and 8 extraintestinal non-bacteraemic infections (1.8%). Of the 438 *Salmonella* isolates only three (0.7%) were *Salmonella enterica* subsp. *enterica* serovar Paratyphi A (n = 2) and *S.* Paratyphi B (n = 1), while 99.3% were non-typhoid salmonella. The distribution of all *Salmonella* serotypes is shown in the Table I. The annual number of NTS infection episodes ranged from 62 in 2000 to 35 in 2006 (data not shown). The most frequently isolated was the serotype *Salmonella enterica* subsp. *enterica* serovar Enteritidis (*S.* Enteritidis; 86.7% of cases), and after that *Salmonella enterica* subsp. *enterica* serovar Hadar (*S.* Hadar; 6.7% of cases). Majority of these NTS isolates were obtained from Department of Gastroenterology and Hepatology and Infectious Diseases (36.7%) and Department of Hematology (26.7%). The annual case number and incidence (cases per 1000 discharges) of adult patients with extraintestinal manifestations during each year is illustrated in Fig. 1. Blood samples yielded most of the NTS isolates (73.3%), followed by urine samples (13.3%), pus samples (10%), and

Table I
The distribution of *Salmonella* serotypes isolated from patients hospitalized at the University Hospital in Cracow during a 7-year study period

Serological type serovar	Sero-groups	No. (%) of isolates from stool samples	No. (%) of isolates from other samples[a)]
S. Enteritidis	D_1	330 (81.3)	26 (86.7)
S. Hadar	C_2	19 (4.7)	2 (6.7)
S. Virchow	C_1	18 (4.4)	–
S. Typhimurium	B	13 (3.2)	–
S. Infantis	C_1	10 (2.5)	1 (3.3)
S. Indiana	B	5 (1.2)	–
S. Bareilly	C_1	2 (0.5)	–
S. Braenderup	C_1	2 (0.5)	1 (3.3)
S. Agona	B	1 (0.2)	–
S. Anatum	E_1	1 (0.2)	–
S. Bovismorbificans	C_2	1 (0.2)	–
S. Hlingdon	D_2	1 (0.2)	–
S. Mbandaka	C_1	1 (0.2)	–
S. Newport	C_2	1 (0.2)	–
Total		n = 405	n = 30

[a)] Including venous blood, urine, pus, central venous catheter, and bronchial washings samples

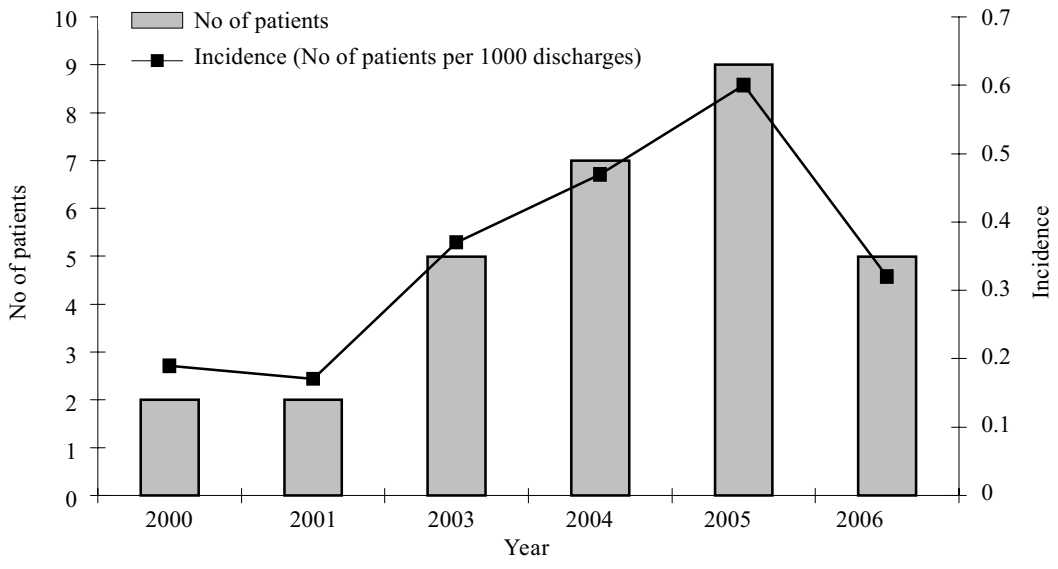

Fig. 1. Incidence and number of patients with extraintestinal salmonella manifestations treated at the University Hospital in Cracow from 2000 to 2006.

Table II
Non-typhoid salmonella infections during the period 2000–2006 (n = 30)

Case	Age/ Gender	NTS Isolate/Source	No. of day(s)[a)]	Isolation from stool sample	Clinical diagnosis
Clinical cases with bloodstream infections (n = 22)					
1	76/F	*S.* Enteritidis/ VB	5 days	+	septicaemia
2	70/F	*S.* Enteritidis/ VB	1 day	–	myeloma
3	31/F	S. Enteritidis/ VB	2 days	+	food poisoning
4	62/M	*S.* Enteritidis/ VB	11 days	–	chronic lymphatic leukaemia
5	30/F	*S.* Enteritidis/ VB	11 days	+	acute gastrenterocolitis
6	59/M	*S.* Enteritidis/ VB	1 day	+	salmonellosis; septicaemia; renal failure; COPD; arterial hypertension; epilepsy
7	60/M	*S.* Enteritidis/ VB	at admission	–	septicaemia; renal transplantation
8	31/M	*S.* Enteritidis/ VB	at admission	+	salmonellosis
9	72/M	*S.* Enteritidis/ VB	ND	+	posthepatitic cirrhosis; virus hepatitis C
10	74/F	*S.* Enteritidis/ VB	4 days	+	septicaemia; bronchitic asthma; cholecystolithiasis; virus hepatitis; nausea; diarrhea; fecal vomiting
11	39/M	*S.* Enteritidis/ VB	25 days	–	aplastic anemia
12	38/M	*S.* Enteritidis/ VB	1 day	+	septicaemia; DM
13	80/M	*S.* Enteritidis/ VB	1 day	+	prostatic carcinoma; COPD; circulatory and respiratory failure; isochaemic heart disease
14	33/F	*S.* Enteritidis/ VB	5 days	+	multiple myeloma; gastrenterocolitis; renal failure
15	56/M	*S.* Enteritidis/ VB	at admission	–	non-Hodgkin lymphoma CTCL
16	40/F	*S.* Enteritidis/ VB	2 days	–	non-Hodgkin lymphoma DLBCL
17	31/F	*S.* Hadar/ VB	1 day	–	non-Hodgkin lymphoma DLBCL
18	64/M	*S.* Enteritidis/ VB	ND	+	septicaemia
19	70/F	*S.* Hadar/ VB	4 days	+	food poisoning; cancer of the breast
20	46/F	*S.* Enteritidis/ VB	1 day	–	SLE
21	30/F	*S.* Enteritidis/ VB	ND	–	septicaemia; HIV infection
22	59/F	*S.* Enteritidis/CVC	16 days	–	acute myeloblastic leukemia
Clinical cases with focal infections (n = 8)					
23	23/M	*S.* Enteritidis/ P	1 day	+	acute suppurative appendicitis; retrocecal abscess; gastroenterocolitis
24	65/M	*S.* Enteritidis/ P	at admission	–	thrombocytopenia; subphrenic abscess (*S.* Enteritidis and *P. aeruginosa* etiology); arterial hypertension; steroid diabetes
25	72/M	*S.* Enteritidis/ P	at admission	–	septicaemia; DM; myocardial infarction; subphrenic abscess; abscess of the spleen
26	75/M	*S.* Enteritidis/ BW	2 days	–	reactivity arthritis; septicaemia; coronary atheromatosis; bilateral pneumonia and bronchitis
27	69/M	*S.* Enteritidis/ U	6 days	–	bilateral pneumonia; thrombocytopenia; secondary anemia; DM; chronic peptic ulcer disease
28	74/F	*S.* Braenderup/ U	5 days	+	gastroenterocolitis
29	36/F	*S.* Infantis/ U	9 days	+	acute myeloblastic leukemia
30	67/M	*S.* Enteritidis/ U	ND	–	chronic renal failure; glomerulonephritis in the course of vasculitis

[a)] Number of hospitalization day(s) until extraintestinal salmonella infection appearance; NTS – non-typhoid *s*almonella; COPD – chronic obstructive pulmonary disease; DM – diabetes mellitus; SLE – systemic lupus erythematosus; NT – not tested; ND – data not available; (+) – present; (–) – absent; F – female; M – male; VB – venous blood; CVC – central venous catheter; U – urine; P – pus; BW – bronchial washings

bronchial washings samples (3.4%). Table II shows the demographic and clinical data in-patients who had bacteraemia or other extraintestinal non-bacteraemic infections, including those patients with and without gastrenterocolitis. The average age of salmonella bacteraemia patients was 42 (30–80 year), but more than 50% of them were older than 60. In nearly more than 50% of patients there was at least one risk factor responsible to dissemination. Eight patients had a localized salmonella infections, including three who had undergone successful surgery. The overall risk factors for non-typhoid salmonella infection with varied manifestations are summarized in Table III. Out of 30 patients with either bacteraemia or focal salmonella infections, 30% had hematological malignancies, 57% had immunodeficiency, 27% had chronic liver, pulmonary and renal diseases, 10% had solid organ cancers, diabetes mellitus or organ abscesses, 7% had hyper-

Table III
Background and manifestations of non-typhoid salmonella with extraintestinal infections

Background and manifestation	Clinical cases (cases numbers)[a)]
Malignancy	Solid organ cancers (3) [Prostatic carcinoma-1, lung neoplastic tumor-1, breast-1[b)]]; Hematological malignancy (9) [Neoplasm dissemination of lymphatic system (1), multiple myeloma (2), chronic lymphatic leukaemia (1), acute myeloblastic leukemia (2), non-Hodgkin lymphoma (3)]
Immunodeficiency[c)]	HIV infection (1), neutropenia (1), use of chemotherapeutic agents (7), use of immunosuppressive agents (2), exclusive corticosteroid use (9), agranulocytosis (3); SLE (1)
Other underlying medical diseases	Gastrointestinal disorders (9), chronic renal failure (3), septicaemia (9), COPD (2), posthepatitic cirrhosis (1), subphrenic abscess (2)[d)], abscess of the spleen (1), retrocecal abscess (1), aplastic anemia (1), acute suppurative appendicitis (1), DM, including steroid diabetes (3); bilateral pneumonia and bronchitis (2), cardiovascular diseases mainly encompassing hypertension (2) and heart failure (2), thrombocytopenia (2); epilepsy (1), skeletal disorder (1)

[a)] Description of abbreviations as in the legend to Table II; [b)] Patient had mastectomy; [c)]Immune dysfunction excluding malignancies;
[d)] Patient had subphrenic abscess evacuation, postoperative drainage, recurrent laparotomy with body, and tail of the pancreas removal due to acute pancreatic necrosis

Table IV
Characteristics and presentations of fatal non-typhoid salmonella bacteraemia (n = 4)[a)]

Case	Gender	Age (years)	Co morbidity	Predisposing intervention	NTS Isolate/Source	No. of day(s)[b)]	Comment(s)/other new diagnoses
1	F	40	Non-Hodgkin lymphoma DLBCL	Chemotherapy; exclusive steroid use	*S.* Enteritidis/VB	2 day illness	Central venous catheter
2	M	75	Reactivity arthritis; coronary atheromatosis; bilateral pneumonia; bilateral bronchitis	Parenteral nutrition	*S.* Enteritidis/BW	2 day illness	Patient after gastrectomy at 1982, and cholecystectomy; bilateral inflammatory infiltration in lungs; lung neoplastic tumo(u)r suspicion; treated due to tuberculosis; respiratory failure; hipox(a)emia; instant circulatory arrest
3	M	60	Renal transplantation	Immunosuppression after renal transplantation (8 years)	*S.* Enteritidis/VB	at admission	Death due to overwhelming sepsis;
4	F	33	Multiple myeloma	Chemotherapy	*S.* Enteritidis/VB	5 day illness	Gastroenterocolitis; renal failure

[a)] Description of abbreviations as in the legend to Table II; [b)]Number of hospitalization days until extraintestinal salmonella infection appearance

tension and 1 patient had reactivity arthritis. Four of 30 patients (13%) died (Table IV).

Most isolates remained highly susceptible to all 5 antimicrobial agents examined, with the exception of four isolates, including *S.* Enteritidis (resistant to ampicillin and trimethroprim-sulfamethoxazole); *S.* Hadar (resistant to ampicillin and ciprofloxacin); *S.* Hadar (resistant to ciprofloxacin) and *S.* Braenderup (resistant to ampicillin and ciprofloxacin). None of the tested isolates demonstrated an ESBL phenotype.

Discussion

Enteric fever is imported to developed countries while non-typhoid salmonella infections occur globally. It is, however, of note that in Poland number of bacterial foot borne infections and intoxications remain high – 19 870 cases (52.0 per 100 000), and 79.6% of them were caused by *Salmonella* (Zieliński and Czarkowski, 2006). Approximately 5% of gastroenteritis develop bacteraemia, and <1% have focal infections such as osteomyelitis, soft tissue infection, urinary tract infection or endocarditis (Miller and Pegues, 2000). Ramos *et al.* (1996) retrospectively reviewed the charts of 183 patients with extraintestinal salmonellosis, and proposed classification of these patients into four groups, including primary bacteraemia, enteritis-associated bacteraemia (secondary bacteraemia), digestive focal infection, and non-digestive focal infection. The greatest risk of acquiring focal infections is associated with the existence of underlying illness or immunodepression (Ruiz *et al.*, 2000). In our study we presented thirty cases of severe diseases complicated by

non-typhoid salmonella infections that occurred over a period of 7 years. Blood cultures were positive in twenty two (73%) cases, including twenty with *S.* Enteritidis, and only two with *S.* Hadar. Nearly half of these sepsis cases had underlying diseases: hematological malignances, solid organ cancers, liver disease, HIV infection, diabetes mellitus, and chronic heart and kidney diseases. In our patients with non-typhoid salmonellosis, the major patients risk factors for bacteraemia were certain immunocompromised conditions. Brown and Eykyn (2000) reported that in patients presenting with non-typhoid salmonella bacteraemia in the absence of gastroenteritis, underlying immunodeficiency should be excluded first. These findings point to the importance of the immune system in the defense against salmonella infection. Five years later, Hsu and Lin (2005) presented clinical data that showed that adult patients (≥18 years) with non-typhoid salmonellosis who had bacteraemia were older, and had more underlying diseases of liver cirrhosis, systemic lupus erythematosus, immunodeficiency, and solid organ cancers than patients who had gastroenteritis alone. Moreover, the same authors using log-logistic regression determined that the independent positive predictors of bloodstream infection in adult were SLE, liver cirrhosis, HIV infection, and solid organ cancers. They also confirmed that immunodeficiency predisposed patients to acquire non-typhoid salmonella bacteraemia. In other study, Ramos *et al.* (1996) revealed the differences between patients with primary and enteritis-associated bacteraemia. The first mentioned one characterized higher severe immunosuppression, and mortality, but lower community acquisition. In the present study nearly more than half of our in-patients with primary bacteraemia had severe immunosuppression due to hematological malignances, systemic lupus erythematosus, HIV infection, and renal transplantation.

We also determined the incidence four cases of non-typhoid salmonella bacteraemia, including three cases of chronic renal failure, and one case of renal transplant recipient followed by our Nephrology Unit. Dhar *et al.* (1991) reported the results of an analysis of 20 cases of NTS infection that occurred over a period of 10 years in 592 renal transplant recipients. This pathology usually occurs when immunosuppression is high – early in the post-transplant period or after anti-rejection therapy. They suggested that despite prolonged antibiotic therapy, relapses occur commonly causing significant morbidity, occasional graft loss and even death.

Bacterial infection is well-described complication of liver cirrhosis, and is a major cause of death (Barrio *et al.*, 1999; Brann, 2001). In this study posthepatitic liver cirrhosis due to virus hepatitis C infection was associated with high incidence of *S.* Enteritidis bloodstream infection. This strain was collected from 72-year old man with virus hepatitis C infection. From the results of a study by Brann (2001), non-typhoid salmonella was an infrequent cause of bacteraemia in cirrhotic patients. The specific risk factors for infection in cirrhotic patients included low serum albumin, gastrointestinal bleeding, intensive care unit admission for any cause, and therapeutic endoscopy.

In non-typhoid salmonellosis, gastroenteritis is the usual presentation and bacteraemia is less common, suggesting invasiveness and severity (Habib, 2004). In our study, the recorded mortality was 4/30 (13%). Three patients had immunosuppressive states, and interventions while the fourth patient were older with more co-morbid diseases, and previous surgical procedures. A recent Danish study showed that increasing age, and increasing levels of co morbidity were independently associated with an mortality, whereas none of the clinical and laboratory variables studied were strong independent prognostic factors (Gradel *et al.*, 2006). Habib (2004) noticed that clinicians need to treat elderly patients and to consider preemptive therapy or even chemoprophylaxis particularly in patients with prior salmonella infection who are likely to develop severe immunosuppression, especially if there is associated lymphopenia.

Another patients had *Salmonella* in pus, bronchial washing, and urine. Among the extraintestinal manifestations of salmonellosis, infection of the urinary tract is infrequent (Gagnon *et al.*, 2007). It occurs when there is a predisposition, such as occult urological problem or immunosuppression. Our patients were predisposed to this rare complication of salmonellosis because they were under corticosteroid therapy or chemotherapy, agranulocytosis, and chronic renal failure. With immune dysfunction, infections often present without gastroenteritis (Brown and Eykyn, 2000) in unusual locations, as seen here with *S.* Enteritidis isolated from subphrenic and spleen abscesses. These strains were collected from 72-year old man with diabetes mellitus (DM) and from 65-year old man with arterial hypertension, steroid diabetes and thrombocytopenia. These patients were successfully treated with drainage of the abscesses. Recently, Yamagata *et al.* (2006) have reported a rare case of *Salmonella* submandibular abscess in 59-year old patient with DM, chronic hepatitis and liver cirrhosis. The authors speculate that an immunocompromised condition can be a critical predisposing factor for *Salmonella* abscesses with different location. Another patient had pulmonary disorder, the presence of comorbid diseases and old age. He was bronchial washing culture positive for *S.* Enteritidis. In a Danish study published in 2007, the acquisition and pathogenesis of more severe NTS infections in debilitated patients was more related to endogenous host characteristic than in healthier pa-

tients in whom exogenous factors may be more crucial (Gradel *et al.*, 2007). We revealed that the incidence rate (mean 0.30/1000 hospital admission/year) increased steadily from 0.19/1000 hospital admission in the 2000 year to 0.32/1000 hospital admission in the 2006 year. The trend of gradually increased annual case numbers or incidence rate has also been reported previously (Gradel *et al.*, 2006; Jean *et al.*, 2006).

We reviewed the susceptibility pattern of *Salmonella* serotypes to a standard battery of five antibiotics in patients with extraintestinal non-typhoid salmonella manifestations at our Hospital in-patients Departments. The results of this study show that multidrug resistance, especially fluoroquinolone resistance, does not represent a serious problem among *Salmonella* isolates collected from the University Hospital medical center as monitored over a period of 7 years. From 22 bloodstream samples collected, two *S.* Hadar isolates were resistance to ciprofloxacin, and one was resistant to ampicillin. These strains were collected from 31-year old woman with non-Hodgkin lymphoma, and from 70-year old woman who had previous history of mastectomy. In conclusion, given this presentation, clinicians need to have a high index of suspicion and to consider preemptive therapy, especially in elderly patients who are likely to develop severe immunosuppression following interventions.

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