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Editorial

Missing children and child helpline

Vijay Kamale

Original Research

1. Spectrum and antibiotic sensitivity pattern of bloodstream bacterial isolates from septicemic neonates in a tertiary care centre in Eastern India.

Bhattacharyya Saugata, Chatterjee Tapabrata

2. Cough Profile and Trends in Cough Management in Children across India: Results of a Multi-centric, Cross-sectional Survey

Paramesh H, Mohanty Nimain , Kamale Vijay, Patra Vikram, Rathod Rohit, Puppalwar Gaurav, Jain Rishi

3. Clinical Profile and Short Term Outcome Of Neonates Requiring Assisted Mechanical Ventilation

Prajakta Dekate, Sachin Damke, Revat Meshram

4. Neurological outcome of neonates undergoing exchange transfusion for hyperbilirubinemia: a study in tertiary care centre in Bihar

Kumar Arpit, Alka Singh, S. R. Choudhary

5. Hand hygiene compliance and efficacy of a multimodal intervention strategy in improving hand hygiene compliance in a tertiary level pediatric intensive care unit

Sham B. Lohiya, R. Rameshkumar, Jayanta Vagha

Case report:

Turner Syndrome with Intra-Hepatic Periportal Cuffing And Non-Cirrhotic Portal Hypertension (NCPH) - A Rare Association

Amonkar Priyanka, Arora Kriti, Mohanty Nimain, Vyas N.L., Preeti Kapoor, Sahu Shilpi

EDITORIAL

Fate of Missing children in India

Vijay Kamale

It is estimated that approximately 45000 children are reported every year from our country. The reasons for missing are generally cited as abduction or kidnapping of children by family members or nonfamily people, runaway children or those forced to runaway by family or due to circumstances unfavorable to child. Problem children like aggressive, hyperactive or those involved in crime or delinquent also seem to be missing occasionally.

Missing children may be exploited by various criminally deviated personalities for obvious reasons known to them. They may become victims of organ trade, traded to countries like gulf for petty jobs or can even fall into prey of cannibals found in many areas of India. Runaway children usually migrate to glamorous cities and fall prey to exploiters and are employed in tea stalls, brothels and beggary etc. Most of these children are coming from poor background that do not have access to authorities or are ignorant, and even if they approach someone their reports also are not taken seriously.

What happens when child is found missing

Missing child is not cognizable offense committed by anyone according to law. First information report is usually not filed and concerned police station just does general entry in station diary. Some media awareness is done depending on case. The database of missing persons is maintained by The Missing Persons Wing at the National Crime Records Bureau (NCRB) in New Delhi. According to child helpline data 2018 around 22000 Children out of 45000 are found and are identified as lost. Rest half children remain untraceable in spite of best effort from Government.

Available NCRB data shows that rate of crime against children has increased from 21.1 in 2015 to 24 per cent in 2016. Kidnapping and abduction are highest registered category followed by POCSO related crime. Juvenile conflicts cases also have increased from 33433 in 2015 to 35849 in 2016.

To rehabilitate the children found and identified as lost Central Adoption Resource Authority (CARA) was found in 2015. CARA mainly deals with adoption of orphans, abandoned and surrendered children through its associated /recognized adoption agencies. The principles governing adoption are laid down.

The child's best interests are of paramount consideration, while processing any adoption placement. The scrutiny of parents is done by special committee, before giving child to prospective parents. The child is preferably given to Indian parents as there are sociocultural environmental issues in foreign country placement.

In spite of best efforts, it is found that only 3-4 % of missing children will find parents and another 10 percent are rehabilitated through adoption. The present drive of finding and investigating missing children with help of ADHAR will be helpful in improving future of missing children in our country.

ORIGINAL RESEARCH:

Spectrum and antibiotic sensitivity pattern of bloodstream bacterial isolates from septicemic neonates in a tertiary care centre in Eastern India.

*Bhattacharyya Saugata**, *Chatterjee Tapabrata**.

*Resident, RSV Hospital, Kolkata. Former DNB resident, Department of Pediatrics, Vivekananda Institute of Medical Sciences, Kolkata. **Professor, Department of Pediatrics, Vivekananda Institute of Medical Sciences, Kolkata.

Corresponding author: Saugata Bhattacharyya, 329/1, Ustad Amir Khan Sarani, Flat B-10, Kolkata-700082 Phone: +919433783176, E-mail:

drsbhattacharyya@gmail.com

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ABSTRACT:

Objective: To determine the antibiotic sensitivity pattern of bacterial isolates from septic neonates so as to identify the most suitable policy for use of empirical antibiotics. Design: Retrospective cross-sectional study

Participants: 126 infants admitted between 1st September 2015 and 30th August 2016, for treatment of suspected sepsis Method: Reports of blood culture done by BacT/Alert[®] system and other relevant data pertaining to suspected

cases of neonatal sepsis were collected from the case records and retrospectively analyzed.

Results and outcome measures: *Commonest organism was E.coli. Resistance to ampicillin, gentamicin and cefotaxime was significant. Overall, 73% of all organisms were susceptible to either carbapenems or glycopeptides while 63% were susceptible to either piperacillin/tazobactam or an aminoglycoside (preferably netilmicin).*

Conclusion: *Carbapenems and Glycopeptides rotated with Piperacillin/tazobactam and an Aminoglycoside (preferably netilmicin) may have to be empirically used in units with similar flora and sensitivity patterns.*

KEYWORDS: *Newborn, Sepsis, Anti-Bacterial agents, Microbial Sensitivity tests.*

INTRODUCTION: Septicemia has been the second most frequent cause of death in newborns after perinatal asphyxia in as recent a time as 2002-03 in India, when an incidence rate of about 16% among hospital born neonates was estimated.^[1] It is still one of the three most important causes of neonatal mortality in this country, the others being prematurity/low birth weight and birth asphyxia.^[2] The pattern of organisms causing neonatal sepsis and that of their antibiotic sensitivity in developed countries ^[3, 4] differ substantially from those in the developing ones.^[5-8] Regional variations are also seen within the geographical limits of developing nations. Having said that, it cannot be

overemphasized that empirical antibiotic therapy is an essential and life saving part of management of neonatal sepsis and any attempt at formalization of policy streamlining such practice requires a thorough knowledge of the regional spectrum of causative organisms as well as their antibiotic sensitivity patterns.

This study was conceived with the above intention.

OBJECTIVE: To determine the antibiotic sensitivity pattern of bacterial isolates from septic neonates so as to identify the most suitable policy for use of empirical antibiotics.

METHODS: A retrospective cross-sectional study was conducted including 126 infants admitted between 1st September 2015 and 30th August 2016, for treatment of suspected sepsis to the NICU of RSV Hospital, Kolkata, a tertiary care hospital, providing level II neonatal intensive care services. Blood samples were collected for culture from all neonates either showing clinical signs of sepsis as described by Young Infants Clinical Signs Study Group^[9] or born to mothers with risk factors for infection including prolonged rupture of membrane for more than 12 hours, fever, UTI, foul smelling and/or meconium stained amniotic fluid. Newborns with gross congenital anomalies and ongoing exposure to antibiotics for probable sepsis were excluded from the study. Aseptically collected samples of blood were cultured in a BacT/Alert[®] 3D system and were sub-cultured if indicated, onto specific media for isolation of

causative organisms. Isolated organisms were identified by colony characteristics, Gram staining and biochemical methods. Antimicrobial sensitivity tests were carried out following Kirby-Bauer's disc diffusion method modified as required according to current CLSI guidelines.^[10] Demographic characteristics of the subjects as well as the blood culture and sensitivity results were collected from hospital records. Organization, descriptive representations and analysis of data were done using STATA[®] version 12SE for Windows[®] statistical software package. Categorical variables and blood culture results were tested for mutual independence using Pearson's χ^2 test.

RESULTS AND OUTCOME MEASURES: During the study period there were 19 (15%) culture positive cases among the 126 infants included in the study.

(Table 1)

Among the 19 pathogenic bacteria isolated, about 74% (n=19) were Gram negative organisms. Predominant among those were *E. coli* (42%, n=19) and *Klebsiella sp.* (22%, n=19). *Staph. aureus* (11%, n=19) and *Staph. epidermidis* (16%, n=19) were the Gram positive isolates. As regards antibiotic sensitivity of the flora, Gram negative bacteria were highly (85%, n=14) resistant to cefotaxime. Ampicillin susceptibility was found to be 29 % (n=14). Only 50 % (n=14) of the entire Gram negative group were susceptible to Aminoglycosides as well as Piperacillin/tazobactam although the figure was slightly better (75 %)

for *E. coli* alone. Best overall susceptibility of the Gram negative flora were to Chloramphenicol (79 %, n=14), followed by Carbapenems (64 %, n=14). As for the Gram positive organisms, half of the *S. aureus* and all of the *S. epidermidis* were resistant to ampicillin. 50% (n=2) of *Staph. aureus* and all of *Staph. epidermidis* were methicillin resistant but were uniformly susceptible to vancomycin, teicoplanin and linezolid. Azithromycin and clindamycin susceptibility stood at 60% (n=5). Overall, 100 %, (n=5) were susceptible to netilmicin, glycopeptides and linezolid. Gentamicin resistance was 50 % (n=2) among *S. aureus* and 100 % (n=3) among *S. epidermidis*.

(Table 2)

DISCUSSION: Our analysis showed a blood culture yield of 15.1 % (n=126) and an overall incidence rate for sepsis of 31.7 per 1000 live births. In this study, early onset sepsis was encountered more often than late onset sepsis, male preponderance prevailed among afflicted (male: female=1.4:1) and prematurity was associated with culture positivity in a statistically significant manner. The causative organisms were mostly Gram negative and *E.coli* was the commonest one. Among Gram positive flora, *S.epidermidis* was most commonly isolated followed by *S.aureus*. With regard to antibiogram of the isolates, very steep resistance to ampicillin and third generation cephalosporins and significant resistance to aminoglycosides were noted among Gram negative

organisms. As for the Gram positive flora, susceptibility to penicillins, macrolides as well as cephalosporins were found to be dwindling.

This was a purely retrospective analysis done without controls. Hence, although prematurity has been linked with increased vulnerability to sepsis, there might have been a selection bias involved. Coagulase negative staphylococci could very well have been contaminant growths since we analyzed cases where only single cultures were taken and response to antibiotics could not have been detected retrospectively.

Similar incidence rates for neonatal sepsis and associations of culture positivity were reported in recent Indian studies.^[6, 11-13] Contrary to our findings, many workers reported *Klebsiella sp.* as the commonest isolate.^[1, 7, 8] Our overall scenario may reflect a principally nosocomial source but such findings are not uncommon and similar scenarios among hospital born neonates in the developing world were recently found and analyzed by Zaidi et al.^[7] In our study, 73% (n=19) of all organisms were susceptible to either carbapenems or glycopeptides providing the highest coverage. The figure for Piperacillin/tazobactam and aminoglycosides (preferably netilmicin) was close (63%, (n=19)). Reports from Pakistan^[14] and JIPMER, Pondicherry^[15] submit that carbapenems and glycopeptides may have to be escalated to the first line of attack in places where significant antibiotic resistance prevails. While we find ourselves in the same boat, our study also indicates that antibiotics with

susceptibility patterns almost similar to those with broadest spectrum coverage can usually be found. We have to utilize that opportunity and although not studied here, rotation between such antibiotics can always minimize the selection of resistant strains in the long run.

CONCLUSION: Carbapenems and glycopeptides can sometimes appear to be the only antibiotics with decent coverage of bloodstream isolates from septic neonates thus making them candidates for empirical use in rotation with other antimicrobials with almost similar effectiveness (Piperacillin/Tazobactam and Netilmicin in our study).

DECLARATIONS:

Contributors: Saugata Bhattacharyya- Determination of study design and methodology, analysis of the collected data, literature search and preparation of manuscript. Tapabrata Chatterjee- Conceptualization, collection of data and revision of the manuscript.

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Table 1: Culture results with respect to patient characteristics

Characteristics	Culture Positive	Culture Negative	p-value*
Less than 72 hours old	14	60	0.151
More than 72 hours old	5	47	
Term infants	2	92	0.000
Preterm infants	17	15	
Male babies	11	54	

Female babies	8	53	0.551
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*Derived from Pearson's χ^2 test, where a p -value <0.05 was considered as statistically significant.

Table 2: Percent isolates susceptible to various antibiotics

	CPM	FLQ	CM B	PCL	PLX N	GLC N	AM G	CPHN 3
<i>E. coli</i>	88	50	75	88	75*	88	75	25
<i>K.pneumoniae</i>	100	50	50	100	100	100	50	None
<i>K. oxytoca</i>	None	None	None	100	100	None	None	None
<i>A. baumannii</i>	None	None	None	None	100	100	None	None
<i>S. epidermidis</i>	None [#]	None	None	100	Not tested	Not tested	100 ^{\$.£}	None
<i>S. aureus</i> [£]	50	Not tested	50	100	Not tested	Not tested	50	50

*this includes 25% *E. coli* which were resistant to colistin but susceptible to polymyxin-B

[#]only 33% was sensitive to Imipenem; ^{\$}all were resistant to gentamicin; [£]all were sensitive to netilmicin.

CPM=Carbapenems (Meropenem, Imipenem & Doripenem),

FLQ=Fluoroquinolones (Ciprofloxacin, Ofloxacin), CMB=Combinations

(Piperacillin/Tazobactam, Ampicillin/Sulbactam), PCL=Phenicol

(Chloramphenicol), PLXN=Polymyxins (Colistin, Polymyxin-B),

GLCN=Glycylcyclines (Tigecycline), AMG=Aminoglycosides (Gentamicin,

Amikacin, Netilmicin), CPHN3=3rd generation cephalosporins (Cefotaxime,

Ceftriaxone).

ORIGINAL RESEARCH:

Cough Profile and Trends in Cough Management in Children across India: Results of a Multi-centric, Cross-sectional Survey

*Paramesh H**, *Mohanty Nimain***, *Kamale Vijay***, *Patra Vikram****,
Rathod Rohit#, *Puppalwar Gaurav##*, *Jain Rishi ###*

*Pediatric Pulmonologist, Lake side centre for health promotion, Bengaluru,

Professors and *Associate Professors, Department of Paediatrics, MGM Medical College, Kamothe, Navi Mumbai; #Medical Advisor, ## Head Medical Affairs and ### Vice President Medical Affairs, Wockhardt Ltd., Mumbai, India

Corresponding author: Dr. Nimain Mohanty, Professor, Department of Pediatrics, MGM Medical College, Navi Mumbai

ABSTRACT:

Objective: *To find the nature of cough associated symptoms and conditions, medication preference in Indian children visiting pediatric outpatient services, with cough as the chief complaint.*

Material and methods: *The survey was conducted in six cities across Indian winter months from October to December 2017. The target population for the survey consisted of 1998 children, involving 200 pediatricians across the country. Data was collected on children having cough, categorized under 6 groups ranging from age 1-2 years to 11-12 years, visiting pediatric OPD / clinics with cough as the chief complaint. Parameters evaluated included duration of presenting cough, history of similar episodes, nature, intensity and frequency of cough, associated symptoms, presence of risk factors, drugs used for treatment of cough, concomitant medications and self-medication, if any.*

Results: Data on 1998 children having cough, aged between 1 to 12 years (58% males; 42% females), was captured in this survey in 6 cities (Bangalore - 350, Ahmedabad - 249, Delhi - 403, Hyderabad - 298, Lucknow - 397 and Mumbai - 301). Over 69% children presented with cough since 5 days prior to OPD visit while only 3% had symptoms lasting over 10 days. Almost half of the children reported 4 to 6 similar episodes of cough in preceding 12 months. 25% of the children were having dry cough whereas 61% had wet cough with no or scanty expectoration. Fever was present as associated symptom in 62.9% cases. Majority (77%) of children had no family history of asthma, allergic rhinitis or tuberculosis. None of them were diagnosed either as pneumonia or tuberculosis on further investigation. First and second generation antihistaminics were prescribed in 76% and 78% children respectively. Antibiotics (50%) and nutritional supplements (12%) were also prescribed besides mucolytics (62%) and expectorants (63%). 83% of children preferred oral medicine. More than half of the children had more than 6 bouts of cough per day. Use of self-medication was however low.

Conclusion: Acute onset and recurrent cough is common in children. Exposures to modifiable risk factors such as environmental pollutants are commonly seen to be associated with pediatric cough. Fever is a common accompanying symptom. Due caution need be observed while prescribing multiple and multi-combination preparations so that same molecule is not present in different preparations, thus avoiding overdosing. Decongestants, antitussives, mucolytics, expectorants and first and second generation antihistamines were commonly prescribed in management of pediatric cough with a view to decrease mucosal oedema, secretions and allergy.

Key words: Cough, children, survey, symptoms

Introduction: Cough is an important natural defence mechanism of respiratory tract. It could also be a warning sign of several respiratory and non-respiratory diseases and is one of the most common reasons for both adults and children seeking medical aid. Acute or short-lived cough often occurs in association with upper respiratory tract infection, is usually of viral etiology, self-limiting and mostly resolves within three weeks¹³. Almost 30% of them have associated multi-trigger wheezing.

Under diagnosis of asthma re-emphasized cough as a symptom being taken seriously. On the other hand, there is increasing evidence that children are inappropriately treated for asthma, based on cough as the sole symptom^{14, 23}. Coughing in children can be distressing and can have a major impact on child's sleep, school performance and ability to play. It may similarly disturb other family members' sleep and be disruptive for school teachers. Considerable parental anxiety is generated in families with a child with problem of coughing^{4,9}.

Cough is the most common pediatric problem managed by family physicians (FP), and it is more common in preschool children than older children. Most cough in children are caused by undifferentiated acute respiratory tract infections—a cough that does not conform to any clear diagnostic syndrome such as croup, whooping cough, pneumonia, or bronchiolitis²⁴. Causes of cough include acute respiratory tract infection, asthma, non-asthmatic eosinophilic bronchitis, exposure to environmental irritants such as - smoke, dust, gastroesophageal reflux, rhinitis, sinusitis, post-nasal drip, laryngopharyngeal reflux, obstructive sleep apnea or drug induced cough. Cough management is based on the cause, type of cough, duration and severity. Symptomatic treatment options for cough include antitussives, mucolytic agents, expectorants

and bronchodilators, whereas definitive treatment depends on the underlying cause. Despite the high prevalence of cough in children, the topic has been poorly researched⁹.

Narayanan et al (16) had conducted a detailed profiling survey in India in patients visiting family physicians with cough as the chief complaint. However, the study involved of a very limited population from pediatric age group. Hence this survey of similar kind was undertaken to understand and generate data on nature of cough, associated symptoms/conditions and the medication preference in Indian children visiting pediatric outpatient departments (OPD) with cough as the major complaint.

Material and methods

This cross sectional questionnaire based survey was conducted among children aged 1 to 12 years, visiting pediatric OPD from 6 cities across India with cough as the chief complaint. The survey was conducted over a period of 3 months, from October to December 2017. It collected demographic details, duration of cough, history of similar episodes in past 12 months, nature, intensity and frequency of cough, associated symptoms, co-morbid conditions, concomitant medications, history of self-medication, adverse effects due to self-medications, classes and duration of drugs prescribed for cough and patient preference for treatment. Intensity of cough was categorized into 3 types; fairly intense (Tiresome, but is able to continue routine), low in intensity (Comfortably carries out routine) and high intensity (Routine life interrupted). Approximately 10 children were enrolled from each site and 250 to 300 from a region.

Statistical analysis

No formal sample size calculation was performed being non-interventional nature of the study. Only standard descriptive statistics is reported in the results.

No comparative statistical analysis is performed. Categorical data are presented as percentages.

Results

A total of 1998 children (58% males; 41% females, 1% not mentioned) were enrolled from 6 cities namely Bangalore (350), Ahmedabad (249), Delhi (403), Hyderabad (298), Lucknow (397) and Mumbai (301).

Age group-wise distribution

Majority (40 %) of children enrolled in this survey belonged to 3-6 years of age (Figure 1). While 1-8 years old comprised 75% of children surveyed.

Duration of Cough

68% children had cough symptoms since 5 days prior to OPD visit while 3% children had symptoms for over 10 days (Figure 2).

History of similar cough episodes

A total of 46% of the children had 4-6 similar episodes of cough symptom in the preceding 12 months (Figure 3).

Nature of cough

A total of 61% of the children had productive cough while 25 % had dry cough with no or minimal sputum (Figure 4).

Intensity of cough

67% of the children had fairly intense symptoms but were able to continue their routine activities while 15% had cough symptoms severe enough to affect their routine life such as -attending school/ kindergarten (Figure 5).

Number of cough bouts per day

37% children reported 2-6 cough bouts per day. More than half of the children had more than 6 bouts and 21% reported more than 20 cough bouts per day (Figure 6).

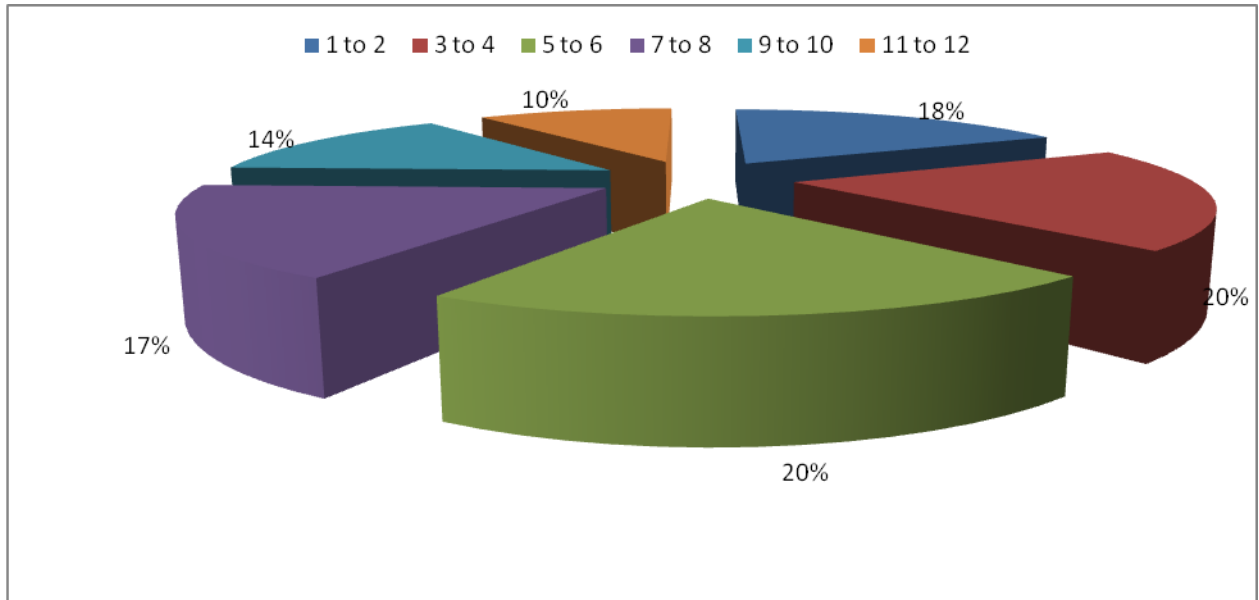


Figure 1: Age group-wise distribution (%) of children enrolled in the Multi-centric survey

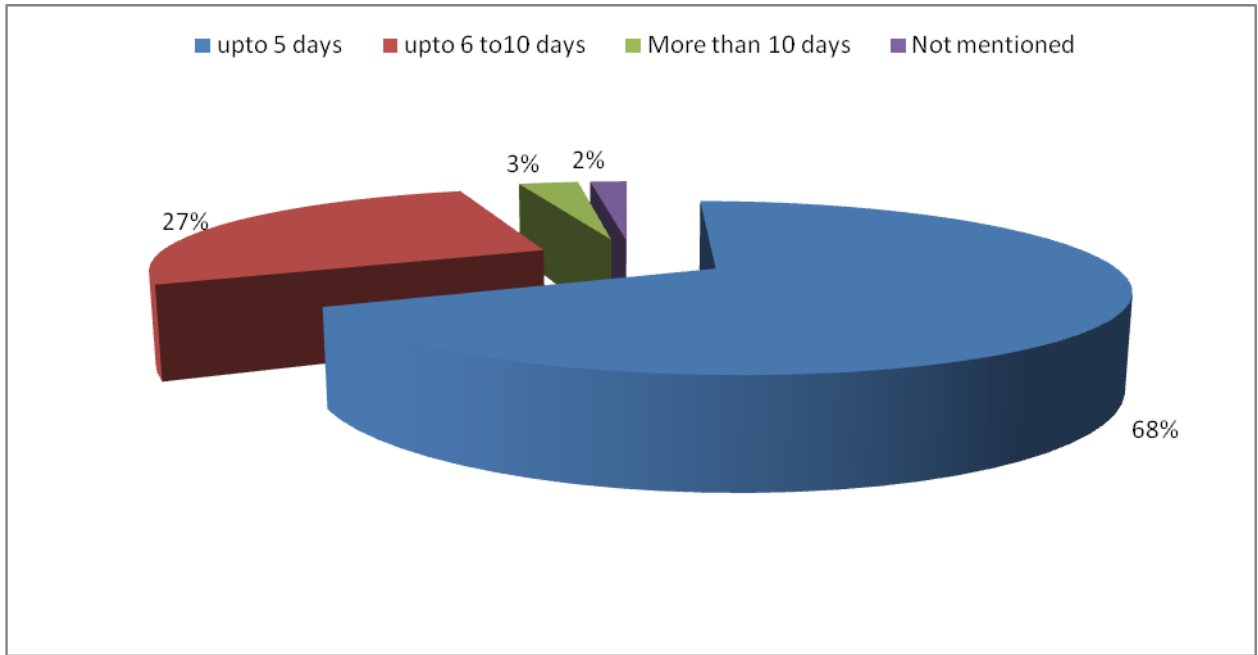


Figure 2: Percent distribution of children based on duration of presenting symptom (cough)

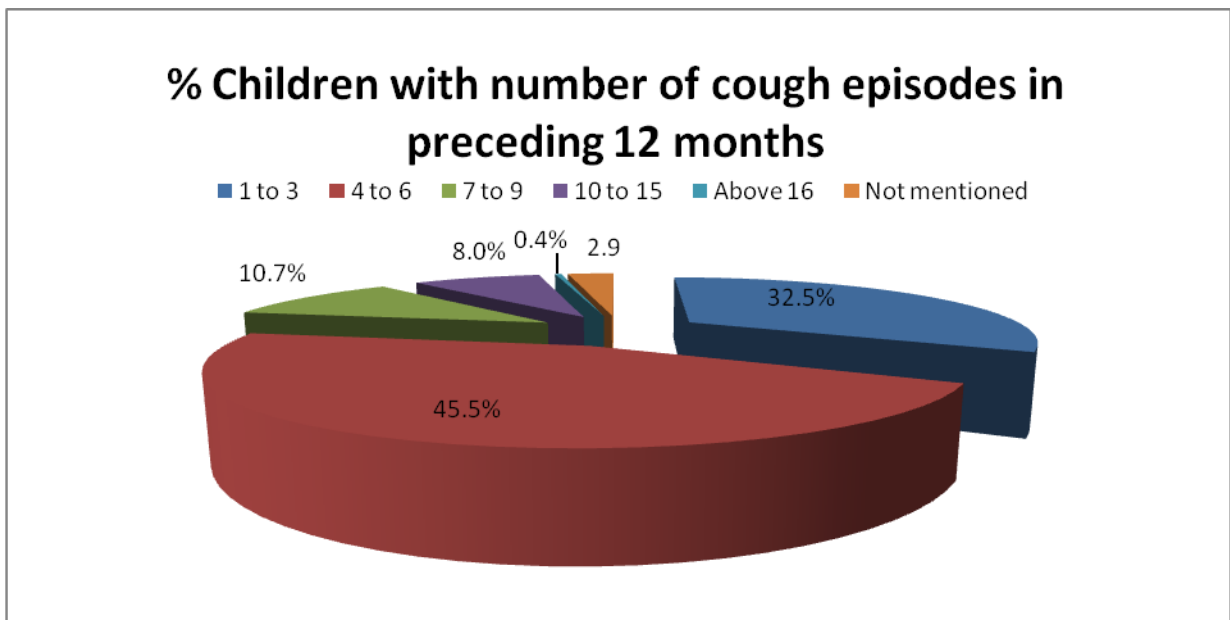


Figure 3: Distribution of children based on number of similar episodes of cough in preceding 12 months

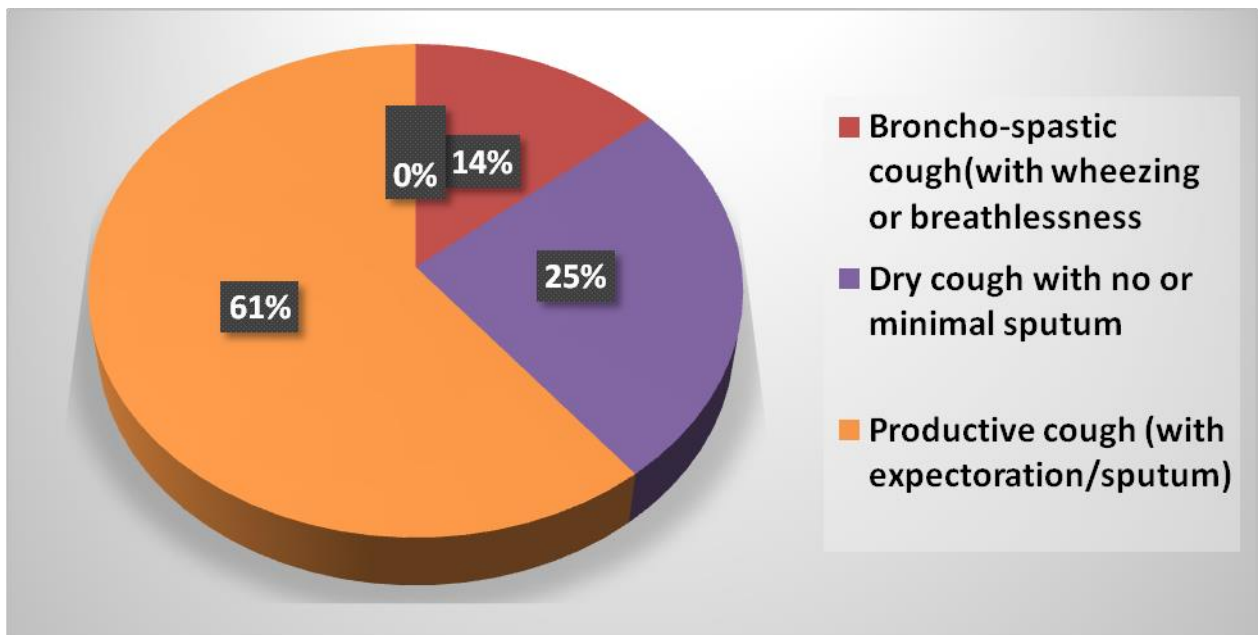


Figure 4: Distribution of children in percentage, based on different types of cough

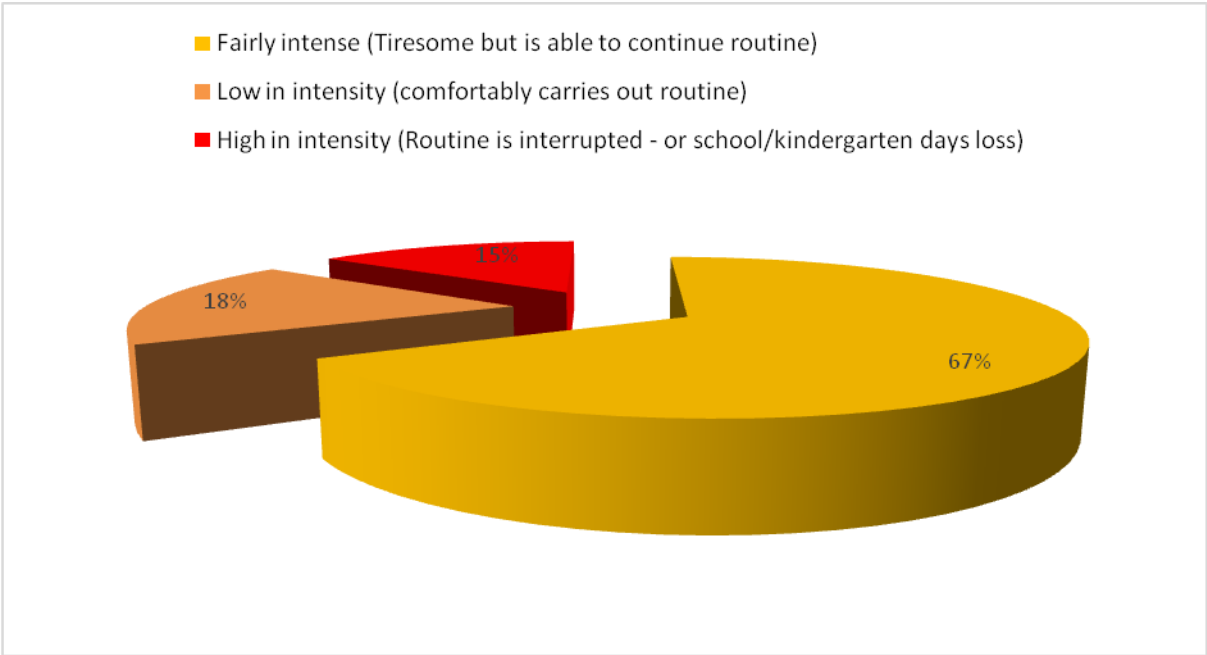


Figure 5: Percent distribution of children based on intensity of cough

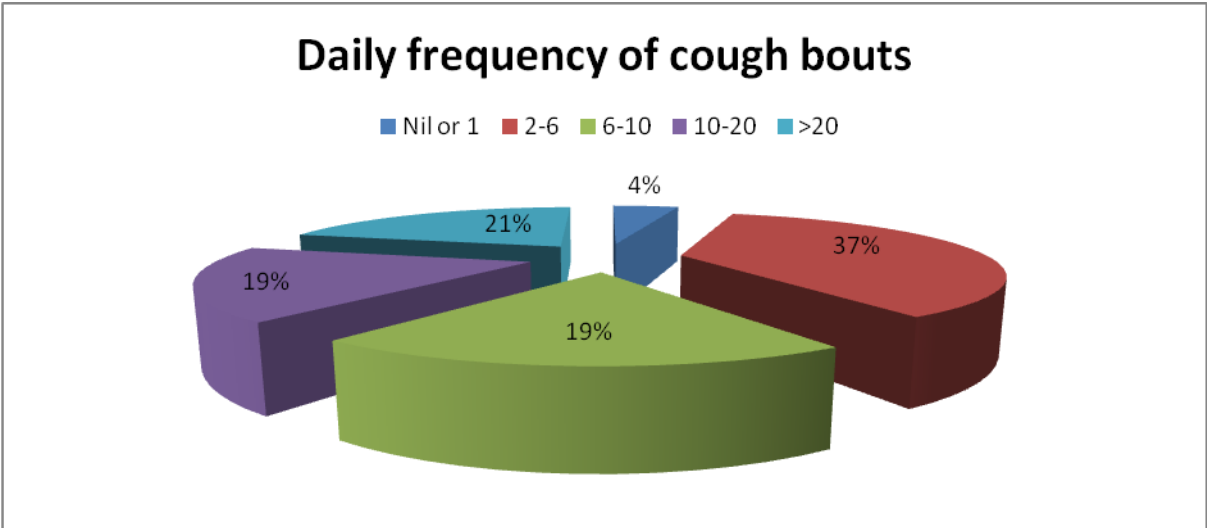


Figure 6: Percent distribution of children based on daily frequency of cough bouts

Associated symptoms

Fever (63%) was the most commonly reported associated symptom with their current cough episode. Other reported symptoms included running nose (53%), sore throat or throat pain (45%), nasal stuffiness (43%), sneezing (40%), headache (39%), sleep disturbance (including snoring) (37%), breathlessness (31%), hoarseness of voice (29%) and nasal irritation or itching (22%). 3% of the children also had fatigue, body ache and skin rashes during the cough episodes (Figure 7).

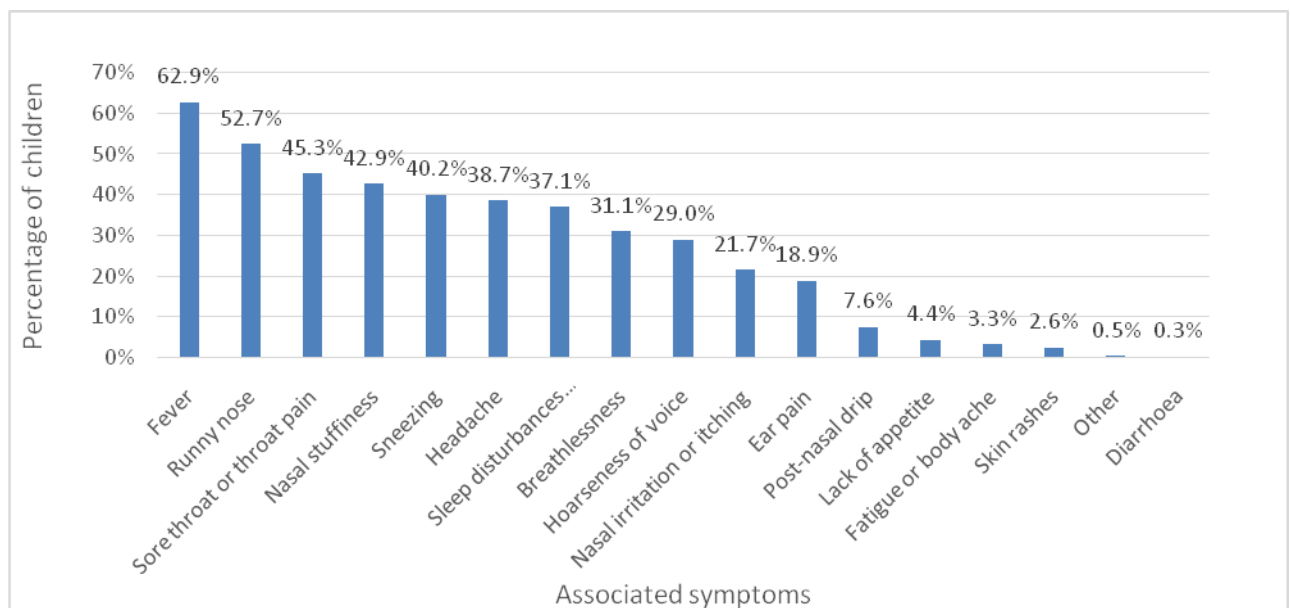


Figure 7: Percentage of children with associated symptoms in addition to cough

Presence of risk factors for precipitation of cough

Associated risk factors for precipitating present cough episode were conditioned/cold air (1%), intake of cold drinks (1%) and chilled water (2%); asthma (2%), malnutrition/ nutritional deficiency (4%) and season/ weather change (7%), reported in less than 10% of children. Exposure to smoking / pollution at home or school (23%), known or suspected immune deficiency

(19%) and allergic rhinitis (15%) were quite frequently associated for their current cough episode. 28% respondents were unaware about any risk factor associated for their current cough episode (Figure 8).

Concomitant medication

22% of the children were taking concomitant medications while remaining majority (78%) were not taking any other medication.

Practice of Self-medication

Although majority (74%) of children had no history of self-medication reported, 26% children were self-medicated for present or in past cough episode(s).

Adverse effects due to self-medication

Sleepiness was the most common adverse effect reported due to self-medication (45%; n=343). Dry mouth 29% (222), gastro intestinal upset 10% (80), lack of sleep 6%(49) and constipation in 7% (57) were other adverse effects reported due to self-medication (Figure 9).

Preference of Formulation

Syrup was preferred by 61% children whereas 13% preferred tablets by grown-up children.

Type of Medications Prescribed for Current Symptoms

78% children received first generation sedative antihistamines while 76% were prescribed second generation non-sedative antihistamines. Antibiotics (50%) and nutritional supplements (12%) were prescribed besides mucolytics (62%) and expectorants (63%) (Table 1). 78% of children were prescribed with

antitussives (61% dextromethorphan, 13% codeine). Majority of cases were prescribed antitussives up to 6 days (Figure 10).

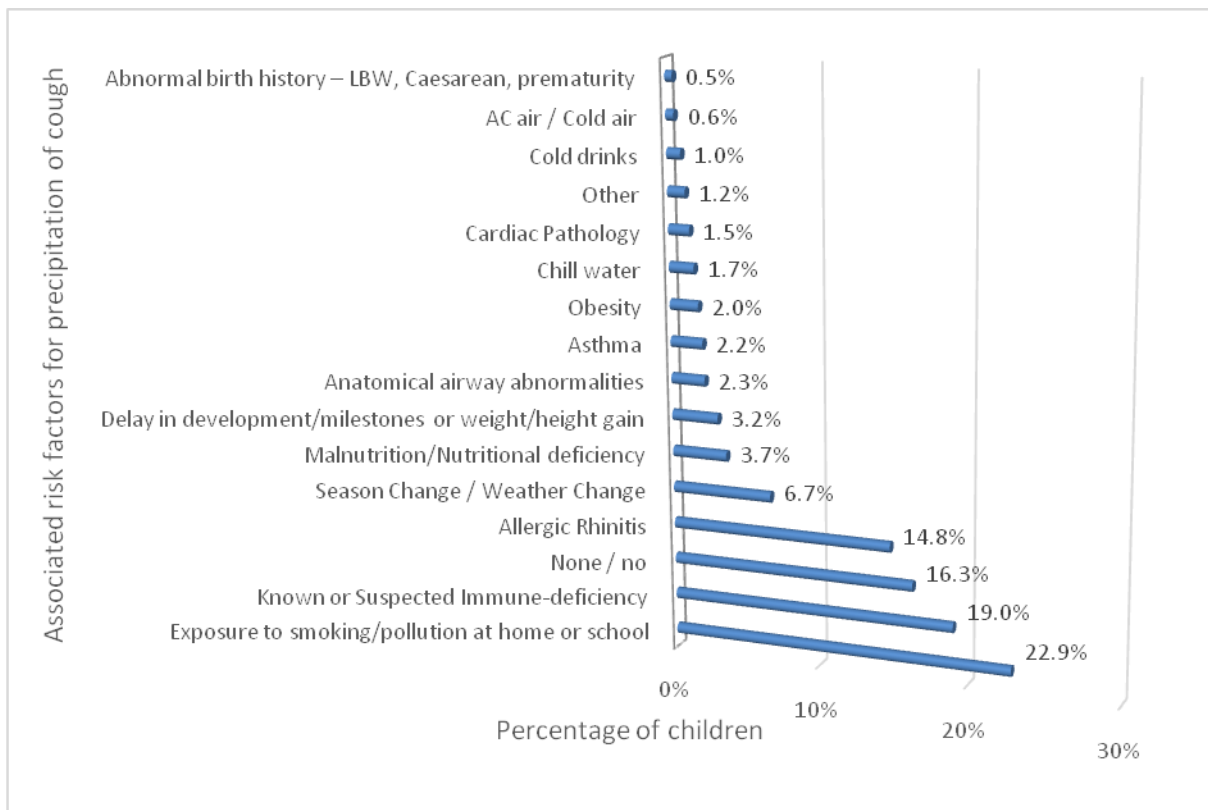


Figure 8: Percentage of children with associated risk factors for precipitation of cough

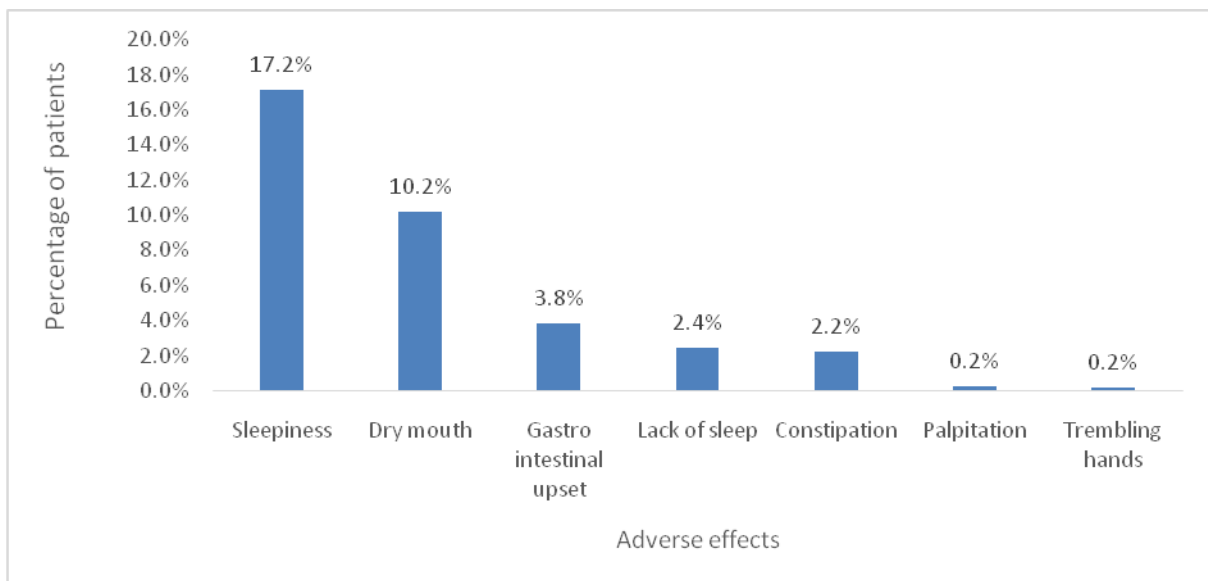


Figure 9: Adverse effects experienced due to self-medications

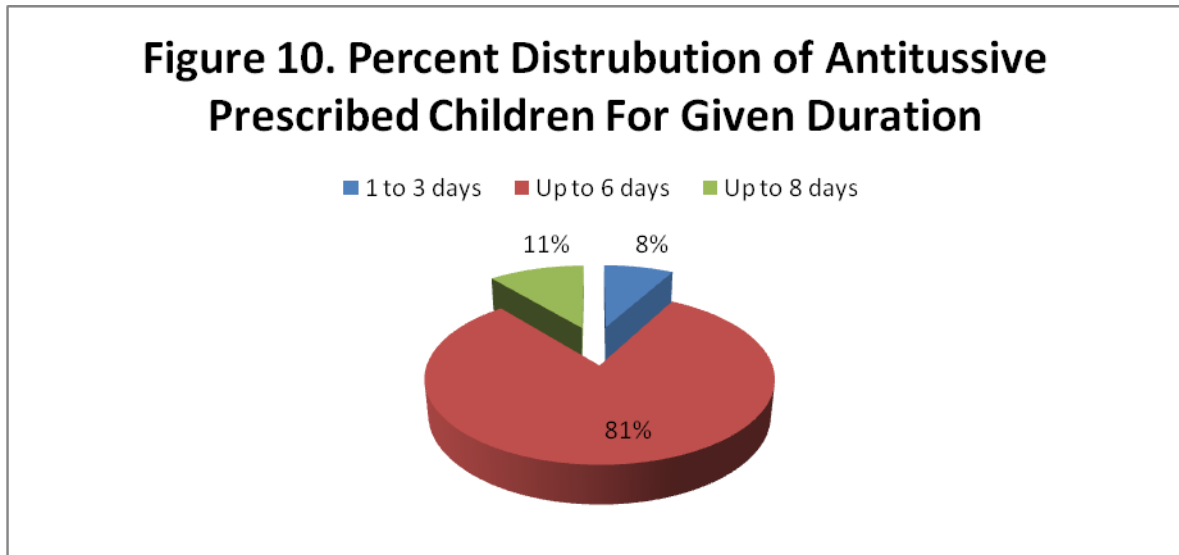


Table 1. Drugs and duration prescribed to the patient for the current cough episode

Classes of Drugs	% of total children (n)	Type of formulation prescribed (% total children*)	Distribution of children prescribed with respective drug for given duration		
			1-3 days, % (n)	Up to 6 days, % (n)	Upto 8 Days, % (n)
1 st generation antihistamines	78 (1558)	Syrup-78	20 (311)	70(1091)	10 (156)
2 nd generation antihistamines	76 (1518)	Syrup-76	30 (456)	40 (607)	30(455)
Mucolytics	62 (1239)	Syrup-62	10(124)	80(991)	10(124)

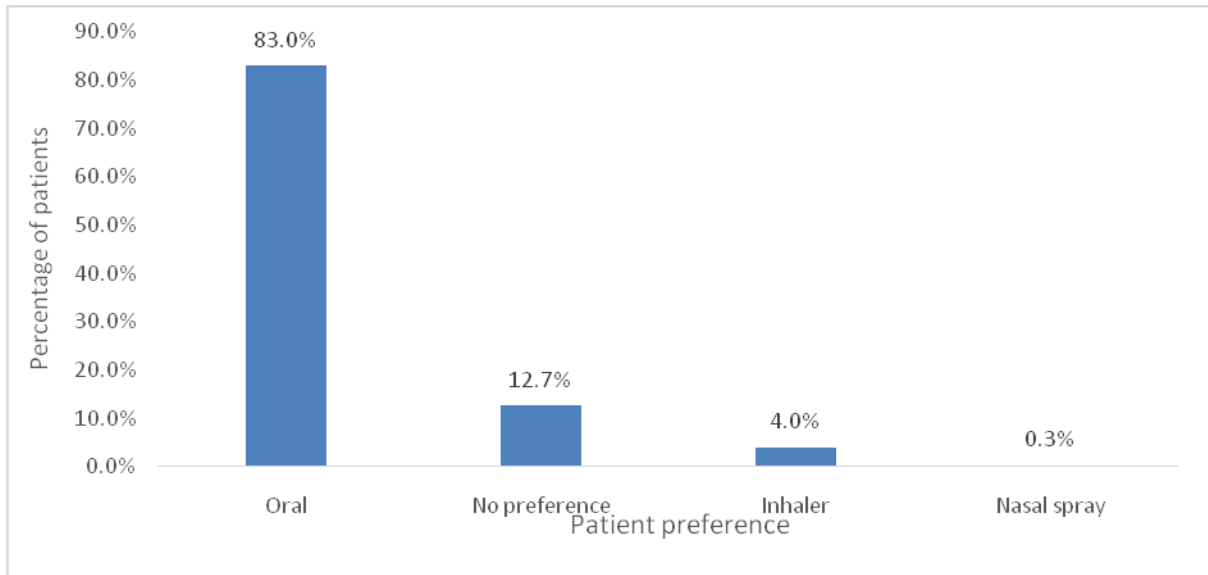
Expectorants	63 (1259)	Syrup-63	35(441)	45(566)	20(252)
Antipyretics/ NSAIDs	69 (1379)	Syrup-68 Tablet-1	30(418)	50(689)	20(276)
Antibiotics	51(1019)	Syrup-50 Tablet-1	50(499)	40(400)	10(100)
Nutritional supplements	13 (240)	Syrup-12 Tablet-1	5 (12)	40(96)	55(132)
Decongestants	50 (999)	Syrup-42 Nasal spray- 8	60 (599)	35 (350)	5 (50)
Antitussives	74	Dextrometho rphan- 61 Codeine- 13	8	81	11
Bronchodilato rs					
Terbutaline	16	Oral- 9 Inhaler- 7	89	8	3
Salbutamol	12	Oral- 5 Inhaler- 7	87	11	2
Levosalbutam ol	15	Oral- 6 Inhaler- 9	75	22	3

*Prescription distribution based on active ingredient mentioned for antitussives

Just 3% of children were prescribed with corticosteroids in the form of nasal spray. 80% of these children were prescribed for just 1-3 days while rest were

advised up to 6 days. (Table 1) Oral route was preferred in majority (83%) of cases (Figure 11).

Figure 11: Percent distribution of children based on preference for route of administration



Discussion

In this cross sectional questionnaire based survey across the country, children presenting with cough were screened and evaluated for different parameters. The survey provides information on important aspects like duration and type of cough, presence of risk factors, self-medication if any and associated adverse effects of drugs on children. The survey was conducted with help of 200 pediatricians from 6 cities across India.

Childhood acute respiratory infection (ARI) is a significant public health problem, especially in developing countries. In an Indian study²² on 397 school children in age group of 5-14 years, 52% of children presenting with acute respiratory infection (ARI) belonged to 5-9 years age group. In our survey, 40% children belonged to 3-6 years age group. An observational study by De Blasio et al⁷ also reported almost half of the children presenting acute cough in 1-5

year age-group. Children in this age group have various habits that promote easy transmission of infections. As such this is the age when children are introduced to out-of-home care and thus susceptible to infections because of lack of previous exposure to common infective organisms. Besides, there are physiological reasons like the immature immune system and dysfunctional eustachian tube predisposing them to upper airway infections¹⁷. Our present study affirms the fact that preschool and nursery age group children are more prone to infections than others.

Classification of cough based on the duration relies on available data related to URTI in children. Cough may continue for 10-25 days in children with common cold or viral respiratory tract infections². British Thoracic Society (BTS) guidelines defined acute cough as a recent onset of cough lasting less than 3 weeks²¹. Different guidelines label chronic cough as ranging from 3-12 weeks. 68% children in this survey had cough up to 5 days prior to their presentation to the OPD. 95% children in this survey can be considered as cases of acute cough since the duration of presentation of cough was less than 10 days. Children in an observational study⁷ showed mean duration of acute cough to be around 4-5 days, ranging from 2 to 21 days.

Acute respiratory infections usually produce 5 to 8 episodes of cough in a year in children; each lasting for 7 to 9 days. 45% Children in our survey reported 4 to 6 similar episodes of cough in preceding 12 months, suggesting underlying asthma or virus induced tracheo-bronchial hyper-reactivity states, more in winter months during which the study was conducted, that too, in the metropolitan cities where the pollution level is much higher.

Cough is usually categorised based on duration of cough rather than frequency. As such, two or more episodes of cough, without any history of viral URI (Coryza, cough and cold) in past one year considered as recurrent cough.

However, recurrent cough in short intervals, even with resolutions, cannot be easily differentiated from persistent chronic cough¹⁸. Thus, recurrent cough episodes seem to be quite prevalent in children in our country.

Children with cough is usually heterogenous, with varied risk factors and comorbid conditions³. Our study population was heterogenous in terms of age group and type of cough. Contrary to usual belief, wet and productive cough was commonly observed in our survey (61%) than dry 25% and bronchospastic cough (14%; n=270). Previous survey conducted by Narayanan et al¹⁶ reported dry cough (57%) more commonly than productive (40%) and bronchospastic (3%) cough. De Blasio et al reported dry cough as more common in their observational study in 433 children⁷. While the Indian study¹⁶ included majorly adult population, our survey was pediatric age specific under 12 years of age. However, there could be other factors in operation, leading to such differences. Environmental factors are supposed to affect the transmission of viral respiratory infections¹⁹. The survey by Narayanan¹⁶ was conducted in two different seasons, our present survey was mostly limited to winter season only when viral (RSV and others) infections are so common, with immune mediated cough. These aspects can be the reason for the observed variation. Despite these findings, the use of antitussives such as - dextromethorphan and codeine was found to be more prevalent (74%; n=1480) in our study. There is a need to understand that viral ARI always not confined to dry cough. Very often than not, the involvement of tracheo bronchial tree with immune mediated mucosal oedema, sticky secretions result in spasmodic and paroxysmal cough in a vicious cycle of vagal stimulation, not amounting to active broncospasm as in asthma. Higher incidence of wet and productive cough in our study conducted during inter months, may be attributable for this patho-physiology. Antitussives, particularly opioids are certainly not desirable. Plenty of fluid intake, frequent saline nose drops, a mild second generation decongestant are good enough with

or without a short course of bronchodilator if at all, in moderate to severe extent of cough. Steroids have no role to play.

De Blasio et al⁷ assessed the intensity of cough as mild, moderate and severe. Wide variation in intensity of cough from low to fairly intense severity was seen in our study, with moderate intensity being more common (58%). Although mild to moderate cough or low to fairly intense cough may not interfere with daily routine, parents might refrain from sending these kids to school, especially if associated with fever, to avoid increase in severity of symptoms as well as prevent spread of infection to other classmates. Cough and cold lead to missed school days for children which ultimately force missed office days for working parents who need to stay at home to care for children¹.

Majority of children in our survey had more than 6 cough bouts per day. 21% children were having even more than 20 cough bouts per day. This can be the reason for early consultation with pediatricians seen in the survey. The previous survey¹⁶ also reported similar results (More than 6 bouts-56%; More than 20 bouts-17%).

Children in our study reported different symptoms including fever, running nose, sore throat or throat pain, nasal stuffiness, sneezing, headache, sleep disturbance (including snoring), breathlessness, hoarseness of voice and nasal irritation or itching. Most of these symptoms are commonly seen with viral respiratory illnesses. Fever, cough and rhinorrhea are the most common symptoms seen with acute respiratory infections and were correspondingly frequent in our study population (fever 63%, rhinorrhea 53%)³. However, Suguna et al²² reported fever in 13.6% of school children with acute respiratory infections. Previous survey, majorly comprising of adults, by Narayanan et al also reported less frequent fever (12%).

There are several risk factors known to precipitate cough. Potts et al²⁰ assessed indoor risk factors for cough and found that tobacco smoke, poor ventilation, coal as cooking fuel, mold and dampness as important contributors. Association of malnutrition, younger age, low coverage of immunization, early childhood mismanagement and respiratory damage has been found to be significant risk factors in development of respiratory illness like pneumonia⁸. In the 5-9 years age group, family history of allergic disorder and asthma, presence of smoke outlet in kitchen, absence of windows in sleeping room are also found to have an independent association with the ARI. In our survey, exposure to smoking or pollution at home or school, known or suspected immune-deficiency and allergic rhinitis were identified as associated risk factors for cough in many children.

Although the effects of cough and cold are temporary, its high prevalence has remarkable bearing on quality of life and economic burden. The typical common cold management is usually through use of antihistamines, antitussives, mucolytics and decongestants. Many consumers are aware of risk of drug interactions of prescribed drug for other comorbid conditions and OTC cough and cold medicines¹¹. Fewer children (22%) in our survey were on concomitant medication leading to decreased chances of drug interaction with cough medication. The practice of self-medication was reported to be less (26%) in the surveyed population which is quite high. A study conducted by Ahmad et al to evaluate self-medication practice in India found that 11.7% of the study population was taking self-medication for respiratory disease. Among the self-medications, use of cough syrup containing antihistamines was common in our study. Sleepiness (45%) was the most common adverse event associated with self-medication followed by dry mouth (29%) which are well-known side effects of anti-histamines, especially first generation agents.

First generation 78% (1560) and second generation 76% (1520) usage of antihistaminics were found to be high. The data also reflects that some of the children were given both generation antihistaminic drugs together. Although, both first- and second-generation antihistamines are blockers of H₁-receptor sites, there is an additional pharmacological activity of the first-generation antihistamines as the competitive antagonism of acetylcholine at neuronal and neuromuscular muscarinic receptors. The effectiveness of first-generation antihistamines in reducing sneezing in colds is supposed to be due to neuropharmacological manipulation of histaminic and muscarinic receptors in the medulla¹⁵. That is why, the first-generation antihistamines are commonly used in cough formulations for prompt relief. But the resulting drowsiness, sticky secretions on bronchial mucosa are counterproductive. As the individual tries to dislodge these dried secretion inducing cough, the rebound vagus stimulation induces a vicious cycle of more and more cough and broncho spasm. The American Academy of Paediatrics stated that OTC medicines are generally safe only if used as per product labelling. AAP raised concerns on chances of increased risk of adverse effects due to usage of multiple multi-ingredient preparations having same active ingredient. Inappropriate dosing of cough and cold medications is another important concern¹². The cross sectional study reported 37% prevalence of multiple antihistamine use for upper respiratory infection in children less than 6 years of age. Practice of prescribing multiple histamines as reported in that study as well seen in the current survey pose a risk of increased adverse effects on children.

Acute respiratory infections are commonly associated with low-grade fever. The symptoms and signs of the common cold start with nasal stuffiness and throat irritation, usually accompanied by low-grade fever, anorexia and myalgia. Sneezing is associated with a watery nasal discharge, which becomes mucopurulent in 1 to 3 days; can persist for up to 10 days in many. Cough

occurs probably due to inflammation of the lower respiratory tract⁵. Antipyretic use was found common (69%) corresponding with high number of children with fever (63%) in our survey. Antibiotic use in childhood URTIs has always been an issue since more than 90% of such infections are of viral aetiology⁵. The same is highlighted in our study with half of the children being prescribed antibiotics albeit for short duration (3 to 6 days) in the majority prescribed. Short courses of decongestants were also commonly seen in 42% of children.

Despite greater number of children reported with wet and productive cough, albeit with scanty expectoration, use of antitussives was paradoxically higher (74%) in our study. This shows wide variation from management protocols and guidelines in clinical practice. Use of dextromethorphan was found to be more common as compared to codeine which is in line with its expected advantages⁷.

More than half of our children preferred syrup over tablet which was quite obvious considering the surveyed age group. The preference can be attributed to swallowing ease and soothing effect of syrups in younger children.

The current survey provides significant insights into patient profile of acute cough among children and its management. Large sample size and enrolment of patients from different regions of the country are the strengths of this study.

Conclusion:

Acute onset and recurrent nature of cough is a common observation in pediatric age group. Exposure to environmental pollutants both at home and school seems to be an important risk factor. Cough in children is often associated with expectoration or sputum production, albeit scanty, contrary to our belief. Grown-up children are able to bring out sputum better while younger ones usually swallow it down, Fever, runny nose and sore throat are the most commonly associated symptoms along with pediatric cough. Decongestants,

antitussives, opioids, antihistamines, expectorants and mucolytics are commonly prescribed by pediatricians for management of cough in children, not always as per guidelines. Prescription of multiple antihistamines needs to be discouraged and awareness is required in treating physicians about risk of drug toxicities when prescribing multiple multi-combination preparations. Self-medication may be harmful for children about which public awareness drives are welcome.

Role of Authors:

Dr H. Paramesh: Concept and study design, Dr. N. C. Mohanty: Study design, Data interpretation, manuscript writing, Dr. V. Kamale: Data analysis and final editing, Dr. V. Patra: Monitoring data collection, first editing, Dr. R. Jain: Dr. R. Jain: Administration, supervision and manuscript writing, Dr. G. Pappulwar: Co-ordination between study centres and manuscript writing, Dr. R. Rathod: Data collection, Tables, figures and manuscript writing.

Conflict of Interest: None

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ORIGINAL RESEARCH:

Clinical Profile and Short Term Outcome Of Neonates Requiring Assisted Mechanical Ventilation

*Prajakta Dekate *, Sachin Damke**, Revat Meshram****

*Post-graduate Student, **Professor & Head, ***Associate Professor

Department of Paediatrics, JNMC, Acharya Vinoba Bhave Rural Hospital, Sawangi, Wardha, Maharashtra, India

Corresponding Author –Dr. Sachin Damke, Professor & Head Department of Paediatrics, JNMC, Acharya Vinoba Bhave Rural Hospital, Sawangi, Wardha, Maharashtra, India

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Abstract: *Assisted ventilation has become an indispensable part of the neonatal intensive care. It is helpful to reduce the high mortality in this group of neonates and identification of risk factors is important.*

Objectives: *To assess the current status of neonatal ventilation in a tertiary care neonatal unit in a rural hospital in central India, to identify the common indications for ventilation, analyze the complications that arise, and evaluate the short term outcome as measured by survival.*

Design: *Hospital based prospective observational study*

Setting and participants: *conducted on neonates who required mechanical ventilation over period of 2 years (1st September 2015 – 31st August 2017).*

Materials and methods: Neonates requiring mechanical ventilation during the study period of 2 years (1st September 2015 – 31st August 2017) were enrolled in the study.

Neonates who received mechanical ventilation for minimum of 6 hours during the study period were included in the study after written informed consent from parents. Babies who expired within 6 hours of life, neonates with birth weight < 500 grams, abrupt termination of ventilator support for any reason and gestational age <26 weeks were excluded.

Results: 206 neonates were included in the study. Males comprised of 56.8% of ventilated neonates. The most common indication of ventilation was birth asphyxia, in 29.1% neonates, followed by neonatal sepsis (22.3%), respiratory distress syndrome (18.4%), and meconium aspiration syndrome (13.1%). Complications were seen in 35.9% neonates, the most common complication was ventilator associated pneumonia (50%), sepsis (40.5%), pneumothorax (16.2%). Survival rate among the ventilated neonates was 45.6%.

Conclusion: Neonates with birth asphyxia and sepsis were the major problems in NICU, which must be addressed to improve outcome.

KEYWORDS: Neonates, mechanical ventilation

INTRODUCTION: Neonatal deaths account for nearly 64% of all infant deaths and 50% of under-five mortality in India. Birth asphyxia, congenital pneumonia, immaturity, hyaline membrane disease, intraventricular haemorrhage, and neonatal infections are leading causes of neonatal mortality in our country⁽¹⁾. Many critically sick babies, who develop life-threatening apnoea or cardiovascular collapse from a variety of causes, need cardiopulmonary resuscitation^(2,3). Assisted ventilation has become an indispensable part of the neonatal intensive care⁽¹⁾. Infants with progressive respiratory distress with impending respiratory failure can be supported and saved by assisted ventilation facilities^(2,3).

Since its introduction into the modern ICUs, mechanical ventilation has undergone continuous evolution. Epidemiologic and environmental factors in

the ICU are important to critical care because they can affect care and mortality (4,5).

OBJECTIVES: To assess the current status of neonatal ventilation in a tertiary care neonatal unit in a rural hospital in central India, to identify the common indications for ventilation, analyze the complications that arise, and evaluate the short term outcome as measured by survival.

Design: Hospital based prospective observational study

Setting and participants: Conducted on neonates who required mechanical ventilation over period of 2 years (1st September 2015 – 31st August 2017).

MATERIAL AND METHODS: This prospective observational study was conducted in a tertiary care hospital, attached to a medical college and neonates requiring mechanical ventilation during the study period of 2 years (1st September 2015 – 31st August 2017) were enrolled in the study.

Neonates who received mechanical ventilation for minimum of 6 hours during the study period were included in the study after written informed consent from parents. Babies who expired within 6 hours of life, neonates with birth weight < 500 grams, abrupt termination of ventilator support for any reason and gestational age <26 weeks were excluded.

The babies were managed as per prevailing protocol. The required data was obtained and entered in a predesigned validated proforma.

Statistical analysis: The results obtained were tabulated and analysed and using the chi square test and multiple logistic regression, p value was calculated. The results were tested at 5% level of significance.

OBSERVATION & RESULTS: We included 206 neonates who were mechanically ventilated and fulfilled the inclusion criteria. Of these, males were 117 (56.8%) and females were 89 (43.2%). 96 (46.6%) neonates were full term

and 110 (53.4%) were preterm. 50 neonates (24.3%) had normal weight i.e. >2.5kg; while 156 (75.7%) were low birth weight babies (Table 1)

Table 1: Distribution of neonates based on birth weight:

Birth Weight (Kg)	Total Number	Percentage (%)
<1	39	18.9%
<1.5	19	9.2%
1.5-2.5	98	47.6%
>2.5	50	24.3%
Total	206	100%

The common indications of ventilation observed are given in table 2, the most common being birth asphyxia, reported in 62 neonates (30.1%). Of the 40 neonates with RDS, 26 were male (65%) while 14 were females (35%).

Table 2: Indication (cause) of ventilation:

Sr. No.	Indication	Total No.	Percentage
1.	Birth asphyxia	62	30.1%
2.	Neonatal sepsis	44	21.4%
3.	Respiratory distress syndrome	40	19.4%
4.	Meconium aspiration syndrome	25	12.1%
5.	Apnea of prematurity	10	04.9%
6.	Persistent pulmonary hypertension of newborn	7	3.4%
7.	Congestive heart failure	5	2.4%
8.	Meningitis	6	02.9%
9.	Tracheo-esophageal fistula	4	1.9%
10.	Congenital diaphragmatic hernia	3	1.5%
	Total	206	100%

Table 3: Ventilation parameters in survivors and non-survivors:

Sr.No	Parameter	Mean(Range)	
		Survivors	Non-survivors
1	PIP(cm of H ₂ O)	13.48(10-18)	15.10(10-24)
2	PEEP(cm of H ₂ O)	6.35(5-9)	7.86(5-16)
3	Rate(/min)	38.07(30-44)	40.46(32-50)
4	FiO ₂	0.67(0.3-1)	0.90(0.4-1)
5	Tidal volume(ml/kg)	7.51(6-10)	9.26(7-10)

Ventilator parameters between survivors and non-survivors were compared in this study. Less ventilator pressures were required among the group of survivors while the requirement of pressures and the other ventilatory settings were increased among those of non-survivors (Table 3). Ninety four (43.6%) neonates were successfully weaned; SIMV with PS was the preferred mode in 53 (56.4%) neonates. Complications were seen in 74 (35.9%) neonates, the most common being ventilator associated pneumonia (Table 4)

Table 4: Neonates with complications of mechanical ventilation:

Sr. No.	Complication	No. of patients	Percentage of total babies ventilated (n=206)
1.	Ventilator associated pneumonia.	37	17.8%
2.	Sepsis	30	14.6%
3.	Pneumothorax	12	05.9%
4.	Pulmonary hemorrhage	7	3.4% %
	Total (n= 206)	74	35.9%

Out of total 206 neonates, we could salvage 94 neonates (45.6%). Of the 39 ELBW babies, only 5 neonates (12.8%) could be salvaged, whereas of the 50 normal birth weight babies, 32 could be salvaged (64%). Thus survival rate is fairly rising with increasing weight of the neonate.

Table 5: Predictors of survival:

Parameters	Value	Total	Survival	P value
Birth Weight	<2.5kg	148	62	0.0033
Gestation	Preterm	110	34	0.0011
Inotropes	Yes	168	70	0.0193
Acidosis (pH<7.2)	Yes	112	30	0.0001
Sex	Male	117	48	0.1580
IUGR	Yes	18	7	0.6257
Asphyxia	Yes	62	30	0.6487
Sepsis	Yes	44	20	1.0000
HMD/RDS	Yes	40	18	1.0000
Blood Products	Yes	84	36	0.5698
Blood Culture	Positive	46	24	0.3197

Using logistic regression, the predictors of survival were birth weight >2.5kg, term gestation, ventilated babies not requiring inotropes and acidosis with $\text{pH} < 7.2$.

DISCUSSION : Assisted ventilation is one of the most important advancement in neonatal medicine which has reduced neonatal mortality considerably. Shah et al⁽⁶⁾ 2013 conducted a similar study in eastern Nepal, and found that birth asphyxia (34%) and sepsis (30.8%), were the most common indications as seen in our study. Mannan et al also concluded asphyxia as the most common indication. While Srinivas et al⁽⁷⁾ conducted a retrospective study at Mangalore and found that, respiratory distress syndrome and neonatal sepsis were the most common indications for ventilation. Similarly, Krishnan et al concluded sepsis as the most common indication.

In a study done by Acharya et al⁽⁸⁾ in tertiary care hospital, Hyderabad, septicemia was the most common complication, followed by air leak, tube block and weaning failure.

Maiyya et al⁽⁹⁾ and Mannan et al⁽¹⁰⁾ had VAP as the most common complications as seen in present study. While Prabha et al⁽¹¹⁾, Bhatt et al⁽¹²⁾, and Singh et al⁽¹³⁾ and Mathur et al⁽¹⁴⁾ had sepsis as their most common complications. In the study by Jahan et al⁽¹⁵⁾ at Bangladesh,, pneumonia & pneumothorax were the common complications of mechanical ventilation followed by neonatal sepsis and pulmonary hemorrhage.

Similar to our study, Sangita et al⁽¹⁶⁾ conducted a study at Surat and had higher mortality. Similarly, Srinivas et al⁽⁷⁾ Iqbal et al⁽¹⁷⁾, Singh et al⁽¹³⁾, also had higher mortalities. Most of the studies had heigher mortality, however, Hossain et al⁽¹⁸⁾ and Mathur et al⁽¹⁴⁾ had 29.4% and 26% mortality respectively.

In our study, the factors such as weight <2.5kg, prematurity and acidosis ($\text{pH} < 7.2$), significantly affected the outcome of neonates. In the study done by Acharya et al⁽⁸⁾, no significant association was observed between birth weight or gestational age and survival rates. He also observed that survival was highest

for neonates ventilated for hyaline membrane disease (34.3%), followed by meconium aspiration (17.1%). In the study by Iqbal et al⁽¹⁷⁾, apnea and sepsis significantly affected the outcome of the patient. In a study done in Eastern U.P⁽²⁰⁾, it was observed that survival was worst in babies weighing < 1.5 kg(40%) and those < 32 wk of gestation(36%).

CONCLUSION: Majority of the neonates on mechanical ventilator were secondary to birth Asphyxia, neonatal sepsis, respiratory distress syndrome and meconium aspiration syndrome. Complications during the course of mechanical ventilation included ventilator associated pneumonia, sepsis, pneumothorax and atelectasis. Survival rate of the neonates who were mechanically ventilated was 45.6%. Most common weaning mode used in this study was SIMV with pressure support, followed CPAP with pressure support.

DECLARATIONS:

Contributors: - **Sachin Damke** - Determination of study design and methodology, **Prajakta Dekat** -collection of data e analysis of the collected data, literature search and preparation of manuscript. **Revat Meshram**- Conceptualization, and revision of the manuscript

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ORIGINAL RESEARCH:

Neurological outcome of neonates undergoing exchange transfusion for hyperbilirubinemia: a study in tertiary care centre in Bihar

Kumar Arpit*, **Alka Singh****, **S. R. Choudhary*****

*Senior Resident, Dept of Paediatrics, Nalanda Medical College Hospital, Patna

**Professor of Pediatrics, Nalanda Medical College and Hospital, Patna

***Professor of Pediatrics, Rohilkhand Medical College and Hospital, Bareilly

Corresponding author: Dr. Alka Singh, e mail id: dralka24@yahoo.in, mob no: 9835217017

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Abstract: Background: Jaundice is one of the most common conditions requiring medical attention in newborn babies. Exchange transfusion is standard method of therapy for immediate treatment of severe hyperbilirubinemia and prevention of kernicterus. As bilirubin is removed from plasma, extra vascular bilirubin equilibrates and binds to albumin in exchanged blood. Within half hour of exchange transfusion bilirubin level returns to 60% of pre exchange level. Guidelines for the implementation of phototherapy and exchange transfusion rely on evidence-based estimates of when the benefit of these interventions exceeded their risks and costs. **Material and methods:** The following study is a prospective study carried out in Hospital for Children and Upgraded Department of Paediatrics, PMCH, Patna. Neonates who underwent exchange transfusion for neonatal hyperbilirubinemia from August 2011 to September 2012 in NICU were included in study. **Result:** In this study most common cause of hyperbilirubinemia requiring exchange transfusion was ABO incompatibility i.e 42.86%, (n=15). Rh incompatibility constituted 22.85% of cases (n=8). In remaining 34.29% cases (n=12) no specific cause could be found. Immediate complications were seen in 7 out of 35 cases (20%). all cases were followed till age of 12 months, at 6 months follow up, out of 34 cases 4(11.76%) showed gross motor and fine motor delay while language and social personal delay was seen in 2(5.88%) and 3(8.82%) respectively. At 12 months follow up out of remaining 32 cases (3 were lost to follow up) 4 cases (12.5%) showed delay in developmental milestones. **Conclusion:** Two most

common cause for hyperbilirubinemia needing exchange transfusion are ABO incompatibility (42.86%) and Rh incompatibility (22.85%). In about 34.29% of cases exact cause could not be found out. Pre exchange bilirubin values strongly correlated with persistent BERA changes (p value < 0.005).

KEY WORDS: *Exchange transfusion, Neonatal hyperbilirubinemia, Kernicterus, Rh incompatibility.*

INTRODUCTION: Jaundice is one of the most common conditions requiring medical attention in newborn babies. Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life, and about 10% of breastfed babies are still jaundiced at 1 month of age.

Kaplan and associates⁷ demonstrated that an imbalance between bilirubin production and conjugation is fundamental in the pathogenesis of neonatal bilirubinemia.

Bilirubin inhibits mitochondrial enzymes, interferes with DNA and protein synthesis⁶, and alters cerebral glucose metabolism⁴. Unconjugated bilirubin initiates a mitochondrial pathway of apoptosis in developing brain neurons⁸ and it inhibits the function of N methyl-aspartate-receptor ion channels⁵.

The region most commonly affected are the basal ganglia, particularly the subthalamic nucleus and the globus pallidus, the hippocampus, the geniculate bodies, various brainstem nuclei, including the inferior colliculus, oculomotor, vestibular, cochlear, and inferior olivary nuclei, and the cerebellum especially the dentate nucleus and the vermis².

Exchange transfusion is standard method of therapy for immediate treatment of severe hyperbilirubinemia and prevention of kernicterus. Exchange transfusion removes partially hemolysed and antibody coated RBCs as well as unattached antibodies and replaces them with donor RBCs lacking sensitising antigen. As bilirubin is removed from plasma, extra vascular bilirubin equilibrates and binds to albumin in exchanged blood. Within half hour of exchange transfusion bilirubin level returns to 60% of pre exchange level.

Exchange transfusion is generally initiated¹

- 1) When phototherapy fails to prevent rise in bilirubin to toxic levels
- 2) To correct anaemia and improve heart failure in hydropic infants with haemolytic disease.
- 3) To stop haemolysis and bilirubin production by removing antibody and sensitized RBCs.

4) In haemolytic disease, immediate exchange is needed when:-

- Cord bilirubin level $>4.5\text{mg/dl}$ and cord haemoglobin level $<11\text{g/dl}$.
- Bilirubin level is rising $>1\text{mg/dl}$ despite phototherapy
- Haemoglobin level is between 11g/dl and 13g/dl , and bilirubin level is rising $>0.5\text{mg/dl}$ despite phototherapy.
- Bilirubin level is 20mg/dl or appears to reach 20mg/dl at the rate it is rising
- There is progression of anaemia in face of adequate control of bilirubin by other methods.

The bilirubin level at which intervention is necessary is still a contentious issue. Various study groups had proposed guidelines regarding initiation of exchange transfusion. Guidelines for the implementation of phototherapy and exchange transfusion rely on evidence-based estimates of when the benefit of these interventions exceeded their risks and costs. Ideally, these estimates should come from randomized trials or high quality, systematic observational studies but such studies are rare. Thus, treatment guidelines must rely on relatively uncertain estimates of risks and benefits and the recognition that using a single TSB level to predict long-term behavioural and developmental outcomes is not reliable and will lead to conflicting results.

Design: Prospective cohort study

Setting: Carried out in Hospital for Children and Upgraded Department of Paediatrics, PMCH, Patna.

Participants: 35 newborns with exchange transfusion were followed for 12 months

MATERIALS AND METHODS: Neonates who underwent exchange transfusion for neonatal hyperbilirubinemia from August 2011 to September 2012 in NICU were included in study. Medical records of patients were reviewed and data was recorded through proper history taking, clinical methods, laboratory investigations and one year follow up. All neonates with bilirubin level compatible with levels for which exchange transfusion is indicated according to AAP nomogram were included in study. Neonates undergoing exchange transfusion due to causes other than hyperbilirubinemia were not included in study, like exchange in cases of:-

a) neonatal polycythemia

b) severe anaemia

c) neonatal sepsis

In this study, isovolaemic double volume fresh whole blood (within 7 days) was used. Exchange was done with neonate under radiant warmer and cardiac and BP monitoring in place. Umbilical vein catheterisation was done under aseptic conditions. Exchange was done with push pull technique. Removal and infusion of blood was done according to standard published guidelines with intermittent infusion of calcium. CBC, serum bilirubin levels, electrolytes, glucose were measured after exchange.

Follow up: - All infants who were included in study were followed at regular interval upto 12 months of age. BERA was done at 3 months of age, follow up and assessment during later period (6 months and 12 months) was done in terms of attainment of neurodevelopmental milestone under following headings:-

- Gross motor
- Fine motor
- Social personal
- Language

OBSERVATION AND RESULTS: In this study amongst 35 cases 18 (51.4%) were male and 17 (48.6%) were female. Majority (80%) of babies in this study were term (n=28), preterm (n=7) constituted only 20% of total cases. In this study most common cause of hyperbilirubinemia requiring exchange transfusion was ABO incompatibility i.e 42.86%, (n=15). Rh incompatibility constituted 22.85% of cases (n=8). In remaining 34.29% cases (n=12) no specific cause could be found. Out of 35 cases most of babies had pre exchange bilirubin level between 20.1-25.0 mg/dl (n=18; 51.43%).remaining 17 were clustered in 15.0-20.0 mg/dl (n=5; 14.29%), 25.1-30.0 mg/dl (n=6; 17.14%) and 30.1-35.0 mg/dl (n=6; 17.14%) respectively. Mean pre exchange bilirubin value was 24.53 ± 4.34 mg/dl as compared to post exchange value which was 13.68 ± 3.44 mg/dl. None of the cases underwent second exchange transfusion in this study.

OUTCOME ON FOLLOW UP: In this study follow up of neonates who underwent exchange transfusion was done for 12 months. At 3 months BERA was done to look for any residual effect of hyperbilirubinemia. Out of 35 cases 4 cases were lost to follow up, 1 at 6 months and rest 3 at 12 months. At 3 month follow up 4 cases (11.43%) showed abnormal BERA records and on further follow up all of these cases showed abnormal development.

Table 1-

Pre exchange bilirubin level(mg/dl)	Affected	Not affected	Total
≤25.0	0	23	23
25.1-30.0	1	05	06
≥30.1	3	03	06

On analysis of data it was found that residual defect at 3 month of life suggested by abnormal BERA was in correlation with initial bilirubin level (p value< 0.005)

Out of 4 cases with abnormal BERA readings 1 had absent waveform, 1 had prolonged latencies III and other 2 showed prolonged latencies V.

Table 2- **BERA findings:**

BERA changes	Cases
Absent wave form	1
Raised threshold	0
Prolonged latencies I	0
Prolonged latencies III	1
Prolonged latencies V	2
Prolonged interpeak	0

Interval I-III	
Prolonged interpeak Interval III-V	0
Prolonged interpeak Interval I-V	0

Table 3-Outcome based on follow up at 6 & 12 months

Duration	Normal	NDD	Attrition
6 months	30	4	1
12 months	28	4	3

In this study all cases were evaluated at 6 and 12 months for residual defects attributed to hyperbilirubinemia. Out of total 35 cases 3 were lost to follow up (1 at 6 months and remaining 2 at 12 months). Out of remaining cases only 4 cases (11.43%) showed neurodevelopmental delay in terms of attainment of milestones of development

Table-4 Pattern of attainment of milestones in cases

Milestones	6 months		12 months	
	normal	abnormal	normal	abnormal
Gross motor	30(88.24%)	4(11.76%)	28(87.5%)	4(12.5%)
Fine motor	30(88.24%)	4(11.76%)	28(87.5%)	4(12.5%)
Language	32(94.12%)	2(05.88%)	28(87.5%)	4(12.5%)

Social personal	31(91.18%)	3(08.82%)	28(87.5%)	4(12.5%)
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In this study all cases were followed till age of 12 months, at 6 months follow up, out of 34 cases 4(11.76%) showed gross motor and fine motor delay while language and social personal delay was seen in 2(5.88%) and 3(8.82%) respectively.

At 12 months follow up out of remaining 32 cases (3 were lost to follow up) 4 cases (12.5%) showed delay in developmental milestones.

Discussion : In present study sample size was of 35 neonates with hyperbilirubinemia. This was comparable to sample size of Salas AA¹⁴ et al (n=56), Spada A⁴ et al (n=57), and Patra K⁸ et al (n=55).

In this study most common cause of hyperbilirubinemia requiring exchange transfusion was ABO incompatibility i.e 42.86%, (n=15). Rh incompatibility constituted 22.85% of cases (n=8). In remaining 34.29% cases (n=12) no specific cause could be found. It is mainly due to lack of investigations in our resource limited setting. This was comparable to that of studies carried out by Hosseinpour Sakha¹² et al where also most common cause was ABO incompatibility (49.3%), Badiie Z¹³ in a similar work also concluded that most common cause of hyperbilirubinemia requiring exchange transfusion was ABO incompatibility, though it constituted 22.1% of cases. Dikshit SK³ et al also had comparable results regarding cause of exchange transfusion i.e ABO incompatibility being most common followed by Rh incompatibility.

In this study mean pre exchange bilirubin value was 24.53 ± 4.34 mg/dl as compared to post exchange value which was 13.68 ± 3.44 mg/dl. None of the cases underwent second exchange transfusion in this study. 51.43% of cases had bilirubin level between 20.1-25.0 mg/dl (n=18). Similar study by Hosseinpour Sakha S¹² et al showed mean pre exchange bilirubin value of 29.59 ± 6.88 mg/dl. Salas AA¹⁴ et al found mean pre exchange bilirubin value of 31.1 mg/d, this explains higher incidence of bilirubin encephalopathy in his study.

In this study all cases were followed for 12 months to study adverse effects associated with hyperbilirubinemia and exchange transfusion. BERA was done at 3 month of age. Remaining follow up was done on clinical basis due to resource limitations. Out of 35 cases 4 were lost to follow up, 1 at 6 month and rest 3 at 12 month. At 3 month follow up 4 cases (11.43%) showed abnormal BERA records and on further follow up all of these cases showed abnormal development. It is comparable to study of Agrawal et al in which 10% of cases (n=30) had persistent BERA changes on follow up. Sharma et al¹⁰ found

persistent abnormal BERA records in 16.7% of cases (n=30), where as Bhandari¹¹ et al, Deorari⁹ et al, Gupta et al found no cases with abnormal BERA record on follow up indicating transient nature of bilirubin encephalopathy. In this study there was significant correlation between serum bilirubin value and persistent BERA changes ($\chi^2=12.053$; p value < 0.005) indicating that higher the bilirubin value greater is the risk of damage to auditory pathway. Study of Bhandari¹¹ et al found no correlation between serum bilirubin value and persistent BERA changes. Whereas studies of Sharma¹⁰ et al, Deorari⁹ et al, Gupta et al also showed correlation between bilirubin level >25 mg/dl and BERA changes.

Summary and conclusion : Two most common causes for hyperbilirubinemia needing exchange transfusion are ABO incompatibility (42.86%) and Rh incompatibility (22.85%). In about 34.29% of cases exact cause could not be found out. It can partly be attributed to resource limited settings in our scenario. Mean day of commencement of exchange transfusion in this study was 4.9. This delay reflects lack of early recognition of problem and scope of improvement in peripheral hospitals regarding early diagnosis of problem. Most of neonates who underwent exchange transfusion had potentially life threatening level of serum bilirubin before exchange, but on follow up only 4 of them showed persistent abnormalities in BERA, rest were normal. This strengthens the fact that exchange transfusion is very effective in rapidly reducing serum bilirubin value and in preventing kernicterus. Pre exchange bilirubin values strongly correlated with persistent BERA changes (p value<0.005), this shows that early intervention and regular monitoring are key in preventing kernicterus and permanent damage due to bilirubin encephalopathy.

DECLARATIONS:

Contributors: - *Kumar Arpit* - Collection of data and Analysis of the collected data, Preparation of manuscript *Alka Singh* -Concept, Guidance,Literature review *S. R. Choudhary* - Study design and Methodology, Revision of the manuscript

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ORIGINAL RESEARCH:

Hand hygiene compliance and efficacy of a multimodal intervention strategy in improving hand hygiene compliance in a tertiary level pediatric intensive care unit

*Sham B. Lohiya**, *R. Rameshkumar***, *Jayanta Vagha****

*Assistant Professor , **Associate professor Pediatrics J.N.M.C. Sawangi. Pediatrics, J.I.P.ME.R. Pondicherry. ***Senior Professor Pediatrics J.N.M.C., Sawangi.

Place of study- PICU, JIPMER Pondicherry.

Address for correspondence. - Dr. Sham b. Lohiya Dept. of pediatrics, 3rd floor A.V.B.R.H. Sawangi.Email- sham.lohiya19@gmail.com Mob number- 8098842537.

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ABSTRACT-: Objective of study was to assess the hand hygiene compliance in health care personnel before and after hand hygiene education and effect of change in hand hygiene compliance on rate of hospital acquired infections.

It is an observational analytical study.

Study was carried out on medical and paramedical staff working or visiting to PICU over a period of 4 months from March 2015 to June 2015.

Surveillance was done by CCTV camera recordings. Two weekly classes on hand hygiene and its importance in PICU were taken by the principal investigator

Total opportunities for HH observed during video surveillance were 10519, out of which 5953 opportunities were used with total compliance of 56%. Hand hygiene compliance in the same period i.e. Mar 2014 to June 2014 was 33%. This is a pre intervention data Hence we can see that compliance improved from 33% to 56% which is significant with p- value < 0.01. Ventilator associated pneumonia (VAP) rate between march 2014 – June 2014 was 22.3/1000 ventilation days. Central line associated blood stream infection (CLABSI) during the same period was 10.06/ 1000 catheter days(unpublished data). In

intervention phase i.e. march 2015 to June 2015, there was significant fall in VAP rate which was 13.42/ 1000 ventilator days, and CLABSI rate which was 2.78/1000 catheter days. There was significant fall in a rate of HAI.

It can be concluded that rate of hand hygiene compliance can be increased significantly by reinforcing its importance repeatedly to medical staff working in I.C.U.s. Only increase in hand hygiene compliance can decrease the number of rate of hospital acquired infections.

INTRODUCTION: Infections by multidrug-resistant organisms (MDROs) are increasing worldwide [1]. Worldwide, the most common bacteria causing health-care associated infections (HAIs) are:

MRSA Methicillin resistant *Staphylococcus aureus*

VRE Vancomycin resistant *Enterococci* spp.

ESBL Extended-spectrum beta (β)-lactamase gram-negative organisms

CRE Carbapenems resistant *Enterobacteriaceae*

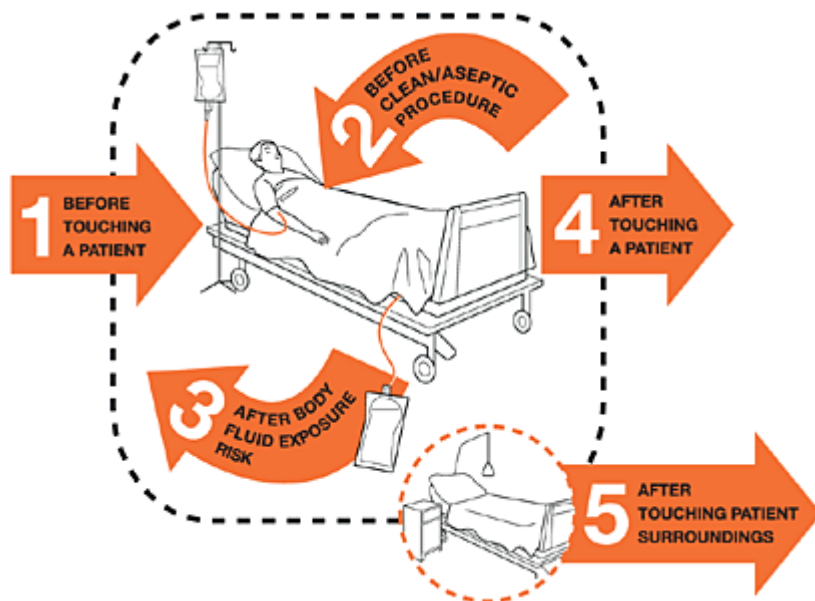
MRAB Multi-resistant *Acinetobacter baumannii*

The spread of MDROs in health-care settings is common and occurs mostly via health-care workers' (HCWs) contaminated hands, contaminated items/equipment and environment.

The importance of hand hygiene in preventing health care associated infections (HCAIs) has been long known since the study carried out by Semmelweis in 1884[2]. Many studies down the ages, have repeatedly demonstrated effective hand hygiene to be the single most effective method in reducing HCAIs [3-4].

Despite this, hand hygiene compliance among health care personnel has remained abysmally poor, especially in the intensive care unit (ICU) [5]. This has been attributed in part, due to the poor design and quality of the information and training imparted to health care workers [6–8].

In order to tackle this problem, the World Health Organization (WHO) developed a concept called “My five moments for hand hygiene” [9]. It describes the reference points for hand hygiene and tells the specific moments when hand hygiene is required to effectively interrupt microbial transmission during the normal care of patients.



There is very little data available on hand hygiene practices among healthcare personnel in India. Thus, we decided to conduct a before–after, prospective, observational study of hand hygiene practices in our ICU, with an interventional strategy based on “my five moments of hand hygiene”

MATERIAL AND METHODS: This observational analytical study was conducted from March 2015 to June 2015 at JIPMER women and children hospital, a tertiary care teaching hospital center in Pondicherry.

Study participants were all healthcare personnel working and visiting in PICU, JIPMER. Health care personnel not willing to give consent for study were only excluded.

Before starting the study verbal consent was taken from all health care personnel in PICU for recording of daily activity. Hand hygiene education module consisted of running of video of hand hygiene daily from 8 am – 9 am in television installed outside PICU. Two weekly classes on hand hygiene and it’s importance in PICU were taken by the principal investigator. Reinforcing the importance of hand hygiene was done in PICU daily bedside. The interventional program targeted resident trainees working/visiting the ICU and all nursing staff working in the ICU.

Posters reinforcing the importance of hand hygiene were already present in PICU. CCTV camera was installed in PICU. CCTV was chosen as a method of surveillance so as to decrease the observer bias in a surveillance done in person

by infection control nurse. Also it reduced the human workload and we were able to observe and note observations even during night time.

Whole day activities were recorded in it for whole week. Weekly once the data in memory card of CCTV camera was viewed after dividing each day in 4 blocks of 6 hours. Out of 6 hours in each block, 1 hour period was randomly selected for viewing the video footage. Particulars of any health care personnel were not revealed anywhere. Before the start of the study period, we discussed all aspects of observations in detail regarding what constituted each hand hygiene opportunity and what a lapse is.

Pre intervention data of hand hygiene compliance from January to June 2014 was collected by random observation from infection control nurse. HAI rate data from same period was retrieved from computer based data from PICU desktop where data of all patients is saved.

Hand hygiene compliance rate in health care personnel in JIPMER PICU was 33% (January- June 2014 unpublished data) .In order to raise it to 60% with 95% confidence interval with precision of 5% minimum number of observations required was 369. With 10% attrition rate (due to environmental or mechanical problem) final numbers of observations were 410. Sample size was calculated by using OPENEPI software version 3.03 updated 22/09/2014. Study was conducted over period of 4 months (From march 2015– june 2015). Total number of hours were 2880 (120 x 24), which were divided into equal blocks of 6 hrs making it total 480 blocks . Out of 6 hours block 1 hour was randomly selected, of which video footage viewed. 420 hours of video recording was studied.

Simple random table was used for randomization. Numbers of blocks were numbered from 1-480. Out of which 420 were randomly selected. Out of 6 hours of period in each block, 1 hr period was randomly selected again by simple randomization table by the person not directly involved in study.

Data collection methods including settings and periodicity

Randomly selected 1 hour of video recording in each block of 6 hours was viewed at the end of one week .Number of opportunities of hand hygiene according to ' **My 5 moments of hand hygiene**' [9] were noted. Out of total opportunities number of times hand hygiene was carried out and number of time lapse of opportunity was noted. Observations involving the health care person

not giving consent for study were not counted. Rate of hospital acquired infection during this 4 month period was noted. Hospital acquired infection was defined as per standard definition. No blood sampling or any other investigation was done for this study purpose.

STATISTICAL ANALYSIS: Both descriptive and inferential statistics were used to analyze the data. Categorical data was described using frequencies and percentages and compared by using chi square test or Fischer's exact test. To present the normally distributed data, mean and standard deviation were used and for Non-Gaussian, median was used. Appropriate parametric (Independent students t test) or non-parametric (Mann Whitney U test) were used to compare the groups.

HAI rate before and after are expressed in HAI rate / 1000 PICU days. HAI episodes were divided in VAP and CLABSI. VAP rate was expressed in VAP rate / 1000 ventilation days. CLABSI rate was expressed as rate/ 1000 catheter days.

All tests were two-tailed and a p value of < 0.05 was considered as significant. SPSS 20.0 software (SPSS Inc. Chicago, Illinois) and Epi Info™ 7 (7.0.9.7, CDC) was used for data analysis.

RESULTS:

Total 420 hours of video footage was viewed.

Total video footage was equally divided in day and night hours. Day was defined as 8 am- 8 pm and night was defined as 8 pm- 8 am.

Shift	N	%
Day	210	50%
Night	210	50%
Total	420	100%

Table 1- distribution of video recording viewed

Total number of opportunities as per WHO my 5 moments of hand hygiene were 10519. Out of which 5953 were utilized. 4566 opportunities were missed. Overall compliance was 56% .

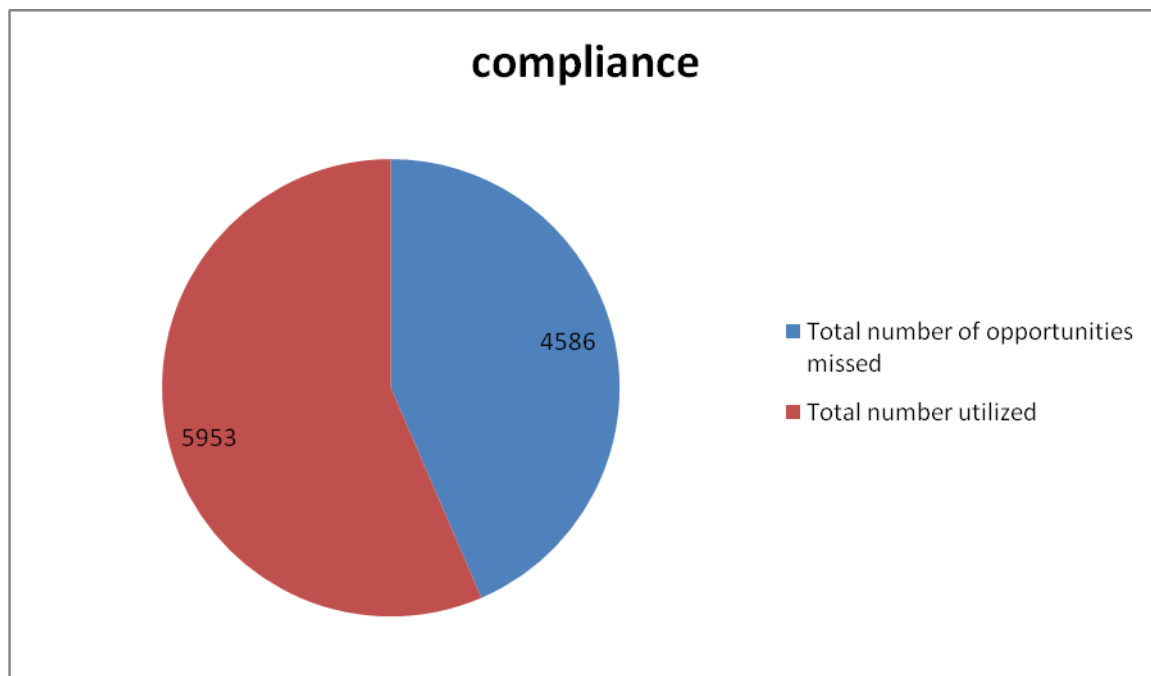


Fig1 – total compliance of hand hygiene

As stated previously, hand hygiene compliance in the same period i.e. Mar 2014 to June 2014 was 33%. Hence we can see that compliance improved from 33% to 56% which is significant with p- value < 0.01

Preintervention HH compliance	Postintervention compliance	t-value	p-value	95% CI	
				UPPER	LOWER
33%	56%	34.887	< 0.01	24.2611	21,673

Table 2 : comparison of hand hygiene compliance before and after

In our study, compliance differed in medical personnel as follows,

Sr. no	Medical personnel	Compliance %
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1	Nurses	77.25
2	Residents	52.25
3	Consultant	98.5
4	Visiting technician	21.75
5	Nursing orderly	8.5

Table 3- HH compliance in different medical personnel

As we can see highest compliance was in consultant followed by nursing staff followed by residents but which differed significantly.

As study was conducted over a period of 4 months, month wise HH compliance also studied which showed highest compliance in June followed by April. Least compliance was found in month of March which was significantly less compared to April, May, and June. This can be attributed to the reason that study commenced in month of March with intervention to improve compliance also started in March showing it's positive effect in subsequent months.

Months	N	Mean (%)	SD	Min.	Max.
March	124	46.43	10.04	21.42	66.60
April	120	63.87	10.64	35.00	83.33
May	124	54.22	13.66	21.42	83.33
June	52	64.45	9.25	37.90	83.33

*Significant difference was observed between March and April/ May/ June (p-value < 0.05)

*Significant difference was observed between April and May (p-value < 0.05)

*Significant difference was observed between May and June (p-value < 0.05)

Table 3- month wise distribution of HH compliance

HH compliance also differed according to ‘5 moments of hand hygiene’ of WHO campaign in a way shown following chart.

Hand Hygiene Practices	Mean (%)	SD	Minimum %	Maximum %
Before contact with patient	64.7377	14.76205	30	100
Before aseptic task	88.7692	21.17954	10	100
After body fluid exposure risk	47.082	20.42326	0	100
After patient contact	37.9286	22.37723	0	100
After contact with patient surrounding	28.1143	22.75818	0	75
Total	55.9671	13.47564	21.42	83.33

Table 4- HH compliance as per ‘My 5 moments of hand hygiene’.

HH compliance was highest before aseptic task, 88.76% followed by “before contact with patient”, 64.73%. Least compliance was seen with “after contact with patient surrounding”, 28.11%.

HH compliance also differed according to shift of the work as in day or night. In the morning hours which were defined as 8 am to 8 pm and night hours defined as 8 pm -8 am. Compliance was significantly less in night hours with mean of 57.36% in morning hours while 54.56 in night hours with p-value < 0.05.

Unpaired T-test	Group	N	Mean	SD	p-value
Shift	Morning	210	57.36	13.38	0.04

	Night	210	54.56	13.44	
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Table 5- HH compliance according to shift of duty

Ventilator associated pneumonia (VAP) rate between march 2014 – June 2014 was 22.3/1000 ventilation days. Central line associated blood stream infection (CLABSI) during the same period was 10.06/ 1000 catheter days(unpublished data). In intervention phase i.e. march 2015 to jun 2015, there was significant fall in VAP rate which was 13.42/ 1000 ventilator days, and CLABSI rate which was 2.78/1000 catheter days.

Discussion : We in our institution, routinely use chlorhexidine based hand rub for hand hygiene required in “my 5 moments of Hand hygiene”. This evidence-based, field-tested, user-centred approach is designed to be easy to learn, logical and applicable in a wide range of settings [9].

We used video surveillance for monitoring of hand hygiene compliance as per these 5 moments of hand hygiene as used previously by Armellino et al [10]. Total 420 hours of video recording was viewed which was equally divided in day and night shift to see the diurnal variation in hand hygiene compliance. Total opportunities for HH observed during video surveillance were 10519, out of which 5953 opportunities were used with total compliance of 56% which was comparable o previous studies by Mathai et al and Salem et al [11,12]. This was the post intervention data. In study by Salem et al hand hygiene compliance increased from 42.9% pre-intervention to 61.4% post-intervention, $P < 0.001$ with similar intervention. In another study by Mathai et al hand hygiene compliance improved significantly to 56% after intervention to improve hand hygiene.

The intervention which we used to increase HH compliance i.e. biweekly classes , bedside reinforcement of hand hygiene importance, similar intervention was used by Mathai et al [11].

In our study HH compliance was maximum in “before aseptic task” 88.76 % , followed by “ before contact with patient” 64.73%. This was opposite to result seen by Mahfauz et al in which before contact with patient was significant risk factors for hand hygiene non-compliance in the hospital [13].Least compliance in present study was with “ after contact with patient surrounding” 28.11%.

Compliance among health care personnel according to their work rank differed significantly. Highest compliance was noticed in PICU consultant with 98.5%. This was differing with previous studies by Mahfauz et al [13]. In study by Mahfauz et al being a physician was significant risk factor for hand hygiene non-compliance in the hospital [13].

Compliance was highest among nurses after consultant (77.25%) while in residents it was 52.25%. Results were similar to previous observations by Mathai et al, Salem et al and Victor et al [11,12,14].

This can be contributed to fact that residents have tighter schedule and more mental stress. This fact tells us that we need to focus on residents more for hand hygiene compliance and give them positive feedback of improved compliance frequently as residents and nurses are the personnel who will be in contact with patients for longest duration.

There was significant fall in HAI in the post intervention period as rate of fall in HAI has already been told in results This can be attributed to increase in hand hygiene compliance significantly as rest of the factors which can affect HAI rate i.e. profile of patient admitted, nurse to patient ratio, doctor to patient ratio was also similar. Similar results were seen by Salama et al. in his study, the rate of overall health care-associated infections/1000 patient-days, fell from 37.2 pre-intervention to 15.1 post-intervention ($P < 0.001$); the rate of bloodstream infections, which fell from 18.6 to 3.4/1000 central-line-days ($P < 0.001$); and the rate of lower respiratory tract infections, which fell from 17.6 to 5.2/1000 ventilator-days ($P < 0.001$) [12].

In present study, we were able to see diurnal variation in hand hygiene compliance as have been previously reported. Compliance during day hours was significantly more than night hours 57.36% and 54.56% with a p-value < 0.05 . Similar observation has been made previously by Sahay et. al. in his study, hand hygiene compliance dropped during the night for doctors (81% vs 46%, respectively, $P < .001$), for nurses (64% vs 55%, respectively, $P = .02$), and for paramedical staff (44% vs 31%, respectively, $P = .01$). This again emphasizes importance of repeated reinforcement of importance of hand hygiene compliance [15].

The HH compliance in duration of 4 months was least in month of March, 46.43 %, while highest in June and April (64.45 and 63.87 % respectively).

Significance of this can be seen as there was not a single c/o of HAI in the form of VAP and CLABSI was noted in the month of April., while in the month of March there were 3 events of VAP and 1 CLABSI amounting to VAP rate of 13.57/ 1000 ventilator days and CLABSI rate of 5.95/ 1000 catheter days. While most of the other factors affecting the occurrence of HAI were same in both months, though not correlated systematically.

Limitations of study:

- 1) Method of collection data of hand hygiene compliance before and after intervention was not same.
- 2) Other factors which might decrease incidence of HAI apart from hand hygiene compliance were not formally studied.

CONCLUSIONS: 1) It can be concluded that rate of hand hygiene compliance can be increased significantly by reinforcing its importance repeatedly to medical staff working in I.C.U.s.

2) Increase in hand hygiene compliance can decrease the number of rate of hospital acquired infections

DECLARATIONS:

Contributors: *R. Rameshkumar* -Conceptualization ,analysis of the collected data and preparation of manuscript. *Jayanta Vagha*-Study design and Methodology.*Sham B. Lohiya*-Literature search, collection of data and revision of the manuscript.

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CASE REPORT:

Turner Syndrome with Intra-Hepatic Periportal Cuffing And Non-Cirrhotic Portal Hypertension (NCPH) - A Rare Association

Amonkar Priyanka, Arora Kriti**, Mohanty Nimain***, Vyas N.L.#, Preeti Kapoor##, Sahu Shilpi###*

*Junior Resident , **Senior Resident, ***Professor Pediatric Gastroenterology , Dept Of Pediatrics , MGM Medical College , Kamothe Navi Mumbai , 410209

Associate Professor and endoscopist , Department of Surgery , ## Professor And Head Of Department, Radiodilogy, ### Professor And Head Of Department, Pathology , MGM Medical College , Kamothe Navi Mumbai , 410209

Corresponding Author: Amonkar Priyanka, Resident

Dept Of Pediatrics, MGM Medical College, Kamothe Navi Mumbai , 410209.

Email: priya11_sa@yahoo.com

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ABSTRACT: Turner syndrome is a comparatively commonly encountered chromosomal disease with well known congenital malformations involving the cardiovascular and renal system in addition to its typical phenotypic characteristics. Liver involvement in Turners syndrome is seldom reported . We describe a case of a 9-year old girl with Turner syndrome, presenting with massive upper gastrointestinal bleed from Grade-III esophageal varices and portal hypertension due to a rare vascular anomaly involving the hepatic vasculature.

KEY WORDS: *Turner syndrome, Non cirrhotic portal hypertension, Non-cirrhotic portal fibrosis, Esophageal varices, hematemesis, Intra-hepatic periportal cuffing*

INTRODUCTION: Approximately 1 in 2,500 live female births is affected by Turner syndrome which is one of the common genetic conditions encountered

in pediatric practice [1]. Cardiovascular and renal malformations are among the well known associations and are usually screened for[2]. In this report we describe a 9 year old child presenting with massive hematemesis and portal hypertension. Although different body systems can be affected to varying degrees in Turner syndrome, gastrointestinal bleeding due to portal hypertension is rare. The main causes of liver involvement in Turner syndrome are vascular disorders of congenital origin, and non-alcoholic fatty liver disease. In the instant case however, liver function tests and hepatic echotexture on sonography were fairly normal, making the evaluation of cause of portal hypertension a diagnostic challenge.

CASE REPORT: A 9 year old girl born in our hospital, a known case of Turner syndrome (confirmed by Karyotyping) presented with 3 episodes of vomiting containing 50-100 ml of blood and black colored stools for past few days. She had no other bleeding manifestations or petechiae. There was no history of fever, chronic cough, epigastric pain, drug intake, jaundice or abdominal distention. Patient had a history of an episode of hematemesis two years back for which she was hospitalized and managed with oral iron supplements in view of iron deficiency anemia. She had splenomegaly and doppler studies were normal at that time. Patient was however lost to follow up and thereafter presented with current symptoms.

On examination (Figure 1) child had typical features of turner syndrome with short stature, low hair line, webbed neck, shield chest, widely spaced nipples and wide carrying angle. Tachycardia and pallor were present. No jaundice or signs of liver failure were seen. Abdomen was soft and not distended. Spleen was soft to firm, 6 cm below costal margin. Liver was not enlarged. Examination of other systems was unremarkable. 3rd episode of hematemesis in hospital amounted to about 200 ml frank blood, rendering her hypertensive and pale. CBC showed severe anemia (Hb 4.6 gm/dL) with a progressive fall in all three cell lines on subsequent tests indicating hypersplenism. Peripheral smear for RBC morphology showed a microcytic hypochromic picture. No parasites were seen. Liver function tests were normal. Stool for occult blood was positive. She was managed with four packed cell transfusions, octeotride and ethamsylate.

Upon hemodynamic stabilization of the patient, further evaluation of suspected variceal origin of hematemesis was done. Upper gastrointestinal endoscopy (Figure 2) confirmed grade III esophageal varices & grade IV

gastric varices which were actively bleeding. Endoscopic band ligation of esophageal varices was done and 3 monthly endoscopies for repeat ligation were advised. Portal venous doppler (Figure 3,4,5) showed normal hepatopedal flow with monophasic flow in main portal vein and loss of respiratory phasicity. Periportal cuffing was noted around main portal vein and in the distal branches of portal vein, indicative of fibrosis. Enlarged spleen measuring 12.8cm was seen in contrast enhanced CT abdomen (Figure 6,7,8), with a normal liver in shape and size. Multiple dilated varices were seen in wall of esophagus. Splenic vein appeared prominent, measuring 10mm and multiple dilated tortuous vessels were seen at the splenic hilum suggestive of perisplenic collaterals. Portal vein and superior mesenteric vein measured 10 mm & 8mm respectively.

Liver biopsy (Figure 9,10,11,12) was performed which showed normal liver architecture with minimal fibrosis, mild steatosis and mild dilatation of sinusoids. PAS positive and diastase negative material was seen within hepatocytes. There was no evidence of cholestasis, bile duct proliferation or infiltration of chronic inflammatory cells. A diagnosis of Turner Syndrome with Grade III Esophageal Varices, Intra-Hepatic Periportal Cuffing and Non Cirrhotic Portal Hypertension was hence made.

DISCUSSION: Cardio-vascular and renal anomalies are known in Turners Syndrome. We present a rare association of portal hypertension due to vascular anomaly (periportal cuffing of portal vein and its distal branches) and NCPF with Turners syndrome in a 9-year old girl presenting with massive UGI bleed from Grade-III esophageal varices. Her splenic vein diameter on doppler was however found to be normal for age, as was the portal vein.

Muller, et al (2008) [1] had reported a 3 year old girl with Turners syndrome presenting with UGI bleed due to pre-hepatic PHT whose liver biopsy had shown anomalous intra-hepatic arteries and veins. Roulot et al (2004) [3] published a cohort of Turners Syndrome cases in the mean age group of 8 +/- 5.2 years showing vascular anomalies in liver. Out of 27 cases whose liver tissue samples were available, 10 showed marked liver architectural derangements, including nodular regenerative hyperplasia in 6, multiple focal nodular hyperplasia in 2 and cirrhosis in 2. These changes were often associated with obliterative portal venopathy and aortic malformation. Out of 17 others, there was mild to moderate portal fibrosis in 15, inflammatory

infiltrates in 9 and nonalcoholic fatty liver disease in 11. Bile duct alterations resembling small duct sclerosing cholangitis were observed in 21 with or without architectural changes. PHT was observed in 4 with marked architectural changes, including 3 in whom refractory ascites or recurrent variceal bleeding developed, needing transplantation. None of the patient without marked architectural changes experienced progressive or decompensated liver disease. There was no evidence of hepato-toxicity from estrogen replacement therapy.

The earlier terminology of NCPF (Non-cirrhotic Portal Fibrosis) has since been changed to NCPH (Non-Cirrhotic Portal Hypertension) to encompass the whole spectrum of vascular anomalies in portal system [4]. However the instant patient is likely to be a case of NCPF in view of periportal cuffing of terminal portal vein branches, minimal fibrosis seen within liver on biopsy and absence of any blocks (eg.thrombus) in the splenic vein or the portal vein branches.

CONCLUSION: Liver involvement in Turners syndrome is rare. High index of suspicion and selecting appropriate investigations and interventions in time is the corner stone to salvage such children. Main causes are vascular disorders, probably of congenital origin, requiring long-term follow-up with drug therapy, variceal ligation, and transfusion under close supervision and may be, liver transplantation in selective cases.

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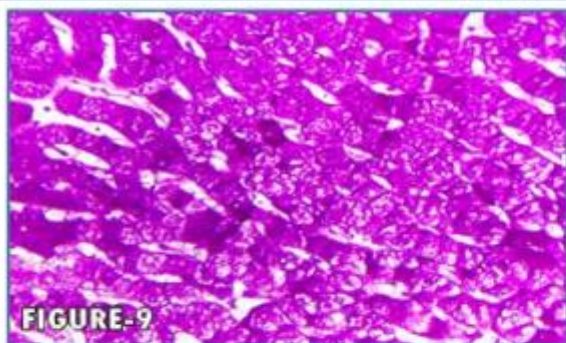
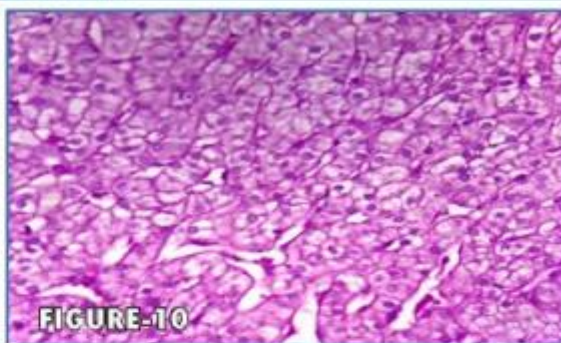
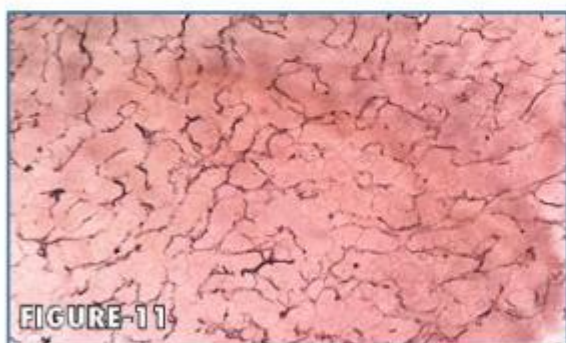
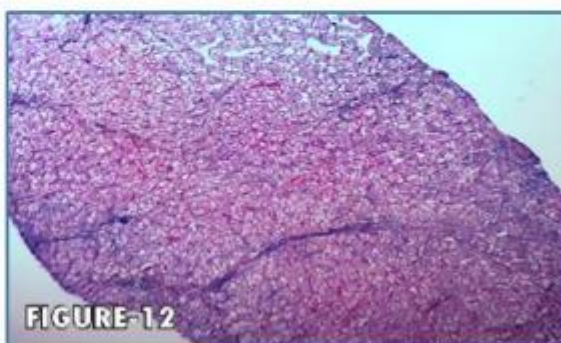
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LIVER BIOPSY**PAS Stain (40X)****Diastase Stain (40X)****Reticulin Stain (40X)****Masson Trichome Stain (10X)**

- Liver architecture normal. Mild steatosis and mild dilatation of sinusoids seen.
- Minimal fibrosis seen (Figure 11, 12).
- No evidence of cholestasis, bile duct proliferation or infiltration of chronic inflammatory cells.
- PAS+ve and Diastase -ve material within hepatocytes seen (Figure 9, 10).

