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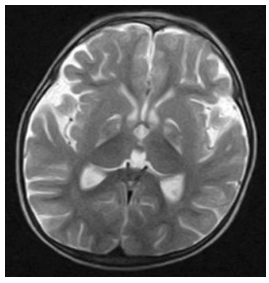

Bilateral symmetrical low T1 and bright flair and T2 abnormality with post contrast enhancement, suggestive of Japanese encephalitis.

Courtesy:Dr Ejaz A. Khan, Shifa International Hospital, Islamabad.

Antibiotics in the Management of Severe Malnutrition with Complications

Malnutrition causes a staggering number of deaths each year. It is directly or indirectly responsible for 50% of child deaths.[1] Pakistan ranks second after Afghanistan in stunting rates among the SAARC countries. According to the recently conducted National nutrition survey of Pakistan, wasting and stunting has increased in the last 10 years.[2] This seems plausible in the face of the many disasters that that the country has faced in the recent years and is still facing. The above data highlights the failure to progress towards the first Millennium Development Goals (MDGs); "to halve between 1990 and 2015 the proportion of people who suffer from hunger". However there is no data on deaths due to malnutrition at the country level. A lot of effort worldwide has been put in for the community management of acute malnutrition (CMAM), with provision of ready to use food supplements (RTUF) and nutritional education. However complicated severe acute malnutrition i.e. weight for height <-3Sd with one of the following: anorexia, lower respiratory tract infection, severe palmar pallor, high fever, severe dehydration, remains neglected particularly in South Asia.[3] Complications increase the risk of death in a severely malnourished child, up to 30% in some case series despite adequate management. The WHO has set up standard guidelines for the management of CSAM, but despite adherence to these guidelines the case fatality is high. There are nutritional rehabilitation units (NRU) in almost all public sectors of the country where large number of children are admitted and receive treatment. However, there is little published data on the reasons for admission in these children, their case fatality and the pathogens identified in these children.

Observational data and discussion with colleagues working in the NRU brings to light the fact that organisms like *Salmonella* Typhi and *para typhi*, *Klebsiella pneumoniae* and *Staphylococcus aureus* are the major pathogens in these children. The antibiotics currently recommended by WHO (ampicillin and gentamicin) provide inappropriate antimicrobial coverage for these organisms in the face of the increasing resistance to commonly used antibiotics.[4,5] Adherence to the WHO recommended regimen in this situation will lead to increase child mortality and it is suggested that data from these units on the microbiology of CSAM should be published as a first step to recognizing the problem. This should later be followed by well conducted randomized controlled trials to determine the most appropriate antibiotic regimen in these children.

It is reemphasized that in a country with such high rates of malnutrition, there is no published data on the recovery rates, death or for that matter any aspect of CSAM in the last 10 years. In the absence of documented data it is difficult to make policy changes in the antibiotic management of CSAM and refining the approach of management of severe malnutrition is a simple way of reducing child mortality in resource limited countries.

References

1. Robert E Black, Lindsay H Allen, Zulfiqar A Bhutta, Laura E Caulfield, Mercedes de Onis, Majid Ezzati, Colin Mathers *et al*. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet Infect Dis*. 2008; 371(9608):243-60.
2. Z .A Bhutta SBS. National nutrition survey Pakistan, Aga Khan University, Pakistan; 2011.
3. WHO. Community-based management of severe acute malnutrition: World Health Organization, World Food Programme, United Nations System Standing Committee on Nutrition, United Nations Children's Fund; 2007.
4. Latif S, Anwar MS, Ahmad I. Bacterial pathogens responsible for blood stream infections (BSI) and pattern of drug resistance in a tertiary care hospital of Lahore. *Biomedica* 2009; 25:101-5.
5. Thaver D, Zaidi AK, Critchley JA, Azmatullah A, Madni SA, Bhutta ZA. Fluoroquinolones for treating typhoid and paratyphoid fever (enteric fever). Cochrane Database Syst Rev. 2008;4.

Dr. Farah Naz Qamar
Assistant Professor,
Department of Pediatrics and Child Health,
Aga Khan University, Karachi, Pakistan.
E-mail: farah.qamar@aku.edu

ORIGINAL ARTICLE

Spectrum of Pathogens of Ventilator Associated Pneumonia among Cancer Patients in Pakistan

Naveed Rashid*, Faisal Sultan*, Syed Hammad Nazeer*, Summiya Nizammudin**, Aun Raza*, Amjad Mahboob*, Nadeem Paul***

*Department of Internal Medicine, Division of Infectious Diseases, Shaukat Khanum Memorial Cancer Hospital & Research Centre, Lahore.
**Department of Pathology, Shaukat Khanum Memorial Cancer Hospital & Research Centre, Lahore.
***Infection Control Nurse, Shaukat Khanum Memorial Cancer Hospital & Research Centre, Lahore

Abstract

Objective
Ventilator associated pneumonia (VAP) is a common complication among patients admitted to the intensive care units (ICU). Local research lacks data regarding its incidence in general or the immunocompromised population. In this study, we aim to determine the incidence and common etiological agents of ventilator associated pneumonia in cancer patients admitted to the intensive care unit (ICU) of a major tertiary care hospital in Pakistan.

Methods
This study was conducted retrospectively by reviewing medical records of cancer patients admitted in the ICU from January 2010 till September 2012.

Results
Out of the 2032 patients admitted into the ICU, 737 (36.3%) were mechanically ventilated. 23 (3.1%) of these fulfilled the diagnostic criteria for VAP (as per National Healthcare Safety Network (NHSN); 10 (43.5%) of these patients suffered from solid organ malignancies while 12 (52.2%) suffered with haematological malignancies. The attributable mortality due to VAP was 60.9%, with 60% mortality in solid organ malignancies and 58.3% mortality in haematological malignancies. VAP rates ranged from 29.4 to 3.2. The most common pathogens identified were *Acinetobacter baumannii*, followed by members of Enterobacteriaceae family and *Candida albicans*.

Conclusions
VAP rates in cancer patients in our institute are high with a high mortality rate.

Key Words
Ventilator Associated Pneumonia, Cancer Patients, Intensive Care Unit

Corresponding Author: Naveed Rashid,
Department of Internal Medicine, Division of Infectious Diseases, Shaukat Khanum Memorial Cancer Hospital & Research Centre, Lahore.
Email : dr.naveedrashid@gmail.com

Introduction
Health care associated pneumonia is the second most common cause of nosocomial infections in United States among patients admitted in intensive care units.[1] Mechanical ventilation is the major risk factor for health care associated pneumonia called as VAP. Incidence of health care associated pneumonia varies from 45% in India to 86% in United States.[1,2] Multidrug resistant (MDR) bacterial pathogens are becoming increasingly associated with VAP.[3,4] The distribution of these bacterial pathogens correlate with early or late onset VAP.[2,3] The risk factors associated with VAP include advanced age, immunosuppression, exposure to broad-spectrum antibiotics, increased severity of illness, previous hospitalization or residence in a chronic care facility and prolonged duration of invasive mechanical ventilation.[4,5] Cancer patients are at risk of acquiring VAP with MDR bacteria due to the presence of more than one of the above risk factors. Therefore, VAP in cancer patients is the leading cause of nosocomial infection as compared to being the second most common cause amongst the general population.[1,6,7] Apart from bacterial causes, some studies have also implicated fungal pathogens as an important cause of VAP especially with early onset.[8] The risk of acquiring VAP due to fungi also increases in this immunocompromised population.[6] Patients colonized with Candida species are 1.58 times more likely to develop VAP and 2.22 times more likely to develop it with *Pseudomonas aeruginosa*.[9]

Limited studies from Pakistan on different aspects of VAP have already been conducted but most are geared towards the knowledge of nursing staff about VAP prevention, infection control education and VAP in children.[10-13] So far, no study has been conducted locally on the etiologic agents of VAP in cancer patients. In this study we evaluated the incidence, mortality and etiologic agents of VAP among cancer patients at a tertiary care hospital of Pakistan.

Materials & Methods
This study was conducted at a major tertiary care hospital in Lahore, Pakistan. The center mainly caters to the management of oncological diseases among other specialities. We retrospectively reviewed the electronic medical records of those cancer patients who were admitted in the ICU from January

2010 to September 2012. A total of 2032 patients were admitted in the ICU during this period, of which 737 (36.3%) patients were mechanically ventilated. We reviewed the records of these mechanically ventilated patients as per the NHSN January 2012 Patient Safety Component Manual related to the diagnosis of VAP.[14] The device days or ventilator days, (the number of patients on a ventilator), were collected daily as part of routine infection control surveillance and were used as denominator for calculation of the quarterly VAP rates.

SPSS version 16.0 was used for data entry and analysis. We calculated the quarterly rates of VAP/1000 device days, mortality in patients who developed VAP and the frequency of the causative organisms for VAP and their antibiotic sensitivity patterns. We also calcultated rates of VAP, device days (DD) and Device Utilization Ratio (DUR) over a three year period (2010-12) from our institute.

Results

Out of 737 patients, 23 (3.1%) patients fulfilled the diagnostic criteria for VAP as per NHSN criteria. Out of these, 16 patients had PNU1 (clinically defined pneumonia), 1 patient had PNU2 (pneumonia with common bacterial and filamentous fungal pathogens and specific laboratory findings) and 6 patients had PNU3 (pneumonia in immunocompromised patients). Demographic details of these patients are given in Table 1. All of these patients had some form of malignancy, 10 (43.5%) patients had solid organ malignancies, 12 (52.2%) had hematological malignancies and 1 patient had a mediastinal mass of unknown etiology. Amongst the solid organ malignancies (n=10) there was one patient each with gastroesophageal cancer, esophageal cancer, sarcoma, breast cancer, rectal cancer, Wilm's tumor, medulloblastoma, Germ cell tumor, thymoma and urinary bladder cancer. Hematologic malignancies (n=12) included eight patients with non-Hodgkin's lymphoma, two with Hodgkin's lymphoma and two with acute myeloid leukemia. VAP rate and device utilization ratio is given in Table 2. There were 29 different microbial (27 bacterial and 2 fungal) isolates identified from 23 patients. The distribution of these 29 isolates from 24 culture specimens (one patient developed VAP twice) is given in Table 3. The resistance pattern of different Enterobacteriaceae (26 isolates) to antibiotics is given in Table 4. There was only one gram positive isolate vancomycin-resistant enterococcus. A total of 14 out of 23 patients (60.9%) died in the ICU with 60% mortality in solid organ malignancies and 58.3% mortality in hematologic malignancies.

Table 1: Characteristics of cancer patients with VAP (n=23)

Cancer Category	Mean age (years)	Age < 18 years	Age ≥ 18 years	Male	Female
Hematologic (n=12)	27.8±17.4	4	8	8	4
Solid organ (n=10)	42.6±27.4	3	7	5	5
Unknown (n=1)	65	0	1	0	1
Total	35.87 ± 23.52	7	16	13	10
%	-	30.4	69.6	56.5	43.5

Discussion

The rates of VAP have been reported to be 25-30% worldwide, with 0-50% mortality. The rates of VAP in our study varied between 3-29% but were associated with significant mortality. In our study 93.1% of causative organisms were gram negative bacteria followed by 6.9% of fungal pathogens. According to a recent study from Korea, amongst general hospital patients the most common pathogen isolated was *methicillin resistant Staphylococcus aureus* (MRSA) while in our study apart from one patient infected with *Enterococcus spp.* (VRE) no other gram positive bacteria were isolated.[3]

Our results showed *Acinetobacter baumannii* as the most common pathogen followed by *Pseudomonas aeruginosa*. Since we could not find a similar study exclusively done in cancer patients in Pakistan, we compared this data to a local study that was conducted on children of with a different spectrum of pathogens. In this *Pseudomonas aeruginosa* was the most common pathogen isolated followed by *Klebsiella species* and *Escherichia coli*. No fungal pathogen was isolated.[13]

Two or more bacterial isolates were found in three of our cases, where *Acinetobacter baumannii* and *Klebsiella pneumoniae* were the common pathogens as compared to poly-microbial isolates in 19.8% cases from a Korean study amongst general hospital patients.[3] In the same study about 69% isolates of *Acinetobacter baumannii* were imipenem resistant. Almost half (47.9%) of the strains of Acinetobacter *baumannii* were multidrug resistant in a study from India.[2] On the other hand, in our case 100% of *Acinetobacter baumannii* were resistant to imipenem. All of these were also 100% resistant to other beta lactam antibiotics while resistance to gentamicin was 92.8%, followed by 85.7% for ciprofloxacin and 71.4% for amikacin. There was no resistance reported against colistin and polymixin B in these isolates. None of the other bacterial isolates were resistant to carbapenems. In contrast to our study, fungal

Table 2: VAP rates and device utilization ratios for a 3 year period (2010 -12)

Year	Quarter	VAP	Device days (DD)	VAP rate /1000 DD (NHSN ratio 3.3)	Patient days	Device Utilization Ratio (DUR) (NHSN ratio 0.44)
2010	1st Q	1	207	4.8	372	0.55
	2nd Q	3	241	12.4	388	0.6
	3rd Q	2	295	6.7	393	0.75
	4th Q	1	313	3.2	470	0.66
2011	1st Q	1	121	8	437	0.27
	2nd Q	1	34	29.4	383	0.08
	3rd Q	4	151	26.5	354	0.42
	4th Q	2	304	6.6	444	0.68
2012	1st Q	1	121	8	437	0.27
	2nd Q	4	303	13.2	603	0.5
	3rd Q	3	212	14.1	544	0.39
Total	11 Q	23	2302	9.99	4825	0.47

Table 3: Microbiologic features of cancer patients with VAP

Culture Source (n=24)	Isolates	Culture Specimens	
		n	%
Tracheal aspirates (n=21)	*Acinetobacter baumanii*	12	50
	Pseudomonas aeruginosa	3	12.5
	Klebsiella pneumoniae	1	4.2
	Stenotrophomonas maltophiia	1	4.2
	Enterococcus spp. (VRE)	1	4.2
	Klebsiella pneumoniae + Stenotrophomonas maltophilia + Enterobacter cloacae	1	4.2
	Acinetobacter baumanii + Pseudomonas aeruginosa + Klebsiella pneumoniae	1	4.2
	Candida albicans	1	4.2
Broncho-alveolar lavage (n=1)	*Candida albicans*	1	4.2
Pleural fluid (n=1)	*Citrobacter freundii + Acinetobacter baumanii*	1	4.2
Blood not explained otherwise (n=1)	*Escherichia coli*	1	4.2

Table 4: Resistance pattern of the pathogens isolated from cases with VAP

Bacterial Pathogens (n=26)	Percentage Drug Resistance									
	Imi/ Merope	Pip/tazo	Colistin/ Polymyxin B	Co-trim oxazole	Genta micin	Amika cin	Cipro	Cefepime	Ceftaz	Tetra-cycline
Acinetobacter baumanii (n=14)	14/14 (100%)	14/14 (100%)	0/14 (0%)	14/14 (100%)	13/14 (92.8%)	10/14 (71.4%)	12/14 (85.7)	14/14 (100%)	14/14 (100%)	14/14 (100%)
Pseudomonas aeruginosa (n=4)	1/4 (25%)	1/4 (25%)	0/4 (0%)	NT*	0/4 (0%)	0/4 (0%)	1/4 (25%)	2/4 (50%)	2/4 (50%)	NT*
Stenotrophomonas maltophilia (n=2)	NT*	NT*	NT*	0/2 (0%)	NT*	NT*	0/2 (0%)	NT*	1/2 (50%)	NT*
Klebsiella pneumoniae (n=3)	0/3 (0%)	0/3 (0%)	NT*	0/3 (0%)	0/3 (0%)	0/3 (0%)	0/3 (0%)	NT*	NT*	1/2 (33%)
Eschericia coli (n=1)	0/1 (0%)	0/1 (0%)	NT*	1/1 (100%)	0/1 (0%)	0/1 (0%)	1/1 (100%)	1/1 (100%)	1/1 (100%)	0/1 (0%)
Citrobacter fruendii (n=1)	0/1 (0%)	0/1 (0%)	NT*	1/1 (100%)	1/1 (100%)	0/1 (0%)	1/1 (100%)	NT*	NT*	1/1 (100%)
Enterobacter cloacae (n=1)	0/1 (0%)	0/1 (0%)	NT*	0/1 (0%)	0/1 (0%)	0/1 (0%)	0/1 (0%)	NT*	NT*	0/1 (0%)

NT* = Not tested

infections are the second most common cause (22.2%) of nosocomial infections in Brazil amongst cancer patients admitted in ICU. The reason for the low rates of fungal infections in our cancer population is not clear but may be attributable to the overall low rates of VAP and the study of a single nosocomial infection i.e. VAP [6].

In our study, 52.2% of cases had hematological malignancies as the underlying diagnosis, while this proportion was 80% among pediatric cancer patients from Thailand and 15% in a European study.[7,15] More than two third of our patients were ≥ 18 years of age. The mean age of patients with solid organ malignancies was higher as compared to those with hematologic malignancies. This finding was in contrast to the European study where there was a negligible difference between the two groups.[7] According to the same European study solid organ malignancies were more common in males i.e. 66.6% as compared to 52.9% males in hematologic malignancies but this pattern is reversed in our cases with 50% and 66.6% males respectively.[7]

The device utilization ratio in our study was highly variable in each quarter ranging from 0.08 to 0.75 with a mean of 0.47 which is quite close to NHSH ratio of 0.44 and is also lower than a similar study done in cancer patients from Brazil.[6] As compared to standard NHSN value of 3.3 VAPs per 1000 endotracheal intubation days, the rate in our study almost always remained variable during the quarter with values as low as 3.2 to as high as 29.4 and a mean value of 9.9. This value is still much lower than 21 VAPs per 1000 endotracheal intubation days noted in a study amongst paediatric cancer patients from Thailand.[15] The difference in values might be secondary to the difference in pattern of age groups involved in the studies.[15]

Mortality in our patients with solid organ and hematologic malignancies was almost same i.e. 60% and 58.3% respectively while it was 20% and 42% respectively in a European study where mortality was calculated for sepsis and respiratory complications in ICU.[7]

The major limitation of our study was the retrospective nature from a single centre. Larger multicentre reports from our country are needed to have a better idea of infection control practices within the country.

Conclusion

Gram negatives were the most common pathogens responsible for VAP in our cancer patients. The rate of VAP per 1000 device days and device utilization ratio in our study was lower as compared to same groups in international studies but associated with a high mortality. Stringent infection control policies can help reduce the burden of this avoidable cause of death.

Conflict of Interest Statement

The authors of this study declare no conflict of interest.

References

1. Richards MJ, Edwards JR, Culver DH, Gaynes RP. Nosocomial infections in medical intensive care units in the United States. National Nosocomial Infections Surveillance System. *Crit Care Med* 1999;27(5):887-92.
2. Dey A, Bairy I. Incidence of multidrug-resistant organisms causing ventilator-associated pneumonia in a tertiary care hospital: a nine months' prospective study. *Ann Thorac Med* 2007;2(2):52-7.
3. Chi SY, Kim TO, Park CW, Yu JY, Lee B, Lee HS, *et al*. Bacterial pathogens of ventilator associated pneumonia in a tertiary referral hospital. *Tuberc Respir Dis* 2012;73(1):32-7.
4. Grgurich PE, Hudcova J, Lei Y, Sarwar A, Craven DE. Management and prevention of ventilator-associated pneumonia caused by multidrug resistant pathogens. *Expert Rev Respir Med* 2012;6(5):533-55.
5. Koenig SM, Truwit JD. Ventilator-associated pneumonia: diagnosis, treatment, and prevention. *Clin Microbiol Rev* 2006;19(4):637-57.
6. Velasco E, Thuler LC, Martins CA, Dias LM, Goncalves VM. Nosocomial infections in an oncology intensive care unit. *Am J Infect Control* 1997;25(6):458-62.
7. Taccone FS, Artigas AA, Sprung CL, Moreno R, Sakr Y, Vincent JL. Characteristics and outcomes of cancer patients in European ICUs. *Crit Care* 2009;13(1):R15.
8. Joseph NM, Sistla S, Dutta TK, Badhe AS, Rasitha D, Parija SC. Ventilator associated pneumonia in a tertiary care hospital in India: role of multi drug resistant pathogens. *J Infect Dev Ctries* 2010;4(4):218-25.
9. Azoulay E, Timsit JF, Tafflet M, de Lassence A, Darmon M, Zahar JR, Adrie C, *et al*. Candida colonization of the respiratory tract and subsequent pseudomonas ventilator-associated pneumonia. *Chest* 2006;129(1):110-7.
10. Meherali SM, Parpio Y, Ali TS, Javed F. Nurses' knowledge of evidence based guidelines for prevention of ventilator-associated pneumonia in critical care areas: a pre and post-test design. *J Ayub Med Coll Abbottabad* 2011;23(1):146-9.
11. Salahuddin N, Zafar A, Sukhyani L, Rahim S, Noor MF, Hussain K, *et al*. Reducing ventilator-associated pneumonia rates through a staff education programme. *J Hosp Infect* 2004;57(3):223-7.
12. Khan MS, Siddiqui SZ, Haider S, Zafar A, Zafar F, Khan RN, *et al*. Infection control education: impact on ventilator-associated pneumonia rates in a public sector intensive care unit in Pakistan. *Trans R Soc Trop Med Hyg* 2009;103(8):807-11.
13. Hamid MH, Malik MA, Masood J, Zia A, Ahmad TM. Ventilator-associated pneumonia in children. *J Coll Physicians Surg Pak* 2012;22(3):155-8.
14. National Healthcare Safety Network (NHSN) Report, CDC. Ventilator associated pneumonia. Available at: http://www.cdc.gov/nhsn/PDFs/pscManual/6pscVAPcurrent.pdf. [Accessed on January 2013]
15. Oberdorfer P, Pongwilairat N, Washington CH. Nosocomial Infections among Pediatric Patients with Neoplastic Diseases. *Int J Pediatr* 2009;72:1320.

ORIGINAL ARTICLE

Slide Positivity Rate of Malaria and its Association with Blood Chemistry in Hospitalized Adults at Bannu, Pakistan

Lubna Khatoon, Yar Muhammad Khan, Salman Akbar Malik

Department of Biochemistry, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan

Abstract

Objective
To assess the slide positivity rate of malaria and to evaluate its association with blood chemistry in adult patients admitted at a hospital in Bannu, Pakistan.

Methods
Blood samples from 3500 patients who presented to a hospital in Bannu for suspected malaria were collected between August to September 2007. The blood films of these patients were examined by Giemsa staining. Biochemical analysis (serum glucose, bilirubin, ALT, AS, creatinine) was performed on all samples that tested positive for malaria and compared to 70 randomly selected samples that were negative for malaria

Results
The slide positivity rate for malaria was 22% (767/3500) for all malarial species. Among them 55 (7.2%) were *P. falciparum*, while 712 (92.8%) were *P. vivax.*

The biochemical features of the 767 malaria positive patients were compared to randomly selected 70 patients to determine the association of malaria with blood biochemistry. Patients with *P. vivax* had higher mean serum creatinine (0.50 vs. 1.07; $p<0.01$) and bilirubin levels.(0.567mg/dl versus 3.07 ; $p<0.01$). Similarly patients with *P. falciparum* also had higher mean levels for creatinine and bilirubin. No significant difference was observed in AST, ALT and glucose concentration amongst malaria positive and negative subjects for either vivax or falciparum.

Conclusion
There is a very high burden of malaria in Bannu district. Both *P. vivax* and *P. falciparum* infections are associated with an increase in mean bilirubin and creatinine levels.

Key Words
Malaria, *P. falciparum*, *P. vivax*

Introduction

Malaria ranks high among health problems in Pakistan. It affects an estimated 300 million people per year worldwide causing more than a million deaths annually.[1] Majority of the fatalities occur in children under five years of age. Pregnant women and non-immune people are at particular risk. The problem has been compounded by the emergence of drug resistant strains of plasmodia and insecticide resistance anopheline mosquito which is a causative vector.[2,3] Climate change affects malaria indirectly by changing the ecological relationship that is important to the organisms involved in malaria transmission (the vector, parasite and host). Indirect forces like deforestation and habitat changes due to climate change may also affect survival of a particular species of *Anopheles*. The three main climate factors that affect malaria are temperature, precipitation, and relative humidity.[4] Climate predicts, to a large degree, the natural distribution of malaria.[5] Epidemics of malaria are caused by a disturbance in equilibrium between host, parasite and vector. *P. vivax* and *P. falciparum* cause different types of epidemics. *P. vivax* epidemics occur mainly in areas with only seasonal transmission and show a bimodal peak, the second peak caused by relapses, whereas *P. falciparum* epidemics grow slowly and then explode causing only one peak of transmission.[6] Malaria in Pakistan is typically unstable and major transmission period is post monsoon i.e. from August to November. Most studies from Pakistan are based on the parasite burden, and most report severe illness due to *P. falciparum*.

The aim of present study was to determine the slide positivity for *Plasmodium vivax* and *Plasmodium falciparum* in hospitalized adults at Bannu district (K.P.K) Pakistan. We also analysed the differences in blood biochemistry of subjects with vivax or falciparum malaria and compared them to malaria negative subjects.

Materials & Methods

Blood sampling and Parasite detection

A total of 3500 people visiting Women and Children Hospital, Bannu with suspected malaria were selected for the study. After taking written informed consent from the patients, finger prick blood was taken from these patients for preparation of slides. Giemsa staining microscopy was adopted for the detection of malaria parasites. Trained technical staff verified species of the parasite. After confirmation of positive cases, 70 subjects were selected randomly for biochemical evaluation. For this purpose blood samples (3-4ml) were taken and serum was separated through centrifugation and stored at –20ºC till further analysis.

Corresponding Author: Lubna Khatoon,
Department of Biochemistry, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan
Email: lubnakhatoonqau@gmail.com

Serum levels of total glucose, bilirubin, alanine amino transferase (ALT), aspartate amino transferase (AST) and serum creatinine were determined by using pre-packed kits of AMP Diagnostics (AMP Medizintechnik GmbH, Graze, Austria). All experimental work was carried out by the Dept. of biochemistry Quaid-i-Azam University, Islamabad.

The study was approved by the ethical review committee of Quaid-i-Azam University, Islamabad.

Statistical Analysis

Statistical analysis was carried out using SPSS version 10.0. Mean and standard deviation is reported for continuous variables and frequencies for categorical variables. A student t-test was used to determine the difference between biochemical parameters of patients with and without malaria. P<0.05 was considered significant.

Results

From August to September 2007, 3500 patients suspected to be suffering from malaria were enrolled. The blood films of these patients were tested for the presence of malarial parasites. Slide positivity rate for malaria was 22%. Of the 767 positive slides only 55 (7.2%) showed *P. falciparum*, while 712 (92.8%) showed *P. vivax*. From the 70 patients with malaria that were randomly selected for biochemical analysis, 42 had *P. vivax* and 28 had *P. falciparum*.

Table 1 and 2 show the mean serum bilirubin, glucose, ALT, AST and serum creatinine level of patients with *P. vivax* and *P. falciparum* in comparison with malaria negative subjects, whose samples were submitted to the lab for malaria but tested negative for the parasite.. There was a significant difference in S.bilirubin and S.creatinine of patients with malaria (both vivax and falciparum) as compared to malaria negative subjects.

Discussion

As presented in results the slide positivity rate in present study was 22%. However, in earlier studies the slide positivity rate reported by Iqbal and co-workers[7] during 1991 was only 9.2%. Similarly, the slide positivity rate from 1973 to 1994 as reported by Malaria Control Program, Pakistan, ranged from 14.09% in 1973 to 3.9% in 1994.[8] In studies conducted during 1983-84 in Pakistan by Strickland and co-workers a slide positivity rate of 37-43% was reported.[9] The low slide positivity rate reported in some of the above studies may have been an under estimation or our report may have overestimated the rates, as the data is from hospitalized patients and is not reflective of the true incidence in the community. Microscopic diagnosis of malaria is the gold standard but it has inherent limitations and is limited by technical expertise. Due to work load or lack of adequately trained staff there may be underreporting of cases.

Table 1: Effect of *P. vivax* malaria on human blood biochemistry

Biochemical Parameters	Control Subjects (n=70)	Patients (n=42)	*p*-value
Glucose (mg/dl)	71 ±23.8	68.34 ±45.31	0.81
Bilirubin (mg/dl)	0.57 ±0.25	03.07 ±2.37	<0.01
ALT (U/l)	15.13 ±8.72	16.40 ±16.40	0.74
AST (U/l)	14.36 ±8.34	18.93±18.50	0.29
Creatinine (mg/dl)	0.50 ± 0.26	01.08 ± .65	<0.01

Table 2: Effect of *P. falciparum* malaria on human blood biochemistry

Biochemical Parameters	Control Subjects (n=70)	Patients (n=28)	*p*-value
Glucose (mg/dl)	71 ±23.87	68.36 ± 45.55	0.81
Bilirubin (mg/dl)	0.57 ± 0.25	03.90 ± 3.0	<0.01
ALT (U/l)	15.13 ± 8.7	16.08 ± 16.40	0.74
AST (U/l)	14.36 ± 8.34	23.76 ± 18.50	0.47
Creatinine (mg/dl)	0.50 ± 0.26	1.20 ± 0.78	<0.01

The present study shows that the prominent species infecting the people in K.P.K is *P. vivax* (92.8%). This is consistent with the results of other similar studies conducted for different areas of Pakistan.[10] A similar study was carried out in Quetta, Pakistan in which a total of 263018 subjects who were screened, the positivity rate was 35%, of which *P. falciparum* was detected in one third of the samples and *P. vivax* in two thirds of the samples which shows that *P. vivax* is the predominant specie in Quetta, which is similar to our results.[11] Data from the province of Punjab (Pakistan) also shows that *P. vivax* is the commonest specie.[12]

Harris *et al* found that 72% of patients with jaundice due to malaria have direct biliruenemia and elevated liver enzymes suggesting hepatocelluler damage.[13] Reports from Thailand and India show an incidence of jaundice in 30-40% of the cases of falciparum malaria although the bilirubin level was predominantly conjugated.[13,14] Our study shows that jaundice is more common in falciparum malaria as compared to vivax malaria.

Data from a study done in Calcutta showed presence of jaundice in 40% and 9.09% cases with falciparum malaria, and *P. vivax* respectively.[15] Bilirubin levels increase due to malarial hepatitis and there is a greater rise in conjugated bilirubin.[16,17] Our study also shows that bilirubin levels increased significantly in cases of both vivax and falciparum.

Most of the previous studies with hypoglycemia and severe malaria

were conducted in children.[18] In Thailand, hypoglycemia was detected in 8% of adults with malaria.[21] Many workers have reported hypoglycemia with severe malaria. We detected hypoglycemia in nearly 11% of the patients with sever falciparum malaria. Shah and colleagues reported hypoglycemia in 2 out of 20 cases (10%) of severe falciparum malaria from Karachi.[19]

Most of the previous studies suggest that children are more prone to hypoglycemia because of limited hepatic glycogen reserve and reduced intake of food during illness.[20] Thai adults with severe malaria had greatly reduced absorption capacity for sugar transport both actively and passively.[21]

Quinine administration can also cause hypoglycemia. Most of our patients have hypoglycemia before quinine administration. This suggests that there are multiple causes leading to hypoglycemia in malaria.[22]

We did not find significant elevation of either ALT or AST. Some of the previous studies report similar results.[23] These also concluded that the number of patients verses time duration against malarial infection does not significantly elevate both AST and ALT. Only two patients showed significant increase over time.

In our study, serum creatinine level was found to be significantly elevated in cases with malaria caused by either *P. vivax* or *P. falciparum*. Most of the studies done earlier have shown that serum creatinine level is significantly increased in severe *falciparum* malaria.[24]

Conclusion

P. vivax is the predominant in district Bannu. Malaria causes significant elevation of serum bilirubin, and creatinine as compared to subjects without malaria. These parameters should be kept in mind during malaria case management and adequate hydration and monitoring of fluid balance should be emphasized.

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Conflict of Interest

This article is original work of authors and has not been submitted elsewhere for publication.

References

1. Cattani J, Davidson D and Engers H. Malaria. In: 11th Program report. Geneva. *Trop Dis Res* 1993; 15-25
2. Cheesbrough M. Medical Laboratory Manual for Tropical Countries. Vol I, Kent, UK: Butterworth & Co, Ltd., 1987; 1: 221-51.
3. Martens WJM, Niessen LW, Rotmans J, Jetten TH, McMichael AJ. Potential Impact of Global Climate Change on Malaria Risk. *Environ Health Perspect* 1995; 103:458-64.
4. Pampana E. A textbook of malaria eradication. Oxford University Press, London. 2nd Edition.1969
5. Bouma MJ, Dye C, Van der Kaay HJ. Falciparum malaria and climate change in the North West Frontier Province of Pakistan. *Am J Tropic Med Hyg* 1996; 55: 131-7.
6. Najera JA, Kavznetzsov RL, Delacollette C. Malaria epidemics: Detection and Control, Forecasting and Prevention. Geneva: WHO, Division of Control of Tropical Diseases Geneva.1998.
7. Iqbal J, Hira PR, Sher A, Al-Enezi AA. Diagnosis of imported malaria by Plasmodium lactate dehydrogenase (pLDH) and histidine-rich protein 2 (PfHRP-2)-based immunocapture assays. *Am J Trop Med Hyg* 1991; 64:20-23.
8. Iqbal J, Sher A, Hira PR, Al-Owaish R. Comparison of the OptiMAL® test with PCR for diagnosis of malaria in immigrants. *J Clin Microbiol*. 1994; 39: 3644–46.
9. Strickland GT, Zafar-Latif A, Fox E, Khaliq AA, Chowdhry MA. Endemic malaria in four villages of the Pakistani province of Punjab. *Trans R Soc Trop Med Hyg* 1987; 81: 36-41.
10. Rafi S, Memom MA, Rao MH, Bilo AG. A change of Plasmodium species infecting children in Karachi over the last decade. *JPMA* 1994; 44:162-65.
11. Azeem SS, Aqleem AS, Nadeem SS, Paracha SM. Endemicity of malaria in Quetta. *Pak J Med Res* 2005; 44: 32-41
12. Prybylski D, Khaliq A, Fox E, Sarwari AR, Thomas G. Strickland Parasite Density And Malaria Morbidity In The Pakistani Punjab. *Am J Trop Med Hyg* 1999; 61: 791–801.
13. Harris VK, Richard VS, Mathai E. A study on clinical profile of falciparum malaria in a tertiary care hospital in south India. *Indian J Malario*l 2001; 38:19–24.
14. Ashley EA, Krudsood S, Phaiphun L, Srivilairit S, McGready R, Leowattana W, Hutagalung R, *et al* . Randomized, controlled dose-optimization studies of dihydroartemisinin-piperaquine for the treatment of uncomplicated multidrug-resistant falciparum malaria in Thailand. *J Infect Dis* 2004; 190:1773-82.
15. Hazra BR, Chowdhury RS, Saha SK, Ghosh MB, Mazumder AK. Changing scenario of malaria: a study at Calcutta. *Indian J Malariol* 1998; 35:111–16.
16. Kochar DK, Kaswan K, Kochar SK, Sirohi P, Pal M, Kochar A, Agrawal RP, Das A. A comparative study of regression of jaundice in patients of malaria and acute viral hepatitis. *J Vect Borne Dis* 2006; 43: 123-29.
17. Prati D, Taioli E, Zanella A. Updated definitions of healthy ranges for serum alanine aminotransferase levels. *Ann Intern Med* 2002; 137:1-9.
18. White NJ, Williamson D, Turner R, Warrell DA, Chanthavanich P, Looareesuwan S, Warrell MJ, Krishna S. Severe hypoglycemia and hyperinsulinaemia in falciparum malaria. *N Eng J Med* 1983; 309:61-66.
19. Shah I, Rowland M, Mehmood P, Mujahid C, Razique F, Hewitt S, Durrani N. Chloroquine resistance in Pakistan and the upsurge of falciparum malaria in Pakistani and Afghan refugee populations. *Ann Trop Med Parasitol* 1997; 91:591-602.
20. Brewster DR, Kwiatowski D, White NJ. Neurological sequelae of cerebral malaria in children. *Lancet* 1990; 336:1039-43.
21. Molyneux ME, Looareesuwan S, Menzies IS. Reduced hepatic flow and intestinal malabsorption in severe falciparum malaria. *Am J Trop Med Hyg* 1989; 40:470–76.
22. Philips RE, Looareesuwan S, White NJ. Hypoglycemia and antimalarial drugs: quinidine and release of insulin. *Br Med J* 1986; 292:1319-21
23. Lell B, Kremsner PG. Clindamycin as an antimalarial drug: review of clinical trials. *Antimicrob Agents Chemotherap* 2002; 46:2315-20
24. Maitland K, Williams TN, Newbold CI. *Plasmodium vivax* and *P. falciparum*: biological interactions and the possibility of cross-species immunity. *Parasitol Today* 1997; 13:226-31.

ORIGINAL ARTICLE

Pathogens causing Bacteremia in Patients with Urinary Tract Infection in Urology and Nephrology Units of a Tertiary Care Hospital in Karachi, Pakistan

Sadaf Baqai, Muhammad Zeeshan, Saleem Hafeez, Syed Kashif Raza, Parpoola Kumari

Department of Microbiology, Sindh Institute of Urology and Transplantation, Karachi, Pakistan

Abstract

Background
In urology and nephrology units the rate of urinary tract infections and its complication is one of the main infective causes of mortality and morbidity. Early and prompt antibiotic therapy based on the knowledge of the prevalent microorganisms can help reduce this rate. The objective of the study was to assess the microbiology and rate of bacteremia causing urinary tract infections in the urology and nephrology unit of our institute.

Methods
This was retrospective study over 4 month period (July to October 2010); 103 paired urine and blood samples from urology and nephrology unit received in the clinical laboratory were analyzed. Microbiological data was retrieved from laboratory data base. Cultures were performed using standard microbiological methods. Organisms were identified using routine biochemical tests. Antibiotic susceptibility testing was performed with Kirby-Bauer disc diffusion method using Clinical laboratory standard institute (CLSI) standards.

Results
Significant bacteriuria was found in 68% and 31% had only bacteremia. *E.coli* was the most commonly isolated organism from blood and urine culture, 60% were extended spectrum beta lactamases producers. About 14% of the patient had concordant organisms in blood and urine cultures and were labeled as urosepsis, while 6% patients had disconcordant results with different organisms in blood and urine and 8% had negative urine culture and positive blood cultures.

Conclusion
Rates of urinary tract infection are high and lead to bacteremia in one third of the patients and can be reduced with stringent infection control practices.

K**ey Words**
Bacteremia, Urinary Tract Infection, Urology.

Introduction

Urinary tract infection (UTI) is one of the major causes of morbidity and mortality throughout the globe especially in hospitalized patients.[1] Systemic infection or bacteremia complicating UTI happens in patients with underlying risk factors that include urinary tract instrumentation (e.g., catheterization, cystoscopy), anatomic abnormalities, urine out flow obstruction or poor bladder emptying, immunocompromised population such as post renal transplant, diabetic and chemotherapy recipients.[2]

Bacteria can enter the bladder with the insertion of the catheter, through the catheter lumen, or from around the outside of the catheter. A biofilm develops around the outside of the catheter and on the uroepithelium. Bacteria enter this biofilm, which protects them from the mechanical flow of urine, host defenses, and antibiotics, making bacterial elimination difficult.[3]

About 15 % of UTI patients have bacteremia at the time of presentation to the hospital and the source of 20% of hospital-acquired bacteremia is the urinary tract. The mortality associated with this condition is about 10%.[4,5] The microbiological spectrum of uropathogens are changing in urology unit with increasing incidence of Gram positive organisms such *Enterococcus faecalis*, *Staphylococcus aureus*, however members of family Enterobacteracea are still the predominant pathogen.[6]

As our institute is the largest urology, nephrology and dialysis unit of the country, this study would provide the baseline data regarding microbiology and the incidence of bacteremia complicating urinary tract infection at our institute. The objective of the study was to assess the microbiology and frequency of urinary tract infection causing bacteremia in our urology and nephrology units.

Materials & Methods

This was a retrospective study conducted in the department of microbiology of the Sindh Institute of Urology and Transplantation (SIUT) from July to October 2010. One hundred and three paired urine and blood samples from urology and nephrology units received in the clinical laboratory were included. All midstream urines (MSU) were processed for quantitative analysis using calibrated 0.001 ml disposable plastic loops and inoculated by Quadrant Technique on Cystine Lactose Electrolyte-Deficient Agar (Oxoid, UK). Plates were incubated overnight at 37°C ambient air using a 0.001 ml loop. Bacterial count of

Corresponding Author: Muhammad Zeeshan,
Department of Microbiology, Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan.
E-mail: dr.zeeshan1@gmail.com

$\geq 10^5$ CFU/ml of a single type was considered significant. About 8-10 ml of blood was collected in BACTEC Standard/10 Aerobic Culture Vials and incubated in BACTEC 9240 for next 5 days. Gram smears were made from all positive vials. Sub-culture on chocolate agar and MacConkey agar (Oxoid, UK) were incubated at 37°C for overnight. Chocolate agar was placed in 5-7% CO_2 environment.

Organisms were identified using sets of different routine biochemical tests according to the organisms; API (analytical profile index - Biomerieux) was used for gram negative rods. Antibiotic susceptibility testing was performed using Kirby-Bauer disc diffusion method using CLSI standards.[7]

Patients with similar organisms in both blood and urine cultures were recorded as having concordant culture while those with different organisms in urine and blood samples were classified as disconcordant.

Results

A total of 103 paired blood and urine samples were received over a period of 4 months. 69% of the samples were from transplant unit and emergency ward while rests were from other medical and surgical units. Most (67%) samples were from males.

Out of total urine cultures received, 70 (68%) had significant bacteriuria; and 31 (31%) had an isolate on blood culture. *E.coli* was the most commonly isolated organism from urine cultures (n=40, 57%) and blood cultures (n=11, 36%). Table 1 shows frequency of positivity of urine and blood cultures. Figure I show the description of 14 patients with disconcordant results. Of the 10 *E.coli* isolated in the concordant pairs, 6 were multidrug resistant. Figure 2 shows the organisms of bacteremia in patients with disconcordant blood and urine results.

Discussion

Patients admitted in urology unit with structural, surgical and functional abnormalities of urinary tract are 2-4 times more at risk for UTI followed by its complications.[8-9] Most of the patients in our institute had some underlying urological and/or nephrology issues.

In our study, 68% samples yielded growth in urine culture whereas one third had bacteremia. The work of Nieuwkoop et. al in community onset febrile UTI showed urine and blood culture positivity rates of 74% and 23% respectively which are comparable to our study.[10]

In our study almost one fifth of the patients had concordant result with similar organisms indicating bacteremia complicating UTI. This result is consistent with infection rate in other urology units varying from 15 to 28%.[11-12]

Among disconcordant patients, only 2 had community associated enteric organisms while rest had hospital acquired pathogens causing central line infections, phlebitis, surgical site infections and UTI.

Table 1: Pattern of culture positivity among 103 patients

Urine Culture	Blood Cultrue	Total n (%)
Negative	Negative	23(22)
Positive	Negative	52 (50)
Negative	Positive	8 (8)
Positive	Positive	20 (19)

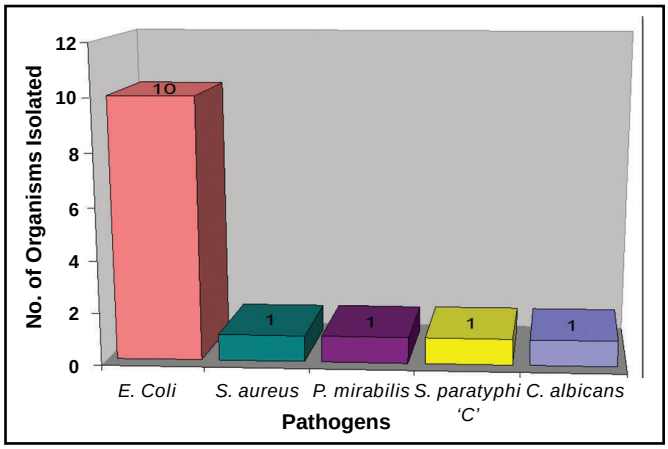

Fig 1. Graphical presentation of organisms causing UTI and bacteremia in the concordant samples

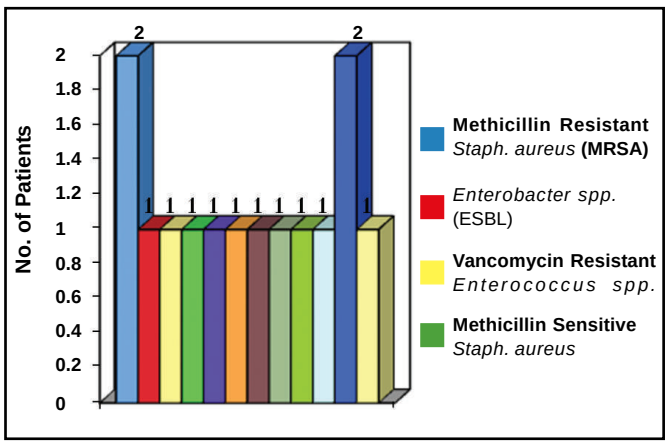

Fig 2. Organisms of bacteremia patients with disconcordant blood and urine results

The microbiological spectrum of positive urine and blood culture were similar to other previous studies comprising *E. coli* as the major etiologic agent. It was also the predominant pathogen in patients who have bacteremia complicating UTI.[13]

Two thirds of the *E. coli* were extended spectrum beta lactamases (ESBL) producers. This is alarming as these clinical isolate are usually difficult to treat and require injectable antibiotics with

prolonging hospital stay and causing a high economic burden specially in institutes like ours which run solely on philanthropy.[14-15,9]

As this was a retrospective lab based study, inaccessibility to patient and hence inability to assess risk factor causing UTI and its complication were the major limitation of our study.

Conclusion

UTI and subsequent bacteremia are high in our setup. Strengthening the infection control practices is the best and most cost effective method of reducing UTIs and its complication.

References

1. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity and economic costs. *Am J Med* 2002; 113: 5S13S
2. Lee JBL, Neild GH. Urinary tract infection. *Medicine* 2007; 35(8): 423-28.
3. Justice SS, Hunstad DA, Seed PC, Hultgren SJ. Filamentation by *Escherichia coli* subverts innate defenses during urinary tract infection. *Proc Natl Acad Sci* 2006; 103(52): 19884–89.
4. Bahagon Y, Raveh D, Schlesinger Y, Rudensky B, Yinnon AM. Prevalence and predictive features of bacteremic urinary tract infection in emerging department patient. *Eur J Clin Microbiol Infect Dis* 2007; 26: 349-52
5. Gould CV, Umscheid CA, Agarwal RK et.al. Guideline for prevention of catheter associated urinary tract infection. *Infect Control Hosp Epidemiol* 2010; 31(4): 319-26
6. Das Gupta R, Sullivan R, Frech G, O'Brien T. Evidence-based prescription of antibiotic in urology: A 5 year review of microbiology. *BJU Int* 2009; 104(6): 760-4
7. Performance standards for antimicrobial susceptibility testing; twentieth informational supplement. 2010. M 100 S20. Vol 30 No 1.
8. Maki DG, Tambyah PA. Engineering out the risk for infection with urinary catheters. *Emerg Infect Dis* 2001; 7(2): 342-7.
9. Abhilasd KP, Veeraraghavan B, Abraham OC. Epidemiology and outcome of bacteremia caused by extended spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella* spp. in a tertiary care teaching hospital in south India. *J Assoc Physician India* 2010; 58: 13-17
10. van Nieuwkoop C, Bonten TN, Wout JW, Becker MJ, Groeneveld GH, Jansen CL, *et.al*. Risk factors for bacteremia with uropathogens not cultured from urine in adults with febrile urinary tract infection. *Clin Infect Dis* 2010; 50(11): e69-72.
11. Budzyriska A, Kaczmarek A, Gospodarek E. Urinary system as a primary source of blood stream infection. *Med Dosw Mikrobiol* 2009; 61(4): 343-50.
12. Rosser CJ, Bare RL, Meredith JW. Urinary tract infections in the critically ill patient with a urinary catheter. *Am J Surg* 1999; 177(4):287-90.
13. Ronald A. The etiology of urinary tract infection: traditional and emerging pathogens. *Am J Med* 2002; 113(1): 14-19
14. Patton JP, Nash DB, Abrutyn E. Urinary tract infection: economic considerations. *Med Clin North Am* 1991; 75(2): 495-513.
15. Tal S, Guller V, Levi S, Bardenstein R, Berger D, Gurevich I, Gurevich A. Profile and prognosis of febrile elderly patients with bacteremic urinary tract infection. *J Infect* 2005; 50(4):296-305.

ORIGINAL ARTICLE

Risk Factors for Pneumonia in Children less than 5 years of age presenting at the Outpatient Clinic of a Primary Health Care in Pakistan

Fatima Jehangir*, Razia Latif**, Ejaz Ahmed Vohra***

*Department of Family Medicine, **Department of Pediatrics, ***Department of Medicine Ziauddin University Hospital Pakistan

Abstract

Background
Pneumonia is one of the leading causes of child mortality in developing countries. We aimed to determine the risk factors for pneumonia among children < 5 years of age in the outpatient clinic of a primary health care in Karachi.

Methods
This case-control study was carried out with 100 cases and 100 controls at primary health care centre at Sikanderabad, Karachi and at the outpatient clinic of Paediatrics at Ziauddin University Hospital Karachi. Controls were healthy children recruited from the immunization clinic or siblings of children visiting the outpatient clinic for reasons other than pneumonia. A questionnaire was used to record the demographic features and predisposing factors for pneumonia like immunization status, breast feeding and nutritional status, educational status of parents and concurrent illness within the family members.

Results
Mean age of the cases was 17.64±14.17, and controls was 24.9±17.53. There was a significant association between pneumonia and lack of breast feeding, lack of immunization, living in overcrowded conditions, low socio economic status, malnutrition, family history of URTI in siblings and LRTI in family members in the preceding 2 weeks. However gender, history of URTI in parents and history of LRTI in the child himself in the preceding 2 weeks were not significantly associated with pneumonia.

Conclusion
Risk factors for pneumonia are re-emphasized as a result of this study and have policy implications for developing strong public health messages for immunization and breast feeding.

Key Words
Lower respiratory tract infections, Upper respiratory tract infections

Corresponding Author: Fatima Jehangir,
Department of Family medicine,
Ziauddin Hospital, Karachi.
Email: fatima_jehangir@hotmail.com

Introduction
Acute respiratory infections (ARI), and pneumonia, are responsible for about one-fifth of deaths among children under age 5 years.[1] There are 4,300 child deaths every day with pneumonia, and a total of 1.5 million child deaths every year from a preventable disease.[2] Most (98%) of the children who die of pneumonia live in developing countries.[3]

Recent estimates from the World Health Organization suggest that pneumonia is responsible for 20% of deaths in children under 5 years causing 3 million deaths per year. Of these deaths, two thirds occur during infancy and more than 90% occur in the developing countries.[4,5]

The increasing focus on the reduction of child mortality in the Millennium Development Goal 4 of "reducing by two-thirds, between 1990 and 2015, the under-five mortality rate", has generated renewed interest in the development of more accurate assessments of the number of deaths in children aged less than 5 years by cause.[6]

The aim of the study was to determine the risk factors of pneumonia among children < 5 years of age in the outpatient clinic of a primary health care centre in Karachi.

Materials & Methods
A case control study was conducted at primary health care center at Sikanderabad Karachi and the outpatient clinics of Pediatrics at Ziauddin University Hospital in Karachi from 1st June 2012 till 30th November 2012. A total of 100 cases with pneumonia and 100 controls < 5 years of age were enrolled. Pneumonia was defined as per WHO guidelines for pneumonia: "The presence of lower chest indrawing with respiratory rate more than 60/minute in infants less than 2 months, > 50/minute in infants 3–12 months and > 40/minute in children 13–60 months." Controls were healthy siblings of children coming to the outpatient clinic for diseases other than pneumonia, or coming for immunization. Written informed consents were taken from the parents of both cases and controls. Children with cleft lip and/or cleft palate, cerebral palsy or mental retardation, any chronic disease like cancer, diabetes, tuberculosis, chronic renal failure and malabsorption syndromes and children with asthma or allergies were excluded.

For both cases and controls history and physical examination was conducted by qualified doctors and risk factors were recorded in a pre-designed performa. Lack of breast feeding was considered if the child had not been exclusively breast fed for first 6 months of life. Overcrowding in the house was defined as more than 2 people inhabiting one room in the house no matter how many rooms are there in the house. Lower socioeconomic status was considered if the combined monthly income of all the earning members of the house was less than Rs. 10,000. Lack of immunization was defined as not or partially immunized as per EPI schedule. Low education in the parents was considered if either of the parent had less than 10 years of continuous school education. Malnutrition was termed when weight of the child was less than 90% according to N.C.H.S.[7]

Data was analysed using statistical programme for social sciences (SPSS) version 17.0. The frequency and percentage was computed for qualitative variables like gender, lack of breast feeding, lack of immunization, overcrowding, low level of education in mother and father, lower socio economic status, upper respiratory infection in father, mother, siblings in the preceding 2 weeks, pneumonia/bronchitis in the child and family members in the preceding 2 weeks and malnutrition. Mean ± standard deviation was computed for quantitative variables like age of the child. Association of each of the categorical variables with pneumonia was assessed with chi-square or Fisher's exact test and the strength of their association was computed by unadjusted odds ratio (95% confidence interval), *p*-value less than 0.05 was considered as statistically significant.

Results

Table 1 shows the demographic characteristics of cases and controls. Table 2 shows the frequencies, *p*-value, odd's ratio and 95% CI of the risk factors for pneumonia. The mean age of the controls was higher than the cases, a larger number of controls were from higher socioeconomic strata and had parents with higher level of education.

Lack of exclusive breast feeding, male sex, overcrowding, lack of immunization, low socioeconomic status, low level of parental education, history of upper respiratory tract infection in siblings in the preceding 2 weeks, pneumonia/bronchitis in the family members in the preceding 2 weeks and malnutrition were found to have significant association with pneumonia whereas upper respiratory tract infection in the parents in the preceding 2 weeks and pneumonia/bronchitis in the child himself in the preceding 2 weeks were not seen to be significantly associated with pneumonia considering.

Discussion

Several socio demographic factors that have been identified earlier as risk factors for pneumonia were highlighted again in this study as significant risk factors for Pneumonia under 5 years of age. Lack of breast feeding is a well-known risk factor for pneumonia. Odds of having pneumonia under 5 years of age is 7.2 times more in children who do not exclusively breast feed for first 6 months of life. Similar results were reported in a study from India.[8]

Table 1: Demographic characteristics of cases and controls

	Cases 100	Controls 100
Gender		
Male	75	60
Female	25	40
Mean age in months	17.64±14.17	24.9±17.53
Socio-economic status		
Low <10000	89	37
Middle 10000-20000	11	54
High >20000	0	9
Maternal level of education		
< Matric	95	57
Intermediate	5	40
University	0	3
Paternal level of education		
< Matric	90	44
Intermediate	9	46
University	1	10
Mean mother's age (years)	23.6±5.49	25.6±4.11
Mean father's age (years)	29.46±5.86	31.33±5.83
Mean weight of the child (kgs)	7.97+2.73	10.89+3.94

Commencing breast feeding early after birth and continuing up to the age of 6 months and continued breastfeeding to the age of 12 months help to maintain a good level of nutrition and immunity against most infections in early childhood. These measures on their own have been estimated to prevent 1,301,000 deaths or 13% of all child deaths.[16]

Although male gender came out to be a significant risk factor but this could be due to differential health seeking behaviour in this part of the world. Pneumonia burden is inversely related to access to healthcare.

Overcrowding was also significantly associated with pneumonia. The possible mechanism may be selection and spread of bacteria and viruses through respiratory droplets.[10]

Similarly, low socioeconomic status has also been reported to be significantly associated with pneumonia in studies from India in 2002 with an OR 4.95.[11]

Unequal distribution of resources has been the major determinant of access to healthcare and disease prevention and control. Only about a fifth of the total health expenditure is borne by the state in high burden countries; the rest comes from the individual or family's 'out-of-pocket' expenses.[12] One of the reasons for lack of immunization could be limited access to

Table 2: Association of common factors with Pneumonia

Variables	Cases	Controls	*p*-value	Odds Ratio	95% CI
Gender (male)	75	60	0.024	2.00	1.09-3.65
Lack of breast feeding	56	15	<0.01	7.21	3.67-14.2
Overcrowding	86	52	<0.01	5.67	2.85-11.27
Low socioeconomic status	89	37	<0.01	13.77	6.5-29.06
Lack of immunization	56	12	<0.01	9.33	4.53-19.19
Low maternal education	95	57	<0.01	14.33	5.36-38.28
Low paternal education	90	44	<0.01	11.45	5.33-24.57
URTI in fathers in preceding 2 wks	11	6	0.311	1.93	0.68-5.45
URTI in mothers in preceding 2 wks	11	6	0.311	1.93	0.68-5.45
URTI in siblings in preceding 2 wks	45	13	<0.01	5.47	2.71-11.06
Pneumonia/Bronchitis in family members in preceding 2 wks	20	6	0.005	3.9	1.5-10.23
Pneumonia /Bronchiolitis in child himself in preceding 2 wks	23	13	0.097	1.99	0.94-4.21
Malnutrition	64	25	<0.01	5.33	2.98-9.8

health care and this is a well-known risk factor for pneumonia with an odd's ratio of 1.54.[9]

There are not many studies linking maternal education with the outcome of pneumonia. Maternal knowledge of symptoms of pneumonia is associated with early recognition and utilization of health care facilities for their children. Educated mothers identify early and avail treatment, however we did not look for the timing of presentation of the cases and their outcomes.

Low level of father's education also is a significant risk factor in the present study with an odd's ratio of 11.45 (CI 5.33-24.57) Results conflict with a study done in India where parents' education was found to have no association with pneumonia under 5 y ears of age.[8] However, Lopez *et al*, Nillay in Turkey found a similar association.[13, 14] The protective effect of parental education against acute respiratory infection could be due to better awareness and care practices.

Upper respiratory infection in both mother and father in the preceding 2 weeks came out to be an insignificant risk factor in the present study. Other studies have shown that URTI in mother is a significant risk factor for pneumonia under 5 years of age with an odd's ratio of 6.53.[8] Upper respiratory infection in the siblings in the preceding 2 weeks and pneumonia /bronchitis in the family members in the preceding 2 weeks proved to be a significant risk factor in this study similar to another study done in India.[8]

Malnutrition was a significant risk factor, similar to another study in Gilgit, Pakistan in 2002 and in India in 2001.[8,9] Another study in Bangladesh in 2009 showed that children with pneumonia and moderate or severe malnutrition are at higher risk of death. For severe malnutrition, OR ranged from 2.5 to 15.1.[15]

The limitations in our study were that the sample size was relatively small and it was done in only two outpatient departments covering mostly the Pathan population, hence generalization is limited. We also did not adjust for confounding and further studies with larger sample size are needed to establish a definite association.

Conclusion

Our study showed that socio demographic factors are important underlying factors for pneumonia and apart from case management, appropriate prevention strategies are needed to decrease child mortality from this common cause of death.

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References

1. Agrawal AS, Sarkar M, Chakrabarti S, Rajendran K, Kaur H, Mishra AC, Chatterjee MK, *et al*. Comparative evaluation of real-time PCR and conventional RT-PCR during a 2 year surveillance for influenza and respiratory syncytial virus among children with acute respiratory infections in Kolkata, India, reveals a distinct seasonality of infection. *J Med Microbiol* 2009;158:1616-22.
2. Black R, Cousens S, Johnson H, Lawn JE, Rudan I, Bassani DG, *et al*. Global, regional, and national causes of child mortality in 2008: a systemic analysis. *Lancet* 2010;375:1969-87.

3. Luby SP, Agboatwalla M, Freikin DR, Painter J, Billhimer W, Altaf A, *et al*. Effect of handwashing on child health: a randomized controlled trial. *Lancet* 2005;366:225-33.
4. World Health Organization. World health statistics 2006. Geneva: World Health Organization; [Online]2006[cited 2009 Sept 6]; Available from URL:http://www.who.int/whosis/whostat2006.pdf. [Accessed on May 30, 2012].
5. Mulholland K: Global burden of acute respiratory infections in children: implications for interventions. *Pediatr Pulmonol* 2003;36:469-74.
6. United Nations Millennium Development Goals. Available from: URL:http://www.un.org/millenniumgoals/ [Accessed on 1 April 2012].
7. Mercedes de Onis. Measuring nutritional status in relation to mortality. Public Health Classics. *Bull of the World Health Org* 2000;78(10):1271.
8. Broor S, Pandey RM, Ghosh, Maitreyi RS, Lodha R, Singhal T, Kabra SK. Risk Factors for Severe Acute Lower Respiratory Tract Infections in Under 5 children. *Indian Pediatr* 2001;38:1361-9.
9. Fatmi Z, White F. A comparison of "cough and cold" and Pneumonia: risk factors for Pneumonia in children under 5 years revisited. *Int J Infect Dis* 2002;6:294-301.
10. Savitha MR, Nandeeshwara SB, Kumar M.J, Farhan-ul-haq , RajuCK. Modifiable risk factors for acute lower respiratory tract infections. *Indian J Pediatr* 2007;74(5):477-82.
11. Mahalanabis D, Gupta S, Paul D, Gupta A, Lahiri M, Khaled MA. Risk factors for pneumonia in infants and young children and the role of solid fuel for cooking: a case-control study. *Epidemiol and Infec* 2002;129:65-71.
12. Neeraj M, Shally A, Girdhar GA. Care-seeking behaviour and out-of pocket expenditure for sick newborns among urban poor in Lucknow, northern India: a prospective follow-up study. *BMC Health Serv Res* 2009;9:61.
13. Lopez BIM, Sepulveda H, Valdes I. Acute respiratory illnesses in the first 18 months of life. *J of pediatr* 1997;1:9-17.
14. Nilay E, Velipasaglu S, Aktekin M. Incidence of acute respiratory infection and the relationship with some factors in infancy in Antalya Turkey. *Pediatr Internat* 2002; 44(1):64-9.
15. Chisti MJ, Tebruegge M, La Vincente S, Graham SM, Duke T. Pneumonia in severely malnourished children in developing countries - mortality risk, aetiology and validity of WHO clinical signs: a systematic review. *Trop Med Int Health* 2009;14(10):1173-89.
16. Jones G, Steketee RW, Black RE, Bhutta ZA, Morris SS. the Bellagio Child Survival Study Group. How many child deaths can we prevent this year? *Lancet* 2003;362:65–71.

ACINETOBACTER : An emerging enemy in tertiary care hospital

Maryam Mukhtar, Sajad Khan, Altaf Ahmed.

Department of Microbiology, Indus Hospital, Karachi.

Abstract

Acinetobacter species is a rapidly spreading nosocomial pathogen. Clinical isolates of this genus are often resistant to multiple antibiotics. Thus this study was conducted to analyze antimicrobial susceptibility pattern and frequency of *Acinetobacter* spp. in hospitalized and outpatients in our set up.

Methods
A total of 232 *Acinetobacter* isolates obtained from various clinical specimens submitted to Indus Hospital diagnostic laboratory from January 2008 to September 2012 were included. Isolates were identified and antibiotic sensitivities were performed using standard microbiological procedures.

Results
Acinetobacter spp was isolated in 232 samples out of 10190 gram negative isolates (2.3% prevalence) from the entire hospital. 72 % were isolated from hospitalized patients. Overall sensitivities of *Acinetobacter* spp against Polymyxin B, Tobramycin, Tigecycline, Meropenem, Imipenem, Cefoperazone/sulbactam, Amikacin, Ceftazidime, Ciprofloxacin, Cefotaxime, Piperacillin – tazobactam and Co-trimoxazole were 88.5%, 84%, 67.2%, 54.6%, 54.6%, 53.6%, 47.4%, 41.2%, 39.2%, 34.1%, 34% and 30.6% respectively. 21 (9%) isolates were detected as multidrug resistant.

Conclusion
Acinetobacter spp especially drug resistant is a great concern of limiting the therapeutic options.

Key Words
Acinetobacter spp, Nosocomial Infection.

Introduction
Genus *Acinetobacter has* emerged worldwide, as a drug resistant infectious pathogen. It causes serious nosocomial infection due to its persistence in the hospital environment and its antimicrobial resistance pattern. *Acinetobacter* spp. can cause a variety of infections including pneumonia, bacteremia, meningitis, urinary tract infections, and skin and soft tissue infections, and the mortality associated with these infections is high.[1] Invasive devices used to facilitate fluid monitoring, administer medications, and provide lifesaving support may also be sources of colonization e.g., in patients with mechanical ventilation, the formation of a biofilm on the surface of the end tracheal tube may be the source of colonization of the lower part of the airway.[2]

Acinetobacter spp are an ongoing challenge and this microorganism has rapidly developed resistance to the majority of antimicrobials, including aminoglycosides, fluoroquinolones, and carbapenems.[3] The reason for multi-drug resistance (MDR) in this organism has been attributed to the intrinsic impermeability of its outer membrane and to its close relationship to the soil and aquatic environment which has made it possible for this organism to acquire highly effective resistance determinants in response to multiple challenges.[4] Based upon resistance, *Acinetobacter* spp. is classified in following categories: MDR *Acinetobacter* spp. is an isolate resistant to at least three classes of antimicrobial agents - all penicillin and cephalosporin (including inhibitor combinations), fluoroquinolones, and aminoglycosides; Extremely / Extensively drug resistant (XDR) *Acinetobacter* spp is resistant to the above three classes of antimicrobials plus carbapenems; Pan drug resistant (PDR) *Acinetobacter* spp is XDR plus resistant to polymyxins and tigecycline.[5]

The present study aimed at determining the frequency of *Acinetobacter* infection and the prevalence of MDR and XDR *Acinetobacter* species obtained from various clinical samples at a tertiary care hospital in Karachi.

Materials & Methods
This study was carried out in the department of microbiology, Indus Hospital, from January 2008 to September 2012. Clinical specimens included blood, tracheal secretion, pus and wound swabs, tissue and other samples. These were inoculated on blood agar, MacConkey agar (Oxoid, UK), and Chocolate agar while urine samples were inoculated on CLED (Oxoid, UK) and incubated at 35°C - 37°C for 24 hours. All suspected colonies were examined and identified by gram stain, absence of motility and negative oxidase and positive catalase test and confirmed by API 20 E (biomerieux, France).

Antimicrobial susceptibility testing of the isolated organisms was performed by the disk diffusion method as recommended by Clinical Laboratory Standards Institute (CLSI).[6] All antibiotic disks were obtained from Oxoid Ltd. Suspension of each isolate

Corresponding Author: Altaf Ahmed,
Department of Microbiology,
The Indus Hospital, Karachi.
Email: altaf_virus@yahoo.com

was prepared so that the turbidity was equal to 0.5 McFarland standards and then plated onto Mueller-Hinton agar (Oxoid, UK). After incubation at 35°C for 18-24 h, diameter of inhibition zones was measured and data were reported as susceptible, intermediate and resistant. Antibiotic disks (Oxoid, UK) used were imipemem (10µg), meropenem (10µg), piperacilin/tazobactam (10/100µg), amikacin (30µg), ceftazidime (30µg), ciprofloxacin (5µg), gentamycin (10µg), co-trimoxazole (1.25/23.7µg), cefotaxime (30µg) polymyxin B (400 units), tobramycin (10µg), tigecyclin (15µg) and cefoperazone-sulbactam (105µg). *Escherichia coli* ATCC 25922 was used as a control strain.

Results

Total culture samples processed during the study period were 37406; pathogenic isolates were 11203 (29.9 %) of which 10190 (91%) were gram negatives bacteria. Overall *Acinetobacter* spp. isolates constituted 2.3% of the total gram negative bacteria (232 out of 10190). The maximum number of *Acinetobacter* isolates were recovered from pus and wound 88 (37.9%) followed by urine 56 (24.1%) and tracheal secretions 39 (16.8%). *Acinetobacter* infections prevalence was found to be very high in hospitalized patients as compared to outpatients (Figure 1).

Out of the total isolates, 117 (50.5%) belonged to the ICU/HDU. The inpatient department (IPD) and the outpatients department (OPD) contributed 49 and 66 isolates respectively (Table 1).

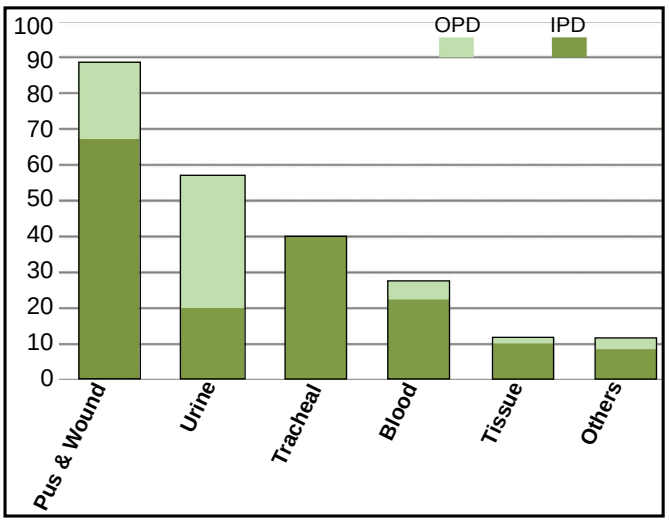

Fig 1. Frequency of *Acinetobacter* spp isolated from various clinical samples of in patients and outpatients (n=232)

Resistance was high for co-trimoxazole (69.4%), piperacillin/tazobactam (66%), and cefotaxime (65.9%). Imipenem and meropenem both showed 45.4% resistance while polymyxin B, tobramycin, tigecycline showed maximum activity with an overall resistance of 11.5%, 16% and 32.8% respectively (Table 2). The frequency of MDR & XDR isolates from IPD & OPD is shown in Table 3.

Table 1: Prevalence of *Acinetobacter* spp among ICU/HDU patients, general ward patients and out patients department

Total Isolates	OPD n(%)	IPD n(%)	
		(General ward)	ICU/HDU
232	66(28.4%)	49 (21.1%)	117 (50.5%)

Table 2: Antibiotics resistance profile of *Acinetobacter* spp. in various clinical samples

Antimicrobial	n	% Resistant
Co-trimoxazole	206	69.4
Piperacillin - tazobactam	168	66
Cefotaxime	229	65.9
Ciprofloxacin	225	60.8
Ceftazidime	238	58.8
Amikacin	226	52.6
Cefoperazone/sulbactam	185	46.4
Imipenem	231	45.4
Meropenem	231	45.4
Tigecycline	70	32.8
Tobramycin	162	16.0
Polymyxin B	147	11.5

Table 3: Frequency of MDR and XDR *Acinetobacter* spp. in OPD/IPD

Resistant Isolates	IPD n(%)	OPD n(%)
XDR	90 (91.8%)	8 (8.2%)
MDR	13 (62%)	8 (38%)

Discussion

Acinetobacter spp. is now recognized as a nosocomial pathogen, capable of causing life threatening infections including pneumonias, septicemias, wound sepsis and urinary tract infections.[5] In addition to hospitalized patients, community-acquired *Acinetobacter* infection is also increasingly being reported.[7] The incidence of outbreak is much more in the regions where temperature is hot and humid, and the organism can survive for long periods on both dry and moist surface. The evolution of this infection commonly occurs in chronically ill patients who have multiple comorbid conditions, are hospitalized for long periods, have multiple invasive procedures, and are of advanced age.

The isolation frequency of our study differs as reported by Siau

et al where *Acinetobacter* spp. was 11% of total gram negative isolates.[8] Maximum isolates were recovered from pus and wound specimens followed by urine, tracheal secretions and blood specimens. These finding highlight the importance of *Acinetobacter* spp causing wound infections, UTI, respiratory infections and septicemia but also as *Acinetobacter* spp having tremendous colonizing potential. It becomes difficult for the clinicians to assess the clinical importance of these isolates whether they are colonizers or true pathogens. In this study maximum isolates were associated from hospitalized patients.

The present study showed a high prevalence of *Acinetobacter* infections in ICU/HDU but it is very difficult to explain the role of acquisition in the ICU, since it does not always act as an infecting pathogen.[9, 10] Antibiotic resistances is a major problem in ICUs thus aggravating the situation. Prolonged hospitalization and mechanical ventilation have been shown to be important risk factors for the acquisition of resistance in *A. baumanii*.[11, 12] Despite intensive efforts, the nosocomial acquisition of *Acinetobacter* spp remains problematic especially in the ICUs.

Susceptibilities of *Acinetobacter* spp. against various antimicrobials are considerably different among countries, cities and even among different wards of the same hospital, therefore, local surveillance studies are important in deciding the most appropriate choice of therapy. The high level resistance to antimicrobials makes the treatment difficult in already serious patients.[13] The resistance in *Acinetobacter* spp originates from resistance genes that are transferred between bacterial species.[14-18] In our study, high level of resistance was recorded for co-trimoxazole, piperacillin tazobactam and cefotaxime. A previous study from Pakistan showed co-trimoxazole resistance as 69%, ciprofloxacin 66% and tigecycline 37% corresponding with our study.[19]

Carbapenems have long been regarded as the agents of choice for multidrug resistant pathogens but resistance rates have risen substantially. The important risk factors for acquisition of imipenem-resistant *A. baumannii* include previous carbapenem use, prolonged hospital/ICU stay, total parenteral nutrition, having a central venous catheter, tracheal tube and urinary catheter or nasogastric tube.[20,21] However, like our study, various studies have shown increasing resistance against imipenem.[22,23] This increasing resistance to these antibiotics is associated with the production of acquired carbapenem-hydrolyzing OXA-type class D beta-lactamases, reported worldwide.

Unfortunately, increased carbapenem resistance in addition to penicillin, cephalosporin, aminoglycoside and fluoroquinolone results in emergence of MDR and XDR *Acinetobacter* spp. The reason of increased frequency of MDR and XDR *Acinetobacter* spp. in our set up vary but may be often linked to inappropriate initial antimicrobial therapy, including administration of sub therapeutic doses of antimicrobial agents, drug overuse, interrupted courses of treatment, and lack of infection control practices. The most active agents *in vitro* against the MDR *Acinetobacter* spp. were polymixin B and tigecycline.

Conclusion

Increasing infections with XDR and MDR *Acinetobacter* is one of the most serious complications that occur in our hospital setting posing serious problems in appropriate antibiotic choices. Eradication of *Acinetobacter* spp. requires adherence to good infection control practices and prudent antibiotic usage. Surveillance for antibiotic resistance may play a significant role in minimizing the spread of this pathogen.

References

1. Jain R, Danziger LH. Multidrug-resistant infection: an emerging challenge to clinicians. *Ann Pharmacotherapy* 2004 Sep; 38(9):1449-59.
2. Lorente C, Del Castillo Y, Rello J. Prevention of infection in the intensive care unit: current advances and opportunities for the future. *Curr Opin Crit Care* 2002; 8:461-4.
3. Shete VB, Ghadage DP, Muley VA, Bhore AV. Multi-drug resistant *Acinetobacter* ventilator-associated pneumonia. *Lung India* 2010; 27(4): 217-20.
4. Bonomo RA, Szabo D. Mechanisms of multi-drug resistance in *Acinetobacter* species and Pseudomonas aeruginosa. *Clin Infect Dis* 2006; 43:S49–56.
5. Manchanda V, Samchaita S, Singh NP. Multidrug-resistant *Acinetobacter*. *J Glob Infect Dis* 2010; 2(3): 291-304.
6. Clinical and Laboratory Standards Institute M100-S21 (2011). Performance standards for Antimicrobial susceptibility testing.
7. Leung WS, Chu CM, Tsang KY, Lo FH, Lo KF, Ho PL. Fulminant community-acquired *Acinetobacter baumannii* pneumonia as a distinct clinical syndrome. *Chest* 2006; 129:102-9.
8. Siau H, Yuen KY, Wong SSY. The epidemiology of *Acinetobacter* infections in Hongkong. *J Med Microbial* 1996; 44:340-7.
9. Bergogue-Berezin E, Towner KJ. *Acinetobacter* species as nosocomial pathogen. Microbiological, clinical and epidemiological features. *Clin Microbial Rev* 1996; 9:148-65.
10. Forster DH, Daschner F Infect D. *Acinetobacter* species as nosocomially pathogens. *Eur J Clin Microbial* Dis 1998; 17:73-7.
11. Rahbar M, Hajia M. Detection and quantitation of the etiologic agents of ventilator-associated pneumonia in endotracheal tube aspirates from patients in Iran. *Infect Control Hosp Epidemiol* 2006; 27:884-5.
12. Mahout S, Ahmed J, Glatt AE. Completely resistant *Acinetobacter baumannii* strains. *Infect Control Hosp Epidemiol* 2002; 23:477-9.
13. Chen HP, Chen TL, Lai CH, Fung CD, Wong WW, Yu KW, *et al.* Predictors of mortality in *Acinetobacter baumannii* bacteremia. *J Microbial Immunol Infect* 2005; 38: 127-36.
14. Fournier PE, Richet H. The epidemiology and control of *Acinetobacter baumannii* in health care facilities. *Clin Infect Dis* 2006; 42(5):692-9.
15. Landman D, Quale JM, Mayorga D, Adedji A, Vangala K, Ravishanker J, *et al*. Citywide clonal outbreak of multi-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in Brooklyn, NY: the pre antibiotic era has returned. *Arch Intern Med* 2002; 162(13):1515-20.
16. Aygun G, Demirkian O, Utku T, Mete B, Urkmez S, Yilmaz M, *et al*. Environmental contamination during a carbapenem-resistant *Acinetobacter baumannii* outbreak in an intensive care unit. *J Hosp Infect* 2002; 52(4):259-62.
17. Wang SH, Sheng WH, Chang YY, Wang LH, Lin HC, Chen ML *et al.* Healthcare-associated outbreak due to pan-drug resistant *Acinetobacter baumannii* in a surgical intensive care unit. *J Hosp Infect* 2003; 53(2):97–102.
18. Mah MW, Memish ZA, Cunningham G. An outbreak of *Acinetobacter*

baumannii in an intensive care unit associated with tracheostomy. *Am J Infect Control* 2001; 29:284-8.
19. Qureshi ZA, Abbasi SA, Mirza IA, Malik N, Amjad A, Sattar A *et al*. Antimicrobial susceptibility pattern of *Acinetobacter* species; one year experience in a tertiary care setting. *Infect Dis J Pak* 2011: 2, 1:269-272.
20. Baran G, Erbay A, Bodur H, Ongoro P, Akinci E, Balaban N, Cevik MA. Risk factors for nosocomial imipenem-resistant *Acinetobacter* baumannii infections. *Int J Infect Dis* 2008; 12:16-21.
21. Cisneros JM, Rodrvguez-Bapo J, Fernandez-Cuenca F, Ribera A, Vila J, Pascual A, *et al*. Risk-factors for the acquisition of imipenem-resistant *Acinetobacter baumannii* in Spain: A nationwide study. *Clin Microbial Infect* 2005; 11:874-9.
22. Lai SW, Ng KC, Yu WL, Liu CS, Lai MM, Lin cc. *Acinetobacter baumannii* bloodstream infection: clinical features and antimicrobial susceptibilities of isolates. *Kaohsiung J Med Sci* 1999; 15: 406-13.
23. Ruiz J, Nunez ML, Perez J, Simarro E, Martinez-Compos L, Gomez J. Evolution of resistance among clinical isolates of *Acinetobacter* over a 6 year period. *Eur J Clin Microbial Infect Dis* 1999; 18: 292-5.

CASE REPORT

Probable Japanese Encephalitis in a Healthy Child: A Case Report

Amna Batool*, Rashid Nazir**, Ejaz Khan*

*Department of Pediatrics, **Radiology, Shifa International Hospital, Islamabad.

Abstract

Japanese Encephalitis (JE) virus is the leading cause of childhood viral neurological infection and disability in Asia. We report a child with acute onset of fever and vomiting, followed by drowsiness and seizures. He had upper motor neuron signs and Neuroimaging showed typical findings of bilateral symmetrical, hyperdense lesions in basal ganglia, consistent with *JE*. His illness resolved after good supportive care.

Key Words

Japanese Encephalitis, Basal Ganglia, *Flavivirus,* Seizures

Case Summary

An eighteen months old previously healthy child presented with low-grade fever and vomiting for 3 days, followed by drowsiness and seizures. There was no history of cough, respiratory distress, loose motions, and rash or drug ingestion. He was previously healthy and was developmentally normal. He was the fourth issue of a consanguineous marriage and the elder siblings were healthy.

On examination he was sick, drowsy and severely dehydrated with acidotic breathing. The pulse rate was 110/min, respiratory rate was 60/min and blood pressure 110/70 mm Hg. The Glasgow Coma Scale (GCS) was 6 and he had generalized hypertonia, hyper-reflexia and positive Babinski sign. The cranial nerves were intact. Rest of the examination was unremarkable.

The provisional diagnosis of meningoencephalitis was made. Initial management included ventilatory, support, intravenous ceftriaxone and acyclovir. Seizures were controlled with phenobarbitone. He was given 70% maintenance intravenous fluids and intravenous soda bicarbonate was started. Initial laboratory evaluation revealed WBC 28800/mm^3, polymorphs 85% lymphocytes 7%, hemoglobin 12 g/dl, platelet count 370,000, marked metabolic acidosis (serum HCO_3 3 mEq/L) with anion gap of 19. Cerebrospinal fluid (CSF) analysis was normal with WBC count 3 cells/mm^3, protein count 25 mg/dl and glucose 84 mg/dl. Blood and CSF cultures were negative. The CSF, PCR *herpes simplex virus* Type 1 and 2 PCR was negative.

Corresponding Author: Ejaz Khan,
Department of Paediatrics,
Shifa International Hospital,
H-8, Islamabad, Pakistan.
E mail: ejazkhan99@hotmail.com

EEG showed diffuse encephalopathy. The CT and MRI brain showed abnormal signals in bilateral globus pallidus which was bright on T2 with FLAIR, isointense to hypointense on T1W images and intense post contrast enhancement (Figure 1). Based on the clinical presentation and the typical neuroimaging findings, final diagnosis of *JE* was made on the basis of the typical MRI findings, although no virological testing was performed. The child was successfully weaned off from ventilator after 3 days. Nasogastric tube feeding was established and regular physiotherapy was started. His GCS gradually improved to 11/15.He received ceftriaxone for 7 days and acyclovir for 14 days. The parents were counseled and the child was discharged home after 2 weeks of hospital stay with full neurological recovery. At follow-up after 2 months he was healthy with no neurological deficit.

Discussion

Japanese encephalitis (JE) virus is the leading cause of childhood

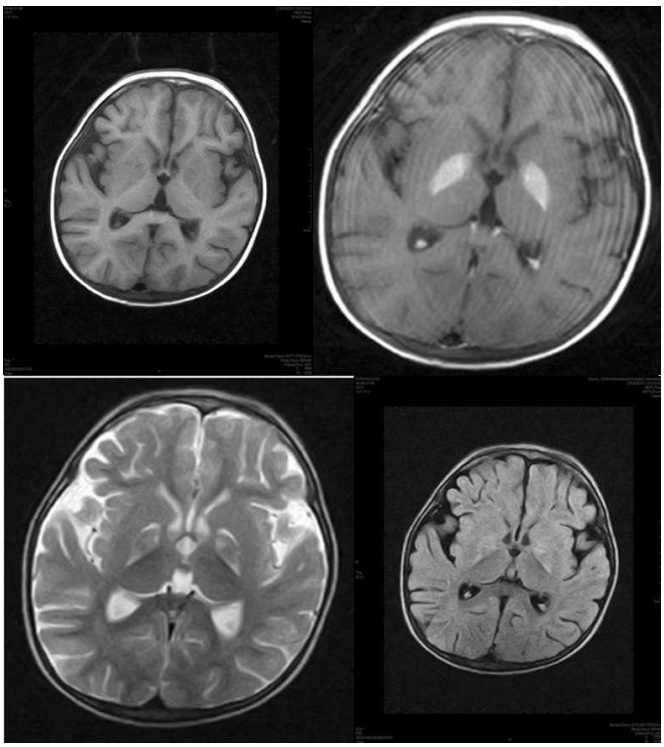

Fig1. Bilateral symmetrical low T1 and bright flair and T2 abnormality with post contrast enhancement. Abnormal signal in bilateral globus pallidus which is bright on T2 and FLAIR, isotense to hypointense on T1W images and has intense post contrast enhancement.

viral neurological infection and disability in Asia.[1] *JE* virus is a mosquito born *flavivirus*. In endemic areas, majority of the adult population has protective immunity due to ongoing environmental exposure.[2] In these areas *JE* typically affects children <15 years of age. In new geographical areas where there is no immunity both adults and children are equally affected. The transmission of *JE* virus occurs in an enzootic cycle involving mosquitoes and vertebrate hosts mainly pigs and wading birds. The *culex vishnui* species, particularly genus *tritaeniohynchus* are the major vectors of *JE* virus.[3]

The clinical presentation may be varied. Halstead et al described a mild case of *JE* infection presenting as aseptic meningitis or non-specific febrile illness.[1] The most common presentation is acute encephalitis. The incubation period is 5 to 15 days. Initially there are non-specific symptoms like fever, diarrhea and rigors followed by headache, vomiting and generalized weakness. Later on movement disorders, mental status changes or focal neurological deficits like paresis, hemiplegia or cranial nerve palsy may develop. In some patients, abnormal behavior or acute psychosis may be the initial presentation. Seizures, which are usually generalized tonic-clonic are commonly seen in children but subtle motor seizures may also be seen. Uncommonly *JE* infection may present as acute flaccid paralysis due to anterior horn cell damage or extrapyramidal involvement presenting as parkinsonian syndrome with flat mask like facies with unblinking eyes, cogwheel rigidity and tremors.[4] In 2007, Chung et al reported a case of *JE* with an unusual presentation of acute flaccid paralysis.[5]

Laboratory evaluation is mostly non-specific. There may be moderate elevation of white cell count, mild anemia and thrombocytopenia. Hyponatremia due to syndrome of inappropriate antidiuretic hormone secretion may be seen. The CSF analysis shows mild to moderate pleocytosis of ten to several hundred white blood cells/mm^3 with lymphocyte predominance, slightly elevated proteins and normal CSF to plasma glucose ratio.

Neuroimaging commonly shows lesions involving thalamus, basal ganglia, midbrain, pons and medulla.[6,7] Thalamic lesions are the most commonly described lesions which are highly specific but less sensitive marker of *JE* infection. *JE* virus-specific IgM antibodies detected in CSF or serum, by enzyme -linked immunosorbant assay (ELISA) is helpful for diagnosis. These antibodies are detected in the CSF of 70-90% cases and their presence in CSF confirms recent central nervous system *JE* infection. Presence of these antibodies in serum may follow vaccination or asymptomatic *JE* infection. Serum antibodies are detectable in 60-70% of all patients in initial days of illness but in nearly 100% patients when samples are taken at least 9 days after the illness.[8,9] Electroencephalogram (EEG) may show various abnormalities like burst suppression, theta and delta coma, epileptiform activity and occasionally alpha coma.[4]

The definite test for *JE* infection is virus isolation or detection of viral RNA with a nucleic acid amplification test (NAAT) on blood or CSF samples. At the time of onset of distinctive clinical symptoms, most patients have low level of viremia and high titers of neutralizing antibodies, virus isolation and NAATs are insensitive for the detection of *JE* virus in blood or CSF.[10] In our case we did not do either antibodies, NAAT or PCR as none of these tests are available. The differential diagnosis of *JE* includes other, post infectious causes and other viral encephalitidies.[11,12]

Important clinical differential diagnoses include central nervous system infections like domestic *arboviral* infections, other viral meningoencephalitis, bacterial meningoencephalitis, early cases of tuberculosis or fungal meningitis, cerebral malaria and post infectious causes.[11,12,13] The radiological differential diagnosis includes many infectious and metabolic abnormalities as shown in table (Table 1).[14] Most of these causes were ruled out by clinical and laboratory evaluation in our patient. We suspected *JE* in our child on basis of clinical, laboratory and radiologic features. Unfortunately PCR is not available to confirm our diagnosis but most likely this was a *JE*-like illness on the basis of clinical evaluation.

Management includes supportive treatment like seizure control, maintaining adequate cerebral perfusion pressure and control of increased intracranial pressure.[15] Use of corticosteroids and interferon alpha *2a* has not been shown to improve outcomes in controlled clinical trials.[16,17]

Kumar *et al* conducted a randomized placebo controlled trial

Table 1: Radiological differential diagnosis of Basal ganglia lesions.[19]

Infectious & Inflammatory Diseases	Metabolic/ Degenerative Diseases	Toxic poisoning	Vascular diseases
Other flavivirus encephalitis, CNS toxoplasmosis, Neuro-Behcets disease	Wilson disease, Wernike encephalopathy, Hypoxic ischemic encephalopathy, Leigh disease, Hypoglycemia, Fahr Disease	Carbon monoxide, menthol, cyanide	Deep cerebral vein thrombosis. vascular occlusion

on 153 Indian children to evaluate the use of ribavirin in treatment of *JE*. This trial showed no difference in outcome between the treatment and control groups.[18]

JE has a high mortality rate of 20-30 % and 30-50 % patients show long-term sequelae. The most common long-term sequelae is upper or lower motor weakness and cerebellar or extrapyramidal signs. Recurrent seizures, severe psychiatric problems, language or cognitive impairment and learning problems may also be seen as long-term sequela.[4]

References

1. Halstead SB, Jacobson J. Japanese Encephalitis. *Adv Virus Res* 2003; 61:103.
2. Tsai TF. New initiatives for the control of Japanese encephalitis by vaccination: minutes of a WHO/CVI meeting, Bangkok, Thailand, 13-15 October 1998. *Vaccine* 2000; 18 suppl 2:1.
3. Van den Hurk AF, Ritchie SA, Mackenzie JS. Ecology and geographical expansion of japanese encephalitis virus. *Annu Rev Entomol* 2009; 54:17.
4. Solomon T, Dung NM, Kneen R, Gainsborough M, Vaughn DW, Khanh VT. Japanese encephalitis. *J Neurol Neurosurg Psychiatry* 2000; 68:405.
5. Chung CC, Lee SS, Chen YS, Tsai HC, Wann SR, Kao CH, Liu YC. Acute flaccid paralysis as an unusual presenting symptom of Japanese encephalitis: a case report and review of the literature. *Infection* 2007; 35:30.
6. Maschke M, kastrup O, Forsting M, Diener HC. Update on neuroimaging in infectious central nervous system disease. *Curr Opin Neurol* 2004; 17:475.
7. Wang HS. Comparison of magnetic resonance imaging abnormalities in Japanese encephalitis and acute necrotizing encephalopathy of childhood. *Arch Neurol* 2004; 61:1149.
8. Solomon T, Thao TT, Lewthwaite P, Ooi MH, Kneen R, Dung NM, White N. A cohort study to assess the new WHO Japanese encephalitis surveillance standards. *Bull World Health Organ* 2008; 86:178.
9. Chanama S, Sukprasert W, Sa-ngasang A, A-nuegoonpipat A, Sangkitporn S, Kurane I, Anantapreecha S. Detection of Japanese encephalitis (JE) virus-specific IGM in cerebrospinal fluid and serum samples from JE patients. *Jpn J Infect Dis* 2005; 58(5):294-6.
10. Burke DS, Lorsomrudee W, Leake CJ, Hoke CH, Nisalak A, Chongswasdi V, Laorakpongse T. Fatal outcome in Japanese encephalitis. *Am J Trop Med Hyg* 1985; 34:1203
11. Solomon T. Flavivirus encephalitis. *N Engl J Med* 2004; 351:370.
12. Solomon T, Hart IJ, Beeching NJ. Viral encephalitis: a clinician's guide. *Pract Neurol* 2007; 7:288.
13. Rao PN Japanese encephalitis. *Indian Pediatr* 2001; 38(11):1252-64.
14. Hegde AN, Mohan S, Lath N, Lim CC. Differential diagnosis for bilateral abnormalities of the basal ganglia and thalamus. *Radiographics* 2011; 31:5–30
15. Tiroumourougane SV, Raghava P, Srinivasan S. Japanese viral encephalitis. *Postgrad Med J* 2002; 78:205.
16. Hoke CH JR, Vaughn DW, Nisalak A, Intralawan P, Poolsuppasit S, Jongsawas V, Titsyakorn U, Johnson RT. Effect of high-dose dexamethasone on the outcome of acute encephalitis due to Japanese Encephalitis virus. *J Infect Dis* 1992; 165:631.
17. Solomon T, Dung NM, Wills B, Kneen R, Gainsborough M, Diet TV, Thuy TT, Loan HT, Khanh VC, Vaughn DW, White NJ, Farrar JJ. Interferon alfa-2a in Japanese encephalitis*:* a randomised double-blind placebo-controlled trial. *Lancet* 2003; 361:821.
18. Kumar R, Tripathi P, Baranwal M, Singh S, Tripathi S, Banerjee G. Randomized, controlled trial of oral ribavirin for Japanese encephalitis in children in Uttar Pradesh, India. *Clin Infect Dis* 2009; 48:400.
19. Amogh N. Hegde, Suyash Mohan, Narayan Lath, C. Tchoyoson Lim, MMed Differential Diagnosis for Bilateral Abnormalities of the Basal Ganglia and Thalamus *Radiographics* 2011;31(1): 5-20

CASE REPORT

Unusual Presentation of Subacute Sclerosing Panencephalitis (SSPE)

Prem Chand*, Poonam Manglani**, Prem Kumar Maheshwari*, Ali Faisal Saleem*, Shahnaz Hamid Ibrahim*

*Department of Paediatrics and child health, Aga Khan University, Karachi, Pakistan
**Elective medical student, Department of Paediatrics and child health, Aga Khan University, Karachi, Pakistan

Abstract
We are reporting the case of a 8 years old boy who presented with hand tremors and aggressive behaviour for one and a half months followed by dystonia and regression of milestones to vegetative state in 15-20 days. There was a significant history of measles at 9 months of age. Diagnosis of Subacute Sclerosing Panencephalitis (SSPE) was made, based on past history of measles, regression of milestones, elevated cerebrospinal fluids measles antibody titer and elevated oligoclonal fragmentation of gamma-globulin. This was an unusual presentations of (SSPE) with rapid detoriation. Our report emphasizes the need for measles vaccine to prevent not only acute infection, but also its rare post infectious neurologic sequelae.

Key Words
Atypical Subacute Sclerosing Panencephalitis (SSPE); Parkinsonism; Milestone Regression

Introduction

Subacute Sclerosing Panencephalitis (SSPE) is a progressive inflammatory disease of the central nervous system caused by a persistent, aberrant measles virus infection.[1] The annual incidence rate varies from one to four per million populations in developed countries.[2] It usually begins insidiously and follows a subacute course with relentless but slow progression to death.[3] SSPE is still high in lower and middle income, and variable in developed countries. Poor vaccination coverage and high incidence of measles could be a possible reason.[1] Most of the patients have a history of measles before two years of age[1] and it takes around 6-8 years after measles infection, for SSPE present clinically. However the range varies between 3 months to 18 years.[1] SSPE usually begins insidiously and follows a subacute course with relentless but slow progression to death. In the typical course of the disease, further clinical stages include stereotypic attacks (myoclonic / atonic), worsening dementia, autonomic failure, mutism, long tract involvement and decerebrate, decorticate rigidity.[5] Clinically, SSPE has a four-stage course over many months to two or more years.[3]

However, in about 10% of patients, clinical manifestations of SSPE are not typical and patients with acute or fulminant course have been reported.[6-8] Atypical presentations are isolated psychiatric manifestations, poorly controlled seizures, or isolated extrapyramidal syndromes like chorea, hemiparkinsonism and stroke.[1] Acute, fulminant course is diagnosed as the patient develops at least 66% neurologic disability (as measured by the neurologic disability index) in the first three months or death occurs within six months.[9] We are reporting a young boy with atypical SSPE manifestations.

Corresponding Author: Shahnaz Hamid Ibrahim
Department of Paediatrics and Child Health
Aga Khan University,
Stadium Road, Karachi, Pakistan.
Email: shahnaz.ibrahim@aku.edu

Case History

An eight year old boy of un-related parents presented in the emergency room with dystonic movement of limbs, posturing and deteriorating Glasgow Coma Scale (GCS). He had 1½ months history of tremors of hands with slurred speech, was not following commands ad had very aggressive behaviour. In addition to this he had gradually lost his cognitive milestones. As disease progressed he started having intermittent posturing movement and later became bed bound. He had been seen by a paediatrician and his initial laboratory investigations including complete blood count, serum electrolytes, urea, creatinine and random blood sugar were unremarkable. The electroencephalogram (EEG) revealed diffuse delta and theta slowing. Initially CSF analysis was not done. MRI brain showed high intensity signals on T2 over peritrigonal area and on the basis of MRI finding he was treated as case of acute disseminated encephalomyelitis (ADEM). He received high dose of methylprednisolone for initial five days followed by tapering dose of prednisolone; however his condition further deteriorated in the next couple of weeks as he developed dystonic movements along with posturing and drowsiness so was referred to our neurology clinic. When he presented to us, he was drowsy with Glasgow coma scale (GCS) 9/15 (E4, M4, V1); intermittent posturing; dystonic movement of arms and legs, generalized increase in body tone; brisk deep tendon reflexes and positive Babinski's response. Rest of the systemic examination was unremarkable. A differential diagnosis of Wilson's disease, Mitochondrial Encephalopathy, Lactic Acidosis and Stroke like episode (MELAS) was made. His CSF analysis, showed leukocyte count of 2 cells/mm3, protein of 4mg/dl and CSF sugar 95 mg/dl with blood sugar 110mg/dl. Serum ceruloplasmin 0.20g/l (0.25-0.45g/l), urinary copper 135µg/dl (80-160µg/dl), serum lactate 4.3 mmol/l (0.6-2.4mmol/l), CSF lactate 2.4 mmol/l (0.6-2.2mmol/l). On Slit lamp examination, Kayser Fleischer (KF) ring was negative. Repeat MRI showed re-demonstration of hyper-intense signals over peritrigonal area bilaterally on T2 weighted images and subtle changes were noted bilaterally in caudate and globus palladium. MR

spectroscopy did not show any lactate peaks in affected area. A repeat EEG showed; diffuse delta slowing without any significant abnormality (figure 1). His CSF showed elevated antibody titer against measles in cerebrospinal fluids and elevated oligoclonal fragmentation of gamma globulin in cerebrospinal fluids which were consistent with SSPE. He was started on Isoprinosine and parents were counselled regarding guarded prognosis and the child was discharged home. He was followed up after nine months, his condition remained static. He continues to be in a vegetative state, and is on immunomodulation therapy.

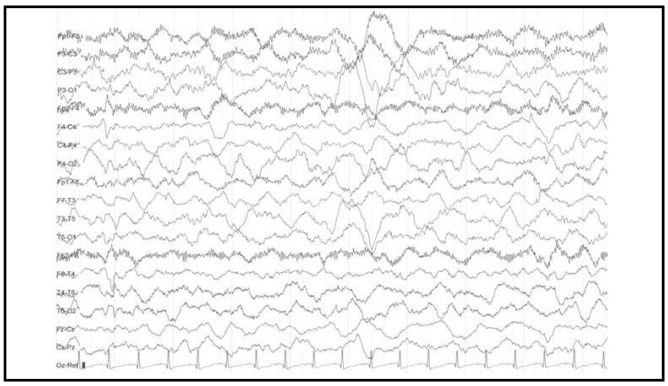

Fig 1. EEG showing Diffuse Delta slowing

Discussion

SSPE is a lethal disease with very little chances of survival once it manifests. The diagnosis of SSPE requires, at least three of the following criteria which include:

(1) A typical clinical picture: personality and behavioral changes, worsening school performance, followed by myoclonic seizures, paresis, dyspraxia, memory impairment, language difficulties, blindness, and eventually obtundation, stupor and coma;
(2) Characteristic EEG changes
(3) Elevated CSF globulin levels greater than 20% of total CSF protein
(4) Raised titers of measles antibodies in blood and CSF
(5) Typical histopathological finding in brain biopsy or autopsy.[1,10] The rate of progression is variable.[3] In the majority, death occurs within 1-3 years after onset of symptoms.[3]

The progression of SSPE can be divided into four clinical stages.[3, 4]

(I) Slowly evolving behavioral and intellectual deterioration;
(II) Various types of involuntary movements;
(III) Severe pyramidal and extrapyramidal hypertonic and disappearance of hyperkinesia;
(IV) Chronic vegetative state and death.

Stage I may last from several weeks to several years, stage II typically lasts from three months to one year, stages III and IV often last from six months to one year.[3]

Clinical profiles of SSPE have revealed varied presentations. Some signs and symptoms of SSPE at an early stage such as hemiparesis, papilledema, headaches, generalized tonic-clonic seizures, nausea, and vomiting can lead to erroneous diagnosis of acute encephalitis, acute disseminated encephalomyelitis or some intoxications, but typical drop attacks, and EEG, CSF and MRI findings can point to the diagnosis of SSPE.[3] At times, SSPE needs to be distinguished from various neurodegenerative conditions characterized by myoclonus, progressive dementia and ocular findings and from some other progressive neurological disorders, such as Lafora disease, Myoclonic epilepsy with Ragged Red fibers, neuraminidase deficiency and Juvenile Ceroid lipofuscinosis.[3]

The treatment for SSPE is still undetermined.[3] Antiviral agents, such as amantadine and ribavirin or immunomodulator (isoprinosine, immunoglobulin and interferon) have been used.[3] However, the result of the treatment of SSPE is not yet satisfactory.[3] Since the treatment of SSPE is only partially effective, immunization against measles remains the only preventive intervention against this fatal disease.[3]

Conclusion

SSPE is a rare but lethal manifestation of measles infection. In any child who presents with atypical manifestations like dystonia, posturing, poorly controlled seizures, deteriorating cognition and dropping GCS, there should be a high index of suspicious for a typical presentation of SSPE.

References

1. Sarkar N, Gulati S, Dar L, Broor S, and Kalra V. Diagnostic Dilemmas in fulminant subacute sclerosing panencephalitis. *Indian J Pediatr* 2004; 71(4):365-7.
2. Garg RK, Karak B, Sharma AM. Subacute sclerosing panencephalitis. *Indian J Pediatr* 1998;35:337-44
3. Herguner MO, Altunbasak S, Baytok V. Patients with acute, fulminant form of SSPE. *Turk J Pediatr* 2007; 49:422-5.
4. Dimova P and Bojinova V. Subacute clerosing panencephalitis with atypical onset: Clinical, computed tomographic, and magnetic Resonance imaging correlations. *J Child Neurol* 2000; 15:258.
5. Griffin DE. Viral infections and related disorders. In: Scheld WM, Whithley RJ, Durack DT (eds). Infections of the Central Nervous System. Philadelphia, New York: Lippincott-Raven; 1997: 47-57.
6. Marjanovic BD, Stojanov LM, Zamurovic DR. Fulminant subacute sclerosing panencephalitis: two cases with atypical presentation. *Pediatr Neurol* 2003; 29:63-5.
7. Dimova P, Bojinova V. Subacute sclerosing panencephalitis with atypical onset. Clinical, computed tomographic, and magnetic resonance imaging correlations. *J Child Neurol* 2000; 15: 258-60.
8. Wight C, Jin L, Nelson CS, Cosby SL and Padfield CJ. Case report: an autopsy proven case of fulminant subacute sclerosing panencephalitis. *Neuropathol Appl Neurobiol* 2003; 29:312-20.
9. PeBenito R, Naqvi SH, Arca MM and Shubert R. Fulminant subacute sclerosing panencephalitis: case report and literature review. *Clin Pediatr* (Phila) 1997; 36:149-54.
10. Dyken PR. Subacute sclerosing panencephalitis. *Neurol Clin* 1985; 3:179 85.

10th Annual IDSP Symposium held at Lahore

Infectious Diseases Society of Pakistan (IDSP) conducted its 10th International Annual Conference on 22-23rd February, 2013, in the academic environment of Shaukat Khanum Memorial Hospital & Research Center, Lahore, along with Shaikh Zayed Hospital. The theme of the symposium was '*Emerging trends*'. Eminent speakers from Pakistan and abroad participated to make this meeting a success.

There were 6 pre-conference workshops on general bacteriology, mycology, epidemiology in infectious diseases, childhood vaccination, zoonosis/rabies and infection control. These workshops were well attended and participants thoroughly benefited and enjoyed them.

The Annual General Body Meeting was attended by executives and key ID (Infectious Diseases) members. The importance of promoting the field of Infectious Diseases, election of new office bearers and other policy matters were discussed. The board members agreed to rename the Society as Medical Microbiology and Infectious Diseases Society of Pakistan (MM-IDSP). It was decided to hold the 11th Annual Conference of Infectious Diseases in Islamabad in 2014 in spring. Scientific sessions were held on the 2nd day. The symposium was focused on problems and challenges that Pakistan is facing in ID. The content of the symposium was broad and comprehensive and highlighted the burning infection issues in Pakistan. Topics covered anti-infective therapy, pediatric infectious diseases, virology, tuberculosis, emerging infectious diseases, preventive and public health, infections in immunocompromised, surgical site infections and HIV. The symposium received full and enthusiastic participation. There were around 130 abstracts received for oral and poster sessions. Eight were selected for oral presentation and certificates of appreciation were given for the best poster presentations.

The meeting was concluded by remarks from IDSP President, Dr Ejaz Khan. Conference organizers, Shaukat Khanum Memorial Hospital & Research Center, Sheikh Zayed Hospital and pharmaceutical companies were thanked for their cooperation, support and hard work. There were many congratulatory comments for holding a very successful and well attended meeting.

Curbside Consultation

An attempt at humor in infectious diseases

Boasting is not a good virtue but as you grey out with years you want to be take pride in what you do best. There is always a fine line but I will leave that to you to judge. Many diagnoses and management options are obvious the moment you see or hear patient's history. I always have loved these and immediately share with those around me especially my residents. I feel exalted when it is confirmed. I can thus *boast* looking at some of the typical or classical cases that are a spot diagnosis as narrated here.

Blog 2: Recognition and bets: Please!

An 18-months-old brought by parents (both doctors) with watery diarrhea since last 7 days. Started with acute watery diarrhea (AWD) and was given "cefaim" (cefxime, *3rd degree* curse for us!). Then the poor thing was given "Rocephin" as he kept throwing up. Developed fever and switched to ciprofloxacin and amikacin combo. Of course he did not settle and was given pipercillin-tazobactam (*Tanzo*! Yummy!). Then they brought the child who was not toxic but dehydrated. Admitted and given IV fluids and no antibiotics. Labs including CBC, stool analysis, blood and stool cultures were normal. Next day all symptoms markedly improved and both doctor parents were given a brief on antibiotic good practices and then IDSP antibiotic guidelines and a copy of article, "When not to use antibiotics….". They were thrilled (as if some new discovery has been made!) They invited me for a talk to their local physicians sometime and I gladly accepted. The curbside question is what antibiotics are good for AWD and what to do when it does not get better? No antibiotics are good for AWD and stop all antibiotics to resolve! It is that obvious!

A 6-year-old girl came with acute onset of sore throat, dysphagia, fever and mild abdominal pain and headache. There was no cough or rhinorrhea or diarrhea. Without examining her, I asked my residents that it will be spot diagnosis. They looked at each other as if I was an alien talking gibberish as there was nothing suggestive yet. I pointed that examine her throat and the diagnosis is there. The pharynx was red with pus on the tonsils that were inflamed and there were multiple petechial lesions on the posterior palate. Thinking of a 2 year old seen few days ago, one of them said it was enteroviral infection! I said possible but wrong! This one is a classical case of *Streptococcal* pharyngitis with acute symptoms as above, no viral symptoms and findings as above (Centor's criteria). We gave amoxicillin for 10 days and did a throat culture that was of course positive. Curbside question: how do you recognize bacterial (strep always) from viral pharyngitis? A good question and very easy I would say! (if you pay attention).

"*Group A streptococcus* or *GAS* is the most frequent bacterial cause of infectious pharyngitis after viruses. Sometimes other bacterial and non-infectious causes also may occur. The etiologic agents are usually respiratory viruses, including *adenoviruses, coxsackie A viruses, influenza,* or *parainfluenza virus*. *GAS* tonsillopharyngitis presents with abrupt onset of sore throat, tonsillar exudate, tender cervical adenopathy, and fever. Remember that there is no viral syndrome such as rhinnorhea or cough."

Finally a typical summer disease that I see every year and is so obvious (even to an insane). This 11-year-old boy's mom was worried as her son was sick for a day with fever, severe headache, vomiting. The resident had examined him and said that it was a viral illness as there is some pharyngitis and no neck stiffness. Seeing these over many years, I was quick to recognize the constellation of this typical disease. The boy was having severe headache and constantly shielding his eyes from the bright light. I asked the boy whether he had any photophobia as well which he did! Bingo! I told the mother this was viral meningitis (most likely non-polio enteroviral) and needs admission and evaluation. The blood counts were normal and the LP showed WBC 350 cells (neutros 75%, lymphos 25%), protein 39 and glucose 66. Gram stain and all cultures were negative. He felt relief and was improved next day. Ceftriaxone was given for 48 hours and then stopped after normal exam and negative cultures. Now unfortunately, we do not have fancy test like Enterovirus PCR in CSF but I can bet this would have been positive. The curbside question is how do you suspect viral meningitis and how to treat best? Viral meningitis is suspected on the basis of an older immunocompetent child, summer time with similar viral syndromes going around in the community, abrupt onset of severe headache, fever, vomiting, photophobia and neck stiffness, CSF with few hundred cells with initial neutros (within 3 days?), normal glucose and protein and negative gram stain and culture, rapid resolution of symptoms after LP. Don't confuse with partially treated meningitis (longer duration, slow resolution, previous antibiotics, cultures /gram stain maybe positive). No treatment in viral meningitis as it is viral. Also the LP itself is diagnostic and therapeutic! Many may feel jittery about this but then things are not rosy in this world!

Suggested readings

1. Dusdieker LB, Murph JR, Murph WE, Dungy CI. Physicians treating their own children. *Am J Dis Child* 1993;147(2):146-9.
2. Wessels MR. Clinical Practice. Streptococcal pharyngitis. *N Engl J Med* 2011:364:8.
3. Glasziou PP, Spinks AB. Antibiotics for sore throat. Cochrane Database Syst Rev 2000; CD000023.
4. Bisno AL, Gerber MA, Gwaltney JM Jr, Kaplan E, and Schwartz R. Practice guidelines for the diagnosis and management of group A *Streptococcal* pharyngitis. Infectious Diseases Society of America. *Clin Infect Dis* 2002; 35:113
5. McIsaac WJ, Goel V, To T, Low DE. The validity of a sore throat score in family practice. *CMAJ* 2000;163:811–5.
6. Ejaz A. Khan. "When not to use antibiotics? A simple guide for prevention of misuse of antibiotics." *Infect Dis J Pak* 2012;21 (2):438-42.
7. Jaffe, M, Srugo, I, Tirosh, E, Colin AA and Tal Y. The ameliorating effect of lumbar puncture in viral meningitis. Am J Dis Child 1989; 143:682.
8. Overall, JC Jr. Is it bacterial or viral? Laboratory differentiation. Pediatr Rev 1993; 14:251.

Ejaz Ahmed Khan
Department of Pediatrics,
Shifa International Hospital,
Islamabad, Pakistan.

Vitamin D Supplementationin Neonates: Can it Reduce Risk of Sepsis?

Romaina Iqbal*, Shiyam Sunder Tikmani**

*Department of community health Sciences, **Department of Pediatrics and Child Health,
Aga Khan University, Karachi, Pakistian.

Dear Editor,

Neonatal infections are a major cause of deaths worldwide.[1,2] It is estimated that approximately 4 million deaths occur annually in developing countries in the neonatal period, attributable mostly to infection, birth asphyxia, and consequences of premature birth and low birth weight[1,3] Pakistan is ranked 3rd amongst 10 countries, contributing to two-third of neonatal mortality worldwide. With an estimated 298000 neonatal deaths annually and reported neonatal mortality rate of 54 per 1000 live births, Pakistan accounts for 7% of global neonatal deaths.[3,4] Most of the research to address neonatal healthis focused on management of neonatal sepsis; however scarce data is available on nutritional intervention to prevent sepsis.

Numerous risk factors for neonatal sepsis have been reported in literature.[5] Vitamin D deficiency could possibly be one of the risk factors for neonatal sepsis. Deficiency of this vitamin has been studied in relation to pneumonia in neonates and sepsis in adults.[6,7] The underlying mechanism may be enhancement of the innate immune response by induction of cathelicidin (LL-37), produced by macrophages and neutrophils.[8] Furthermore, there is corroborative evidence in the form of higher frequency of sepsis in winter as compared to summer, higher rates for African-Americans than white Americans, and comorbid diseases linked to low serum 25-hydroxyvitamin D [25(OH)D]. Based on the above mentioned data it was hypothesized that higher serum 25(OH)D levels could reduce the risk of neonatal sepsis.[9] Thus, it would be worthwhile to test the hypothesisthat supplementation of pregnant women or newborn with vitamin D may possibly have a protective effect in newborns against sepsis, in a large cohort study. A simple intervention of supplementing infants with vitamin D may hence help to reduce the neonatal mortality due to infection.

References

1. Lawn JE, Cousens S, Zupan J. 4 million neonatal deaths: When? Where? Why? The Lancet. 2005;365(9462):891-900.
2. Who U. Why are 4 million newborn babies dying each year? Lancet. 2004;364:399-401.
3. Bryce J, Boschi-Pinto C, Shibuya K, Black RE. WHO estimates of the causes of death in children. The Lancet. 2005;365(9465):1147-52.
4. Stoll BJ. The global impact of neonatal infection. Clinics in perinatology. 1997;24(1):1.
5. Yancey MK, Duff P, Kubilis P, Clark P, Frentzen BH. Risk factors for neonatal sepsis. Obstetrics & Gynecology. 1996;87(2):188-94.
6. Jeng L, Yamshchikov AV, Judd SE, Blumberg HM, Martin GS, Ziegler TR, et al. Alterations in vitamin D status and anti-microbial peptide levels in patients in the intensive care unit with sepsis. Journal of translational Medicine. 2009;7:28.
7. Karatekin G, A Kaya ÃS. Association of subclinical vitamin D deficiency in newborns with acute lower respiratory infection and their mothers. European journal of clinical nutrition. 2007;63(4):473-7.
8. Mookherjee N, Rehaume LM, Hancock REW. Cathelicidins and functional analogues as antisepsis molecules. Expert opinion on therapeutic targets. 2007;11(8):993-1004.
9. Grant WB. Solar ultraviolet-B irradiance and vitamin D may reduce the risk of septicemia. Dermato-endocrinology. 2009;1(1):37.

Instructions to Authors

Scope

The Infectious Diseases Society of Pakistan sponsors the Infectious Disease Journal of Pakistan (IDJ). The Journal accepts Original Articles, Review Articles, Brief Reports, Case Reports, Short Communications, Letter to the Editor and Notes and News in the fields of microbiology, infectious diseases, public health; with laboratory, clinical, or epidemiological aspects.

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All articles are peer reviewed by the IDSP panel of reviewers. After that the article is submitted to the Editorial Board. Authors may submit names and contact information of 2 persons who potentially could serve as unbiased and expert reviewers for their manuscript, but IDSP reserves the right of final selection.

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Manuscripts must be formatted according to submission guidelines given below, which are in accordance with the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" (originally published in N Engl J Med 1997;336:309-15). The complete document appears at www.icmje.org. Please submit one complete copy of the manuscript and all enclosures to **The Managing Editor, Infectious Diseases Journal of Pakistan, Department of Pathology and Microbiology, The Aga Khan University, Stadium Road, P.O. Box 3500, Karachi 74800, Pakistan.** An electronic copy of the manuscript must also be sent to maahin1@yahoo.com and pak_idj@yahoo.com**.** All manuscripts submitted to IDJP must be accompanied by an Authorship Declaration stating that *'The authors confirm that the manuscript, the title of which is given, is original and has not been submitted elsewhere.Each author acknowledges that he/she has contributed in a substantial way to the work described in the manuscript and its preparation'*. Upon submission a manuscript number will be assigned which should be used for all correspondence.

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Title page

This should list the (i) title of the article, (ii) the full names of each author with highest academic degree(s), institutional addresses and email addresses of all authors. (iii) The corresponding author should also be indicated with his/her name, address, telephone, fax number and e-mail address. (iv) A short running title of not more than 40 characters (count letters and spaces) placed at the foot end of the title page.(v) a conflict of interest statement should also be included in this section.

Abstract

Abstract should not exceed 250 words and must be structured in to separate sections headed *Background, Methods, Results and Conclusions*.

Please do not use abbreviations or cite references in the abstract. A short list of four to five key words should be provided to facilitate.

Background

The section must clearly state the background to the research and its aims. Controversies in the field should be mentioned. The key aspects of the literature should be reviewed focusing on why the study was necessary and what additional contribution will it make to the already existing knowledge in that field of study. The section should end with a very brief statement of the aims of the article.

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Please provide details of subject selection (patients or experimental animals). Details must be sufficient to allow other workers to reproduce the results. The design of study and details of interventions used must be clearly described. Identify precisely all drugs and chemicals used, including generic name(s) and route(s) of administration All research carried out on humans must be in compliance with the *Helsinki Declaration*, and animal studies must follow internationally recognized guidelines. The authors are expected to include a statement to this effect in the Methods section of the manuscript. A description of the sample size calculation and statistical analysis used should be provided.

Results

Present results in logical sequences in the text, tables and illustrations. Articles can have a maximum of 5 illustrations (in a combination of figures and tables) per article. The results should be in past tense and repetition of results presented in the tables should be avoided. Exact *P*-values should be reported along with reporting of OR and RR with their Confidence Intervals where applicable.

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Emphasize the new and important aspects of the study and conclusions that follow from them. Do not repeat the details from the results section. Discuss the implications of the findings and the strengths and limitations of the study. Link the conclusions with the goals of the study but avoid unqualified statements and conclusion not completely supported by your data.

Acknowledgments

Acknowledge any sources of support, in the form of grants, equipment or technical assistance. The source of funding (if any) for the study should be stated in this section. Please see below for **format of References, Figures and Tables**.

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Authoritative and state of the art review articles on topical issues are also published, with a word limit of 2000. It should consist of critical overview of existing literature along with reference to new developments in that field. These should be comprehensive and fully referenced. Articles should contain an Abstract; Main Text divided into sections, Conclusions and References.

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V. Letter to the Editor
These may relate to material published in the IDJP, topic of interest pertaining to infectious diseases, and/or unusual clinical observations. A letter should not be more than 300 words, one figure and 3-5 references.

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Announcements of conferences, symposia or meetings may be sent for publication at least 12 weeks in advance of the meeting date. Details of programs should not be included.

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Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by Arabic numerals (in superscript). References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification of the particular table or illustration. Bibliography should be given in order.Authors, complete title, journal name (Abbr), year, vol, issue, page numbers. According to "Uniform Requirements of Manuscripts submitted to Biomedical Journals", as cited in N Engl J Med 1997; 336:309-15.

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Illustrations should be numbered, given suitable legends and marked lightly on the back with the author's name and the top edge indicated. Original drawings may be submitted although high quality glossy photographs are preferable. They should be kept separate from the text. If possible, figures should be submitted in electronic format as either a TIFF (tagged image file format) or JPEG format. Minimum resolution for scanned artwork is:

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Authors should refrain from plagiarism and should double check their work before submitting it for publication. Adequate references should be provided for text from other sources.

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3. Vote according to constitution of the society.

ASSOCIATE MEMBERS:

All the members shall have the right to:
1. Participate in programs of the society.
2. Receive all publication including quarterly ID Journal free of cost.

Please send your Application form by hand or by mail only.
Membership fee will only be received in cash/ cross cheque/ pay order or bank draft made out to Infectious Disease Society of Pakistan.

Mailing Address and Contact Nos:

Infectious Diseases Society of Pakistan
21 G /1, Block - 6, P.E.C.H.S., Shahrah-e-Faisal, Karachi.
E-mail: idsp123@yahoo.com