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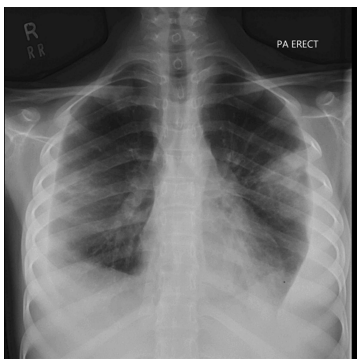

14 years old girl with bilateral pleural effusion and consolidation. Her Sputum Gene xpert is positive for tuberculosis with no Rif reisistance.

Courtesy: Dr Ali Faisal Saleem, Aga Khan University, Karachi.

Pediatric sepsis: Efforts for improvement in outcome

Sepsis is a major burden on health care. In developed countries case fatality rate is around 20 to 30 %.[1] Overall almost 4,500 death per year is reported in United States alone.[2] For developing world, although exact figure is lacking, sepsis is the leading cause of death in children.[3]

Defining the true incidence of sepsis is difficult because most uncomplicated cases do not come to the hospital. More over many children get admitted with other diagnosis associated with underlying infection, in which the criteria for sepsis are not recorded.

Usual presentation for sepsis is fever, tachypnea, tachycardia, altered mental status and signs of shock. Difficulty is that clinical signs and symptoms consistent with established criteria usually occur late in the course of illness. Early manifestations are often non-specific and can occur in many other disease processes. Children may not be able to tolerate the cardio-respiratory compromise associated with sepsis and delay in treatment can rapidly lead to multiorgan dysfunction syndrome which carries a bleak prognosis, hence, vigilance and high index of suspicion is advised.

The important therapeutic principles for pediatric sepsis management include rapid recognition of sepsis, early source control, antibiotic administration, reversal of shock, treatment of associated metabolic derangement and supportive care including nutrition and glycemic control.

Antibiotics are the cornerstone of management and should be started within the first hour of recognition of sepsis after obtaining appropriate cultures.[4] If obtaining a specific culture is delayed, antibiotics should not be withheld. Ideally IDSA guidelines should be followed. Both antibiotics overuse and misuse should be avoided. Once antibiotics are started patient should be thoughtfully evaluated on a daily basis, because there is increasing trend of antibiotic resistant pathogen and broad spectrum antibiotic use is one of the important contributing factors for this fact.[5]

Establishment of antibiotic stewardship team along with the microbiologist, infection control nurse, infection disease consultant and clinical pharmacist are important for proper utilization of local antibiogram. Routine bacterial surveillance and study of their resistance patterns is essential for formation of antibiotic policy guidelines, and such study should be carried out in every hospital.

Another helpful modality is collection of regional multicentre epidemiological data for pediatric sepsis, as knowledge of our own specific infection pattern will aid in prevention of sepsis through vaccination, anticipatory guidelines and early recognition of causative organisms. Sepsis remains a significant problem in pediatrics ,especially in resource limited countries We know a lot about what needs to be done and how to do it. We need to do it, now

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ORIGINAL ARTICLE

Maternal Knowledge and Practices Regarding Prevention and Treatment of Common Cold in Children Under 6 Years of Age

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Abstract

Background
Acute respiratory tract infection is the most important human health problem and has high economic cost. Prevalence of acute respiratory infection in Pakistan is 16% out of which 10% is common cold. Parents frequently administer over-the-counter medications to their children for this illness with their attendant risks. We conducted this KAP survey to assess mother knowledge and practices related to management of common cold among children younger than six years of age.

Methods
A cross-sectional study, consisting of 301 mothers selected on non-probability convenience sampling basis, was conducted at Ziauddin hospital Karachi.

Results
Mean age of mothers was 31 years; 61% (n=184) had received at least primary education; 83% (n=250) were house wives and 61% (n=184) belonged to low income family. Eighty one percent (n=245) mothers had knowledge about home remedies regarding common colds. Thirty six percent (n=108) of mothers were counseled by health care providers regarding safe home remedies. Only 20% (n=60) mother had knowledge about hand washing as a means of prevention for spread of common cold while 36% (n=108) mothers knew that good ventilation would prevent the spread of common cold. Home remedies were practiced by 67% (n=203) of the participants while 37% (n=113) mothers practiced self-medication.

Conclusion
Home based therapies for common colds are commonly used in our country. Many are complementary to other treatment modalities. Mothers had poor knowledge regarding spread of common cold.

Key words
child, common cold, respiratory tract infection

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Introduction
Respiratory tract infections have a high incidence and lead to high economic costs. Acute Upper Respiratory Tract Infection (URTI) is the second most common diagnosis in physician's offices[1] and the most common discharge diagnosis at emergency department.[2]

A survey conducted in Pakistan[3] in 2011 showed prevalence of ARI in Pakistan is 16%, out of which 10% is common cold and also revealed that ARI (cough/flu, pneumonia and severe pneumonia) was more prevalent in urban than in rural areas across Pakistan.

Colds is a self-limiting viral infection which usually presents with runny nose, cough, and congestion. The mean duration of URTI in young children is 7-9 days. On an average a child experiences 6-8 spells of Acute Respiratory Infection (ARI) per year, which is similar in both developing and developed countries.[4]

To treat cold, parents frequently administer over-the-counter (OTC) medications to their children that may have risks,[5,6] lack of proven,[7,8] efficacy with no endorsement by professional organizations such as the American Academy of Pediatrics[9] and the Food and Drug Administration (FDA).[10] Supportive care and safe home remedies remain the only recommended treatment for common cold.[4]

A study was conducted in India[11] on this issue; however in our country such data is lacking. Health education programmes are only effective if based on KAP. Therefore this study was conducted to help develop a better understanding and provide baseline data on the existing practices of treatment of common cold in mothers of young children.

Material and Methods
We conducted this cross-sectional KAP study during August-October 2013 at OPD of Kemari campus, Ziauddin Hospital, Karachi. Mothers of children under six years of age were enrolled by using non-probability convenience sampling. Mothers with at least one child below the age of six years, coming to the hospital for their own illness or their childâ€™s illness or an accompanying women with a child <6 year old,

were interviewed. However foreigners and mother having psychiatric disorder were excluded from the study. The sample size was calculated to be 301 with a CI of 95%, absolute precision of 0.05 and prevalence of knowledge and practice of mothers to be 23%. Informed consent was taken from participants. Their anonymity, autonomy and beneficence were given top priority. Their confidentiality was strictly maintained and they had complete liberty not to answer any question or quit at any time during the study. They were informed that withdrawal from study would not affect their due care at the above mentioned hospital. Questionnaire was developed in easy and understandable language. It was administered by researchers. Problematic questions and any queries were explained to the mother.

Data were entered into SPSS-20 and were password protected. Main Independent variables included age, education, occupation, and monthly income while the main dependent ones were knowledge and practices on common cold, type of home remedy and type of self-medication. Mean and SD were calculated for continuous variables like age. Frequencies were calculated for categorical variables like socioeconomic status, educational status, use of antibiotic in children and use of honey in infants in common cold. Multiple response analysis was done on variables like knowledge and practices of mothers on common cold, type of home remedy and self-medication.

Results

More than half had received at least primary education. Majority were house wives and belonged to low income family (Table 1). Eighty one percent mothers had knowledge about home remedies regarding common colds. Forty four percent mothers considered home remedies to be more effective in common cold, while 34% considered OTC medicines and 15% considered antibiotics as an effective treatment modality.

Table 1. Demograpic features of mothers. n=301

Demograpic features of mothers	Number (%)
Age (years) (means±SD)	30.5 ± 5.84
Maternal Education, n (%)	
Non formal	116 (39)
Primary	94 (31)
Secondary	59 (20)
Higher secondary	17 (6)
Graduation	14 (5)
Maternal Occupation, n (%)	
Working Women	48 (16)
House wife	250 (83)
Monthly Income, Rs/month	
<15,000	181 (61)
15,001-30,000	92 (31)
>30,000	25 (8)

For source of information "Her mother" was the most frequent (38%) while "Husband" was the least frequent source (5%). Only 36% of mothers were counseled by health care providers (HCPs) regarding safe home remedies "Keeping child clean" was the most preferred choice regarding personal hygiene (50%) while for environmental hygiene it was "Keeping house clean" (80%). Only 20% mother had knowledge about hand washing as a means of prevention for spread of common cold while 36% mothers knew that good ventilation would prevent the spread of common cold.

Home remedies were practiced by 67% of the participants while 21% always visit to doctor for treatment of common cold (Table 2). Honey and Joshanda were more popular home remedies tried by the mothers for common cold (Table 3). In self-medication OTC medicines were the most preferred choice (Table 4). Two hundred and fourteen (72%) mothers used honey in infants in common cold.

Discussion

In this study, mothers were chosen for the interview because they are the ones, who are more involved in their children and accompany them to the hospital.[12,13] In the present study, knowledge about home remedies for common cold was 81% which is contrary to S. Kaskade's study[11] which showed that

Table 2. Practice regarding treatment of common cold (n=301)

Multiple responses	Number (%)
Home remedies	203 (67)
Self-medication	113 (37)
Always visit doctor	63 (21)
Rest/sleep to child	30 (10)
None	2 (.07)

Table 3. Type of home remedy (n=203)

Multiple responses	Number (%)
Honey	142 (70)
Joshanda	126 (62)
Hot tea	116 (57)
Steam inhalation	65 (32)
Ginger tea	61 (30)
Vicks	43 (21)
Saline nasal dropes	39 (19)
Brand	15 (7)

Table 4. Type of self-medication (n=113)

Multiple responses	Number (%)
Ibuprofen/paracetamol	56 (50)
OTC/cough/cold syrup	96 (85)
Antibiotics	28 (25)
Homeopathy	8 (7)
Other	1 (.08)
None	1 (.08)

58%. Forty four percent of mothers considered home remedies as more effective in common cold, while 34% considered OTC, 15% antibiotics and 5% considered homeopathic drugs assisted in eradication of common cold. In a study conducted in Malaysia twenty eight percent of the parents believed their children needed antibiotics for upper respiratory tract infection (URTI).[14] As many as 44% of individuals surveyed believed that antibiotics assisted in eradicating colds while 63% believed that OTC medications were efficacious in relieving cold symptoms.[15]

Efforts to find the source of knowledge for home remedies showed that "Her mother" (38%) and her "Mother-in-law" (27%) were the main sources of information. Contribution of mass media regarding knowledge on home remedies for common cold was only 16%, which should be reinforced. In a study conducted in Nepal,[16] it was shown that 33% of mothers get health related information through newspapers/TV and other media. Thus giving health information through public media. This may be useful in enhancing and promoting practices of mothers on common cold.

In the present study only 36% of mothers' were counseled by health care providers regarding safe home remedies and self-limited nature of common cold. This emphasizes the need of educational programs for HCPs to improve the case management of URTI. Kumar *et al*[17] in his study, showed poor knowledge in private practitioners regarding identifying and management of ARI. Health education is cost effective by reducing the use of unnecessary medications; knowledge of symptoms will also improve satisfaction of patients.

Knowledge about personal hygiene was blunted to keeping child clean or house clean in majority of mothers; with small number i.e. 20% knew about the importance of hand washing. This again emphasizes the need for health education of mothers as hand washing is the most effective way of prevention of spread of common cold.[18]

Home remedies were practiced by 67% of the participants. The result is similar to the studies carried out in Ethiopia,[19] where it was found 64.4% and that done in New Delhi[20] 52%. On the contrary, use of home remedies was much lower in studies conducted in Multan[21] and Lahore[22] in Pakistan where it was 40% and 23% respectively.

Although various modalities of home remedies were used by the mothers, either alone or in combination, to treat common cold in children in the present study honey and joshanda were the most popular home remedies tried by the mothers for common cold. In contrast, in a study conducted in New Delhi,[23] honey and ginger were the two most popular home remedies. This could be due to the cultural differences.

In the present study, self-medication was practiced by 37% of mothers. In contrast, in a study conducted in Multan[21] it was 58% and Khartoum State Sudan 74% where it was alarmingly high.[24] Lack of consultancy practices in mothers for rational drug use in children suffering from common colds might be the major reason for this increased frequency of self-medication.

OTC drugs have adverse effects and no proven efficacy in common cold, yet a large number of mothers (85%) do use them. Similar results were posted on the FDA website.[25] Contrary to this finding, in a study conducted by Kapoor *et al*,[20] it was shown that use of cough syrup in management of mild ARI was only 0.9%.

Previous studies conducted by different groups, exhibited different percentages of antibiotic use in URTI; Chan *et al*[14] (68%), Bhanwra *et al*[26] (46%), Nyquist *et al*[27] (44%) and Watson *et al*[28] (42%). However in present study use of antibiotics without prescription was low (25%), which is similar to the findings of Panagakou *et al*[29] and Farhad *et al*[30] where such use of antibiotics was 10% and 5% respectively.

Honey is a preferable treatment for cough and sleep difficulties associated with childhood URI above the age of 1 year. However it should not be given to children under 1 year[31] of age because of the risk of infantile Botulism.[32] In our study the use of honey in infants for treating common cold is alarmingly high (i.e.) 70%.

Conclusion

Mothers visiting the Kemari campus, Ziauddin hospital have substantial knowledge about home remedies in common cold but use of OTCs is also high. Their knowledge regarding spread and prevention of common colds were poor. We found insufficient counseling regarding safe home remedies by their health care providers. We found high use of honey in infants in study population.

Recommendations

- Education of caregivers and healthcare providers regarding natural history of common cold and its symptomatic treatment is needed, emphasizing safe home remedies options for symptomatic relief of the common cold in children.

- Role of media in raising health awareness about common cold may be more effective.

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Role of Medical Grade Honey in Curing Infectious Wounds: A non randomized trial

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Abstract

Objective
To determine the efficacy of two weeks continuous application of "medical grade honey"in clearing bacterial infection from infected wounds.

Material and Methods
This was a quasi experimental design conducted in the department of plastic surgery, SIMS/ Services Hospital Lahore during 1st July 2013 to 31 December 2013. Consecutive subjects with post-traumatic and post-surgical infected wounds admitted through plastic surgery out-patient department were screened for eligibility criteria and after informed consent, were asked for participation in the study. Only patients with positive culture of the wound swab were included. Honey dressing over the wound was applied on daily basis and culture of the wound swab was done after one week. Patients with positive culture after one week were continued on honey dressing for another one week and again the wound swab was sent for culture.

Result
Out of 150, twenty patients (13%) failed to have regular follow ups and were lost. 130 patients who completed follow up had mean age25.76±15.75 years and median age 22 years, 72 (55 %) were male and 58 (45 %) were female, had mono-microbial bacterial growth. 70(53.8 %) patients showed negative culture after one week of application of honey dressing, 43(33 %) patients become negative after two weeks of application of honey dressing and remaining 17(13 %) Patients did not show any response to honey dressing even after two weeks of the continuous dressing. The outcome was not associated with age, gender and type of growth.

Conclusion
The data presented here argue for a greater use of medicinal-grade honey in wound care, particularly where antibiotic resistance is an issue.

Keywords
Medical Grade Honey, Positive wound culture, Negative wound culture, infected wounds.

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Introduction
Honey has been used for its healing properties for centuries and has been used to dress wounds with favorable results. The emergence of antibiotic resistance and growing interest in "natural" or "complementary" therapies has led to an interest in honey dressings. Much of the research to date has been related to honey's antibacterial properties. However, the healing properties claimed for honey also include stimulating new tissue growth, moist wound healing, and fluid handling and promoting epithelialization, medical gradehoney does appear to be a valuable addition to the wound management formulary.[1]

A number of recent studies have shown that honey is an effective infection control agent in specific situations, particularly in wound care.[2] The current issues surrounding antibiotic resistance, and a growing body of evidence supporting the use of honey as a dressing for a wide range of wounds, has increased interest in its use in the clinical setting.[3-9] Honey provides a moist healing environment and can prevent (if used early enough) or rapidly clear existing wound infections. Several other properties make it an attractive wound dressing: honey debrides wounds and removes malodor; it reduces edema and exudates, prevents or minimizes hypertrophic scarring and hastens healing.[2]

Recent studies in human beings and other species have demonstrated the beneficial wound healing properties of honey, and medical grade honey dressings are available commercially in equine practice.[10] Certain honeys are now available in the form of various sterile products licensed for use in wound care in Australia, Canada, the European Union, Hong Kong, New Zealand and USA.Manuka (*Leptospermum scoparium*) honey from New Zealand has been found to have substantial levels of non-peroxide antibacterial activity associated with an unidentified phytochemical component, denoted as Unique Manuka Factor (UMF).[11]

Manuka honey from New Zealand is often considered to be a medicinal product of special value due to its high level of antimicrobial activity. Honey is high in sugar (~80%) and is relatively acidic (typical pH ranges from 3.2 to 4.5), making it unsuitable for most microbial growth.[12] Most honeys, when diluted with water, produce hydrogen peroxide, which is toxic to microbes.[13] in the stability of nectar flavonoids during honey elaboration and ripening in the hive were shown to be due to hydrolytic enzymatic activity and to oxidation probably related to hydrogen peroxide (glucose-oxidase) activity.[14]

In addition, some types of honeys possess an extra, florally derived antibacterial activity.[15] This activity is largely restricted to certain Leptospermum honeys from New Zealand and Australia (colloquially known as Manuka and jelly bush honey, respectively). Leptospermum honeys are particularly well suited to therapeutic use as they are very stable during storage and in the presence of body fluids, and they show no toxicity towards mammalian cells.[13] Two laboratories have recently reported that the activity of Leptospermum honeys correlates with the presence of methylglyoxal, an alpha-oxoaldehyde that reacts with macromolecules such as DNA, RNA and proteins.[17-16] Toxicity issues with methylglyoxal have been raised.[18]

Although there are a number of studies showing that honey is effective against common pathogens, it is not commonly used in infected wounds. Bacterial pathogens have developed resistance to antibiotic introduced into clinical practice.[19] Today, most bacteria that cause infections in hospitals are resistant to at least one antibiotic[20] and some are resistant to all commonly employed antibacterial drugs.[21] There is an urgent need for new antibiotics with novel modes of action, but few are currently under development.[22] Many large pharmaceutical companies have abandoned antimicrobial research as the cost of bringing new drugs to market is not being recovered, in part because micro-organisms so rapidly develop resistance to new products.[19] Staphylococcus aureus is one of the most commonly acquired pathogens in both the community and the hospital settings, and it is particularly problematic in skin and wound infections.[23] The emergence of methicillin resistant S. aureus (MRSA), and, more recently, vancomycin-resistant strains[24], has seriously compromised treatment options. Multi-drug resistance is, likewise, a major problem among the Enterobacteriaceae, which are the most frequent pathogens isolated by clinical microbiological laboratories.[25] Many hospitals are now also seeing the emergence of intrinsically resistant pathogens that were previously uncommon. For example, Acinetobacter sp. causes a multitude of infections in skin and soft tissue, with a high associated mortality and a particularly broad spectrum of resistance phenotypes.[26] In one hospital study, 89% of Acinetobacter sp. isolates were resistant to at least three classes of antibiotics, and 15% were resistant to the nine antibiotics tested.[27] Multi-drug resistances limits treatment options and results in the use of more expensive or more toxic drugs, with corresponding increase in patient morbidity and mortality.[28-30]

More information on the spectrum and mode of activity of honey is required for it to gain widespread acceptance as a therapeutic agent in conventional medicine. Therefore, we conducted this study to observe the role of medicinal grade honey in clearing wounds from bacterial infections.

Material and Methods

After approval from ethical review board of services institute of medical sciences, aquasi experimental study was conducted among patients with post-traumatic and post-surgical infected wounds admitted through outpatient department of the plastic surgery department of services hospital Lahore to determine the bactericidal and bacteriostatic effects of medical grade honey on infected wounds. The study was completed in six months starting 1st July 2013. Infected wound was defined as a wound with positive mono or poly bacterial culture showing growth of bacteria other than normal skin flora. Medical Grade Honey was applied at a dose of 5g/20 cm^2 once a day. Role of honey means the ability to clear bacterial infection from a wound. It was judged by wound swab cultures which may be positive or negative and mono-microbial or poly-microbial by standard laboratory technique for bacterial growth. Outcome was defined in terms of clearing the infection from the wound.

Using consecutive, non-probability sampling, 150 patients with infected wounds on limbs, abdomen and trunk due to trauma and surgery, up to 80 years of age and of either sex were offered to be enrolled in the study. Use of any systemic or topical antibiotic for at least 48 hours had been ascertained through history and medical record. Patients whose wounds showed negative wound cultures were excluded along with those who had history of malignancy, immunosuppressant drugs, diabetes as determined by history, medical record and laboratory report. History of allergy to any bee-product was elicited and those with allergy were excluded. Patients requiring oral or intravenous antibiotics for systematic sepsis determined by total leukocyte count > 12000/mm3 and neutrophilia were excluded too.

Patients were screened consecutively for the eligibility criteria and those found eligible were asked for giving the informed written consent. Eligible patients who provided written consent were included in this study. Each patient was interviewed and evaluated by the principle investigator regarding demographic information such as name, age, and gender and eligibility criterion. Data was recorded on a pretested and predesigned proforma.

A uniform protocol of dressing was designed and a single trained dresser (Operation Theater assistant) was allocated for once daily dressing ofthis included patient in day care surgery room.Each patient had to undergo cleaning of the wounds with 0.9% saline solution under aseptic conditions. None of the antiseptics were used. Medicinal grade honey was applied uniformly across the wound and covered with simple gauze. This procedure was repeated once daily in the morning on outdoor basis. Culture swab was taken again at end of first week before dressing. Those with positive culture after one week were continued for honey dressing during another week and again third culture was sent after second week of the study. The study was stopped after the second week of study. The variable under consideration was the wound cultures either becoming negative (i.e. clearance of the bacterial infection) or remaining positive (i.e. persistence of the bacterial infection).

Data collected was entered and analyzed using statistical package for social sciences (SPSS) version 21. The descriptive statistics

like age was presented in the form of mean ± standard deviation while sex, type of infection, outcome as frequency and percentage. Chi square test or Fischer exact test were used to determine the statistical difference between outcome and age groups/gender/type of infection. ANOVA was applied to determine statistical difference in mean age across three groups of bacterial clearance at week 1, 2 and no clearance. A value of p = 0.05 was considered as significant.

Result

A total 150 patients were included in the study. Out of 150 twenty (13%) patients failed to have regular follow up and were lost. Out of 130 patients, 72 (55%) were male and 58 (45%) were female. The patients were divided into four age groups. The first age groups patients aged 0-20 years (n=61) 47%, in second age group patients aged 21-40 years (n=49) 3769 %, in the third age group patients aged 41-60 years (n=16) 12.30 % and in the fourth age group patients aged 61-80 years (n=4) 3% (Table 1). Mean age came out 25.76±15.75 years while median age was 22 years. Cultures of most of the patients (88%) yielded poly-microbial infection.

70 (53.85 %) patients showed negative wound culture after one week of application of honey. In the remaining 60 patients, 43 (71.66 %) patients wounds, become negative after two weeks of application of honey and remaining 17/60 (28.33 %) wounds did not show any response and hence showed positive culture after two weeks of application of the honey dressing. When these results were cross-tabulated for common confounders and effect modifiers like age, age groups, gender and mono versus poly-microbial infection, the resultant difference was non-significant (Table 3). ANOVA test was used to determine the mean difference in age distribution among three groups with clearance of infection at week 1 and 2 and no clearance, F statistics were also non-significant (p value= 0.976)

Table I: Descriptive statistics of sampled population (n=130)

Characteristics	Groups	Count	Percentage
Age in Years	20 and below	61	46.92
	21-40	49	37.69
	41-60	16	12.30
	Above 60	4	3.07
	Mean ± SD	25.76±15.75	
Gender	Male	72	55.39
	Female	58	44.61
Microbial Growth	Mono-microbial	16	12.3
	Poly-microbial	114	87.7

Discussion

Honey has an unusually broad spectrum of antimicrobial activity, its significant antibacterial properties have been well documented;[31-32] however, few studies to date have used a readily available, registered, medical grade honey, making it difficult to apply these findings in clinical practice. Other studies have found similar results when using Leptospermum honey

Table 2: Frequency distribution of sampled population by Duration of Honey Dressing and outcome (n=130)

	Duration of Honey Dressing		
	0 day	1 week	2 week
N	130	130	60
Positive culture report	130(100%)	60(46.15%)	17(28.33%)
Negative culture report	0(0%)	70(53.85%)	43(71.66%)

Table 3: Cross tabulation of culture report/Outcome with confounders and effect modifiers

Characteristics	Groups/Outcome	Culture Report/Outcome			p Value
		Negative after 1st Week	Negative after 2nd Week	Positive after 2nd Week	
Age in Years	20 and below	33	20	8	0.62*
	21-40	28	15	6	
	41-60	6	8	2	
	Above 60	3	0	1	
Gender	Male	39	23	10	0.92**
	Female	31	20	7	
Microbial Growth	Mono-microbial	10	6	0	0.27*
	Poly-microbial	60	37	17	

*using Pearson chi square test ** using Fischer exact test

from New Zealand.[33-35] The emergence of extensive resistance to antibiotics has arguably occurred due to their overuse and misuse, and it is widely recognized that sub-lethal concentrations of antibiotics favor the development of a resistant phenotype.[36] Recent studies attribute the antibacterial activity of Medical Grade honey to methyl-glyoxal[16-17] Methyl-glyoxal detoxification pathways have been identified in bacterial cells, as these must deal with some level of endogenous methyl-glyoxal production.[37]

A combination of antimicrobial agents is known to slow or prevent resistance. While the low pH, high sugar content and hydrogen peroxide production in honey all play a part in it antibacterial activity. Honey is a complex substance with over 200 components.[38] Cross resistance often occurs via a generic structural modification, such as decreased cell wall permeability, decreased drug accumulation or increased drug efflux, and the cross protection conferred by biocides against other antimicrobials is of increasing concern.[39-40] Medical Grade (Leptospermum) honey has been shown to be effective against non-bacterial pathogens, such as the yeast Candida[41] and dermatophytes, which are filamentous fungi.[42]

Conclusion

The data presented here argue for a greater use of medicinal-grade honey in wound care, particularly where antibiotic resistance is an issue.

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ORIGINAL ARTICLE

Prevalence and Etiology of Urinary Tract Infections in Febrile Children

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Abstract

Introduction
Urinary tract infections (UTI) represent major burden on the community. UTI concomitantly presents with other infections. Antibiotics are usually started empirically irrespective of the sensitivity pattern.

Objective
To determine frequency of UTI in febrile children and compare the demographic and clinical feature of cases with or without UTI. We also report the pathogens causing UTI and their sensitivity pattern in our set up.

Material and Methods
This was a cross sectional study conducted at the Paediatric unit of Civil hospital Karachi from December 2006 to December 2007. Patients up to fourteen years of age of either gender with fever (101ºC) for less than two weeks were enrolled after written consent. History and physical examination was recorded in a proforma. Urine D/R and culture was sent within one hour of its collection. The data was entered and analyzed using SPSS version 10. Frequencies are reported for demographic variables and sensitivity pattern. the difference between demographic and clinical features of patients with and without localizing signs of UTI were compared using Chi square test, P-value of <0.05 was considered as significant.

Results
200 patients were enrolled in the study. Out of them 24 (12%) patients had UTI. *E. coli* was the most commonly isolated pathogen accounting for 12 (50%) cases. Most of the pathogens were sensitive to aminoglycosides, fluoroquinolones and fosfomycin.

Conclusion
Gram negative organisms are common pathogens of UTI and most are still sensitive to conventional antibiotics.

Key words
Febrile children, UTI, Pathogen

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Introduction

UTI is a commonly diagnosed bacterial infections in childhood with high frequency in first three years of life.[1-2] The prevalence of UTI is 3-5% in girls compare to 1-3% in boys.[3] In infants the incidence of UTI is more in males than females due to higher incidence of obstructive anomalies of the urinary tract in boys but after the first year of life, UTI is more frequent in girls than boys because of small urethra in females and increase chances of vaginal contamination with fecal flora[4] and beyond two years the male to female ratio is 1:10. UTI is more common in uncircumcised boys.[4] Fever is the commonest clinical feature of UTI in neonates, infants and young children whereas older children present with urinary symptoms (Dysuria, Polyuria, increase frequency, urgency).[5-6] Clinical features are vague and non specific in infants so the diagnosis of UTI is often missed and may lead to misdiagnosis followed by ill health and renal damage.[7]

UTI is an important cause of bacteremia due to gram negative organism e.g. *E. coli, Proteus, K. Pneumoniae, and Pseudomonas*.[8] Urinanalysis provides presumptive evidence of UTI, a quantitative urine culture before initiation of antibiotic therapy is considered gold standard for the diagnosis of UTI.[9-10]

Recognizing UTI is very important to prevent long term sequelae like renal scaring, hypertension and chronic renal failure. To ensure optimal treatment with antibiotics it is necessary to know the causative organisms and their sensitivity pattern so that appropriate antibiotics can be prescribed to prevent these long term sequelae. The aim of the study was to determine the frequency of UTI in febrile children along with isolation of pathogens in urine and their sensitivities and to compare the demographic differences between cases with or without UTI. The outcome of the study helps us in prioritizing the choice of antibiotic therapy in children with UTI so that long term renal damage can be prevented. The objectives of the study are to determine the proportion and etiology of urinary tract infections in febrile children with or without localizing symptoms.

Material and Methods

This cross sectional study was conducted in the Pediatric unit, Civil Hospital Karachi. It is a 1800 bedded public sector tertiary care hospital and provides health facilities to urban, periurban and rural areas of Sindh. Department of Paediatrics compromises of 200 beds and busy outpatient clinics with approximately 500 patients/day and emergency care 200-300 patients/day. It was

one year study from 21st Dec, 2006 to 20th Dec, 2007. Two hundred patients were included in the study through non-probability convenience sampling technique from both the outpatient and inpatient departments. Patients' up to fourteen years of age of either gender with complaints of fever of 101 degree centigrade for less than two weeks were included in the study. Patients who were very sick, chronically ill, received antibiotics within the last 48 hours, refused to give written consent or had structural anomalies of urinary tract were excluded from study.

The study physician explained the purpose, procedure, risks and benefits of the study to the parents and written consent was taken from them. An interview along with complete physical examination was performed and a urine sample for microscopy and culture and sensitivity was sent for all enrolled patients. Urine was collected following standard aseptic measures and sent to lab within an hour of its collection. The culture was considered positive if $>10^5$ single bacterial pathogen/ml were detected.

Data was entered and analyzed on SPSS version 10.0. Mean ± standard deviation is presented for age. Frequency and percentage are reported for categorical variables like sex, age group, circumcision, voiding habits, urinary tract infections and causative organisms. Chi square test was applied to compare the different variables. P-value of <0.05 was considered significant.

Results

Out of 200 patients, 118 (59%) were less than 5 years of age with female were predominance. All patients were febrile with mean temperature of 101.3±1.4 0F. Low grade and high grade fever was recorded in 70%and 30% patients respectively. Dysuria was most common localizing symptom accounting for 30 (15%) cases. Out of 200 patients 162 (81%) has normal voiding pattern, 126 (63%) were toilet trained and 74 (37%) had enuresis. Other symptoms like vomiting in 36 (18%) cases, diarrhea in 22 (11%) cases, reluctance to feed in 26 (13%) cases and fits in 10 (5%) cases were observed. Amongst 200 febrile children 24 (12%) had urinary tract infection (Table 1). None of the children had received used any prior antibiotics.

Among patients with positive urine culture 22 (91.6%) had a single pathogen, *E. coli* was most commonly isolated organism (Table 2). Sensitivities of the pathogens are given in Table 3. Comparison of features of children with or without UTI is summarized in Table 4.

Discussion

UTI is a significant problem in children. The factors responsible for the consequences of UTI are the non-specific clinical presentation in children and lack of appreciation of high morbidity and mortality associated with UTI and the spectrum of micro organisms associated with it. Significant bacteriuria has been documented in febrile infants and children even with alternative diagnosis of fever.[11, 12]

Table 1: Demographic and clinical features of the subjects enrolled with suspected UTI (n=200)

Demographic and clinical features	Frequency (%)
Age groups (Mean±SD)	4±2 years
5 years	118 (59)
More than 5 years	82(41)
Sex	
Male	96 (48)
Female	104(52)
Low grade fever	**140(70)**
101ºC	78(39)
102ºC	62(31)
High grade fever	**60(30)**
103ºC	38 (19)
104ºC	22(11)
Dysuria	30(15)
Polyuria	16 (8)
Flank pain	6 (3)
Ureteric colic	6 (3)
Poor stream	4(2)
Normal	62(81)
Holding urine	26(13)
Incomplete urination	10(5)
Toilet trained	126(63)
Bed wetting	74 (37)
Vomiting	36 (18)
Reluctant to feed	26 (13)
Diarrhea	22 (11)
Constipation	4 (2)
Fits	4 (2)

Table 2: Frequency of pathogens isolated from urine in patients with UTI (n=24)

Pathogen	Frequency	(%)
Single pathogen	*22*	*91.6*
E. coli	12	50
Klebsiella Pneumoniae	6	25
Proteus spp	2	8.3
Pseudomonas spp	2	8.3
Polymicrobials	*2*	*8.3*
E. coli and *staphylococcus aureus*	2	8.3

Table 3: Antibiotic sensitivity of the pathogens isolated in urine culture

Antibiotics	Organisms			
	E. coli	Klebsiella	Pseudomonas	Proteus
Augmentin	8	6	0	2
Ceclor	10	2	NT	2
Cefixime	4	2	0	2
Cipro/oflox	10	4	2	2
Nalidixic acid	2	4	0	2
Gentamicin	10	4	2	0
Amikacin	10	4	2	2
Fosphomycin	12	6	0	2

Table 4: Comparison of demographic and clinical features in cases with or without UTI

Features	UTI		P-value
	Yes	No	
Demographic features			
Age up to 5 years	12	106	0.23
Age more than 5 years	12	70	
Female	16	88	0.09
Male	8	88	
Toilet Trained	14	112	0.35
Bed wetting	10	64	0.38
Circumcision	4	60	0.0001
Clinical features			
Low grade fever (Temp =102ºF)	14	76	0.005
High grade fever (Temp =103ºF)	10	50	
Dysuria	6	24	0.12
Polyuria	4	12	0.10
Flank Pain	4	2	0.002
Ureteric colic	0	6	0.46
Poor Stream	0	4	0.59
Vomiting	8	28	0.04
Reluctant to feed	6	20	0.06
Diarrhea	8	14	0.001
Constipation	0	4	0.59
Holding Urine	6	20	0.06
Incomplete urination	4	6	0.021

In our study majority (59%) of children less than five years age and females were predominant. A study conducted in Yemen reported similar results.[13] A study in Lahore by Waqar *et al* reported UTI was common in patients between one to five years of age.[17]Among 200 febrile children 24 (12%) had UTI in this study. This finding is comparable to a study in India conducted in 2003, which concluded incidence of UTI in febrile children as 10%.[13]A quarter of the subjects had dysuria on presentation, a much higher frequency (68%) has been reported in other studies. Female preponderance has been documented worldwide in all settings.[12, 13] This is due to short urethra of females and perineal contamination. In our study febrile children with UTI had diarrhea and vomiting in 33.3% cases. Diarrhea was significantly associated with UTI; reported by many studied conducted in India.[14, 15]

In our study UTI was common in uncircumcised males, similar findings have been reported by other investigators. This finding is due to colonization of bacteria in foreskin that may cause contamination of urine.[12, 13]

E. coli was the most commonly isolated organism followed by *Klebsiella* pneumoniae. *E. coli* was common reported organism in the study at Yemen[16] and a study conducted in Ayub Teaching Hospital, Abbottabad reported similar results comparable to our study. However a few studies have indicated a lower percentage of *E. coli* and higher infection with *proteus* and *Klebsiella*.[17] *Proteus* was isolated from 2 male subjects. This has been explained on the ability of the *Proteus* species to swarm the long urethra of males and ascend to cause infection.[11]

E.coli was sensitive to co-amoxiclov (66.6%), quinolones (83.3) and resistant to nalidixic acid and co-trimoxazole (83.3%). Unlike our study, in Yemen, *E. coli* were sensitive to nalidixic acid (70%).

Conclusion

It is concluded from the study that urinary tract infection is common in febrile children predominantly involving females. Gram negative organisms are common pathogens of UTI and most are still sensitive to conventional antibiotics.

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Nosocomial Infections in Neonatal Intensive Care Unit at The Children's Hospital, Lahore

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Abstract

Objective
To determine the spectrum and sensitivity pattern of nosocomial pathogens in NICU of a tertiary care hospital, in Lahore.

Methodology
A cross-sectional study, conducted at the department of neonatology, Children's Hospital & Institute of Child Health (ICH), Lahore. Neonates admitted in neonatal intensive care unit, during the study period of 18 months showing clinical signs of infection after 72 hours of hospitalization and those with a pathogen on second blood culture that was different from the first culture were included in the study. Neonates whose stay in hospital was = 72 hours; who died or left against medical advice prior to the diagnosis of nosocomial infection; Blood culture with more than one isolate; and neonates with severe congenital malformations were excluded from the study. Blood culture samples were taken using standard technique and processed by conventional method in microbiology lab.

Results
In our study, a total of 140 neonates fulfilled the inclusion criteria and 30 % acquired nosocomial infection. Male gender (n=98; 70%) and low birth weight (n=90; 64%) babies had a significantly higher proportion as compared to appropriate for gestational age babies (n=47, 33.6%) (p=<0.001). *Klebsiella* spp. (n=41; 29·3%) were the most common nosocomial pathogens followed by CoNS (n=40; 28.6%). Gram negative microorganisms were sensitive to meropenem, tazobactem + piperacillin and amikacin. Gram positive microorganisms were sensitive to amikacin and vancomycin. Male gender (p=0.04), prematurity (p=0.01), LBW (p=0.001) and gram negative septicemia (p=0.001) were associated with higher mortality.

Conclusion
Gram negatives are predominant nosocomial pathogens in our neonatal intensive care unit. A combination of either meropenem with vancomycin or tazobactem+ piperacillin with amikacin can be used effectively asinitial empiric antibiotic therapy in our center.

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Key words
Nosocomial infection, sensitivity pattern, microorganisms.

Introduction
Neonatal deaths account for over a third of the global burden of child mortality.[1] Every year 2.9 million babies die within the first month of their lives, accounting for 44% of the under-five mortality.[2] Most of these deaths take place in the developing world, where mortality from sepsis may be as high as 85%.[3] With an estimated 298,000 neonatal deaths annually and a reported neonatal mortality rate of 55 per 1000 live births, Pakistan accounts for 7% of global neonatal deaths.[4,5,6]

Neonatal infection is an important cause of morbidity, prolonged hospital stay and mortality among infants, particularly those born preterm and of very low birth weight (VLBW).[7]

Nosocomial infection (NI) is defined as infection occurring at any site which was acquired during hospitalization and results from inoculation with an organism that was not present or incubating in the patient at the time of admission.[8] Most reports from the western world indicate that the incidence ranges from 6% to 25%.[9]

The most frequent NI are bloodstream infections associated with an intravascular catheter and pneumonia, especially ventilator-associated pneumonia followed by skin, soft tissues and urinary tract infections.[10, 11] Risk factors for NI among neonates include prematurity, LBW, invasive procedures, indwelling vascular catheters, endotracheal tubes, immunological immaturity, alterations in the skin and/or mucous membrane barriers, total parenteral nutrition, frequent use of broad-spectrum antibiotics and prolonged hospital stay.[12]

Different organisms cause NI; in the developed world gram positive organisms are associated with 70%, gram negative with 18%, and fungi with 12% of NIs.[13]

In developing countries, gram negative rods are major pathogens of NI in neonatal intensive care unit (NICU).[13] In Pakistan, gram negative bacilli; *Klebsiella pneumonia* and *Pseudomonas aeruginosa* (41.4%) predominate followed by *Escherichia coli* (11.2%), *Streptococcus pneumonia* (8.5%), *Enterobacter* (8.3%) and *Candida albicans* (1.9%).[14, 15]

WHO recommends developing institutional protocols based on their local sensitivity pattern. This study was designed to assess the spectrum of NI in our NICU and to determine the sensitivity pattern of NI so the best possible empiric antibacterial can be identified. There is less local data available hence this study also help us to identify the incidence of NI pathogens and mortality and morbidity associated risk factors in our NICU.

Study Methods

A prospective, observational, descriptive cross sectional study was carried out at the Neonatology Department of the Children's Hospital and the Institute of Child Health, Lahore-Pakistan from September 2012 to February 2014. A sample size of 140 cases was calculated using 95% confidence level, 5.5% margin of error taking an expected percentage of sensitivity of gram negative bacteria as 12% for cefotaxime, $N=z^2(p)(1-p)/d^2$, where z is a constant value, p is prevalence/frequency of disease, d is margin of error.[34] Informed written consent was taken from every parent or guardian.

All the neonates admitted in neonatal intensive care unit, who did not have clinical signs of sepsis defined as having 2 out of 4 criteria of SIRS plus suspected or proven infection,[16] (lethargy, hypotonia, feed intolerance, tachypnea/apnea, tachycardia/ bradycardia, hypothermia 95.9°F and hyperthermia 98.9°F after 72 hours of hospitalization and/or whose second blood culture grew a pathogen different from the first one were included in the study.

Demographic details (age, gender, birth weight, gestational age), clinical information including history of previous hospitalization, initial diagnosis at the time of admission and their outcome (alive or dead at the time of discharge) were noted on a pre-designed proforma. Blood culture samples were taken by recommended method, in a culture vial containing triptic soya broth (provided in routine from hospital microbiology lab) in a ratio of 1:9, and were sent immediately to the department of microbiology, where it was incubated at 37°C and checked by the conventional method.[37] Microbiological data including blood culture, micro-organisms and their sensitivity pattern was recorded from blood culture report.

Neonates whose stay in hospital was ≤ 72 hours, babies who expired or left against medical advice before the clinical diagnosis of infection, whose culture report showed growth of multiple organisms, babies with severe congenital malformations and babies whose parents did not give consent were excluded from the study. The collected data was analysed using SPSS version 17. Qualitative data like gender, history of previous hospitalization, initial diagnosis at the time of admission is presented as frequencies. Quantitative data like age, birth weight, gestational age, is presented in the form of Mean ± SD. Statistical test between dependent and independent variables was done using Chi-square test ($\alpha 2$). P-value ≤0.05 was considered significant.

Results

A total of 480 neonates were admitted in the NICU during the study period, 154 neonates were enrolled in this study out of which 140 met the exclusion criteria, leading to a nosocomial infection rate of 30% in our unit. Therefore, statistical analysis was carried out on 140 patients. The demographic details are given in the Table 1.

Only seventeen percent of the patients acquiring NI had previous hospitalization. Eleven different types of pathogenic bacteria were isolated from their blood cultures. The number of gram negative bacilli was significantly higher as compared to gram positive organisms (p-value=0.001)as shown in Fig.1.

Distributionof the pathogens is given in Table 2, *Klebsiella* had low sensitivity to ciprofloxacin (46.8%). *Pseudomonas* spp. & *Acinetobacter* showed sensitivity to meropenem and ceftazidime in all cases. Though *Pseudomonas* were also sensitive to amikacin (83%) and tazobactam + piperacillin (81%), *Acinetobacter* showed resistance to tazobactam + piperacillin

Table 1: Demographic data of study population

Characteristics			p-value
Gender	Male	98 (70%)	0·001
	Female	42 (30%)	
Gestational age	Preterm	74 (53%)	0.4028
	Term	66 (47%)	
Mean age at infection (±SD)		18±3.67 days	
Weight at admission (Kg)	LBW	90 (64%)	0.001
	AGA	47 (34%)	
	LGA	3 (2%)	

Table 2: Spectrum of nosocomial pathogenic bacteria

Gram Staining	Pathogenic bacteria	Total No (%)
Gram positive organisms (n = 46)	*Coagulase negative Staphylococcus*	40 (29%)
	Enterococcus	4 (3%)
	Staphylococcus aureus	3 (2%)
Gram negative organisms (n = 94)	*Klebsiella*	41 (30%)
	Pseudomonas spp.	24 (17%)
	Enterobacter	10 (7%)
	Acinetobacter	8 (6%)
	E. coli	4 (3%)
	Serratia marcescens	2 (1%)
	Pantoea	2 (1%)
	Citrobacter	2 (1%)

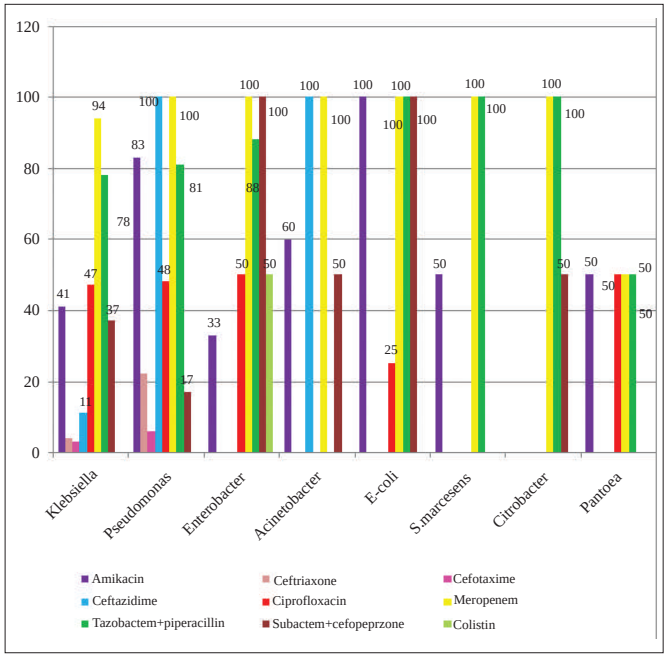

Fig: 1 Sensitivity pattern for common gram negative organisms

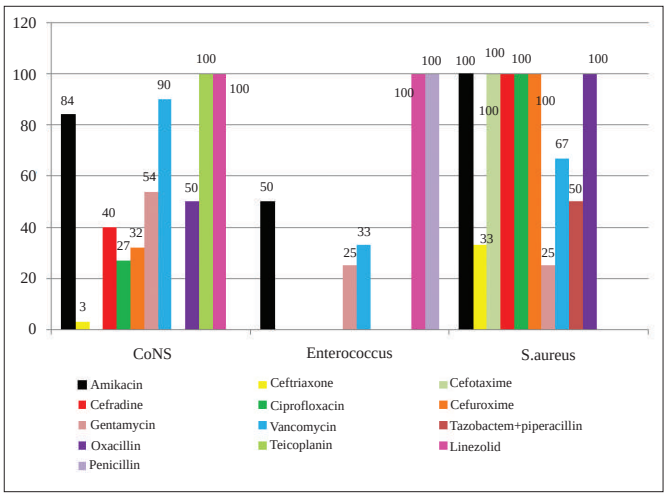

Fig:2 Sensitivity pattern of gram positive organism

in 67% cases. *Enterobacter* was sensitive to meropenem and sulbactam + cefoperazonein all cases,tazobactam + piperacillin (88%) and ciprofloxacin (50%). *E. coli* were showed resistance to ciprofloxacinin 75% of the cultures. Other gram negative rods like *S.marcescens* and *Citrobacter*showed a similar sensitivity pattern i.e. 100% sensitivity to meropenem andtazobactam + piperacillin. *Pantoea*were sensitive to amikacin (50%) and ciprofloxacin(50%).

The sensitivity pattern in gram positive organisms showed that CoNS were sensitive to linezolid and teicoplanin in all cases tovancomycin (90%) and toamikacin (84%) while resistant to ciprofloxacinin 73% and to 3rd generation cephalosporins in 70-90% cases. *Enterococci* were sensitive to penicillin and linezolid in all cases and resistant to vancomycinin 67 % (VRE) and to gentamycin in75% cultures.

Staph. Aureus were sensitive to ciprofloxacin, amikacin, cefradine, cefuroxime and oxacillin in all cases and tovancomycinin 67% cultures. Resistance to ceftriaxone was found in 67% cases.

The determination of outcome in relation to gestation revealed significantly higher mortality in preterm septic patients as compared to term babies p=<.001(OR0.33,CI 0.15-0.73) and in LBW in comparison to AGA babies p=<.001, OR0.23, CI0.08-0.61). Also, higher number of male babies expired as compared to females (p =0.11). The details are shown in the Table 3.

Discussion

NIs are a reason for enormous mortality and morbidity in terms of impaired cognition and poor neuro developmental outcome. They increase the cost of intensive care, prolong hospitalization by several weeks and are responsible for most of the deaths.[17] The rate of nosocomial infection in our study is 30%, different studies reported from the western world quote different figures ranging from as low as 6% to as high as 25.6%.[38,39] This variation is because of difference in practicing aseptic measures, lack of overcrowding in the developed world and improved staff to patient ratio which is in contrast to a resource limited country like us. Male gender, prematurity and low birth weight are considered as potential risk factors for neonatal infections.[18,19,20] These are similar to factors highlighted in a NI surveillance done by NeonIN in England.[7] Males are four times more affected than females and the possibility of a sex-linked genetic basis for host susceptibility is postulated.[19] Bonde and Wilcox showed that specific gender difference in South Asia is due to reduced care seeking for girls as compared to boys.[21] Similar results were presented by Imtiaz *et al* in their study done in Pakistan in 2005.[22] Low birth weight babies due to their prolonged hospitalization, late establishment of feeds and use of formula feeds are candidates for NIs. A study done in China by Horng and colleagues in 2004 revealed that LBW babies were potential candidates for NIs when compared with AGA babies.[23] The findings of our study are in conformity to above studies and show that significantly higher number of males and LBW babies acquired NIsin our NICU. However, prematurity was not a significant risk factor for NIs in our study, which may be due to the smaller sample size as compared to above studies. Therefore, a multicenter study with larger sample size is suggested.

Pathogens causing NIs and their antibiotic susceptibility patterns may differ between countries and centers and also they change over time. Different microbial culture studies of septic neonates conducted at various hospitals in Africa and Asia have shown *Klebsiella, Pseudomonas, Enterobacteriaceae, and E. coli* as

Table 3: Outcome of the study participants

Outcome		Discharge	Death	p-value	OR (CI)
Gestation	Preterm	35 (53%)	26 (39%)	0.005	0.33(0.15-0.73)
	Term	56 (76)	14 (19%)		
Birth weight	LBW	52 (58%)	43 (48%)	0.001	0.23(0.08-0.61)
	AGA	36 (77%)	7 (15%)		
Gender	Male	69 (70%)	25 (26%)	0.11	1.87(0.82-4.19)
	Female	22 (52%)	15 (36%)		
Gram staining	Gram +ve	34(37%)	7(18%)	0.02	2.79(1.14-7.49)
	Gram-ve	57(63%)	33(83%)		

OR: Odds Ratio, CI: Confidence Interval.

predominant gram negative organisms and *Staph. Aureus* as commonest gram positive organism.[24,25,26] In India the study done by Kamath, Mallaya and Shenoy in 2010, 72% of bacterial isolates were gram negative bacilli comprising *Klebsiella*, *Pseudomonas* spp., *E. coli*, *Enterobacter*, and *Acinetobacter*.[32] The most common pathogen implicated in neonatal nosocomial sepsis is reported to be CoNS in the developed countries.[27,28] The neonatal surveillance network in England as well as different workers in United States and Israel also reported CoNS to be the commonest nosocomial pathogen followed by *Enterobacteriaceae and Staph. aureus.*[7,29,30] In our settings we noticed predominance of *Klebsiella* in our unit followed by CoNS, *Pseudomonas* spp., *Enterobacter* and *Acinetobacter*. The predominance of gram negative rods in our study is similar to above studies done in developing countries of our region where gram negative rods are predominant.[32] This similarity in results is probably due to common problems like under staffing, poor hygiene and overcrowding in the resource limited countries.[27] On the other hand the results are in contrast to developed countries, where CoNS is the commonest pathogen implicated in NIs. This difference might be due to less number of invasive procedures and indwelling catheters used in developing countries in general. Although standard precautions were observed, high percentage of *CoNS* in our study may be related to possible contamination from skin during blood sampling and we did not use two culture technique as mentioned in other studies.[31]

In a study done in Pakistan in 2005 by Rabia Shams, gram negative rods were common as compared to gram positive organisms. And resistance to antibiotics like amoxicillin, ampicillin, ceftriaxone and cefotaxime was noticed. Quinolones and imipenem had less resistance and vancomycin was effective in 100% of staphylococcus group.[33] Another study conducted in Pakistan, in 2009 on the multidrug resistant microorganisms by Hannan *et al* showed that most effective drugs against gram negative rods were carbapenems and sensitivity pattern of gram positive cocci showed that more than 50% of CoNS and *Staph. Aureus* were resistant to penicillin, but vancomycin and linezolid were found to be effective against them which is comparable with gram positive sensitivity pattern in our study. Shrestha *et al* in India and Bas AY in Turkey, reported that gram negative bacilli were resistant to ampicillin, cefotaxime, gentamicin and amikacin and resistance to penicillin was 100% in gram positive bacteria.[34, 35]

The gram negative sensitivity pattern in our study shows similar results i.e. resistance to third generation cephalosporin. The resemblance is due to the use of third generation cephalosporin as first line. The sensitivity pattern reported in our study does not match with the results reported in a study from Israel where resistance to meropenem and amikacin was common.[29] A study done by Afif *et al* reported 100% of MRCoNS and Enterococci which were not sensitive to penicillin, CoNS in our study were resistant to oxacillin (MRCoNS) in half of the cases and enterococci were sensitive to penicillinin all cases. This change in antibiotic resistance pattern might be due to difference in local susceptibility data and different choice of empirical antibiotics in different regions.[36]

In a study done by Makhoul *et al*, mortality was more with gram negative sepsis (26.2%) as compared to gram positive (8.7%),[29] which is in accordance with our study results which showed significantly high mortality with gram negative sepsis ($p = 0.0017$).

One limitation of the study is that CoNS contamination in our study has not been ruled out by two culture techniques as in other studies.

Conclusion

Though, both gram negative and gram positive bacteria cause

NIs in NICUs, gram negative are predominant. A combination of meropenem with vancomycin or tazobactem+ piperacillin with amikacin can be used effectively as empirical antibiotic therapy.

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ORIGINAL ARTICLE

Modified Early Warning (MEW) Score: a low cost tool in predicting in-hospital outcomes of acutely ill medical patients.

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Abstract

Background
Modified Early Warning (MEW) scoring system is a simple bed-side tool which can be administered by a nurse. We conducted this study to look at the utility of a MEW scoreis a marker of in-hospital outcomes of acutely ill adult medical patients and can be effectively utilize for early detection of warning signs.

Methods
One hundred and twelve age-matched patients who were admitted the medical service from the emergency room of our hospital over a 6 month (August 2010 - February 2011) period were included. MEW scores of these patients were calculated once at the time of admission; the patients were followed till their discharge or death. Fischer's exact test was used to calculate statistical differences in outcome between the groups.

Results
Patients were categorized into 4 groups based on their MEW Scores: group 1:0-1, group 2: 2-3, group 3:4-5 and group 4: score of >5;26 patients died. There was no mortality in group 1. Mortality was significantly higher in group 4 (MEWS>5) when compared with group 2 (MEWS 2-3, p= <0.001; Fisher exact test) and with group 3 (MEWS 4-5, p=<0.001; Fisher exact test).

Conclusions
A single calculation of MEWS at the time of admission is a reliable predictor of in-hospital mortality in our patients. Acutely ill patients and those at imminent risk of deterioration are identified quickly on the basis of clinical criteria alone, making MEWS a cost-effective tool in triaging patients, prioritizing admission to high dependency areas and predicting outcomes. MEWS can be used at secondary and tertiary care centers in a resource-poor country to identify patients in need of urgent intensive care.

Key words
MEWS, prediction of in-hospital outcome, resource-poor settings

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Background
Most critically ill patients who are admitted to the intensive care unit (ICU) due to cardiopulmonary arrest or sepsis, show clear and detectable signs of deterioration in the hours preceding these events in up to 80 % of cases.[1-4] Prompt recognition of preventable causes of in-hospital mortality through complete and timely measurement and documentation of vital signs is key element of all patient-safety endeavors.[5] Clinical impression is of paramount importance but clinical judgment alone has a low sensitivity in gauging severity of critical illness.[6] To aid detection of deteriorating patients on the general wards, track and trigger (TT) systems have been developed. 'Early warning score' or 'track and trigger systems' allow timely recognition of patients with potential or established critical illness.[6] The risk of deterioration in heterogeneous groups of patients can be quantified on a numerical scale and through pre-defined escalation protocols, facilitate objective decision-making to ensure a suitable management response.[7-8] Appropriately derived and validated scores help to optimize individual patient management through improved risk stratification and prognostication.[9]

Track and trigger systems now have an established role in enhancing the detection of critical illness in hospitalized patients. They rely on the measurement of vital signs either in the form of single-parameter systems, based on the deviation of a single parameter from normality, or as multiple-parameter tools, which rely on the calculation of a score based on a multitude of parameters: aggregate-weighted track and trigger systems (AWTTSs).[10] Diagnostic performance of TTs has been shown to vary widely.[11,12] Although TTs, including the Modified Early Warning Score (MEWS), have been widely adopted throughout the world[13,14] the workings of these systems in clinical practice have not been fully elucidated. Predictive capabilities vary between different studies.[15]

MEWS has been derived from "Early Warning Scores" (EWS) which was primarily developed as a tool to trigger skilled, experienced senior help for at-risk patients. Regular use of EWS ensured earlier and more appropriate intensive care referrals and its evolution into MEWS has further increased its potential for identifying at-risk patients.[16]

Recently, implementation of MEWS has been reported as the

only intervention which was associated with an improvement of outcome[17,18] and failure of the afferent limb, i.e. failure of recognition of clinical deterioration was associated with increased mortality.[19]

MEWS is a simple bed-side tool which can be administered by a physician or a nurse. We conducted this study to look at the utility of MEW score in identifying in-hospital outcomes of acutely ill medical patients who presented to the Emergency Room at the Aga Khan University Hospital, a tertiary care referral center in Karachi, Pakistan.

Methods

One hundred and twelve adult patients who were admitted from the emergency room to the medical wards were recruited after obtaining informed consent through non-probability, purposive sampling. The study was conducted over a 6 month period (August 2010 till February 2011). Terminally ill, day-care patients, burns and trauma cases and those with surgical problems were excluded. MEW Score on admission was calculated once by a medicine resident and a third year medical student. Patients were followed till their discharge from the hospital or expiry.

Statistical analysis on outcome differences between the 4 groups was performed using Fischer's exact test using the Statistical Package for Social Sciences software (SPSS Version 17.0).

Ethical approval

The study was approved by the Ethical Review Committee of The Aga Khan University.

Results

Mean age of the patients was 52±2 years (range 15-90 years). There were 56 males and equal number of age-matched females. Out of 56 males, 45(80%) were discharged and 11(20%) died; 41(73%) female patients were discharged and 15 (26.78%) died.

Mean systolic B.P was 129±28 mm Hg (range 60 to 220) mmHg. Mean pulse was 106±24 (range 49-180). Respiratory rate was reliably recorded in all patients; mean respiratory rate was 25±7 (range 12-52). Mean temperature was 37±0.8ºC (range 36 -40). Seventy three patients (65%) were alert and awake, 21 (19%) were responsive to verbal commands, 17 (15%) responded to painful stimuli and one patient was unresponsive on admission.

Patients were categorized into 4 groups based on their MEWS cores: group 1:0-1, group 2: 2-3, group 3:4-5 and group 4: score of >5.

Table 1 shows different groups of patients according to MEWScores and their outcomes. There was no mortality in group 1 (MEWS of 0-1). Mortality was significantly higher in group 4 (MEWS>5) when compared with group 2 (MEWS 2-3, p=<0.001) and with group 3 (MEWS 4-5, p=<0.001) (Fig 1).

Discussion

Early warning systems are useful in rapid identification of patients who require close monitoring and aggressive treatment to ensure a good outcome. A major initiative is currently directed towards reducing mortality from treatable conditions like sepsis, early and aggressively to reduce mortality. One of the evidence-based strategies for identification and monitoring of admitted medical patients who may need close monitoring and higher level of care, is utilizing scoring systems which rely on a composite of clinical markers like Modified Early Warning (MEW) scoring system. A previous study form Pakistan reported a reliable association between in-hospital mortality and high scores on Early Warning Scoring System.[21] Simple scoring systems which do not require any laboratory parameters or additional staff training and skills provide an important means of identifying patients who are at high risk, especially in resource poor countries like Pakistan, where healthcare systems are poorly financed and emergency rooms are overcrowded. Use of a reliable and validated scoring system in the emergency room would help identify patients who are in urgent need of intensive care and appropriately triage those who are vitally stable and not in imminent danger of shock or cardiac arrest. Suboptimal quality of care prior to admission to high dependency unit can lead to mortalit.[22] The number of patients that can be

Table 1. Medical Early Warning Signs Score

MEW SCORE	3	2	1	0	1	2	3
Pulse		≤ 40	41 - 50	51 – 100	101-110	111-129	≥ 130
Respiratory Rate		< 9		9 -14	15-20	21-29	≥ 30
Temperature (°C)		< 35		35-38.4		= 38.5	
AVPU Score	Un-responsive	Reacting to pain	Reacting to voice	Alert	Reacting to voice	Reacting to pain	Un - responsive
Systolic BP (mm Hg)	< 70	71-80	81-100	101-199		≥ 200	

monitored and treated in intensive care units and high dependency units is restricted because of resource limitations world-wide and more so in Pakistan, making it crucial to select appropriate patients who would benefit most from critical care.[23]

Use of MEWS at a predetermined frequency has been shown to improve outcomes in hospitalized patients.[14,17,18,19] We were only able to record the MEW Scores, i.e. the afferent limb of the system; the real impact would follow once the efferent arm of the system with a proper escalation protocol is implemented.[14] Better triaging, increased frequency of monitoring, transfer to high level of care, early detection of sepsis and initiation of bundled care are all linked to accurate identification of patients with possible sepsis and high likelihood of deterioration.

In a third-world country, a simple, low-cost, validated tool, based on clinical observations can be used not only to monitor patients for potential critical illness and adverse events, but also for appropriate triage in the emergency room.

The two common causes of preventable morbidity and mortality in hospitalized patients are sepsis and cardiac arrest. The addition of MEWS improves early detection of critical illness at the expense of reduced specificity[2] but reduces mortality.[17-18]

Table 2. Demographic features of the study population

Characteristics	Minimum	Maximum	Mean	Standard Deviation
Systolic B.P (mmHg)	60	220	128.50	27.96
Pulse (beats per min)	49	180	105.72	24.28
Respiratory rate (breath per min)	12	52	25.46	6.94
Temperature (^{0}C)	36	40	37.17	0.78
MEW Score	1	10	3.8	2.0

Table 3. MEW SCORE at the time of death

Categories	Frequency (%)
2-3	5 (5)
4-5	7 (6)
>5	14 (13)
Total expired	26 (23)
Discharged	86 (77)
Total patients	112 (100)

In a resource-poor setting, MEWS presents a cost effective tool which only requires a priming of the nursing staff, who are already assigned with the task of recording vital signs. Accurately recorded readings and appropriately calculated scores can significantly influence patient outcomes and have already been shown to be instrumental in averting preventable adverse outcomes.

Competing interests

The authors declare they have no competing interest.

Authors' contributions

All the authors have contributed to this study. BJ and AA conceived the study; BJ drafted the manuscript. MA and AM examined the patients and collected the data. NT performed the main statistical analyses and interpreted the results. All authors have read and approved the final manuscript.

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Etiology, Prognostic Factors and Outcome of Fulminant Hepatic Failure at The Children's Hospital Lahore.

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Abstract

Background
Fulminant hepatic failure (FHF) in children is a devastating disease, with guarded prognosis and ultimate outcome. Viral hepatitis is very common reasons for this acute fulminant hepatitis.Patients in developing countries like Pakistan are referred late where treatments are inadequate and improper. Subtle signs and laboratory parameters pointing to bad prognosis are missed and treatment is started late. We aimed to study behavior of fulminant hepatic failure due to viral etiology, determine the prognostic factors and outcome in children.

Methods
It is cross sectional study conducted at department of Gastroenterology, Hepatology and Nutrition, The Children's Hospital and Institute Of Child Health Lahore during Jan 2010 till Dec 2013. Children younger than 15 years of age with admitting diagnosis of fulminant hepatic failure due to viral etiology were enrolled. Their grade of encephalopathy, liver function tests, viral markers, coagulation profile, and serum potassium levels were recorded on a proforma. Discharge disposition (alive or dead) were study outcome. Chi square and p-value were calculated.

Results
During three year period 108 children were admitted with fulminant hepatic failure due to suspected viral etiology. Among them 65 (60%) were males. The etiologies were: 40(37%)were due to hepatitis A, 18(23.6%)were due to non A –Eviral hepatitis, 13(12%) were due to hepatitis B, 1(0.92%) was due to hepatitis E while 4 (3.1%)were due to co-infection(Hepatitis A & typhoid fever).Out of 108 patients admitted with fulminant hepatitis 53(49%) survived, 39(36%) expired while 16(17%) left against medical advice. Children who had a higher grade of encephalopathy grade IV had bad prognostic outcome with 13 (77%)dying (p=<0.001), while those with lower grade of encephalopathy had a good outcome with 100 % survival in grade 1 encephalopathy. In grade II encephalopathy 22 (92%) survived and in grade III encephalopathy 22 (48%) survived. Delay between the first symptom of liver disease and the onset of hepatic encephalopathy (within 10 days versus more than 10 days), lower plasma albumin (less than 2.5 g/dL), higher prothrombin time (more than 60 seconds) on admission were more likely to die of fulminant hepatic failure (p=<0.05).

Conclusions
Fulminant hepatitis is a potentially fatal disease. In our study hepatitis A and B were the most common viruses causing fulminant hepatic failure.Children with fulminant hepatic failure with severe coagulopathy, hypoalbuminemia and hypokalemia on admission and prolonged duration of illness before the onset of hepatic encephalopathy are more likely have a significant mortality and morbidity.

Key words
Acute Viral hepatitis, fulminant hepatic failure (FHF), coagulopathy

Introduction

Fulminant hepatic failure (FHF) in children is a devastating disease, a final path way of variety of insults to liver, with guarded prognosis and ultimate outcome.[1] Patients in developing countries like Pakistan are referred late where treatments are inadequate and improper. Subtle signs and laboratory parameters pointing to bad prognosis are missed and treatment is started late. Unfortunately they are not referred to centers equipped with resources to treat them efficiently and timely. There is a need of standardized diagnostic and management strategy. There is lack of randomized controlled trial pertinent to children particularly from centers without liver transplantation facilities. Pakistan currently facing the same problem with lack of multidisciplinary approach to these children, where early intervention might be essential in preventing long term morbidity and major mortality linked with FHF in children.

Fulminant hepatic failure is due to various reasons, including toxins, drugs, metabolic diseases and hepato tropic viruses. [2] Viral hepatitis is very common reasons for this acute fulminant hepatitis.[3] Fulminant hepatic failure is a rapidly evolving clinical condition in pediatric age group. It is complex and rapid final common pathway for many diverse diseases, known and unknown alike.[4-6]

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Management requires a multidisciplinary team including pediatrician, pediatric hepatologist, intensivist, and liver transplant surgeon. In countries like Pakistan where pediatric liver transplant program isn't available it's very pertinent to know the prognostic indictors that will guide to outcome, counseling of families and early referral to neighboring country where liver transplant can be done.

This study was conducted to investigate the viral etiology and assess outcome in relation to the etiology and laboratory parameters. It was very relevant to do this study as the prognostic factors we want to study if catered for in time can change the outcome and also can help buy time while arranging for liver transplant.

Methods

It was an observational prospective study, conducted at The Gastroenterology ICU of the Children's Hospital, Lahore from Jan 2010 - Dec 2013. 108 patients of fulminant hepatic failure with suspected viral etiology admitted during that period were included in this study.

Patients with fulminant hepatic failure due to other causes e.g. metabolic, drug induced, autoimmune and chronic liver disease were excluded from the study.Viral markers for hepatitis A to E (anti HAV IgM, HBsAg, anti HCV antibody, anti HEV IgM) were determined by ELISA method. Age, sex, duration of stay in ICU, durations of symptoms, presence of pallor, jaundice, edema, span of liver, splenomegaly, Ascites and stage of encephalopathy were recorded on set proforma.

Fulminant Hepatic failure was defined as per second World Congress of Pediatric Gastroenterology, Hepatology, and Nutrition, proposed a detailed classification and definition of liver failure in children,[7] where hyper acute liver failure is defined as coagulopathy due to acute liver dysfunction of up to 10 days total duration by clinical criteria. Acute liver failure is defined as coagulopathy due to acute liver dysfunction of more than 10 days, but less than 30 days total duration by clinical criteria. Sub-acute liver failure is defined as coagulopathy due to acute liver dysfunction of more than 31 days, but less than 6 months total duration by clinical criteria. All definitions imply absence of previous liver disease.

Relation between outcome and different laboratory parameters like Serum ALT, Serum albumin, hypoglycemia, thrombocytopenia, deranged renal functions and coagulation was also made from that proforma. These variables were tabulated and Chai-square test was applied for P-value. The collected data was analyzed by using statistical program SPSS Version 16.0.

Results

During study period, total of 108 patients of fulminant hepatic failure of suspected viral etiology were collected. Out of which 65 (60%) were male and 43 (40%) were female. Six (5.5%) were less than 1 year of age, 58(54%) patients were between 1 – 5 years of age, 27(25%) were between 6 – 10 years while 17(16%) patients were more than 10 years of age (Fig. 1).

From 108 patients, 16 patients got LAMA. From 92 remaining patients, 5 (6%) were in stage I, all of which survived. Twenty four (26%) patients were in stage II out of which 22 (92%) survived and 2 (8%) expired. Forty six (50%) were in stage III, out of which 22 (48%) survived and 24(52%) expired. Seventeen (19%) patients were in stage IV, out of which 4 (24%) survived and 13 (77%) expired. Sixteen (14%) patients were having thrombocytopenia, out of which 5(31%) survived and 11(69%) expired. Seventeen (15%) patients were having hypokalemia, out of which 8 (53%) survived and 9 (47%) expired. Fourteen (13%) patients were having hypoalbuminemia, out of which 3 (23%) survived and 11 (77%) expired. Fourteen (16%) patients were having renal failure, out of which 2(14%) survived and 12 (86%) expired. All patients were having deranged coagulation profile. PT was <1 minute prolonged in 34 (31%) patients out of which 28 (82%) survived and 6 (18%) expired. PT was >1 minute prolonged in 74 (69%) patients out of which 31 (55%) survived and 43 (45%) expired (Table 1).

Viral etiology was known in 76(70%) patients. 40 (37%) were due to Hepatitis A, 18 (23.68%) were due to non A – E viral hepatitis, 13 (12%) were due to Hepatitis-B, 1 (0.92%) was due to Hepatitis E, 4 (3%) were due to co infection (Hepatitis A and Typhoid fever).

Fifty four (50%) patients develop encephalopathy within the 10 days of jaundice, out of which 16(30%) expired and 38(70%) survived. 17(15%) patients develop encephalopathy within the 11-20 days of jaundice, out of which 6(35%) expired and 11(65%) survived. 21(19%) patients develop encephalopathy after 20 days of jaundice, out of which 17(80%) expired and only 4(20%) survived (Fig.2).

Out of 108 patients of FHF which were included in this study 53 (49%) were discharged, 39(36%) were expired and 16(17%) left against medical advice.

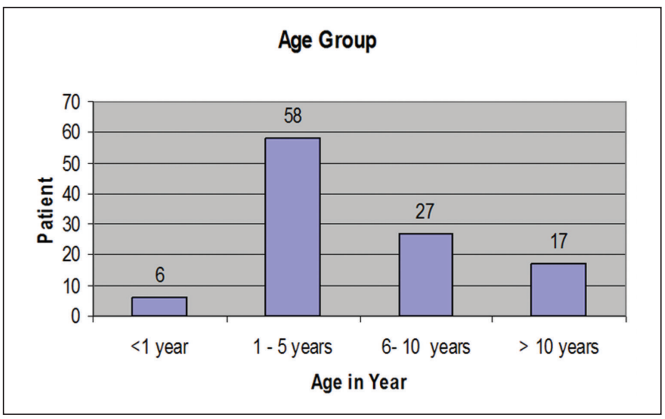

Fig. 1: Age distribution of patients

Table 1: Stage of encephlopathy and laboratory parameters

Features	No. of Patients N (%)	Survived N (%)	Expired N (%)	P-value
Stage of Encephalopathy				
I	5(5.5)	5(100)	0(0)	<0.001
II	24(26)	22(92)	2(8)	
III	46(50)	22(48)	24(52)	
IV	17(18.5)	4(23.5)	13(76.5)	
Thrombocytopenia (<150,000)	16(14)	5(31)	11(69)	0.008
Hypokalemia < 3.5	17(15)	8(53)	9(47)	0.101
Serum Albumin < 2.5	14(13)	3(23)	11(77)	0.002
Deranged renal functions	14(16)	2(14)	12(86)	0
Deranged coagulation				
< 1 min	34(31)	28(82)	6(18)	0.014
> 1 min	74(69)	31(55)	43(45)	
Onset of Encephalopathy				
< 10 days	54(49.68)	38(70)	16(30)	<0.001
10 - 20 days	17(15.64)	11(65)	6(35)	
> 20 days	21(19.32)	4(19)	17(81)	

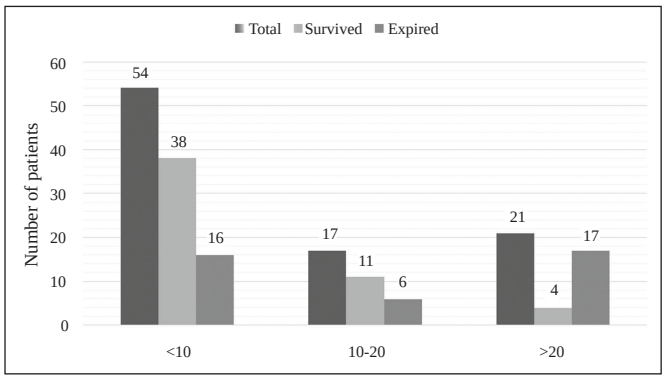

Fig. 2: Duration between onset of jaundice and onset of encephalopathy

Discussion

Fulminant hepatic failure is caused by hepatitis viruses and by drugs. Important clinical presentations are jaundice, coagulopathy, and encephalopathy. Diagnosis is clinical. Treatment is mainly supportive, sometimes requiring liver transplantation. Viral hepatitis tops the list of causes in developing countries, while drugs are the commonest reason for acute liver failure in western world. Viral hepatitis now comprises only one-eighth of all ALF cases in the United States.[8]

Less common causes include metabolic disorders and vascular disorders which include hepatic vein thrombosis (Budd-Chiari syndrome), ischemic hepatitis, portal vein thrombosis, and hepatic sinusoidal obstruction syndrome. Metabolic causes include Reye syndrome, and Wilson disease. Other causes include autoimmune hepatitis, metastatic liver infiltration, and sepsis.In developing countries, the etiologies are similar but are dominated by infectious etiologies, among which hepatitis A is the most common.[4]

Fulminant hepatic failure typically presents in normal healthy child with non specific signs and symptoms or variable durations with or without jaundice. In an icteric patient or any other significant signs of liver disease, Symptoms may persist or wax and wane for days or weeks before the child is brought to medical attention.

However, in the presence of clinical signs of liver disease injury or encephalopathy, or if laboratory investigations obtained reveals hepatic dysfunction, the clinical scenario encompassing acute liver failure can be recognized.

Our study of 108 subjects has provided useful clues regarding viral etiology, presentation, bad prognostic factors including clinical and lab parameters andoutcome of patients with FHF admitted at The Children's Hospital and Institute of Child Health, Lahore.

The high frequency of acute liver failure associated with hepatitis

A in our study is similar to the observed in Santiago,[7] Buenos.[8] Another study done locally in Pakistan also demonstrate fulminant course associated with hepatitis A.[9] A study from Agha Khan Hospital, Karachi also points out to association of hepatitis A with fulminant hepatic failure in children.[10]

In our study the best outcome was seen in patients who developed encephalopathy within 10 days of appearance of jaundice with 70% survival rate & patients who developed encephalopathy between 11 – 20 days of appearance of jaundice 65% while only 4% survived in patients who developed encephalopathy after 20 days of encephalopathy.

In a study of 376 cases of FHF in adults, O'Grady and colleagues found that 60% of cases were hyper acute, 24% acute and 16% sub acute. The best chance of survival was in the hyper acute group (36%) compared to acute (7%) or sub-acute (14%).[10]

In our study, most common cause of FHF was Hepatitis A followed by non A-E and hepatitis B. High rate of mortality was associated with patients who had hepatitis A. Hepatitis A is also a common cause of super infection in patients of chronic liver disease due to other reasons with very high fatality. AKU study also shows similar high mortality 30% in patients who had hepatitis A and presented with fulminant hepatic failure.[10] Our study confirms various previous reports of fulminant course of hepatitis A and rapid progression to death which is predictable from many laboratory and clinical parameters.[11,12,13,14,15.] A retrospective case study done in 74 patients with acute liver failure revealed hepatitis A (14/21 patients, 66.7%) was the most frequent infectious agent.[16]

Hepatitis B virus as a cause of ALF is less common in children[3].In another study out of 100 cases of ALF, 45 were due to non–A-E hepatitis.[17]

In the absence of liver transplantation which alters the outcome of Liver failure, outcome depends on various clinical and biochemical factors.

In our study, there are different predictors of poor outcome which include hypoalbuminemia (<2.5g/dl), deranged coagulation, GI bleeding, hypokalemia, deranged renal functions, thrombocytopenia, spontaneous bacterial peritonitis delayed onset of encephalopathy and stagy IV encephalopathy.

Multivariate logistic regression analysis showed that the presence of raised intracranial pressure at the time of admission, prothrombin time >100 sec on admission, older age and onset of encephalopathy seven days after onset of jaundice were associated with poor prognosis.[18]

In a study of 31 cases of FHF in children, showed that poor outcome was related to the grade of encephalopathy, prolonged prothrombin time (>90 second), GI hemorrhageand renal failure.[19]

Another study revealed that higher plasma bilirubin (299 micromol/L versus 80 micromol/L), higher prothrombin time (62 seconds versus 40 seconds) or lower alanine aminotransferase (1288 IU/L versus 2929 IU/L) levels on admission were more likely to die of fulminant hepatic failure.[20]

Infection is found to be a marker for poor prognosis in patients of FHF.[21] A study in 41 children with FHF, showed the presence of GI bleeding, the degree of coma, and serum bilirubin to be independent predictors of mortality.[22] In our study, 30% had ascites.Ascites has been reported in 16.5–55% of children with FHF.[23]

Conclusion

Fulminant hepatic failure in children due viral hepatitis is a common entity in our country and has significant morbidity and mortality. It is one of major cause of admissions in our liver ICU. Hepatitis A is a leading underlying cause which can easily be prevented by vaccination, followed by non A – E viruses. All predictors of the poor outcome defined in this study if promptly addressed can significantly reduce the final outcome and can also help the treating physician to plan early referral for transplantation.

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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 and Figures 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:

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

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.
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