Childhood Acute Lymphoblastic Leukemia: Need of a National Population Based Registry

Outcome of childhood acute lymphoblastic leukemia (ALL) in India, although improving, has not kept pace with >80% cure in developed nations [1]. In contrast to resource-plenty nations, there is paucity of accurate epidemiological data [2,3]. Out of the estimated >10000 new ALL patients in India annually, few are adequately treated. Therapy refusal and abandonment and loss to follow-up and lack of reporting of cancer related mortality are major challenges [1].

Although, national cancer registries exist, there are fraught with several limitations including under-reporting, under-diagnosis, and limitations in personnel and technological expertise [2,3]. Hospital based registries are likely inadequate and may underestimate the true disease burden. Although efforts by investigators in a few cities are commendable, there has been a lack of prospective and precise and nationwide effort to report all the cases with a separate focus on childhood malignancies, especially ALL [3,4]. In addition, investigators have suggested a plausible increase in incidence of ALL with wide variation in incidence in different geographic locales [2,4].

Thus, there is a clear need of accurate estimation of incidence and epidemiology of childhood ALL in India to be able to estimate the true disease burden. A national population based childhood ALL registry with high-resolution data collection would be pivotal to achieve these goals. This in turn is important for identification of pattern of disease and its change, risk factors for prognosis, delineating the biology of disease and management lacunae in ALL an Indian setting. Furthermore, organized efforts are imperative to prevent both under diagnosis and reporting with emphasis on reporting of all events and cases. Establishment of such registry would require multimodal and multilevel efforts involving governmental and non-governmental/voluntary organizations, cancer-treatment centers, infrastructural facilities, finances and ongoing surveillance for quality assurance.

A 'National Childhood ALL Registry' would serve as a stepping stone in introduction of remedial measures to improve the ALL survival. We earnestly request the Indian Academy of Pediatrics to contribute to this mound which would undoubtedly help in improving the outcome of childhood ALL in India.

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Pediatric BLS Updates 2010

Pediatric basic life support forms the basis of rapid and effective Cardio pulmonary resuscitation (CPR) in infants and children, which ultimately is associated with return of spontaneous circulation. The main emphasis is on high quality CPR. Recent pediatric data shows an overall survival of 33% for pulseless arrest from in-hospital pediatric arrests [1].

The new guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care were published in October, 2010, by American Heart Association, in accordance with the established five yearly changes in the guidelines [1]. In the same month, almost a

TABLE I CHANGES IN THE PEDIATRIC BASIC LIFE SUPPORT

	2005 recommendations	2010 recommendation [1]	Reasons for change
1.	Use of the "A-B-C" (Airway, Breathing/ventilation, Chest compression) in basic life support sequence.	A change in sequence to C-A-B" (Chest compressions, Airway, Breathing) for adults and pediatric patients (children and infants, excluding newborns). "Look, Listen, and Feel" has been removed.	• Majority of victims who require CPR are adults with VF in whom chest compression are more important than ventilations [4]. • There is a delay in ventilations by about 18 seconds for the lone rescuer and by even a shorter interval for 2 rescuers. • It offers consistency in teaching, for all age groups.
2.	Recovery position was not recommended in infants and small children.	Recovery position is recommended in children.	If there is no evidence of trauma, recovery position helps to maintain a patent airway and decrease the risk of aspiration
3.	Rescuer should press down 1/3 to ½ the depth of the chest with each compression.	Rescuer should press atleast 1/3 the anterior – posterior diameter of the chest or approximately 1½ inches (4 cms) in infants and 2 2 inches (5 cm) in children	Inadequate chest compression depth is common even by the health care providers [5]. Compression to ½ the anterior- posterior diameter may not be possible.
4.	A chest compression rate of approximately 100 per minute	A chest compression rate of atleast 100 per minute.	Delivery of more compressions during CPR is associated with better survival and an important determinant of return of spontaneous circulation.
5.	In 2 thumb- encircling hands technique, thorax is to be squeezed at the time of chest compression.	Not recommended	There is no data which shows the benefit from a circumferential squeeze.
6.	There are no different recommendations for trained *versus* lay rescuer.	If a lay rescuer is not trained in providing ventilations, or is unable to do so, the rescuer should continue with chest compressions (Hands – Only or compression – only CPR) until help arrives	High quality chest compressions generate blood flow to the vital organs. Compressions only are easier for an untrained rescuer to perform.
7.	No recommendations for use of Automated External defibrillator (AED) in infants less than 1 year of age [6].	For infants a manual defibrillator is preferred. If a manual defibrillator is not available, an AED with a pediatric attenuator is preferred for infants. If neither is available, an AED without a pediatric dose attenuator may be used.	Shockable rhythms respond to electric shocks (Defibrillation) which ultimately decides the survival. There is minimal myocardial damage with good neurological outcomes [7].

similar set of revised guidelines for cardiopulmonary resuscitation were published by European Resuscitation Council [2]. Both these guidelines for basic Life Support recommend that all rescuers should start with chest compressions on a victim who is found unresponsive and not breathing (or gasping). However, asphyxial arrests are more common than cardiac arrest in infants and children, and ventilation are important for resuscitation in pediatric age group, which is further substantiated by a recent pediatric study which showed that resuscitation results for asphyxia arrests are better with a combination of compressions and ventilation [3]. Some of these major changed in the pediatric basic life support are highlighted in ***Table* I**.

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Efficacy and Safety of Azithromycin for Typhoid Fever

I have some concerns about the interpretation of data in the paper by Aggarwal and colleagues on efficacy and safety of azithromycin for uncomplicated typhoid fever [1]. While many children in the study sample had typhoid fever, evidence is unconvincing that all of them had the specific disease. The inclusion criteria included at least 4 days of fever with clinical features suggestive of typhoid fever, such as abdominal pain (present in 69%), diarrhea or constipation (61%), splenomegaly (27%) and hepatomegaly (73%). While the sensitivity of such a spectrum would be high to include typhoid fever, the specificity would be quite low, except for splenomegaly. This suspicion is strongly supported by the very low blood culture yield (17 children, 15.5%). Moreover, other diagnostic possibilities were not excluded or apparently even considered.

If the diagnosis is not firm, the drug trial is on slippery grounds. Azithromycin is well known to be safe. As for efficacy, azithromycin is active against several pathogens and as pointed out above, such agents could have been the cause of fever in some children. Its efficacy evaluation against typhoid fever in this study is not valid since the case definition was not stringent enough. Moreover, children seen with fever on the fourth day, with only mild discomfort and no localizing signs may well be left alone with symptomatic support and close monitoring; their recovery cannot be attributed to the drug therapy. Many children with uncomplicated fever have surprised pediatricians by their recovery without antibiotic treatment, while their blood cultures have yielded *Salmonella typhi*. The data on the 17 culture-proven cases, of whom 16 completed the study – their response and final outcome are essential to consider the efficacy of the drug, but they are not specifically mentioned. The report says that 5 of them "required add-on antibiotics" [1], suggesting treatment failure in one-third.

Three questions arise. One, what are the indications to start an antibiotic in children with fever of less than one week and without specific diagnosis? Second, what are the criteria to diagnose typhoid fever when blood culture result is negative and when blood culture was not attempted? Third, what are the criteria to choose azithromycin in typhoid fever in preference to other inexpensive oral drugs? These questions have no answer in the paper. The IAP Task Force's guideline on treatment of enteric fever seems to have been ignored by the investigators; it includes azithromycin as an 'alternative' agent for treating uncomplicated typhoid fever [2]. However, the IAP Task Force did not provide minimum diagnostic criteria – clinical and laboratory – for typhoid fever, but apparently alludes that blood culture is essential [2].

In short, the present study cannot be taken as a precedent to diagnose typhoid fever without defined criteria. The rationale to choose azithromycin as the first drug to be given when typhoid fever in 'suspected' or even 'diagnosed' needs further clarification. Perhaps azithromycicn is justified when no cause for fever is available but the child is ill, the cause is suspected to be infection which could include a variety of agents including *S typhi*.