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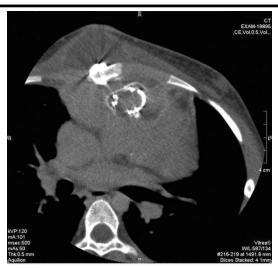
CONTENTS **PAGE #**



Contegra valve endocarditis

Courtesy: Dr Nadeem Aslam, Aga Khan University, Karachi.

Measles Havoc - Time to get back to Strengthen Routine Immunization

Despite a safe and cost-effective vaccine, measles is still one of the leading causes of global childhood mortality. In 2011, there were 158,000 measles deaths globally – about 430 deaths every day or 18 deaths every hour. Pakistan is measles endemic country with an estimated 1.7% is a measles associated mortality in children aged younger than 5 years, with periodic epidemics every 2 to 3 years.[1,2] Given these high figures, it was concluded that measles eradication should be a vital part of achieving the Millennium Development goal aiming towards achieving reduction in childhood mortality. With the year 2015 approaching fast, it is unlikely that such a goal will be achieved by our nation. Efforts have been made to bring this into effect. However, they seem to have had little impact on the bigger picture in Pakistan.

Vaccination is the only solution, and strengthening routine immunization is a critical component of the strategy to control and eliminate measles. Until 2007, the EPI system of Pakistan had only a single dose of measles vaccine as part of the schedule which was administered at the age of nine months. In the Pakistan Health and Survey (2006-2007), only 50-60% country wide coverage was noted for the single dose of measles vaccine. Surveillance in the year 2007 showed that despite the EMRO region achieving 90% reduction in mortality as was the goal, outbreaks still occurred all over Pakistan with an incidence rate of 2 per 1000 in children less than five years of age. This was taken into account and the second dose of measles vaccine was added to the EPI schedule. Also, supplementary immunization activity (SIA) was conducted in the years 2007-2008 in order to facilitate the achievement the above stated goal. In spite of all these measures, coverage achieved with EPI as well as SIAs has remained poor and is a cause of concern. In a survey conducted by Sana et al, it was found that in Karachi, the largest metropolitan city of the country, 12% of the children had received the second dose of this vaccine and only 3% of the parents had reported being vaccinated by SIAs, such that a year after the SIA program of 2007-2008 only 55% of the children (12-59 months of age) were found to be immunized against measles.[3]

The prevention of childhood diseases through increased access to immunizations is one of the greatest success stories in global public health and now this is the demand at our end too. Good measles coverage is the foundation for high levels of immunity to measles in the community and we are lacking behind in this aspect.[4] During the recent outbreak of measles a team from Aga Khan University surveyed the affected part of Sindh and identified the inadequacy of routine immunization due to multiple causes including unawareness of masses, improper technique for vaccine storage including disruption of cold chain, and power failure as the hurdles in overcoming this failure. Lack of coordination at all level is another cause of suboptimal immunization.[5] Furthermore, malnutrition complicates the issue of achieving adequate immunity to the vaccine.

These periodic outbreaks are alarms for us now to get back to our basic strategy – strengthen the immunization coverage. What we need is to educate the masses regarding the benefits of routine immunization, treat malnutrition (according to WHO guidelines), strengthen the infrastructure in out-patient (BHU) facilities with focus on cold chain and teaching and training of health care providers.[5] To ward off the disease all it takes is two doses of an inexpensive and safe vaccine.

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ORIGINAL ARTICLE

Fecal Carriage and Antibiogram of Extended Spectrum Beta-lactamase Producing Enterobacteriaceae in Patients at a Tertiary Care Hospital in Rawalpindi

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Abstract

Objective
The presence of extended spectrum beta-lactamase (ESBL) producing Escherichia coli in the gut not only contributes to extra-intestinal infections, but can also result in the transfer of antimicrobial-resistance genes to other susceptible strains carried as commensals in the gut flora, resulting in increased treatment failures, increased mortality and a higher cost of care. We aim to determine the fecal carriage and antimicrobial susceptibility pattern of extended spectrum beta lactamase producing enterobacteriaceae in patients at a tertiary care hospital in Rawalpindi.

Methods
We conducted a descriptive study at the Department of Microbiology, Army Medical College/National University of Sciences and Technology, from January 2012 to June 2012 on fecal samples from patients of Military Hospital, Rawalpindi, Pakistan.

Two hundred and twelve fecal samples were tested for extended spectrum beta lactamase (ESBL)enzyme by double disc method; Co-Amoxiclav (AMC) (20µg/10 µg) disc placed in the centre with Aztreonam (AZT) (30µg) and ceftriaxone (CRO) (30µg) discs. Antimicrobial sensitivity was then carried out for each by the modified Kirby-Bauer disc diffusion method.

Results
From the 212 fecal samples, fifty eight isolates were extended spectrum beta-lactamase producers with majority of the (38.76%) samples from admitted patients. *Escherichia coli* was the most frequently isolated (69%) ESBLproducing organism. The antimicrobial susceptibilities were higher for Carbapenem (100%), Tigecycline (98.3%), Amikacin (94.8%), Piperacillin/ Tazobactam (75.8%)and Cefoperazone/Sulbactam (63.8%) as compared to Ciprofloxacin (48.3%), Gentamicin (51.7%) and Co-Amoxiclav (32.75%).

Conclusion
This study shows an alarmingly high fecal carriage rate of extended spectrum beta lactamase producing Enterobacteriaceae in our setting.

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Key Words
ESBL producing enterobacteriaceae, *Escherichia coli,* fecal carriage, *Klebsiella pneumoniae.*

Introduction
The incidence of extended-spectrum β-lactamase (ESBL)-producers has increased all over the world. Over the past few decades, ever-increasing use of antimicrobial agents has led bacteria to acquire various resistance mechanisms. *Extended spectrum* β-*lactamases* (ESBLs) are acquired enzymes produced by a variety of gram negative bacteria. They are inhibited in vitro by Clavulanic acid.[1,2] ESBL producing organism confer resistance to penicillin, cephalosporins, and monobactams. They cannot hydrolyze cephamycins and are inhibited by Clavulanic acid (CA).[2] Like ESBLs, plasmid-mediated AmpC β-lactamases have a broad substrate profile that includes penicillin, cephalosporins, and monobactams. In contrast to ESBLs, they hydrolyze cephamycins and are not inhibited by commercially available β-lactamase inhibitors.[3] ESBLs are primarily produced by and spread rapidly amongst enterobacteriaceae, in particular *Klebsiella pneumoniae* and *Escherichia coli*. These organisms are of enormous clinical and microbiological significance and are associated with severe infections.[4] The presence of ESBL often makes empiric antibiotic treatment ineffective.[5] The transfer of ESBLs also results in increasing resistance to non-β-lactam antibiotics such as the quinolones.

Although, the carriage of ESBL producers is expected to be present in general population, its occurrence has rarely been reported. Fecal carriage of ESBL producers has mainly been detected in nosocomial outbreak investigations. There are only a few studies done during non-outbreak situations among patients in community settings. Transmission of such bacteria usually occurs via the fecal-oral route, either directly or indirectly through hand contact with healthcare workers, and is also facilitated by overcrowding.[6] Colonization with ESBL-producers is considered a prerequisite for infection. The presence of ESBL-producing *Escherichia coli* in the gut not only contributes to extra-intestinal infections, but can also result in the transfer of resistance genes to other strains of *Escherichia coli* and other organisms within the gastrointestinal tract. The spread of ESBL-producing organisms to the community can be related to previous hospital acquisitions and by the overuse of antibiotics in the

community. *Escherichia coli* and *Klebsiella pneumoniae* are the most common species of enterobacteriaceae carrying ESBL-encoding genes.[7] Therapy of infections caused by extended-spectrum beta-lactamase producers with an antimicrobial agent to which they are resistant results in treatment failure, higher cost of care and increased mortality. Knowledge of the local antimicrobial susceptibility pattern of enterobacteriaceae is very helpful in early treatment of patients.

The aim of this study was to determine the fecal carriage and antibiogram of extended spectrum beta-lactamase producing enterobacteriaceae in patients at a tertiary care hospital in Rawalpindi.

Materials and Methods

This was a descriptive, cross sectional study carried out in the Department of Microbiology, Army Medical College/National University of Sciences and Technology, affiliated with an 1100 bedded tertiary care, Military Hospital, Rawalpindi. A total of 212 fecal samples with enterobacteriaceae strains isolated from 1st January, 2012 to 1st June, 2012, by non-probability, convenience sampling were included in the study. The patients included in this study were those who presented with gastrointestinal symptoms. No further details were available for these patients. The isolated enterobacteriaceae are not considered pathogenic in age above 2 years generally and we reported the fecal samples carrying these as normal in age above 2 years. Only *Escherichia coli* are labeled as pathogenic in children age less than two years and rest of the members of enterobacteriaceae mentioned are non pathogenic in this age group. So we labelled it fecal carriage instead of infection.

The samples were received from admitted as well as outdoor patients of the hospital as ordered by their respective physicians for investigating gastrointestinal symptoms. Samples were inoculated within 4-6 hours of receipt in the laboratory on deoxycholate citrate agar (DCA) and Mac-Conkey agar plates simultaneously. All the inoculated plates were incubated under aerobic conditions at 35^0C for 24-48 hrs. The bacterial colonies which were catalase positive, oxidase negative, glucose fermenting gram negative rods were considered members of the enterobacteriaceae family. Further speciation was done by using Analytical Profile Index 20 E (BioMerieux,USA). All the isolates were screened for ESBL production by the Clinical and Laboratory Standards Institute (CLSI) double-disc method. We performed the method using an Amoxicillin–Clavulanic acid (AMC) (20 µg/10 µg) disk placing it in the centre with Aztreonam (AZT) (30µg) and ceftriaxone (CRO) (30µg) discs each 25 mm apart from AMC. Strains producing ESBL were defined as those showing zone enhancement of ≥ 5 mm between AMC and either of CRO or AZT[8]. The enterobacteriaceae showing no synergy between CRO/AZT and AMC discs were excluded from the study. *Klebsiella pneumonia* ATCC 700603 and *Escherichiacoli* ATCC 25922 were used as positive and negative controls, respectively. Antimicrobial susceptibility testing was performed using Mueller Hinton agar (Oxoid,UK) according to modified Kirby-Bauer disc diffusion method following CLSI guidelines[9]. Antimicrobial susceptibilities were tested for Amoxicillin–Clavulanic acid (20µg/10 µg), Ceftriaxone (30µg), Aztreonam (30µg), Amikacin (30µg), Gentamicin (10µg), Meropenem (10µg), Sulfamethoxazole / Trimethoprim (1.25/23.75µg), Cefoperazone/Sulbactam (75/30µg), Piperacillin / Tazobactam (100/10µg), Tigecycline (15µg) and Ciprofloxacin (5µg) (Oxoid, U.K).

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 19. Frequencies and percentages were calculated qualitative variables.

Results

During the 6 month study period, 212 fecal specimens were received which were included in the study (normally all fecal samples carry enterobacteriaceae). Of eighty-three (39.15%) samples received from outdoor patients, eight (9.64%) showed ESBL producing enterobacteriaceae strains. Of 129 (60.85%) enterobacteriaceae isolates recovered from indoor patients, fifty (38.76%) were ESBL producers. Overall, fifty eight (27.36%) of the total 212 fecal samples were ESBL producers. *Escherichiacoli* was the most frequently isolated ESBL producing organism (69%). The proportion of ESBL producing *Escherichia coli* was 70% (35/50) in indoor and 62.5% (5/8) in outdoor patients respectively. Following in frequency were *Klebsiellap neumoniae* (20.7%), *Citrobacterfreundii* (6.9%) and *Enterobacter species* (3.4%).Table 1 shows their frequencies in descending order.

Age of fecal ESBL carriers ranged from 2 months to 65 years. The faecal samples of children in 0-2 years age group contributed 77.8% (165) of the total and 25.45% (42/165) were ESBL producers. Age distribution of faecal ESBL carriers is shown in figure1 and the distribution of the various ESBLs by age is shown in table 2.

Multidrug resistance was prevalent among the ESBL producing enterobacteriaceae, but no pan-resistant strain was isolated. All were sensitive to carbapenems (meropenem) but resistant to trimethoprim-sulfamethoxazole. Fifty seven (98.3%) were

Table 1: Source and frequency of ESBL producing (n=58) Enterobacteriaceae

Organism	Origin		Total isolates
	Hospitalized	Non-hospitalized	
Escherichia coli	35	5	40
Klebsiella pneumoniae	11	1	12
Enterobacter species	2	0	2
Citrobacterfreundii	2	2	4
Total isolates	50/129 (38.76%)	8/83 (9.64%)	58/212 (27.35%)

Table 2: Age-wise Distribution of Faecal ESBL Carriers (n=58)

Age (years)	Organism				Number (Percentage) of faecal carriers
	Escherichia coli	*Klebsiella pneumonia*	*Enterobacter species*	*Citrobacterfreundii*	
0-2	29	9	2	2	42 (72.4%)
2-20	4	3	0	0	7 (12.1%)
21-40	2	0	0	2	4 (6.9%)
41-65	5	0	0	0	5 (8.6%)

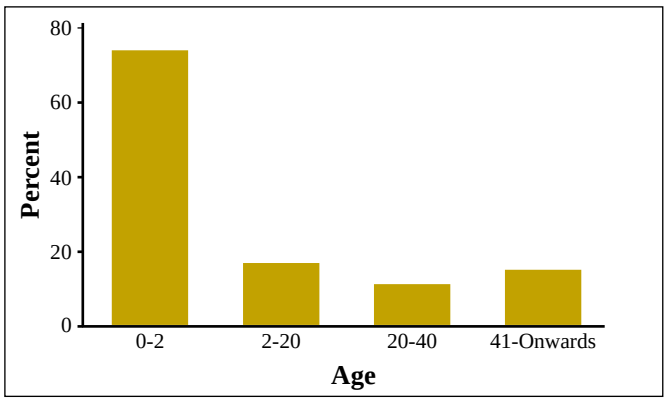

Fig 1. Bar Chart Showing Age-wise Distribution of Faecal ESBL Carriage (n=58)

susceptible to tigecycline and fifty (94.8%) to amikacin. The susceptibilities for different beta lactamase inhibitor combinations showed variable results. Those for ESBL producers against piperacillin/tazobactam and cefoperazone/sulbactamwere75.8% (44/58) and 63.8% (37/58), respectively, but this decreased to 32.75% (19/58) for amoxicillin-clavulanic acid combination. The susceptibilities of ESBL producers for the quinolones (ciprofloxacin) and aminoglycosides (gentamicin) were 48.3% (28/58) and 51.7% (30/58), respectively. The details of the susceceptibility patterns are presented in Table 3.

Table 3: Susceptibilities for different antibiotics against ESBL producing enterobacteriaceae

Antibiotics	Susceptibility Percentages of ESBL Producing Enterobacteriaceae	
	Sensitive (%)	Resistant (%)
Trimethoprim-sulfamethoxazole	0	100
Tetracycline	8.6	91.4
Amoxicillin-clavulanic acid	32.8	67.2
Ciprofloxacin	48.3	51.7
Gentamicin	51.7	48.3
Cefoperazone/ sulbactam	63.8	29.3
Piperacillin/ tazobactam	75.8	24.2
Amikacin	94.8	5.2
Tigecycline	98.3	1.7
Meropenem	100	0

Discussion

ESBL-producing enterobacteriaceae have emerged worldwide and have also been reported recently in outpatients in many countries. Our rate of fecal carriage was higher than that reported by Husicova *et al* in 2012 who found 15.87% in their patients.[10] Similarly, Kader and Kamath[11] reported fecal ESBL-producers carriage rate of 12.7% in 2009. The increase in ESBL fecal carriage rate from 1.9% to 5.0% over 2 years was reported by Tham J. in 2012.[8]

Fecal carriage rate of ESBL-producing enterobacteriaceae was significantly higher in hospitalized as compared to outdoor patients in our study. Similar findings were reported by Husam *et al* showing 15.4% and 4.5% fecal ESBL carriage rates among inpatients and outpatients, respectively.[12] These rates were 6.8% and 3% respectively in a study by Tham J.[8] Fecalcarriage rate of 13.7% was reported by Kader and Kamath[11] in community patients.

Escherichia coli was the most frequent ESBL producer in our study and similar were findings of the studies by Lonchel *et al* and Tham J. with rates of 66.7%[13] and 83%[8], respectively. Husicova *et al* also found *Escherichia coli* as the most frequent fecal ESBL isolate (89.7%) in the community setup.[10] This isolate is an important and common component of nosocomial infections especially in younger children and elderly people. The Infectious Diseases Society of America has listed *Escherichia coli* and *Klebsiella pneumoniae* as two out of the six pathogens for which new drugs are urgently required in order to battle against development of resistance.[14]

We found a high proportion of ESBL producers in fecal samples of children of 0-2 yrs age group which coincides with the findings of Isendahl *et al* who reported 27% carriage in children

aged 0-3 months.[15] Among the 411 children enrolled in a study on French people by Birgy *et al* 4.6% fecal samples carried ESBL producers.[16]

All ESBL producers were sensitive to meropenem. Carbapenems are regarded as the antibiotic of choice and mainstay of treatment against severe infections by ESBL producers.[4] We report higher susceptibility for Tigecycline, Amikacin and β-lactamase inhibitor combinations and similar results were found by Paterson and Bonomo in 2005.[2] Kelesidis *et al* in 2008 evaluated 26 studies for in-vitro susceptibility to Tigecycline of multidrug resistant (MDR) enterobacteriaceae (including ESBL-producing) and reported 99.8% *Escherichia coli*, 92.3% *Klebsiella pneumoniae* and 91.3% *Enterobacter* species as susceptible to tigecycline.[17] We report low susceptibilities of ESBL producers to ciprofloxacin and gentamicin and 100% resistance to sulfamethoxazole/trimethoprim. Another study in 2012 by Lonchel *et al* reported additional resistance of ESBL producing isolates to ciprofloxacin, gentamicin and sulfamethoxazole/trimethoprim but none was found resistant to amikacin or meropenem.[13] Quinolone resistance was high in ESBL-producing *Escherichia coli* (81.9%) and *Klebsiellap neumoniae* (48.4%), in a study by Isendahl *et al* in Guinea-Bissau.[15] ESBL-associated resistances found by Andriatahina *et al* were higher for trimethoprim-sulfamethoxazole (91.3%), gentamicin (76.1%), ciprofloxacin (50%), but not for amikacin and imipenem.[18] A study in Rawalpindi showed 100% susceptibilities of ESBL producers's for carbapenems, 84% for tazobactam/piperacillin, 81% for sulbactam/cefoperazone, 12% for fluoroquinolones, 13% for cotrimoxazole, 59% for amikacin and 18% for gentamicin[19] respectively. We found similar antimicrobial patterns in our study. Tazobactam/ Piperacillin has been shown to be more effective against ESBLs as compared to amoxicillin/clavulanate and similar to other reports.[20]

We could not ascertain the duration of stay in the hospital as well as the time at which the sample was collected from patients, thus we cannot conclude when the actual carriage of these ESBL producing Enterobacteriaceae occurred. The sample size from outdoor patients was relatively small, further, we also did not assess the types of beta-lactamase enzymes as molecular analysis of the samples was not done.

Conclusion

A quarter of the fecal samples collected from in- and outpatients in a tertiary care hospital in Rawalpindi yielded ESBL producing enterobacteriaceae. ESBL producing *Escherichia coli* was the commonest isolate. Appropriateness of betalactamase inhibitor combinations should be based on culture sensitivity tests.

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ORIGINAL ARTICLE

Awareness of Transmission of Hepatitis B, C and HIV amongst Health Care Workers at a Tertiary Care Hospital in Karachi

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Abstract

Objective
Transmission of infections to health care workers by needle stick injuries is a huge health problem. Unfortunately there is little data in this regard from Pakistan. We aim to assess the knowledge of health care workers (HCW) regarding transmission of Hepatitis B, C and HIV at a tertiary care center of Karachi, Pakistan.

Methods
A cross sectional study was conducted on the knowledge of HCW including physicians, nurses and technicians of Ziauddin University. A structured questionnaire including their demographic information and their understanding of universal safety precautions was filled by a trained HCW during October and November 2012. Data were entered and analyzed using SPSS version 20.0. Percentages of categorical variables were determined and compared using Chi- square test. Means were compared by using one way anova. P value of <0.05 was considered significant.

Result
Two hundred HCW participated in the study. Majority were males (51%) and physicians (n=88, 44%), between the age of 26-35 years. Most of the participants were on job for approximately three years. Only 30% of the participants were above the mean score for knowledge which was 24.3±2. The mean score of universal precautions was 7±0.7. Knowledge of technicians and nurses was better than the doctors, with the main source of information being media, internet, television and radio.

Conclusion
Knowledge about spread of blood borne infections and universal precautions in health care workers is inadequate and requires continuous sensitization and address.

Key words
Blood-borne infections, health care workers, universal precautions.

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Introduction
Blood borne infections are transmitted through the exposure of contaminated blood, and as a result pathogenic microorganism like hepatitis B and C and human immunodeficiency virus (HIV) can be transmitted. The prevalence of hepatitis B antigen and hepatitis C antibody in healthy adult Pakistani population is 2.4% (range; 1.4-11%) and 3.0 % (range; 0.3-31.9%) respectively.[1] Moreover, the prevalence of HIV in Pakistan is 0.05%.[2]

Studies have reported that the incidences of needle stick injuries is high among health care workers (HCW) ranging from 14.5 to 53%.[3] Most incidences occur during venipuncture and recapping the needles after use.[4] Zafar A has reported that 45% of health care workers have needle stick injuries and the frequency is high amongst doctors.[5]

The risk associated with transmission of hepatitis B virus to a non-immune HCW is 2% if the source patient is Hepatitis B e antigen negative, to 40% if the patient is positive for the Hepatitis B e antigen.[6,7] Risk of HIV transmission after percutaneous exposure to HIV infected blood is approximately 0.3%.[8] Average incidence of anti-HCV seroconversion after needle stick or sharps exposure from a known anti-HCV-positive source patient is 1.8% (range, 0 to 7%).[9]

Unsafe injections are one of the major reasons for the rise in blood borne infections in Pakistan.[10] WHO defines a safe injection as one that does not harm the recipient, the health care worker or the community.[11] Injections are unsafe if they are reused or the needles are used on more than one patient without sterilization. Risk of transmission of blood borne infections is very high due to the use of poor quality syringes in Pakistan. WHO has reported that approximately 80% of the injections used in Pakistan are unsafe.[12]

An exposure to blood borne infections poses a serious risk to health care workers. They are at potential risk of these infections due to needle stick injury, exposure of other body fluids e.g. amniotic fluid, pleural fluid etc. Since the key to improving the attitude and practice of health care workers is accurate and updated knowledge, therefore we aim to assess the knowledge of transfer of hepatitis C & HIV due to needle stick injuries and assess knowledge regarding universal precautions amongst health care workers.

Methods

A cross sectional study was conducted on 230 health care workers selected conveniently. They comprised of 88 doctors, 85 nurses, and 27 technicians. Ethical clearance was obtained from the ethical review committee of the university.

A structured questionnaire was administered between October and November 2012. The questionnaire comprised of respondents demographic data, knowledge of transmission of blood borne diseases i.e. HCV, HBV and HIV (11 questions) and knowledge of universal precautions (8 questions). Source of updating knowledge was also asked (4 questions). Knowledge of vaccinations available for HCV, HBV and HIV was also assessed. The answers were True/Yes and False/No type. One (1) point was given for each correct answer. Data were entered and analyzed on SPSS version 20.0

Quantitative variables are presented as mean and standard deviation, while qualitative variables presented as frequency and percentages. For categorical variables chi square test was applied. Means were compared by one way anova. P value of < 0.05 was considered significant.

Results

Out of 213 questionnaires, 200 were returned with a response rate of 93.8%. 51% of the participants were male and 49% were females. Majority (49.5%) of the participants were between 26-35 years of age. Job duration of 51.5% participants' was almost 3 years.

Out of 33 questions, regarding the transmission of diseases, break up was 11 questions each for HBV, HCV and HIV. Proportion of the correct answers for the knowledge is given in Table 1. (Mean score was 24.3±1.98), minimum score was 20 and maximum was 32 out of 33 questions. Only 30% of participants scored above the mean score for knowledge. The mean score of doctors, nurses and technicians is shown in Table 2. Comparison of the mean knowledge by year of service and by different age groups did not reveal statistically significant difference. The mean score of knowledge of universal precaution was 7±0.77. Comparison of different health care groups is given in Table 3.

Regarding the knowledge for vaccination available for the blood borne infections, 57% of respondents wrongly believed that there is a vaccine available for HCV. 22.5% believed that there is no vaccination available for HBV. Regarding the source of knowledge it was found that majority of the respondents used media i.e. internet, television and radio as a source of updating their knowledge.

Discussion

This study showed several interesting facts regarding the knowledge of health care workers which highlights the need of adding infection control in the curricula at an undergraduate level in both public and private sectors.

The mean knowledge score for transmission of disease was found to be 24.3 that was 73.5% of the possible score. Whereas a study conducted in Malaysia shows the mean score of knowledge to be 79.6%.[13] Out of all the participants, technicians had higher mean score of knowledge of transmission of blood borne diseases. Some misconceptions were revealed during this study like donating blood could be a reason for acquiring blood borne diseases; and only 11% respondents gave a correct answer.

Another misconception was regarding recapping of needles. Most of the doctors believed that recapping was essential on the contrary majority of nurses and technicians thought it should be avoided. In a study by Alam M, 29% of HCWs responded

Table 1: Frequency of correct responses for knowledge of blood borne infections given by the participants

Variables	Hepatitis C		Hepatitis B		HIV	
	n	%	n	%	n	%
Insect Bite	19	9.5	21	10.5	15	7.5
Needle Sharing	200	100	177	88.5	199	99.5
Donating Blood	20	10	20	10	26	13
Receiving Blood	200	100	200	100	200	100
Unprotected Sexual intercourse	195	97.5	200	100	199	99.5
Eating with patients	14	7	59	29.5	18	94.3
Mother to fetus	200	100	198	99	200	100
Breast Feeding	155	77.5	161	80.5	170	85
Dental procedure	200	100	198	99	199	99.5
Sharing razors	199	99.5	200	100	200	100
Shaking Hands	198	99	200	100	200	100

Table 2: The mean score for knowledge of Transmission of blood borne disease amongst the various cadres of HCW

Profession	Mean ± SD
Doctor	23.5 ± 1.89
Nurse	24.8 ± 1.74
Technician	25.0 ± 2.18

Table 3: Comparison of knowledge regarding universal precautions among the various groups of health care workers

Options	Doctor n (%)	Nurse n (%)	Technician n (%)	p-value
Wearing gloves while handling blood products or body fluids	86 (97)	84 (98.8)	27 (100)	0.552
Avoiding I/V drug abuse	88 (100)	85 (100)	27 (100)	--
Practicing safe sex	88 (100)	85 (100)	27 (100)	--
Hand washing	80 (90)	59 (69.4)	15 (55.5)	0.001
Recapping needle	14 (15.9)	3 (62.3)	21 (77.7)	0.001
Use of safety needles or cannulas	88 (100)	84 (98.8)	25 (92.5)	0.20
Paying 100% attention while handling sharps.	88 (100)	85 (100)	27 (100)	--
Avoiding unnecessary injection	84 (92)	68 (80)	19 (70)	0.001

that recapping should be done.[14] It means that HCWs especially doctors need to be educated regarding recapping needle since studies showed that incidence of needle stick injury while recapping is high. Zafar A, reported that needle stick injuries during recapping is 11%.[4] It is also documented that 10-25% needle stick injury occurred during recapping the needle after sampling.[15] It makes it essential that the policy of no recapping of needles should be implemented by infection control department.

Regarding vaccination, 57% HCW believed that there is a vaccination available for HCV. On the contrary 22.5% believed that there is no vaccination for HBV. The update on vaccination of health care workers and universal precautions of blood borne diseases are the key to safe practice in hospital settings. CME, workshops and lectures should be arranged to update the knowledge of HCW on a periodic basis.

This study has few limitations which include convenience sampling and it is a single center study. The actual practices of HCW were not observed during this study but the information revealed regarding their knowledge needs to be addressed.

Conclusion

Knowledge of health care workers regarding the transmission of blood borne infections and universal precautions is inadequate. Misconceptions about donating blood and recapping needles after blood sampling should be addressed at all levels.

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ORIGINAL ARTICLE

Ceftriaxone versus Ampicillin in the Treatment of Pneumonia in Children

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Abstract

Objective
To compare the clinical response, adverse effects and cost of ampicillin with ceftriaxone in the treatment of pneumonia in children between 2 months to 5 years of age at a tertiary care hospital in Karachi.

Methodology
This cross sectional study was conducted at the pediatric ward of Aga Khan University Hospital, Karachi over a period of 6 months, between January to June, 2010. We enrolled a total of 150 patients with clinical or radiological diagnosis of pneumonia as per the definition of World Health Organization. They were divided into two groups on the bases of the treatment received. Group A received intravenous ampicillin while in group B ceftriaxone was given. The clinical response (absence of fever, and return of respiratory rate to baseline and absence of retractions.), adverse effects and cost of both drugs were evaluated.

Results
There were 150 patients with the diagnosis of pneumonia in the study. Group A comprised of 64 (42.7%) children while there were 86 (57.3%) children in group B. The clinical response (97% vs. 95%; p=0.99), mean length of hospital stay (5.5±1 vs. 5.6±1.5 days; p=0.556) and adverse effects (6.3 % vs. 3.5%; p=0.46) were comparable in both the groups. However, there was a statistically significant difference in daily cost of drugs (114.6±13.2 vs. 391.5±19.4 PKR; p=<0.001) and total cost of drugs (829.8±81.7 vs. 2413.3±291.8 PKR; p= <0.001) irrespective of other in-hospital charges between the two groups.

Conclusion
There was no statistical difference in clinical response, length of hospital stay and adverse effects in both drugs; however, ampicillin was cheaper than ceftriaxone. Therefore, ampicillin should be the drug of choice in childhood pneumonia to reduce the overall cost of the treatment in a hospital setting.

Key Words
Pneumonia, ampicillin, ceftriaxone, cost

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Introduction
Pneumonia is a significant cause of mortality and morbidity in childhood throughout the world, more so in developing countries.[1,2] It accounts for almost 28-34% of all under 5 deaths globally. In Pakistan alone there are an estimated 15 million pneumonia cases in children leading to 200,000 child deaths each year. Patients suffering from community acquired pneumonia can often require hospitalization and the total economic burden caused by pneumonia is estimated to be 9 billion dollars in the United States alone.[3]

Pneumonia is caused by both viruses and bacteria, and yield of diagnostic tests to detect these pathogens in only 44-85%of pediatric cases. The most common pathogens are Streptococcus pneumonia (pneumococcus), Haemophilus influenza, Respiratory syncytial virus (RSV) and Mycoplasma pneumonia.[4,5] For the management of pneumonia, it is important to define the likely etiology and grade the severity of the infection. Few studies on antimicrobial treatment of pneumonia include concomitant microbiological information, although there is substantial evidence from recent in vitro studies to indicate that resistance to commonly used antimicrobial agents is increasing; ampicillin and ceftriaxone are still the treatment of choice in uncomplicated community acquired pneumonia in children.[7-9] A microbiology based study observed that overall 26% of isolates of pneumococcus showed intermediate susceptibility to penicillin, and 40% showed intermediate susceptibility to ceftriaxone; none were fully resistant to these antibiotics.[10] Ampicillin or penicillin, generally provides adequate coverage for the fully immunized child in communities without substantial prevalence of penicillin-resistant *S. pneumoniae*.[4] However some authors recommend a third-generation cephalosporin (eg, ceftriaxone) for children younger than 12 months and those who are not fully immunized and/or children with more severe illness because they provide coverage for a broader range of pathogens, including penicillin-resistant *S. pneumoniae*, and beta-lactamase producing pathogens (eg, *H. influenzae*), than does ampicillin.[4,11,12] Thus ampicillin and ceftriaxone are still the treatment of choice in uncomplicated community acquired pneumonia in children.[7-9]

The bulk of deaths from childhood pneumonia occur among families belonging to poor socioeconomic status who have higher exposure rates and are at high risk for developing pneumonia than more affluent people.[13] They have reduced access to preventive and curative services due to financial

constraints and this is the main driving force behind revised strategies for reducing the burden of deaths due to childhood pneumonia in developing countries.[14,15] In Pakistan, cost effectiveness is an important factor considering the prevalent poverty and low economic investment in the health sector.

The objectives of this study are to compare the clinical response, adverse effects and cost of intravenous ampicillin with intravenous ceftriaxone in the treatment of pneumonia in children at a tertiary care hospital.

Materials and Methods

This prospective cross sectional study was conducted in the pediatric ward of the Aga Khan University Hospital, Karachi over a period of 6 months, between January and June, 2010. Non probability, convenience sampling technique was used. Children between the ages of 2months-5years with diagnosis of pneumonia as defined by WHO in Integrated Management of Childhood Illness (IMCI) guidelines and received injectable ampicillin or ceftriaxone for treatment for at least 5days during their stay in hospital were included in the study. Children with chronic respiratory diseases, complex congenital heart disease, gastro esophageal reflux, immunodeficiency, any malignancy and children requiring intubation were excluded from the study.

Patients were divided into two groups based on their treatment regimen to assess the clinical response, adverse effects, cost as well as the duration of hospitalization between two groups. Children in group A received intravenous ampicillin (100mg/kg/day in 4 divided doses) while children in Group B received intravenous ceftriaxone (50-65mg/kg/day once daily dose).

Clinical responses were defined at day 5 as improvement of the clinical signs, absence of fever, and return of respiratory rate to baseline and absence of retractions.

For data entry and analysis, SPSS version 20.0 (IBM, Chicago, USA) was used. Mean and standard deviation of age, weight, temperature, heart rate, respiratory rate, and duration of hospital stay were computed, while frequency (percentage) for gender, nasal flaring, grunting, crackles, wheezes, adverse effects, clinical response were calculated for group A and group B. Chi-square (or Fisher's Exact) or t- test was performed to compare proportion difference between groups for clinical response and adverse effects, p-value of <0.05 was considered significant.

The study was approved by the Ethical Review Board (ERB) of Aga Khan University, Karachi.

Results

A total of 217 patients with the diagnosis of pneumonia were enrolled in the study. Sixty seven patients were excluded from the study because 13 parents refused to consent, 7 had complex congenital heart disease, 27 had malignant disorders, 2 patients required intubation because of respiratory failure, 4 had a secondary diagnosis of gastro esophageal reflux disease and 14 patients had reactive airway disease with pneumonia. Remaining 150 patients were divided into 2 groups. In group A, there were 64 (42.7%) patients while in Group B there were 86 (57.3%) . Out of 150 patients, 105 (70%) were male and 45 (30%) were female and most cases (n= 108, 72%) were < one year of age (n=46 in group A and 62 in Group B) Baseline characteristics and clinical feature at presentation of the patients were comparable in both groups (Table 1).

Clinical response between two groups was comparable (96.8% vs 95.3%) (table 2). Mean duration of hospital stay of group A was 5.5±1 compared to 5.6±1.5days for group B (p=0.556). Two patients from each Group A (3.2%) and Group B (2.4%)

Table 1: Baseline characteristics and clinical feature of all treated patients.

Variable	Group-A n=64 (%) or Mean ±SD	Group-B n= 86 (%) or Mean ±SD
Male	46 (72%)	59 (69%)
Mean weight in Kg	7.6±0.5	7.2±0.4
Mean Age in months	9.7±9.5	11.7±11
Clinical Features		
Mean Respiratory Rate	48±2	53±2
Wheeze	38 (59%)	54 (63%)
Crackles	50 (78%)	66 (77%)
Nasal Flaring	30 (47%)	44 (51%)
Grunting	8 (13%)	13 (15%)
Fever	60 (94%)	78 (91%)

Table 2: Clinical Response, duration of hospitalization, adverse events and Cost of treatment

Variable	Group-A n=64 (%) or Mean ±SD	Group-B n= 86 (%) or Mean ±SD	p-value
Improvement in clinical signs	62 (97%)	82 (95%)	0.99
Adverse Effects (Rash, Diarrhea, Anaphylaxis, Phlebitis)	4 (6.3%)	3 (3.5%)	0.460*
Mean Length of Hospital stay (days)	5.5±1	5.6±1.5	0.556
Average per day cost of drug (PKR)	114.6±13.2	391.5±19.4	<0.001
Total cost of drug during In-Hospital Stay (PKR)	829.8±81.7	2413.3±291.8	<0.001

*Fisher's Exact test applied as sample size were < 5

left against medical advice. Two patients needed a change of antibiotic therapy due to worsening of symptoms and one patient from Group B was expired because of respiratory failure.

Overall adverse effects were observed in 7(4.7%) patients, in group A, 3 patients had diarrhea and 1 patient had phlebitis at the site of cannula. In group B, 2 patients had diarrhea, while 1 patient had generalized erythematous rash, after which the medication was stopped for few hours and then repeated with increased dilution and with injectable antihistamine.

Daily cost of antibiotic in group A was 114.6±13.2 PKR and group B was 391.5±19.4 PKR ($p < 0.001$). The total cost of the drug for duration of 5 days of hospital stay also included the charges of cannula, fluid drip, and container which cost additional 175 PKR, irrespective of hospital bed charges. In group A, the total cost of the drug for at least 5 days including the additional charges of the cannula and the drip set were 829.8±81.7 PKR while in group B, it was 2413.3±291.8 PKR ($p < 0.001$).

Discussion

Pneumonia is the leading cause of childhood death in Pakistan.[6] WHO recommends co-triamoxazole and penicillin for the treatment of pneumonia, oral or injectable.[16] Recently there are studies comparing the efficacy of macrolides vs. conventional therapy.[16-17] The evidence from these studies indicates that treatment with amoxicillin compared to co-triamoxazole produces satisfactory rates of clinical cure and has similar efficacy for the treatment of community acquired pneumonia in children.[18] But with the emergence of resistant organisms, third generation cephalosporin appear to be a good choice in the treatment of pneumonia in children.[19] Our study shows that both intravenous ampicillin and ceftriaxone are effective for WHO defined pneumonia.[20] Rates of clinical response and adverse effects were almost the same in both treatment groups, as was shown in the results.

Both these antibiotics are recommended for the treatment of pneumonia and are commonly used in tertiary care hospitals but the major difference between the two is that the cost of ceftriaxone is almost 3 times higher compared to ampicillin. Pakistan is a low income country along with India, Bangladesh, Sri Lanka and cost of a drug is a major issue in a low income country considering the low budget allocated for health care facilities.[21]

The major strength of our study is the report on the cost per patient of ampicillin and ceftriaxone for the treatment of pneumonia in a tertiary care hospital keeping in view a similar clinical response of both these drugs. Intravenous ampicillin has the benefits of lower cost of therapy, as compared to intravenous ceftriaxone which costs three times more. Overuse of antibiotics and antimicrobial resistance is of concern especially for respiratory pathogens like Streptococcus pneumonia and Hemophilus influenza[19]. A simple antibiotic like penicillin (ampicillin) can help to contain the spread of antimicrobial resistance. Most children were cured with a simple antibiotics like ampicillin, which is good news for the management of pneumonia.[22]

This is single centre based study and has a limited number of patients so results should be generalized with caution.

Conclusion

We conclude that there was no statistical difference in clinical response and adverse effects for either ampicillin or ceftriaxone; however ampicillin was cheaper than ceftriaxone. Therefore, ampicillin should be the drug of choice for pneumonia in children to reduce the overall cost of the treatment in a hospital setting

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ORIGINAL ARTICLE

Frequency of Thrombocytopenia in Children with Acute Vivax Malaria

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Abstract

Objectives
Malaria causes more than 300 million acute illnesses and approximately one million deaths annually. Worldwide it is one of the 5 killers in the pediatric population. Hematological changes especially anemia and thrombocytopenia are considered as hallmark for malarial infection that leads to severe complications and fatality. The aim of this study is to determine frequency of thrombocytopenia in children with acute vivax malaria.

Method
A cross sectional descriptive study conducted at the pediatric medical unit of National Institute of Child Health Karachi over a period of 6 months (October 2009 to March 2010). All patients admitted with acute febrile illness of less than seven days with signs and symptoms suggestive of acute malaria were considered for the study. Peripheralsmear examination for malarial parasite (MP) *Plasmodium vivax* was taken as gold standard. Those with positive MP were then included in thestudy after taking consent. Platelet counts were performed with both automated analyzer and manually. Data was collected on a structured proforma.

Results
A total of 78 children with acute febrile illness of less than seven days with positive *P. vivax* were included in this study. Most (48.7%). of the children were between 5 to 8 years of age. The average age of the children was 4.24±2.13 years. Out of 78 patients, 42(54%) were male. Chills was the most common symptoms that was observed in 74.4% cases followed by sweating (71.8%), splenomegaly (38.5%), headache (37%), body ache (29.5%) and fatigue (15.4%). Thrombocytopenia was observed in 73% (57/78) cases.

Conclusion
In this study a highfrequency of thrombocytopenia was observed in patients with acute vivax malaria.

Key Words
Acute Malaria, *plasmodium vivax*, thrombocytopenia, frequency

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Introduction

Malaria is an acute and chronic illness characterized by paroxysms of fever, chills, sweats, fatigue, anemia, and splenomegaly.[1] Malaria causes more than 300 million acute illnesses and approximately one million deaths annually.[2] Worldwide it is one of the 5 killers in pediatric population.[3] Around 800,000 children under the age of five die from malaria every year, making this disease one of the major causes of infant and juvenile mortality.[4] Malaria is present in more than 109 countries.In addition to its health toll, malaria puts a heavy economic burden on the endemic of countries and contributes to the cycle of poverty.

Pakistan has been classified as a country with moderate malaria prevalence by WHO Annual Parasite Incidence (API) during year 2003 is 0.8 / 1000 population.[5] There is variation in prevalence malaria from province to province and area to area. Sindh and Baluchistan are the most affected provinces.[6,7] Estimated number of annual malaria episodes due to *P. vivax* and *P. falciparum* in Pakistan is 1.5 million and accounts for 12.5% overall disease burden of the country.[2,8] *P. vivax* is the most common type, out of all species of malarial parasites affecting human beings and contributes 70 to 80 million new cases to the annual worldwide burden of disease but it remain to be less investigated when compared to *P. falciparum.* Although *P. falciparum* malaria is considered the most severe form of malaria producing serious disease and mortal consequences but in the last few years an increase in the number deaths due to *P.vivax*, with a significant proportion occurring in children has been reported.[9]

Hematological changes are considered as hallmark for malarial infection that lead to severe complications and fatality. The hematological abnormalities that have been reported are anemia in 65%, thrombocytopenia in 60-80%,leucopenia and/or leukocytosis 20-30%and rarely disseminated intravascular coagulation.[10,12] Anemia and thrombocytopenia are the most common complications in both severe and non-severe clinical malaria cases and is responsible for much of the morbidity and great mortality, particularly in children.[10,12] Biosynthesis and regulation of thrombopoietin (TPO), the main growth factor for megakaryocytes and thrombocytopoiesis, seems to be normal or increased in patients with malaria.[13]

Thrombocytopenia during the clinical course of *P. falciparum* malaria has been consistently reported. However thrombocytopenia is infrequently reported for vivax in pediatric patients. Current studies suggest that thrombocytopenia can be used as an indicator for acute vivax malaria in patients presenting with pyrexia of unknown origin from high malaria endemic area.[12,13] The present study was therefore undertaken to determine the actual burden of thrombocytopenia in children with acute vivax malaria from our population.

Methodology

This cross sectional descriptive study was conducted at the Pediatric Medical unit, National Institute of Child Health Karachi, over a period of 6 months from October 2009 to March 2010. Non probability purposive sampling technique was used. 78 pediatric patients of age 1 month to 12 year with acute febrile illness of less than seven days and positive plasmodium vivax specific trophozoites and schizonts on microscopic examination of thick and thin blood smearusing Giemsa staining were included in the study. Patients having thrombocytopenia due to any other cause like typhoid fever, dengue fever, ITP, and hematological malignancies were excluded from the study.

Data was entered and analyzed using the SPSS Version 20.0.Median age of children with IQR is reported. Frequency with percentage was computed for categorical variables like age groups, gender and presence of thrombocytopenia.

Results

A total of 78 children with acute febrile illness of less than seven days with positive *P.vivax* on slide were included in this study. Most (n=38, 48.7%). of the children were between 5 to 8 years of age. Median age of the children was 4 year (IQR:3,6)

Out of 78 patients, 42(54%) were male and 36(46%) were female with male to female ratio of 1.17:1. Chills was the most common symptoms that was observed in 74.4% cases followed by sweeting 71.8% , splenomegaly 38.5 %, headache 37 %, body ache 29.5%, and fatigue 15.4% as presented in Table 1.

Thrombocytopenia was observed in 73% (57/78) cases. Regarding gender, thrombocytopenia was approximately similar in male and female (71.4% vs. 75%). presence of thrombocytopeniaby age groups is shown in Table 2 and severity of thrombocytopenia given in Table 3.

Table 1: Symptoms of vivax malaria in children (n=78)

Symptoms	Number (%)
Chills	58 (74.4%)
Sweating	56 (71.8%)
Splenomegaly	30 (38.5%)
Headache	29 (37%)
Body Ache	23 (29.5%)
Fatigues	12 (15.4%)

Table 2: Frequency of Thrombocytopenia in Children with Vivax Malaria (n=78)

Age Groups	Thrombocytopenia Number (%)
≤ 1 Years	8/10 (80%)
2 to 4 Years	20/30 (66.7%)
5 to 8 Years	29/38 (76.3%)

Table 3: Severity of Thrombocytopenia in Children with Vivax Malaria (n=57)

Thrombocytopenia Severity	Number (%)
150000-10000	32 (56%)
10000-50000	13 (23%)
<50000	12 (21)

Discussion

Malaria continues to be a major public health problem in Pakistan.[2,8] Plasmodium vivax malaria is prevalent in many regions of the world. It accounts for more than half of all malaria cases in Asia and Latin America with an at risk population of 2.5 billion persons and causes approximately100–300 million clinical cases each year.[14,15]

Hematological changes associated with malaria are well recognized. Thrombocytopenia is associated with falciparum and vivax malaria. Severity of thrombocytopenia correlated well with type and severity of malaria.[16] We found low platelets in 73 % of our cases. Aartikumar *et al*[13] from India reported thrombocytopenia in 24/ 27 (88.8%) of vivax malaria patients. Erhart *et al*[17] reported a likelihood of malaria 12-15 times in thrombocytopenic falciparum (414) and vivax (646) malaria patients with fever compared to febrile non malaria patients, defining thrombocytopenia as the key indicator of malaria. Lathia *et al*[18] suggested thrombocytopenia alone is one of the strongest predictor of malaria (sensitivity 60% and specificity 88%). Other workers who reported thrombocytopenia in vivax malaria are Abro *et al*[10] (81%) and Ammarah J *et al*[3] (72%).

The mechanism of thrombocytopenia is not very clear in malaria, but it probably the consequence of several factors like bone marrow failure, spleen pooling, consumptive coagulopathy with removal of platelets from circulation, direct parasitization, and direct immune phenomenon.[10] Kelton *et al*[19] demonstrated presence of immune complexes generated by malarial antigen in malaria infected patients which may play a role in peripheral

destruction of platelets. Spleen has been implicated as a site of excess sequestration. In our study 13/30 (43%) patients with splenomegaly developed thrombocytopenia. In acute malaria platelets are found to be hypersensitive and there is increased concentrations of platelet-specific proteins such as beta thromboglobulin (ßTG), platelet factor 4 (PF4).[16] These hypersensitive (hyperactive) platelets enhance haemostatic responses, and may be this is why bleeding episodes are rare in acute malarial infections, despite the significant thrombocytopenia. In our study also we did not observed any bleeding tendency even with platelet counts as low as 25,000.

In this study males were predominant (54%) as compared to females (46%) and male female ratio was 1.17:1 which is similar to reports by Jalal-ud-din *et al*[20] and Idris M *et al*.[21]

In our study most of the children were below 5 years of age (51.3%). A study done on malaria in pediatric age group by Jamal MM *et al*[3] reported 62.5% patients below 5 years, and according to WHO malaria is the leading cause of mortality among children <5 years of age.[22]

In the present study chills were the most common symptoms observed in 74.4% cases Percentage of rigors and chills associated with malaria fever were reported by Farooq MA *et al*.[7] as 65% and as 79% by Trampuz A *et al*.[23] Therefore fever associated with rigors or chills is the strong suggestive indicator for malaria infection, and children with these symptoms should be evaluated for malaria.

In this study fatigability was reported in 15.4% while Akbar JU[24] reported it in 80% of malaria case. In our study body ache was observed in 29.5%, while Echeverri M *et al*.[25] reported body pain in 58% and headache in 99%, while in this study headache was present in 37% that resembles to study done by Farooq MA *et al*.[7]

Conclusion

A high frequency of thrombocytopenia was observed in pediatric patients with acute vivax malaria.Any child from malarial high endemic are with acute febrile illness should be investigated for malaria. A larger multi central study needed to determine the association of thrombocytopenia with malarial species especially vivax.

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ORIGINAL ARTICLE

Haemorrhagic Manifestations of Dengue Haemorrhagic Fever in Children

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Abstract

Objective
The World Health Organization (WHO) declares dengue fever and dengue hemorrhagic fever to be endemic in South Asia. Pakistan has faced world's largest epidemic of dengue in 2011. We aim to determine the haemorrhagic manifestations of dengue haemorrhagic fever (DHF) in children.

Methodology
This cross sectional study was conducted in the department of Paediatrics, King Edward Medical University/ Mayo Hospital, Lahore from May to October 2011. A total 50 children of age ≤12 years consistent with clinical case definition of DHF were enrolled by consecutive sampling. Haemorrhagic manifestations (Positive tourniquet test, petechiae, ecchymoses or purpura, or bleeding from mucosa, gastrointestinal tract, injection sites, or other locations) were recorded. Diagnosis of dengue infection was confirmed by acute phase serum sample for dengue IgM & IgG (ELISA).

Results
Among 50 cases of DHF, mean age was 6±2 years. Majority (62%) were >5 years of age. Among haemorrhagic manifestations, petechiae was the most common observation (70%) followed by positive tourniquet test (50%) and mucosal bleed (30%) while GI bleed was observed in 4% cases only. As the severity of DHF increased, positivity of tourniquet test decreased. In non-shock patients, tourniquet test was positive in 67% of patients while it was positive only in 34% of patients with shock. Mucosal bleed was observed in severe cases (46%). Major bleed was uncommon.

Conclusion
Petechiae was the most common (70%) haemorrhagic manifestation observed in children with DHF.

Key Words
Children, Dengue haemorrhagic fever, Haemorrhagic manifestations, Tourniquet test

Introduction

World Health Organization (WHO) declares dengue fever (DF) and dengue hemorrhagic fever (DHF) to be endemic in South Asia. WHO currently estimates 50 million dengue infections worldwide every year.[1] Dengue virus is now endemic in Pakistan. The first recognized epidemic of dengue haemorrhagic fever (DHF) in Pakistan was recorded from Karachi in 1994-5.[2] Subsequent episodes were reported in 2005-6 and in 2008.[3] Pakistan faced world's largest reported epidemic of dengue in Lahore in 2011.[4]

The standard tourniquet test (TT), which reflects both capillary fragility and thrombocytopenia, is performed to predict the haemorrhage in DHF. However, the test may be negative or only mildly positive during the phase of profound shock. It usually becomes positive, sometimes strongly positive after recovery from shock.[5] Local and international studies have evaluated the hamorrhagic manifestations of DHF. Riaz *et al*[6] from Karachi reported 81% haemorrhagic manifestations in DHF. Garg *et al*[7] from India reported bleeding in 61% cases in children of DHF.

There is limited data from Pakistan regarding dengue in children, we therefor conducted this study to determine the haemorrhagic manifestations in dengue haemorrhagic fever (DHF) in children in the 2011 epidemic of dengue fever assuming the antibody mediated enhancement phenomenon due to dengue infection during past years.

Methods

This cross sectional study was conducted in the department of Paediatrics, King Edward Medical University/ Mayo Hospital, Lahore from May to October 2011 in dengue epidemic. This study was approved by Ethical Review Board of King Edward Medical University, Lahore. There was no conflict of interest between the authors. Informed verbal consent was obtained from parents before enrolment. Total 50 children of age ≤12 years consistent with clinical case definition of DHF were enrolled from the inpatient department by consecutive sampling. The diagnosis of DHF was based on following WHO case definition listed below.[5]

- Acute onset of fever of two to seven days duration.
- Haemorrhagic manifestations: Positive tourniquet test, petechiae, ecchymoses or purpura, or bleeding from mucosa, gastrointestinal tract, injection sites, or other locations.
- Platelet count ≤100 000 cells/mm^3
- Objective evidence of plasma leakage: Rising haematocrit/haemoconcentration ≥20% from baseline or

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decrease in convalescence, or evidence of plasma leakage such as pleural effusion, ascites or hypoproteinaemia/ albuminaemia.

Table 1 shows the criteria used to grade DHF[5]. TT was performed in all the cases. An appropriate sized blood pressure cuff was chosen according to the length of the upper arm of the subject. TT was performed by inflating a blood pressure cuff to a point midway between the systolic and diastolic pressures for five minutes. Results of the TT were rechecked by a second observer. The test was considered positive when 10 or more petechiae per square inch are observed. Children presenting with shock were resuscitated first with parenteral fluids. Haemorrhagic manifestations, other than positive TT (petechiae, ecchymoses or purpura, or bleeding from mucosa, gastrointestinal tract, injection sites, or other locations) were recorded. A 1ml heparanized venous sample was obtained with aseptic measures and complete blood count was recorded. Right lateral decubitus chest films to detect pleural effusion and abdominal ultrasound for ascites were done. On 5th day of fever, acute serum sample for dengue IgM & IgG were obtained and tested for anti-dengue immunoglobulin M (IgM) and IgG antibodies using an enzyme-linked immunosorbent assay (ELISA). The Human ELISA kit was used and serology was determined by calorimetric detection method. Results are presented as frequency tables.

Table 1: Criteria used to grade DHF

Grade	Sign & symptoms	Laboratory
DHF-I	Fever and haemorrhagic manifestation (positive tourniquet test) and evidence of plasma leakage	Thrombocytopenia <100 000 cells/ mm3; HCT rise ≥20%
DHF-II	As in Grade **I plus** spontaneous bleeding	Thrombocytopenia <100 000 cells/ mm3; HCT rise ≥20%
DHF-III	As in Grade **I or II plus** circulatory failure (weak pulse, narrow pulse pressure (≤20 mmHg), hypotension, restlessness)	Thrombocytopenia <100 000 cells/ mm3; HCT rise ≥20%
DHF-IV	As in Grade **III** plus profound shock with undetectable BP and pulse	Thrombocytopenia <100 000 cells/ mm3; HCT rise ≥20%

Results

All 50 cases of DHF had positive IgM in acute phase serum. Thirty one (62%) patients were ≥5 years of age. Mean age was 6±2 years. Fifty eight percent (n=29) of the patients were male (Figure I).

Overall, 34% of patients fit the WHO category of DHF-I, followed by DHF-III (30%), DHF-IV (22%) and DHF-II (14%). Among haemorrhagic manifestations, petechiae was the most common observation (70%) followed by positive TT (50%) and mucosal bleed (30%) while GI bleed was observed in 4% cases only (Table 2).

As the severity of DHF increased, positivity of TT decreased. In patients with DHF-I or DHF-II, TT was positive in 67% patients while it was positive only in 34% of patients with circulatory compromise (DHF II and DHF IV). Similarly, mucosal bleeding was more commonly seen in severe cases (46%). Major bleeding was an uncommon event.

Table 2: Haemorrhagic manifestations in DHF (n=50)

Grade of DHF	Total n (%)	Tourniquet Test positivity n (%)	Petechiae n (%)	Purpura n (%)	Ecchymoses n (%)	Mucosal bleed n (%)	GI tract bleed n (%)
DHF-I	17 (34)	11 (65)	13 (76)	02 (12)	00 (00)	00 (00)	00 (00)
DHF-II	07 (14)	05 (71)	04 (57)	03 (43)	00 (00)	03 (43)	00 (00)
DHF-III	15 (30)	07 (46)	10 (67)	02 (13)	01 (06)	07 (47)	01 (06)
DHF-IV	11 (22)	02 (18)	08 (73)	02 (18)	01 (09)	05 (73)	01 (09)
Total	50 (100)	25 (50)	35 (70)	09 (18)	02 (04)	15 (30)	02 (04)

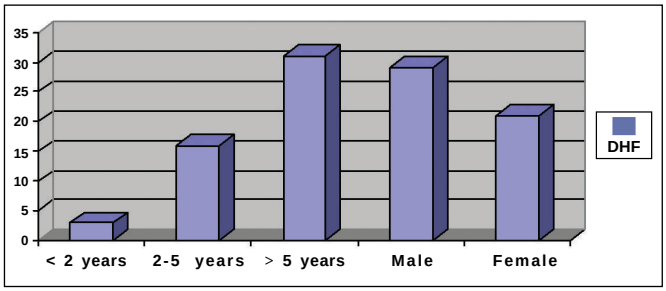

Fig 1. Age and sex distribution of DHF (n=50)

Discussion

In the present study, males were predominantly affected by DHF. Most of the children were 5 year of age or above. Our results are comparable with Ahmed *et al*[8] from Pakistan, Gorg *et al*[7] from India and Kalayanarooj *et al*[9] from Thailand.

According to WHO case definition of DHF, haemorrhagic manifestation is one of the essential criteria in the diagnosis. In the present study, 50% of DHF cases presented with positive TT. In this study, as the severity of DHF increased, positivity of TT decreased. In non-shock patients, TT was positive in 67% patients while it was positive in only 34% of shock patients. The difference may be due to the fact that the TT is usually negative during the phase of profound shock. There are many children with dengue infection, at risk of dengue shock, who do not have a positive TT, so it is critical that a negative test should not be interpreted as signifying that the child does not have dengue infection. Our results are supported by Kalayanarooj *et al*[9] who reported 65% positive TT in children with DHF with decreased positivity in shock patients. In dengue epidemic of Pakistan, Iqtadar *et al*[10] in adults reported 52% positive TT in DHF which is similar pattern reported by our study in younger age group.

Among haemorrhagic manifestations, petechiae was the most common observation (70%) in present study, followed by mucosal bleed (30%). We observed that mucosal bleeding is more in severe cases of DHF (46%). In Karachi epidemic in 2006, Riaz *et al*[6] observed 81% bleeding tendencies in DHF. Qureshi *et al*[11] reported 38% mucosal bleed as haemorrhagic manifestations in DHF while Ansari *et al*[12] found 53% mucosal bleed. Similar results are reported by Lodhi *et al*[13] and Ahmed *et al*[14] locally and Kalayanarooj *et al*[9] internationally. Garg *et al*[7] in a comparative study between Karachi epidemic and Delhi epidemic reported similarities and observed bleeding in 61% of case as haemorrhagic manifestation in DHF.

Present study reported major bleed as a very uncommon finding of dengue in children. Ahmad *et al*[14] from Pakistan and Gorg *et al*[7] from India reported 2% and 5% major bleeding respectively. This may be due to the fact that we sampled our patients from inpatient and better management could have prevented the major bleed during hospital stay.

This study is among the first reports of haemorrhagic manifestations in DHF in children in Lahore epidemic of dengue. Limitation of this study is that due to less sample size, the results are not generalizable.

Continuous education of clinicians is recommended for the early recognition of haemorrhagic manifestations of DHF in children for early diagnosis and management. Shock remains the major cause of death in dengue haemorrhagic fever. Therefore, early recognition and strict fluid management is the key to success.

Conclusion

Petechiae are the most common hemorrhagic manifestation observed in children with DHF, however the results need to be verified in a larger study.

Acknowledgements

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CASE REPORT

Bovine Contegra Valved Conduit Endocarditis Caused By An Unusual Micro-Organism, Gemella Morbillorum: A Case Report

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Background
Different surgical techniques are used for right ventricular outflow tract reconstruction, including homo or porcine xenografts, which have several limitations, including lack of availability, early degeneration and tissue ingrowth. Contegra, a bovine jugular vein graft, because of its easy availability and tissue characteristics is an alternative to overcome these limitations. It has a naturally integrated valve in it. Isolated endocarditis of contegra valve conduit is extremely rare.

Case Presentation
We report the case of a 17 years old male with endocarditis of bovine contegra valve conduit, secondary to a rare micro-organism, *Gemella morbillorum.* This occurred five years after surgery of right ventricular outflow tract reconstruction with bovine jugular vein, contegra, for pulmonary atresia and ventricular septal defect.

Conclusion
We believe that the presentation of this case highlights the importance of unusual organisms in the diagnosis of endocarditis.

Back Ground
A variety of prosthetic conduits and homografts for right ventricular outflow tract re-construction have been developed in recent years. Homografts, being considered as the most reliable option undergo early degeneration and calcification, particularly in very young patients[1], and therefore, fail to be the best choice in long term follow up.[2] The recently developed bovine contegra valve conduit (Medtronic Inc., Minneapolis, MN, USA) has led to short term success in experimental animal studies,[3,4] as well as in humans.[5,6] It consists of a bovine jugular vein which contains a venous valve with three leaflets that open to allow the forward flow and close to prevent the backward flow of blood. It functions like the patient's natural pulmonary artery valve.

The contegra pulmonary valve conduit can be used in children and young adults under the age of 18 years.[7] Isolated endocarditis of the pulmonary valve is uncommon and usually occurs in conjunction with tricuspid and /or left sided valvular endocarditis.[8]

We describe a case of 17 years old male patient with endocarditis of bovine contegra valve conduit, secondary to *Gemella morbillorum* infection, five years after right ventricular outflow tract re-construction.

Case Presentation
A 17 years old male presented to our clinic with complaints of fever, sweating, fatigue and weight loss. He was diagnosed to have pulmonary atresia, ventricular septal defect and patent ductus arteriosus. He underwent ventricular septal defect closure, Patent ductus arteriosus ligation and right ventricular out flow tract reconstruction with contegra pulmonary valve conduit eight years prior to presentation. He also required revision surgery in the form of conduit replacement five years back because of calcification and severe obstruction.

On admission, he was pale with blood pressure of 110/68 mmHg, pulse rate of 110 beats per minute and body temperature of 39ºC. Cardiac auscultation revealed clear sounds and ejection systolic murmur maximum on the second left intercostal space. Lungs were clear on auscultation. ECG showed sinus rhythm with a heart rate of 110 beats/minute and right ventricular hypertrophy along with right axis deviation.

Laboratory data showed high erythrocyte sedimentation (80 mm in first hour) and C-reactive protein (20.7 mg/dl), low hemoglobin value (9.6 gm/dl), low platelets count (142 x 10^3/cm), markedly increased total leukocyte count (33.8 x 103/cm) with high percentage of granulocytes (92.8%) and high serum creatinine concentration (1.3 mg/dl). All other laboratory findings were within normal reference range. Three blood cultures were drawn from different sites; all of them grew *Gemella morbillorum*, sensitive to meropenem, vancomycin, ceftriaxone and chloramphenicol. Chest X- ray showed cardiomegaly along with minimal left sided pleural effusion.

Transthoracic echocardiography demonstrated calcification in right ventricular outflow tract along with multiple vegetations on the bovine contegra valve leaflets. Continuous wave Doppler assessment of the Contegra valve showed increased pressure gradient (maximum pressure gradient of 75 mmHg). There was right atrial and ventricular enlargement with moderate right ventricular systolic dysfunction. CT angiography was also

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performed which revealed multiseptated abscesses involving the contegra valve leaflets.

The patient was admitted in cardiac intensive care unit for monitoring and empirically treated with antibiotics (meropenem and vancomycin) and other supportive care.

After one week of intensive therapy, calcified infective bioprosthesis was replaced with a new conduit, size 22 mm contegra.

Post-operatively, patient remained well and was discharged home in two weeks. He completed total of six weeks of intravenous antibiotics, two weeks of meropenem and vancomycin followed by four weeks of ceftriaxone and rifampicin. Repeat blood cultures at three and six weeks were sterile.

He was regularly followed in cardiology clinic and is doing well at 9 month follow up visit.

Discussion

Since introduction in 1999, contegra valve conduit (Medtronic Inc., Minneapolis, MN, USA), which consists of a bovine jugular vein, is successfully used in patients for the right ventricular outflow tract re-construction. It has several advantages including easy availability, compared with homografts or porcine xenograft.[5, 6]

Right sided infective endocarditis represents about 5-10%[9], whereas the pulmonary valve endocarditis is less than 2% of all cases of endocarditis, and usually it is accompanied with other congenital heart anomalies.[10]

The results of contegra bovine conduit for reconstruction of right ventricular outflow tract and pulmonary artery are encouraging, with good short and medium term results.[6, 11, 12] Although endocarditis of the contegra conduit was shown to be very rare in the follow up of these patients, having a stenotic conduit/valve is a risk factor.[18] Breyman[5], followed up the highest number of patients that underwent this correction (71 patients) and did not register any case with endocarditis, as well as other researchers.[11, 12]

Shebani and colleagues[13] report 64 patients operated with contegra conduit, and detected only one patient with endocarditis early after operation. BajraktariG[14], reported a case of MRSA endocarditis of bovine contegra valve conduit in a 20 years old male.

Only 23 cases of endocarditis caused by *Gemella morbillorum* have been reported in the literature, with the vast majority involving native (non-prosthetic) valves.

Gemella morbillorum is an anaerobic gram positive coccus. It is normal flora of the oropharynx, however, infections when found are similar to *Viridans Streptococci.*

To the best of our knowledge, there have been only three previous reports of endocarditis due to *Gemella morbillorum* involving prosthetic valve and one of the case was associated with intravenous drug abuse.[15] This is believed to be the third reported case in an individual with prosthetic valve who was not an intravenous drug user, and first case report involving contegra pulmonary valve conduit.

We present case of a 17 years old male patient with endocarditis of bovine contegra valve conduit, five years after placement, secondary to *Gemella morbillorum* infection. We consider that our case is a complex one, not referred before in the literature.

Significant clinical isolates of *Gemella morbillorum* reported in the literature have generally been sensitive to penicillin G and ampicillin.[16] Nevertheless, more recent data suggest some emerging penicillin and macrolide resistance.[17] In our patient, the organism was sensitive to penicillin, ceftriaxone and vancomycin. We treated our patient with two weeks of meropenem and vancomycin and four weeks of ceftriaxone and rifampicin.

Conclusion

We present a patient with endocarditis of bovine contegra valved conduit with an unusual pathogen, *Gemella morbillorum.* To our knowledge, this is the first case report of *Gemella morbillorum* endocarditis of bovine contegra valve conduit, which is used for re-construction of right ventricular outflow tract obstruction. This case illustrates the importance of considering unusual organisms in the diagnosis of endocarditis.

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CASE REPORT

Acute Dengue Myositis in a Child. Case Report and Review of Literature

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Abstract

Myositis is a rare complication of dengue fever. We are reporting a case of a seven year old boy who presented with generalized body aches and fever, followed by bilateral lower limbs pain, weakness and inability to walk. He had low platelets, high Creatinine Phosphokinase (CPK) levels and positive dengue antigen. He was given supportive management and was discharged in stable condition.

Introduction

Dengue is transmitted by the bite of an *Aedes* mosquito infected with any one of the four dengue viruses belonging to the genus *Flavivirus*.[1] According to World Health Organization (WHO) over 2.5 billion people, comprising over 40% of the world's population are at risk of dengue.[2] Most seriously affected regions are South East-Asia and Western Pacific regions. The commonest symptoms are mild to high grade fever, severe headache, pain behind the eyes, arthralgia, myalgia, and rash. Acute dengue myositis is characterized by fever and myalgia (with or without muscle weakness). It has a wide clinical spectrum that ranges from mild proximal asymmetrical weakness of the lower limbs to rapidly progressive severe limb, trunk and respiratory muscle weakness.[3] Usually, dengue myositis is considered a benign illness although severe fulminant myositis, resulting in the death of a patient, has been reported infrequently.[4] Rare cases of dengue myositis with respiratory paralysis are reported in literature.[5] Elevated CPK levels remain the most sensitive indicator of myositis. Serum CPK is used is a diagnostic tool in dengue myositis, but it does not predict the severity of the muscle involvement and paralysis.[6,7] The main histopathological changes described in dengue myositis include perivascular mononuclear infiltrate and lipid accumulation. Other histopathological abnormalities observed included an increase in the number of mitochondria, foci of myonecrosis, and fiber type grouping. The exact pathogenesis of severe fulminant myositis is not clear.[8] The proposed mechanisms of dengue myositis includes direct viral invasion of muscle and immune mediated damage of muscle fibers. Muscle biopsy in patients with dengue myositis has varied findings from inflammatory infiltrate to foci of myonecrosis.[5,9] We are reporting a case of a young boy who presented with high grade fever with generalized body aches and difficulty in walking. His clinical and laboratory examination showed signs of myositis and later on, his dengue antigen came positive. He was discharged home with full recovery.

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Case History

A 7 year old previously well child presented in the emergency department with complaints of fever and generalized body aches for past four days. Fever was acute in onset, intermittent, high grade, without rigors or chills, relieved temporarily with antipyretics. The maximum daily documented fever was 104^0F. Body aches were generalized, were increasing in intensity and were more prominent in the lower limbs, leading to an inability to bear weight and difficulty in walking and standing. There were no other significant systemic complaints and rest of the components of history was unremarkable. On examination the child was pale and sick looking. Locomotor examination showed muscular tenderness in all four limbs; pain in the right shoulder, both hip and knees and right ankle joint along with pain in the calf muscles and anterior surface of thighs without any signs of inflammation. Rest of the systemic examination was unremarkable. Viral and enteric fever with myositis were in the list of differential diagnosis and he was worked up accordingly. Initial workup in the emergency showed lymphopenia (WBC $3.3x10^9$/L, N 64%, L 25%) along with thrombocytopenia ($105x10^9$/L). Reversal of SGPT (31 IU/L) to SGOT (277 IU/L) ratio was observed. Muscle enzymes showed a high creatinine phosphokinase (CPK) 2979 (46-171 IU/L), lactate dehydrogenase 954 (155-290 IU/L) and aldolase-B 22 (5-20 IU/L). Dengue antigen NS1 later came out to be positive. He was admitted in the ward. He was hydrated with intravenous fluids, antipyretics and non-steroidal anti-inflammatory drugs were given. His vitals were monitored. Initially he also received injection ceftriaxone for presumed enteric fever, which was discontinued after 72 hours. His platelets decreased to 53 $x10^9$/L and then recovered to 123 $x10^9$/L on discharge. His clinical condition improved markedly in 72 hours. He remained vitally stable, his fever subsided, muscle tenderness decreased and he started bearing weight and then started walking without support. He was discharged on the 4th day of hospital admission. He was followed up in clinic for two consecutive weeks. His muscle enzymes normalized and he remained stable during the two week follow-up period.

Discussion

Dengue myositis is a rare entity in children. It is a dynamic disease beginning with a nonspecific, acute febrile illness, progressing to severe disease during fever defervesce and ending in a convalescent phase.[8] A case series of seven patients (two

paediatric) with varying clinical severity including two cases of severe fulminant myositis was reported from India. Three of them developed acute severe fulminant myositis that required mechanical ventilator support.[5] Some of them developed exceptionally elevated CPK level, as our patient, who developed high CPK level with difficulty in walking and unable to bear weight. A brief review of the reporrted cases of dengue myositis is shown in Table 1.

High CPK level is one of the diagnostic hallmark of acute myositis.[10] There are certain other laboratory tests available, including aldolase B. In a recent study from Egypt, 109 patients out of 110 with dengue fever had elevated serum creatinine phosphokinase levels. Myalgia was found in 64 (63.4%) patients, with severe levels in 12 patients. Mild proximal muscle weakness, mainly in the lower limbs, was found in 3 patients. Three patients with lower limb weakness recovered completely. The creatinine phosphokinase ranged from 200 to 8000 U/L.[5]

In addition to dengue virus infection, mild to moderate muscle involvement can occur with several acute viral infections and this was kept in mind before the diagnosis of dengue viral myositis was made. Influenza virus-associated myositis is one such possibility. Myositis caused by influenza virus is self-limited, usually resolving within few days. It is often seen during influenza epidemics.[10] The other possible causes like enteric fever and malaria were also excluded by documenting negative blood culture and MP ICT. Though non availability of dengue PCR at our hospital is a limitation but a temporal association of acute myositis with dengue fever suggested dengue virus as a cause of muscle involvement. Acute dengue myositis although a benign illness may result in respiratory muscle paralysis apart from trunk and lower limbs weakness and the patient may require ventilator support.[4]

Incidence of dengue fever has increased globally. Currently there are no vaccines available to prevent dengue. A number of candidates vaccines are in clinical trials to evaluate immunogenicity, safety and efficacy. No chemoprophylaxis or antiviral medications are available to treat patients with dengue. However standard precautions are recommended with attention to the potential for blood borne transmission.

Conclusion

Dengue myositis is a rare entity in children. A high index of suspicion in dengue endemic areas is needed to diagnose and manage as per management guidelines.

Table 1: Features of Dengue myositis in children

Author (Year)	Age (Yr)/ Gender	Presentation	Investigations	Recovery
Ahmed R et al (2007)[9]	5/F	Fever, Difficulty in walking	Dengue IgM	Recovered
Piliwal et al (2010)[5]				
7 cases , 2 pediatric	5/M	Flu like illness, Quadriparesis, Neck trunk	CPK 509 IU/L	Recovered
	3/M	Weakness, Flu Like Illness, Lower limb proximal weakness	CPK 874IU/L	Recovered
Sungle SA (2010)[7]	16/F	Fever, Severe malaise, Myalgia	Dengue IgM, CPK 310 IU/L SGOT 120 IU/L	Recovered

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How to Control Rabies in Pakistan: Collaborative Planning and Seminar- with RIA, IDSP, EMRO, UVAS, CVA

A meeting was held on March 22nd 2013at the University of Animal Sciences (UVAS), Lahore just ahead of the IDSP Conference, to discuss Control of Animal Rabies in Pakistan. Those present at the meeting were Dr. Naseem Salahuddin, President Pakistan Chapter of Rabies in Asia and Member WHO Expert Panel on Rabies, Dr. Quaid Saeed (EMRO), Prof Abdul Rahman, President Commonwealth Veterinary Association (CVA) from Bangalore, India, Prof M.K. Sudarshan, Principal Kempegowda Medical College, Bangalore, India, and President Rabies in Asia; Prof. Nasim Ahmed, Dean Faculty of Veterinary Sciences, Prof Masood Rabbani, Dr. Zafar Qureshi and Dr Aneela Durrani of UVAS.

All participants agreed that Animal Rabies Control is pivotal to Human Rabies Control, and that UVAS could play the central role. A task force would be set up from the faculty of UVAS. Prof Abdul Rahman, who has immense experience in animal rabies control, would facilitate its establishment. Prof M.K. Sudarshan cautioned that legal issues regarding animal culling would not be well received by international donors.

On March 23, a seminar on Human Rabies Control was held as part of the Tenth Annual ID Conference at Shaukat Khanum Memorial Hospital. Dr. Naseem Salahuddin set the stage with "Rabies: A Neglected and Fatal Disease". She lamented that health care givers in most urban hospitals, and particularly in rural health centers, manage animal bite exposures inadequately. Poor knowledge, application and practices, as well as non-availability of cell culture vaccines and rabies immunoglobulin (RIG) contribute to this appalling state. The obsolete sheep brain vaccines (sample vaccine) is still being produced and distributed to rural health centers where exposed persons are more likely to get bitten by stray animals. In Pakistan most rabies deaths occur in rural areas.

Prof Abdul Rahman stated that 50% of infections in humans originate in animals. He gave a wide-ranging lecture on zoonosis, and shared his experiences in the international field. The incidence of human rabies in India is 20,000 per year. He emphasized animal rabies prevention should be done in a humane manner; the most effective method of reducing animal rabies is by mass vaccination of stray and pet animals. Prof Rahman is a strong advocate for the "one health approach"- a concept that promotes partnership among multiple disciplines including human and veterinary medicine.

Prof M.K. Sudarshan spoke about the state of rabies in India. The population of India is 1.2 billion, most of who live in poverty, where infectious diseases are rampant. Despite set backs, rabies related activities have accelerated: India is the world's largest producer and exporter of quality antirabies vaccines and rabies immunoglobulin (RIG). India officially discontinued nerve tissue vaccine nearly a decade back and is approved for the practice of low dose intradermal vaccine for postexposure prophylaxis (PEP). The Association for Prevention of Rabies in India (APCRI) and Rabies in Asia (RIA) organize active programs for rabies awareness among school children and use innovative ideas at annual World Rabies Day each year. Dr Sudarshan presented IDSP with two sets of DVDs, journals and Indian literature on rabies.

Dr Quaid Saeed of EMRO held forth a proposal for Road Map for Rabies Prevention in Pakistan. He expounded on his plan for setting up ten PEP centers in each province of Pakistan where health care givers would be trained in PEP management with cell culture vaccine.

Dr Wolfgang Bender, Head of Medical Affairs International Novartis Vaccines spoke about the history of rabies vaccines and the modern method of PEP, with special reference to countries with cost constraints. He emphasized that infiltration of RIG into deep animal bite wounds was essential to save an individual from rabies, but was frequently missed.

Curbside Consultation – Fever Phobia

An attempt at Humor in Infectious Diseases

Fever phobia is as rampant these days, as in the biblical times, besides of course many other dreaded things in life. Both healers and health seekers (children and parents) react to any fever as if it is the end of the world. Aggressive and potentially dangerous intervention and therapy of fever is also common.

"*Fever phobia and inappropriate treatment for febrile children is present among caregivers of patients seen in a pediatric emergency department (PED). Level of education may be a factor in fever knowledge and practices. Overly zealous, potentially harmful home practices and unnecessary PED visits for the assessment and treatment of fever in children is widespread among caregivers surveyed in the PED.*"[1]

"Mild fever is misclassified by many as high, and they actively reduce mild fever with incorrect doses of antipyretics. Although some parents acknowledge the benefits of mild fever, concerns about brain damage, febrile convulsions and death from mild to moderate fever persist irrespective of parental education or socio-economic status.……."[2]

As physicians it has become knee jerk reaction to do things most of the times that do not make sense. All sorts of diagnostic tests and antibiotics or combos are tried without even a second thought what one is dealing with and how the poor patient may suffer in the process! But alas! Today's healers are now a lazy lot of non-thinkers! When confronted they mostly will give an excuse: "It is an individual preference!" "This plan works and I do not have to worry about missing things in fever" Most fevers in children will end with a prescription for an antibiotic. Patients fever phobia will persist but we as physician augment this to the hilt!

We as physicians must be cognizant of the fact that fever can mean a serious underlying disorder. However acute fevers in normal healthy child with no major findings (except maybe focal cause such as URI, OM) is reassuring and mostly needs supportive care only! Although a child who has some underlying problem with such a scenario may also have a self-limiting illness (mostly) but approach may be slightly different. I cannot ignore that. But here I will dwell on true stories that will make my point clear as how fever phobia is "eating in our lives" and our pockets! (I have stopped telling lies after my dear mother made me promise not to tell lies when I was 5 yrs. old!)

Blog 2: Recurrent fevers!

1. Recurrent URI: Cause of concern?

A 2 years old boy with fever. Mother is concerned that her son had repeated fevers and coughs at least once a month. She shows a bundle of prescriptions with TNTC (too numerous to count) antibiotics of all sorts. A careful history from mother reveals that these illnesses are brief with rhinorrhea, cough and fevers. Every time the child has fever she runs to her local physician who is happy to dole out his favorite prescription of antibiotics. The mother is all hyped up in thinking that by using these antibiotics something catastrophic has been averted. She now demands that last person to cure these fevers! (Someone recommended me: Grrhh). So I spent the next 20 minutes reassuring that her healthy thriving son has recurrent viral URIs like any child is destined to have! He or she will need careful monitoring and limited evaluation if required. Those who are sick/toxic, recurrent or prolong illness or are immune compromised will need more extensive workup. The curbside question is what to do about these recurring URIs in such a child? The curbside answer is that these viral URIs (6-10/year) is normal. Also answer lies in the details of the illnesses that one has to go through rather than doing all the fancy diagnostic to unravel something sinister that this child may have!

2. Malaria: Know your species to treat

A 10 yr. old referred for recurrent fevers. The history otherwise is unremarkable. Have had many diagnostic workup and many antibiotic courses. Going through the old labs done outside I come across a positive blood smear for plasmodium vivax (being treated as P falciparum!) Used the combination Artemether+lumefantrine three times with good response but did not use primaquine (or even thought about it despite three visits!). Getting primaquine is not easy sometimes but that is what is needed and works. Curbside side question: Doc why is this malaria not cured? The curbside answer simply put: Use the correct antimalarial and for radical cure of P vivax it is imperative to cure acute infection and to clear the hypnozoites to prevent relapses. Thus the best combination for vivax is chloroquine + primaqune. Vivax is still sensitive to chloroquine through out the world except in Indonesia and has lesser relapse rate than with artemether + lumifantrine combo.[3]

3. Recurrent fever since many years

A 7-year-old boy came with fever since last 4 years almost every month! The parents said I was their last hope, as he had seen many many doctors, peers, hakeems and what not! As they relate his history I examine him and found him to be healthy and well nourished. Had been subjected to many diagnostic tests including multiple smears for malaria, serology for typhoid and TB (bad tests!), numerous x-rays, urine analysis, routine tests, immunoglobulin levels, etc. He has taken tons of antibiotics, antimalarials and a TB course; the record they kept was meticulous. I knew the diagnosis was in history and so I ask the parents to repeat what happens: He starts with abrupt onset of documented high fever, sore throat, anorexia, some neck swelling without any other major GI or respiratory symptoms. Lasts 3-4 days and resolves mostly when he takes

medicine including and antibiotic! (in my mind I calculate at least 48 courses at least). These episodes recur after every 3-4 weeks exactly (mother says fever occurs every 25 days!). In between he remains well and has remained healthy with no hospitalization. So the last curbside side question for today is: What is the diagnosis in a well thriving child with repeated febrile episodes associated with sore throat, lymphadenopathy, lasts 3-4 days and recurs with almost precision every 3-4 weeks for many years? The curbside answer is that described in 1987 it is a well entity now in literature and coined as PFAPA (Periodic Fever, Aphthous stomatitis, Pharyngitis, and cervical Adenitis):[4-6]

"…….periodic episodes of high fever (>39°C) lasting 3 to 6 days and recurring every 3 to 8 weeks, accompanied by aphthous stomatitis, pharyngitis, and cervical adenitis in children."

Diagnosis is clinical as no test is available but must be distinguished from other periodic fevers (juvenile rheumatoid arthritis, cyclic neutropenia, Behçet disease, tick-borne relapsing fever and other hereditary periodic fever syndromes such as familial Mediterranean fever and hyperimmunoglobulinemia D syndrome). These can be distinguished on basis of accompanying pattern of fever, periodicity, accompanying symptoms or signs, specific lab tests and cultures. Therapy for PFAPA is supportive but single dose oral steroids will result in immediate defervescence. Some have advocated other drugs and even tonsillectomy.[5,6] It resolves once the child gets older.

These are few examples to point that to a specific cause of recurring fevers. Of course you need to carefully look for other causes such as specific infectious, malignant, and autoimmune disorders. Lastly I must admit that being in the business of infectious disease it may sound easy for me but I urge everyone out there to think back, read and think again to make sense of some of these patients. Do not fear all fevers, work up or treat unnecessarily. Specific non-antibiotic related therapy exists and must be thought about! Good luck to you!

Suggested readings

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Tragedy of Our Times

As I saw my next patient in front of me one Tuesday morning I knew this would be a "good" one. New patient, for second opinion, looks sick, loads of papers, early morning and I feel excited and relaxed today to such a case that may be a challenge and bring some relief for the patient! Maybe! Asmara was a 10 years old girl from a village of Punjab. She looked frail and had an anxious look in her eyes avoiding contact when I talked to her.

Her mother said that although previously healthy she has been sick since the last 20 months with fever off and on, weight loss and progressive back swelling. She had visited many doctors since and was also admitted once. All kinds of tests were done and diagnosed with tuberculosis (TB) in July 2007. She was given treatment for TB for 8 months at the local TB center with first line four-drug regimen.

After mild relief for few months she again started having low-grade fever, poor weight gain, anorexia, back pain and swelling that had persisted. She was again started on standard four- TB drugs for another 4 months. However with no improvement she was started on 2nd line TB-drugs, which she had been taking since last 10 months. She now came for a second opinion and with continuing symptoms and new onset facial rash and a limp.

The family denied any TB exposure. She had been immunized in early childhood and had 4 healthy siblings. Her father works in a local factory. She was in class three when she left school because of her illness.

The physical examination showed a limping, stunted girl, pinkish papular facial rash, large gibbus swelling but no lymphadenopathy or hepatosplenomegaly. I meticulously went through the child's previous records. The only significant of note findings were anemia, high ESR and a spine x-ray showing kyphoscoliosis and destroyed vertebrae. Her treatment included isoniazid, pyrazinamide, rifampin and ethambutol as initial therapy. Current drugs included ethambutol, ethionamide, ofloxacin and pyrazinamide with amikacin given for initial three months.

Diagnosis was a no brainier as in summary a young girl who has been sick since 2 years with spinal TB and has failed first and second line therapy despite compliance.

So here it sets in motion my thoughts to plan her future management. I face the mother and explain my rationale of admitting the child for confirming the diagnosis of drug resistant TB and how tissue may be needed for that purpose. They agree and I order few basic admission labs to begin with. I had planned a spinal MRI and US of hip, abdomen and back. It revealed a large left sided paraspinal fluid collection with evidence of extension along multiple lumbar vertebra.

After discussion with the interventional radiologist the fluid was aspirated under CT guidance for gram stain, culture and AFB smear and AFB culture. After admission I made a verbal contract with parents that they will abide by our treatment plan that includes long hospitalization, regular labs and expensive medications. They agreed given the long suffering they and the child had endured so far. We started with a newer regimen ensuring that we have "plenty of drugs", include all classes and are available. Our drugs were PZA, ethionamide, ethambutol and levofloxacin for 18 months and parenteral amikacin for first 9 months. All stains and cultures eventually turned to be negative to my utter dismay of course!

We kept her hospitalized for first 2 months. While in hospital she started to gain weight and her fever settled after about 20 days. She became a darling of the ward with small smiles whenever I visited her and looked forward to my daily visits. She initially showed her reluctance to stay in hospital but I gave her small "pep" talks to keep her going. So after 2 months when I was sure that she has shown enough signs of improvement I discharged her on home therapy with once daily amikacin injections and the other four drugs. She followed after every 2-3 weeks with weight check, physical and monitoring of her renal function. She gained 3 kilogram in first 2 months and then another 2 over next 12 months. In the clinic I found her more and more healthy but still quite and shy as compared to other kids of her age.

At my last visit at 16 months there was persistent mild limp with gibbus swelling that had improved a lot as well. I told the family that hopefully we could stop her medications if her follow-up spinal MRI shows resolution of the spinal abscess. However Asmara has not returned since last more than two years.

So here is a story of a poor family with a child afflicted with probable drug resistant TB that may be due to poor compliance, therapy that could have been better at first suspicion and the complexity of keeping a child in hospital for a long time and the costs that are beyond an average Pakistani. The urgent need to do invasive diagnostic procedures, physician's despair when TB cultures turn out negative despite your best efforts, availability and choice of second line drugs for TB and losing a patient to follow-up when you know you are just round the corner to win a big race makes it a frustrating experience. But there is a silver lining in the story of family that went along with advice of a relenting physician as long as they could and positive response to therapy that makes us go everyday to help such Asmara's in future!

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Vitamin D Status in Children: From Deficiency to Toxicity

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Dear Sir/Ma'am,

Vitamin D is a hormone that regulates calcium metabolism. Children less than five years require 400 to 600 IU of vitamin D per day. The deficiency of vitamin D is a problem throughout world especially in Pakistan where the prevalence of vitamin D deficiency was 41.1% according to National Nutrition Survey of Pakistan in 2011. In Pakistan intramuscular injections of vitamin D3 are being given to manage vitamin D deficient status, as per WHO recommnedation. Injection vitamin D3 is available in 600000 IU (15 mg).

Vitamin D toxicity has been attributed to a variety of factors including over-the-counter vitamin D supplements and dosing errors. It is very difficult to recognize signs of vitamin D toxicity because clinical signs are nonspecific and children may be brought to hospitals with severe dehydration, fatigue, muscle weakness, constipation and metastatic calcification It is imperative that careful history about over –the- counter supplementation, doses and frequency should be taken from parents in order to diagnosis and initiate treatment.In case seriesfrom America and India in 2012 and 2013 respectively,it was reported that children treated for vitamin D deficiency showed toxicity. The treatment of vitamin D toxicity includes restriction of vitamin D and calcium intake.

We raise the consideration that with heightened awareness of vitamin D deficiency and increased prescription of pharmacologic vitamin D to children less than five years of age, an increased risk of toxicity is also emerging. Recommendations for vitamin D therapy require reexamination for safety in this age group. Also efforts should be made to educate doctors, not to irrationally prescribe vitamin D.

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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.

Criteria for publication

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.

Submission of the Manuscript

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.

Manuscript Categories

I. Original Articles

Articles should report original work in the fields of microbiology, infectious disease or public health.The word limit for original articles is 2000.

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.

Materials and Methods

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.

Discussion

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**.

II. Review Articles
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.

III. Brief Reports
Short clinical and laboratory observations are included as Brief Reports. The text should contain no more than 1000 words, two illustrations or tables and up to 10 references.

IV. Case Reports
Instructive cases with a message are published as case reports. Routine syndromes or rare entities without unusual or new features are invariably rejected. The text should contain no more than 1000 words, two illustrations or tables and up to 10 references. The authorship should not exceed 3-4 persons.

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.

VI. News and Views
Informative, breaking news updates in infectious diseases from around the world (approx. 200 words).

VII. Notices
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.

References
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.

Tables and Figures
Data reported either in a table or in a figure should be illustrative of information reported in the text, but should not be redundant with the text. Each table must be presented on a separate sheet of paper and numbered in order of appearance in the text. Table should be numbered consecutively in Arabic numerals. Tables andFigures legends should be self-explanatory with adequate headings and footnotes.Results which can be described as short statements within the text should not be presented as figures or tables.

Illustrations
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:

- Black& white line illustration (e.g. graphs): 600 dpi
- Black & white halftone illustrations (e.g. photographs): 300 dpi
- Color illustrations: 400 dpi (note that color images should be split CMYK not RGB)

Plagiarism
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.

Authorship criteria
Those who have contributed sufficiently to the conceptualization, design, collection and analysis of data and writing of the manuscript should be granted authorship. Ideally all authors should be from the same department except for studies that are multi center or multispecialty.

Instructions updated - April 2012.
Editor IDJ

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MEDICAL MICROBIOLOGY & INFECTIOUS DISEASES SOCIETY OF PAKISTAN

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