ORIGINAL ARTICLE

Shigella infections: A two year experience in cancer patients

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Abstract

Objective: To identify clinical and microbiological characteristics of Shigella infections among cancer patients.

Methods: The retrospective study was conducted at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, and comprised medical records from December 2011 to November 2013 which were reviewed to identify persons with laboratory-confirmed Shigella infections. Demographic information, clinical history, seasonal variation, microbiological details, treatment given, and outcomes in term of symptoms resolution and mortality at two weeks were noted.

Results: Shigella infection was diagnosed in 45 cancer patients. The mean age of the patients was 36.02±19.30 years (range: 1-64 years), with 35(78%) patients being >18 years of age. Overall, 16(35.5%) patients had presented during winter months and 40(89%) presented as emergencies. Diarrhoea was present in 44(98%) patients and among them 20(45%) had dysentery whereas 28(64%) had fever and 21(47%) had abdominal pain. Of the total 45 cases, 41(91%) had isolates from stool.. Besides, 39(87%) Shigella isolates were further speciated and Shigella flexneri was the most commonly isolated serotype in 25(64.1%). Overall, 42(93%) strains were sensitive to cefixime and ceftriaxone. Mean duration of symptoms resolution was 3.92±1.51 days (range: 1-10 days). No mortality was noted at 2 weeks.

Conclusions: Shigella flexneri was the most common serotype isolated. Majority of the isolates were sensitive to 3rd generation cephalosporins (cefixime/ceftriaxone).

Keywords: Shigella, Cancer, Drug resistance, Pakistan. (JPMA 66: 37; 2016)

Introduction

Shigellosis is a recognised global health problem, but developing countries continue to bear the major brunt of mortality and morbidity caused by this disease. The estimated annual number of Shigella episodes is been reported to be around 164.7 million, with 163.2 million occurring in the under-developed region (with 1.1 million deaths).[1] The Shigella genus has been divided into four sero-groups: S. flexneri, S. dysenteriae, S. boydii and S. sonnei. All of these sero-groups are known to cause shigellosis. Most commonly they are associated with dysentery, but can also cause bloodstream infections (BSI). BSI is usually seen in patients with underlying conditions like diabetes mellitus, malnutrition, post-organ transplantation and immunocompromised status.[2]

Prompt treatment with appropriate antimicrobial agents shortens the duration and severity of the illness and reduces microbial carriage and further spread of infection in the community. This strategy can be further facilitated with prior knowledge of local patterns of susceptibility which is essential to optimisze guidelines for empirical therapy. But the emergence and dissemination of multidrug-resistant strains of Shigella has complicated the therapeutic management of cases of shigellosis, especially when the target population is profoundly immunocompromised.[3]

Although a number of studies have been conducted across Pakistan[4-7] that have analysed antibiotic resistance rates in Shigella species in the general population, but no study has evaluated the clinical characteristics of shigellosis in immunocompromised patients. International data on this subject tends to be scant as well. Hence, the current study was planned to evaluate the clinical and microbiological characteristics of Shigella infection among cancer patients and to analyse the antibiotics resistance pattern in this population.

Materials and Methods

The retrospective descriptive study was conducted at Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCHRC), Lahore, Pakistan, and comprised medical records from December 2011 to November 2013.Only records of patients concomitantly suffering from cancer and with positive stool or blood cultures for Shigella species were included in this study.

Medical history and clinical details were retrieved from the electronic database. Patient's demographic information, clinical history, seasonal variation, microbiological details,

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treatment given, and outcomes in term of symptoms resolution and mortality at two weeks were documented.

All stool samples had been processed in the hospital's microbiology laboratory according to standard methodology. Colonies morphologically suggestive of Shigella species were identified by conventional biochemical reactions (urea, citrate, triple sugar iron, indole, motility) and further checked by analytical profile index (API) 20 E (Bio Murex, France). Serotyping was performed via the slide agglutination tests using antisera systems (BD Diagnostic Systems). Antibiotics susceptibility testing was performed by the Kirby Bauer disk diffusion method against ampicillin (10ug), ceftriaxone (30ug), cefixime (5ug), cotrimoxazole (trimethoprim-sulfametoxaole) (25ug), chloramphenicol (30ug) and ciprofloxacin (5ug). Escherichia coli ATCC 25922 and Klebsiellapneumoniae ATCC 700603 were used as the quality control strains.

Data analysis was performed using SPSS 19.Continuous variables were presented as mean and standard deviation, while categorical variables were presented as frequencies and percentages.

Results

Shigella infection was diagnosed in 45 cancer patients. The mean age of the patients was 36.02±19.30 years (range: 1-64 years), with 35(78%) patients being >18 years of age. Overall, 16(35.5%) patients had presented during winter months of December, January and February, and 40(89%) presented as emergencies. Diarrhoea was present in 44(98%) patients and among them 20(45%) had dysentery whereas 28(64%) had fever and 21(47%) had abdominal pain. Of the total 45 cases, 41(91%) were isolated from stool.

Serotyping for Shigella species was introduced in the mid 2012 at our centre. Prior to that all isolates identified on API 20E were reported as Shigella species. This group had

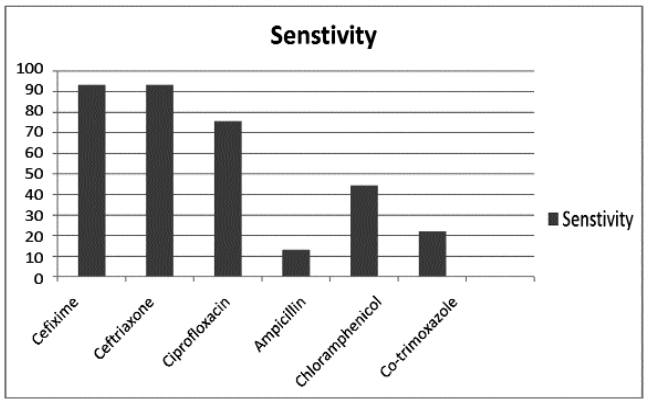

Figure: Overall sensitivity patterns of Shigella isolates.

Table: Demographic characteristics.

Characteristic	N (%)
Age (years)	
Less than 18	10 (22.2%)
≥ 18	35 (77.8%)
Gender	
Male	27 (60%)
Female	18 (40%)
Primary Diagnosis	
Haematological	18 (40%)
NHL	8 (44.4%)
HL	4 (22.2%)
ALL	4 (22.2%)
CLL	2 (11.1%)
Solid Tumours	27 (60%)
CA breast	8 (29.6%)
Head & Neck	6 (22.2%)
Ewings Sarcoma	3 (11.1%)
Others	10 (37.1%)
Shigella	
Shigellaflexneri	25 (55.6%)
Shigelladysentriae	6 (13.3%)
Shigellaboydii	4 (8.9%)
Shigellasonnei	4 (8.9%)
Shigella species	6 (13.3)
Sample	
Stool	41 (91.1%)
Blood	4 (8.9%)
Presentation	
Emergency	40 (88.9%)
Inpatient	5 (11.1%)
Means	
Age	36.02±19.30 (1-64)
ANC	4.02±4.10 (0-17.1)
Days (Symptoms resolution)	3.92±1.57 (1-10)

NHL: Non-Hodgkin lymphoma
HL: Hodgkin lymphoma
ALL: Acute lymphocytic leukaemia
CLL: Chronic lymphocytic leukaemia
CA: Cancer antigen
ANC: Absolute neutrophil count.

6(13.3%) of our isolates. The remaining cases 39(87%) Shigella isolates were further speciated and S. flexneri was the most commonly isolated serotype in 25(55.5%) (Table).Overall, 42(93%) strains were sensitive to cefixime and ceftriaxone (Figure).

Mean duration of symptoms resolution was 3.92±1.51 days (range: 1-10 days). No mortality was noted at 2 weeks.

Discussion

Majority of our patients were older than 18 years of age with a mean age of 36 years. Shigellosis primarily affects children and young adults, but in our study majority were adult patients. In endemic countries, shigellosis occurs

throughout the year with majority of cases occurring in the monsoon and hot humid season.[7] On the other hand results of our study reflect a higher incidence of cases during the winter months followed by an increase of cases noted during the monsoon season.

Previously published papers have identified S.flexneri as the most frequent species isolated from Asia.[8-10] Our findings reflect the same in our serotyped group. Prior results from Pakistan also suggest S. flexneri to be the most commonly isolated species.[5] All previous studies were done on the general population and none is available in cancer population to compare our findings with.

Four of our patients had Shigella in their bloodstream. Three of them were under 6 years of age, while one was a 45-year-old female. Adult female had growth of S. flexneri from central as well as peripheral line. Only one child was neutropenic. All the species isolated were S. flexneri. The three paediatric patients had fever along with dysentery whereas the adult female had no gastrointestinal symptoms. There are case reports of Shigella blood stream infection in infants[11] in acquired immunodeficiency syndrome (AIDS) patients[12] and in patients post-renal transplant.[13]

All these cases were due to S. flexneri like our bacteraemic patients. Our study population was all cancer patients who were immunocompromised due to malignancy and the treatment they were receiving, so they were also prone to Shigella bacteraemia.

Available data also shows an increasing trend in antibiotic resistance among Shigella species from developed as well as developing countries.[8,14] Data from Pakistan also reports higher rates of resistance to commonly used first-line drugs for Shigellosis like ampicillin, chloramphenicol and co-trimoxazole. Our study results also confirm a higher resistance pattern of ampicillin, co-trimoxazole, chloramphenicol and ciprofloxacin. A study conducted by Zafar and colleagues also reveals higher resistance to these agents, with the highest resistance found against ampicillin followed by cotrimoxazole, chloramphenicol and ciprofloxacin, respectively. Hence, these agents can no longer be considered appropriate for the empiric treatment in our patient population.[5]

Overall resistance to ceftriaxone and cefixime in our study isolates was low (7%), suggesting that third-generation cephalosporins are still effective for the treatment of acute shigellosis in our population. Till final antimicrobial susceptibility results arrive, these can be continued as part of the empiric therapy strategy.

There were several limitations in our study. It was a retrospective review and it was not possible to identify the source for acquiring the Shigella infection. Secondly, the number of patients was small and it was conducted at a single centre so these results cannot be generalised. Thirdly, in 13% of patients,Shigella serotypes were not identified.

Conclusions

S. flexneri was the most common serotype isolated. Majority of the Shigella isolates were sensitive to 3rd generation cephalosporins (cefixime/ceftriaxone).

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