From the desk of editor-in-chief:

Dear all, warm regards

The time runs very fast. As we are all aware, the first year of the life of an individual is very critical for future growth and development similarly the first year of this publication saw many critical hurdles, obstructions and hiccoughs. But, ultimately the infancy of NIJP has passed off without any significant murmurs, flutters or fibrillations. As usual everything was not running smoothly during the infancy. There were some hurdles, obstructions, and limitations in continuing the project. But, all these ultimately resulted in strengthening and building our self confidence and removing the feelings of inferiority complex.

There was immense support, cooperation and guidance from various parts throughout the country. Many articles, case reports, writes – up started pouring in. The support from reviewers was also good and encouraging though many of them have taken their own time and preferences. The support from pharma industry has also started trickling gradually.

We expect similar cooperation, support and guidance for the future issues or volumes. We hope to continue this venture with new zeal and zest in the coming years. We hope that in the coming years, we will receive more and more contributions from different parts of the country on various hot topics, current issues, recent advances and latest developments.

Wishing you all a very happy, prosperous and glorious new year…….

Yours
Dr Satish Tiwari
Editor- in- Chief
Editorial:
Conflict of Interest: Controversy and Confusion
Dr. Satish Tiwari*, Dr. Chhajer CM, ** Dr. R K Agarwal***

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The globalization and industrialization of human race has many positive and negative impacts in the society. The physical comforts and amenities, in the name of development has become the necessity of life. The technical advances and invasion by media has further increased these needs. This has resulted in the growth of many multinationals with their focused vision of monetary gains. The increasing inequalities in the community not only mean that there has been no improvement in the standard of living of the poor and that they are still living in poverty, in spite of economic growth but it is also causing a hindrance in the future economic growth. The top few people like; capitalists, government officials, highly educated salaried peoples and a few corrupt politicians have undoubtedly benefitted by economic growth but the majority of population has remained deprived of the so called developmental economic benefits. Even the middle class is under duress due to the increasing cost of livelihoods and the physical needs.

Health Needs

All these changes have not only affected the financial status of the society but also have major impact on the health of the individual and health needs of the community. This has also resulted in the emergence of group of people or companies with “conflict of interests” so as to reap the benefit of these societal needs. Health sector can’t remain exception to these global developments. In this era of technical advances and ‘medical tourism’ each and every aspect of health sector is affected by conflict of interests (COI). In many cases, these individuals do not believe the relationship influences their medical advice, research or prescribing habits -- although clearly the drug industry would not continue devoting millions of dollars to this type of marketing if it did not pay off. But even prominent researchers and expert physicians are often being influenced by the industry, whether they realize it or not.

The Food Industry

The food and nutrition are one of the basic needs of any society. But, the misconceptions and confusions regarding diet continue to be fixed and deep rooted in the minds of people. These inadequacies are exploited by the people with conflicts of interest by projecting a specific food having magic effects, as energy boosters and as brain developers / enhancers. The exaggerated health claims associated with commercial food have taken the toll of many lives. They have been responsible for the continuous prevalence of nutrition related morbidity and mortality in spite of regular health programs.

Those having COI in the artificial or commercial food have come out openly in
favor of market based food. According to them, the Indian market completely lacks affordable complementary foods for infants from poor families or for poor children during or recovering from illness. This is one of the main causes of acute undernutrition among children younger than 2 years, affecting their physical and cognitive development. The Indian food industry is not developing cheap complementary foods because of the marketing prohibitions and the lack of a specific mandate in the international code or IMS Act. It is also likely that because of this legal barrier, public health experts and civil society do not mobilize support on the matter. The WHO 2001 guidelines on complementary feeding must be developed to formulate an international code for the promotion and production of complementary foods. This would set the necessary standards and enable national governments and civil society in India to actively advocate production and marketing. (1)

The Vaccination Industry

Immunization or vaccine industry has frequently been a talking point whenever the issue of conflict of interest is discussed. One is compelled to admit that murmurs of dissent are always heard whenever a new vaccine is recommended. The situation now is such that any vaccine, news related to it, media report, press note, communication or recommendation creates flutter amongst the hyper-excitable academic experts, which hardly dies down before the next wave sets in. Perhaps, the truth evades and controversy, contradiction and confusion prevail as most of us grope in dark. Many a times there are allegations and counter allegations amongst the experts. Committee on immunization of Indian Academy of Pediatrics felt that persons qualified to serve as an expert for the Committee may have personal interests related to the subject of their expertise. At the same time, it is imperative that situations be avoided in which such interests may unduly affect, or may be perceived to affect, an expert's impartiality or the outcome of work in which he/she was involved. Thus, all office bearers and members of IAPCOI (including its subcommittees) should disclose any financial, professional or other interests relevant to the subject of the work or meeting in which they will be involved and any interest that could significantly affect the outcome of the meeting or work. They are also asked to declare relevant interests of others who may, or may be perceived to, influence their judgment, such as immediate family members, employers, close professional associates or any others with whom they have a substantial common personal, financial or professional interest. (2)

Pharmaceutical Industry

In July 2012, leading pharmaceutical major GlaxoSmithKline started issuing advertisements saying that nearly five lakh babies die in India due to Rotavirus. The aim was clearly to ensure that Rotavirus vaccines become a part of the mandatory vaccines that are given to new born babies and infants. What makes this advertisement interesting is that it did not promote a particular company but the need for the vaccine. In other words, here was a sly attempt by the pharmaceutical companies to unite and look forward to ‘creating’ a new
market. Dr Nalini Abraham, a Delhi-based medical practitioner, objected to the advertisements featuring the Rotavirus vaccination being broadcast freely on television channels and filed an official complaint with the Advertising Standards Council of India (ASCI) alleging that the advertisement misrepresents facts as it demonstrates that vaccines are the only way to reduce incidents of infection. (3) Medical fraternity comprises of experts who have a basic instinct of realizing what is true and what is false, what is neutral opinion and what is vested interest, do we wish to take away even that from them and consider them as a herd to be dictated by a few shepherds?

Breaking the drug industry's strong hold on the conventional medical industry will not be easy -- after all, the drug industry spends nearly twice as much on promotion as it does on research and development – but increasing numbers of people are now waking up to these harsh realities, and that is instrumental in getting the tide to turn.

Publications and Research

It's well known that studies funded by industry or conducted by researchers with industry ties tend to favor corporate interests. That's why it probably comes as no surprise that many so-called "experts" are very much on the drug industry's payroll -- but they masquerade as independent medical experts or even state officials during their "day jobs." All research institutions, international organizations and international donor agencies have direct/indirect funding from industry. The interpretation in positive terms is “corporate social responsibility” the negativity is “Bribery”. To draw a line between this is very difficult because of the gray zone that exists. The conflict of interest within this practice is obvious, which is why the drug industry often keeps quiet on their actual payments, as do the medical professionals involved. Although many medical, educational and research institutions require faculty members to disclose such potential conflicts of interest, many do not actively monitor employees' activities. (4) Researchers and certainly those who sit on government panels are supposed to disclose these types of relationships with the drug industry, but they often don't and little is done about it.

Health Facilities (Five Star Hospitals)

In the present era of modernization and urbanization, newer and newer multi specialty hospitals or private medical colleges are mushrooming for providing the so called latest medical services and facilities. But, their interests are very obvious and they are seen as money or profit making business tycoons in the name of providing medical care. The malpractices, over investigations and unjustified surgeries are some of the fields which expose their COI. These Five star hospitals are catering to the needs of classes and not the masses, which still remain unprivileged and unattended as far as their health needs are concerned.

Role of Government

The role of government is very vital in all these issues. But, it is unfortunate that rather than planning some long term policy to curb this from society, our politicians remain busy in mud-slinging and raising
insignificant issues in parliament. Obviously there are unseen underpinnings of many vested interests behind the policy paralysis, but our leaders should ask themselves for a minute when alone, can there be any issue more important than the future of our younger generations, who will shoulder the responsibility of nation building in the coming years?

**Role of Judiciary**

The law makers and judiciary have come out with many enactments to improve the deteriorating situation. But, no wonder the things happen very much under the nose of the law and law makers. Courts pass orders but, neither, the law enforcing agencies are strong enough to enforce the various Acts, nor, they are allowed to be strong by those who are in power for the obvious reasons. Various industries have big hold on governance, often by unfair and shady clout in the corridors of power. Industry buys and influences decision making in its favor.

**Role of Medical Councils**

Regulations of medical councils have also been questioned with regards to conflict of interests. The “Indian Medical Council (Professional Conduct, Etiquette and Ethics) (Amendment) Regulations, 2009, clause 6.8 and its sub clauses; defines Code of conduct for doctors and professional association of doctors in their relationship with pharmaceutical and allied health sector industry. A medical practitioner shall not accept any travel facility inside the country or outside, including rail, air, ship, cruise tickets, paid vacations etc. from any pharmaceutical or allied healthcare industry or their representatives for self and family members for vacation or for attending conferences, seminars, workshops, CME program etc as a delegate. A medical practitioner shall not receive any cash or monetary grants from any pharmaceutical and allied healthcare industry for individual purpose in individual capacity under any pretext. Ensure that the source and amount of funding is publicly disclosed at the beginning itself. In dealing with pharmaceutical and allied healthcare industry a medical practitioner shall always ensure that there shall never be any compromise either with his / her own professional autonomy and / or with the autonomy and freedom of the medical institution. A medical practitioner shall not endorse any drug or product of the industry publically. Any study conducted on the efficacy or otherwise of such products shall be presented to and / or through appropriate scientific bodies or published in appropriate scientific journals in a proper way”.

**Role of Society**

Morality and social concerns doesn’t stand a chance before the greed of money. People are neither students, nor prisoners who can be fettered. The human right includes freedom of choice, and if our choice is wrong, who can be held responsible? If one desires to burn his hands in the fire, how long can one stop him? Who can put the reason into his mind that fire is for lighting, not for burning? (5) That’s the way the circle runs. It is a rock solid system as old as the hills and it works with regularity and precision. As long as the pattern persists, money is generated in the system and as long as money changes hands, everyone is happy including traders, manufacturers,
middleman, officers and everyone. The people should be taught the ill effects and the conflicts of interests of the stake holders. There are numerous ways to drive home the point, only if there is the vision and planning.

The need of the hour is awareness, which should go hand in hand with all legal measures or punishments. And awareness doesn’t just mean ads in newspaper or warnings in media. It should start right from the school or classrooms. However, it may be easier said than done. India is supposed to be country of poor and illiterate, reasoning is often diluted, deflected and distorted. The real problem lies in the misguidance and misconceptions strengthened by those having conflict of interests. True, every effort should be made to develop the alternatives and while some of them are already available, yet, something complete and comprehensive is still awaited. In essence, it will be prudent for the experts to figure out at the earliest what and how it should be resolved.

References:

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5) Bhargava A. Root out Gutkha menace. The Hitvada, 2012; 16th Dec Nagpur p.6 (Col. 3-6)
Research Study: 
Clinical and Laboratory Profile of Wilson Disease in Children: A Study at a Teaching Hospital of North India
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Keywords: Wilson disease, Hepatic manifestations, Neurologic manifestations

Abstract

Background: Wilson disease (WD) is an inherited autosomal recessive disorder with varied manifestations.

Objective: The present study was aimed to know about the types and range of clinical and laboratory features of this disease in pediatric patients as observed during a period of three years.

Material and Methods: Fourteen patients suffering from Wilson disease attending the pediatric ward of this hospital during a period of three years, between July, 2009 and June, 2012, were included in the present study. The diagnosis was based on established clinical and laboratory criteria. All the cases were labeled on the basis of features, as those with hepatic, neurologic or mixed manifestations.

Results: The most frequent clinical manifestations were splenomegaly, jaundice, hepatomegaly and neurological findings, mostly in the form of dystonia or gait disturbances; K-F ring was detected in all patients. Findings of the study show that though, WD presented mainly with features of liver disease in childhood, a significant number were found with neurologic manifestations.

Conclusion: On the basis of results, Wilson disease should be considered in all young patients of chronic liver disease with negative viral markers. Neurologic WD, mostly with extrapyramidal manifestations occurs frequently in childhood unlike in the West.

Introduction

Wilson disease (WD), also known as hepatolenticular degeneration was first described by Kinnear Wilson in 1912 [1]. It is an inherited disorder, transmitted in an autosomal recessive manner, in which absent or reduced function of ATP7B protein leads to decreased hepatic excretion of copper. Worldwide prevalence of WD is 30/1,000,000 population [2]. While the disease usually presents with liver manifestations in children and young adults, neurological manifestations are more common in later life. The spectrum of liver disease can be highly variable, ranging from an asymptomatic case with only biochemical abnormalities, to acute liver failure. Neurologic type usually presents in the third decade of life but can be seen in childhood [3]. Although the disease is rare and has variable clinical presentation, yet it appears to be more common in India than in the
West [4]. Uttar Pradesh (U.P.) is the most populous, multicultural state of India comprising one sixth of Indian population but there has been a paucity of work on this disease in the state. The present study is one of the few such studies carried out in the state of U.P. The study was conducted at Shri Ram Murti Smarak (SRMS) Institute of Medical Sciences, Bareilly, situated in the western part of U.P., wherein we have done an analysis of clinical and investigatory profile of WD patients admitted at the Pediatric Department of our hospital.

Material and Methods

An analysis of all children labeled as WD in the pediatric ward of SRMS Institute of Medical Sciences, Bareilly, during a period of 3 years, i.e., between July, 2009 and June, 2012, was carried out. In all patients, a detailed history regarding the type and onset of symptoms was taken and a thorough clinical examination was done, including the slit lamp examination to visualize the KF ring. All the patients were subjected to the following investigations -

1. Urinary copper excretion per day
2. Serum ceruloplasmin level
3. Serum copper level

The diagnosis of WD was made using the scoring system developed at the 8th International Meeting on Wilson disease and Menkes disease, Leipzig in 2001[5]. This scoring system, recognized as a standard method worldwide, is based on clinical and laboratory findings. (Table 1) Only those meeting the criteria for the established diagnosis of WD, i.e., having a score of 4 or more were included in the study. As can be

<table>
<thead>
<tr>
<th>1. K.F. rings</th>
<th>Present</th>
<th>Absent</th>
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<tr>
<td></td>
<td>2</td>
<td>0</td>
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</table>

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<tr>
<th>2. Neurological Symptoms</th>
<th>Severe</th>
<th>Mild</th>
<th>Absent</th>
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<tr>
<td></td>
<td>2</td>
<td>1</td>
<td>0</td>
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<tr>
<th>3. Serum Ceruloplasmin</th>
<th>&lt;0.1 g/L</th>
<th>0.1-0.2 g/L</th>
<th>&gt;0.2 g/L (normal)</th>
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<tbody>
<tr>
<td></td>
<td>2</td>
<td>1</td>
<td>0</td>
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<tr>
<th>4. Coombs Negative Hemolytic Anemia</th>
<th>Present</th>
<th>Absent</th>
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<tr>
<th>5. Liver Copper (in the Absence of Cholestasis)</th>
<th>&gt;5xULN (&gt;4µmol/gm)</th>
<th>0.8 – 4 µmol/gm</th>
<th>&lt;0.8 µmol/gm (normal)</th>
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<td></td>
<td>2</td>
<td>1</td>
<td>-1</td>
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<tr>
<th>6. Urinary copper (in the absence of acute hepatitis)</th>
<th>&gt;5xULN after d- penicillamine</th>
<th>&gt;2xULN</th>
<th>1-2x ULN</th>
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<tr>
<td></td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
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<tr>
<th>7. Mutation analysis</th>
<th>On both chromosome detected</th>
<th>Detected on one chromosome</th>
<th>No mutation detected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
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<table>
<thead>
<tr>
<th>Total score</th>
<th>Evaluation</th>
</tr>
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<tbody>
<tr>
<td>4 or more</td>
<td>Diagnosis established</td>
</tr>
<tr>
<td>3</td>
<td>Diagnosis possible, more investigation needed</td>
</tr>
<tr>
<td>2 or less</td>
<td>Diagnosis very unlikely</td>
</tr>
</tbody>
</table>

Table 1: Scoring System Developed at the 8th International Meeting on Wilson’s disease, Leipzig 2001 (Based on clinical and laboratory findings)
seen in the tables 2 and 3, all our patients had K.F. rings and also had >2x Upper limit of normal (ULN) 24 hour urinary copper excretion. Thus, every patient of our study earned a score of 4, only for these 2 findings, even if we do not take into account other findings, e.g., ceruloplasmin levels, which would raise the score further, meaning thereby that the diagnosis of WD was beyond doubt in all our cases. Besides dividing the patients on the basis of age, they were labeled as ‘with hepatic manifestations’, ‘neurologic manifestations’ or ‘mixed manifestations’. While jaundice, hepatomegaly, splenomegaly, ascites or signs of liver failure were classified as hepatic manifestations, dystonia, dysphasia, abnormal movements (tremors /chorea/ athetosis), seizures and gait disturbances were considered neurologic manifestations; those having a mixture of both types were labeled as mixed manifestations. Only the history of jaundice did not qualify a patient to be labeled as having hepatic manifestations.

Results

In the present series, 14 children - 9 males (64.28 %) and 5 females (35.71%) - with the diagnosis of WD were studied. The lowest age was 7 years and the highest, 15 years, with the mean age of 11.9 years (fig 1). Different modes of presentation are listed in table 1, which shows that overall 8 (57.14%) patients presented with hepatic manifestations while neurologic manifestations were seen in 4 (28.57%) patients only; 2 (14.28%) children had both hepatic and neurologic manifestations. The relative distribution of clinical manifestations in the two age groups can also be seen in the same table, which clearly shows that neurologic manifestations were seen mainly in the second decade of life. The same is evident in figure 1 also which depicts the presenting manifestations as hepatic, neurologic and mixed in the two age groups. An interesting finding was that all the patients had K-F ring in eyes as seen on slit lamp examination; in some of them it was visible with naked eyes. The biochemical parameters of the patients studied are shown in table 2. Besides the above investigations, cranial imaging was also done but only in those with neurologic or mixed manifestations. In all these cases hypodensities in basal ganglia and thalami region were noted. Cortical atrophy was also seen in two patients.
dose of 75mg/day in three divided doses along with pyridoxine (40 mg/day) supplementation. They were advised a low copper diet and use of copper free utensils. For extrapyramidal symptoms, symptomatic treatment was given. All the patients were followed at least up to a 3 month period to evaluate the effect of treatment, to notice any adverse drug reactions and also to observe the development of any new symptoms or signs. Fortunately most of the patients showed improvement in general condition and in none of the cases any significant adverse effect or any new features were noted.

Discussion

In the present study, majority of the WD patients in the first decade of life presented with hepatic manifestations, a finding in conformity with that of most other studies [6,7]. This can be explained by the fact that the disease is characterized by excessive accumulation of copper in liver, brain, eyes and other tissues, but due to impaired hepatic storage and excretion, the copper first accumulates in the liver. Therefore, the usual presentation during the earlier age is hepatic disease [8]. The mean age of onset in the present study was 11.9 years. This is different from the findings of studies done in the central part of India and Europe, but is in conformity with some studies from the northern and the western parts of India [9,10,11,12]. Although, most workers describe the neurologic manifestation predominating only after 20 years of age, in our study, a significant number of patients had neurologic manifestations in the second decade of life [13]. Some other studies from India have found that neurologic manifestations tend to occur earlier in the Indian subcontinent owing to traditional practice of cooking and eating food in copper utensils [14,15]. Neurologic manifestations were present in 42.8% of cases in our study (including the mixed type of presentation). Among these manifestations, dystonia and gait disturbances were the predominant features followed by dysphasia, seizures and tremors. In a study from West India, tremors and speech disturbances were the commonest neurologic abnormalities followed by dystonia, while in a series from Eastern India, dystonia variety was most frequent [12,16]. In the present study, in none of the neurologic type of WD patients, there was history of jaundice or any symptom suggestive of hepatitis occurring earlier, which indicates that contrary to common belief, liver disease should not be expected.
in all pediatric WD patients and it is not infrequent to find pure neurologic WD in children.

Among the hepatic group, a history of self resolving hepatitis or jaundice was present in about one third (35.71%) of cases; evidently, WD had not been thought of before. As it is very difficult in hepatitis cases to distinguish viral from metabolic causes, especially in developing countries, where investigatory facilities are limited, a high index of suspicion is necessary in order to screen for WD in any case of unexplained hepatitis.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>First decade (5-10 yrs)</th>
<th>Second decade (11-15 yrs)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum ceruloplasmin &lt;20 mg/dL</td>
<td>3</td>
<td>10</td>
<td>92.85%</td>
</tr>
<tr>
<td>24 hour urinary copper excretion &gt;100µg/24 h*</td>
<td>4</td>
<td>10</td>
<td>100%</td>
</tr>
<tr>
<td>Serum copper &lt;75mg/dL</td>
<td>3</td>
<td>5</td>
<td>57.14%</td>
</tr>
</tbody>
</table>

Table 3: Investigatory profile of Wilson disease patients

In all cases, excretion was >200µg/24 h, i.e., >2x ULN (upper limit of normal)

The biochemical parameters are shown in table 2. In the present study, increased 24 hour urinary copper excretion was present in all the patients. Though, abnormal findings were found in all cases in which neuroimaging was done, there was no correlation between them and the clinical severity of the disease.

On follow up, 9 (64.28%) patients showed improvement within 6-8 weeks. Deterioration was, however, noted in 5 (35.17%) patients, in whom the drug was withdrawn for 1-2 weeks and then restarted. While 3 (21.42%) of them showed improvement on re-initiation of the drug, 2 (14.28%) patients failed to show any significant improvement.

**Conclusion**

In summary, Wilson disease should be strongly considered as a diagnostic possibility in any child with unexplained liver disease, particularly in the absence of viral markers and in the presence of neurologic manifestations. Neurologic manifestations tend to occur earlier in our country unlike in the West. Lack of hepatic involvement usually delays the diagnosis in neurologic type which is unfortunate, because early and correct diagnosis can prevent the devastating consequences as the Wilson disease is a treatable condition.

**Acknowledgement**

We are thankful to our Head, Prof A K Rathi, for his guidance and support in conducting the study. We are also thankful to the management of the Institute for giving us the permission to carry out this study and all other help rendered in this regard.

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Research Study:
Prescriptions Audit and cost indicators in treatment of Diarrhea among children under 5 years of age

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Key Words: Diarrhea, Dehydration, Prescription Audit, ORS, Zinc, Poly-pharmacy

Abstract

Objective

The present study evaluated the pattern of drug use and cost of management of acute diarrhea in childhood.

Method

Questionnaire was designed factoring patients’ demographic profile, history, disease severity, prescription regimen, nutritional advice and cost of therapy.

Result

A total of 102 prescriptions {70% outpatient department (OPD) and 30% (in patient department (IPD))} for acute childhood diarrhea were analyzed. Maximum children were in the age group of 6 months to 1 year (47.4%). Male were 60% and female 40%. The average number of stools per day at the time of presentation was 4. Of them, 80% had watery diarrhea and 20% had presence of mucus in stool. Tenesmus was reported in 25% of cases. Clinical diagnosis was made as ‘Viral diarrhea’ in 75% cases and as ‘Bacterial diarrhea’ in 10% of them. 15% were labeled as ‘Loose motion’ pending laboratory confirmation. 60% had some dehydration and 15% had severe dehydration and were hospitalized. Nutritional advice was given to 92% cases and 72% were advised to continue more frequent breastfeeding on the prescription in writing. The average number of drugs per prescription was 4. Total cost of therapy per prescription was Rs 66/- for OPD and Rs 264/- for hospitalized cases. The percentage of drug prescription by generic name was 99%. Zinc was prescribed in 98% and oral rehydration solution (ORS) also in 98% cases. Injectables, including intravenous fluid, were given to 30% (All IPD cases). Antibiotics were prescribed in 22% patients, the most common drug being Cefixime for OPD cases and Ceftriaxone for IPD cases by brand names. Antibiotic use correlated well with 25% invasive (Bacterial) diarrhea. There was no use of probiotics, antisecretory or antimotility agents. Most common concomitant medications prescribed were paracetamol and domperidone.

Conclusion

The prescribing pattern in childhood acute diarrhea by and large was found to be in conformity with the WHO guideline in the teaching hospital. However, Poly pharmacy, prescription by brand names and high average cost per prescription (Excluding the hospital related charges other than medications for IPD cases) are still matters of concern.
Introduction

The World Health Organization (WHO) defines diarrhea as the passage of unusually loose or watery stools, at least three times in a 24 hr period. However, it is the consistency of the stools rather than the number that is most important. Frequent passing of formed stools is not diarrhea. Diarrheal diseases account for about 8.2 per cent of the total burden of disease in India, contributing about 22 million of Disability Adjusted Life Years (DALYs) lost, the highest among communicable diseases (1). According to National Family Health Survey (NFHS)–III, about 9 per cent of children under age five in India had diarrhea in the two weeks preceding the survey. Every 30 seconds a child dies due to diarrhea globally.

Diarrhea remained the second most important cause of death among children under five in India (16%), next to pneumonia (17%). It is a major cause of hospitalization and death of young children, particularly the under nourished (2). Acute diarrhea among children account for about 3 million deaths worldwide under 5 years. On average, any child under 3 years of age will have 1 to 3 episodes of diarrhea every year, mostly of viral etiology.

Based on a meta-analysis of randomized placebo controlled trials, the Indian Academy of Pediatrics (IAP) published guidelines for effective management of acute diarrhea in 2004 (4). The guidelines focused on the use of low osmolarity ORS and zinc in acute diarrhea; use of antibiotic only in dysentery where indicated and also focused management of diarrhea in severely malnourished children, being the very high risk group. These guidelines were further revised in 2006 (5). Since diarrheal diseases contribute significantly to both morbidity and mortality and have serious economic consequences for the family as well as the nation, it is necessary to analyze the pattern of drug use in acute diarrhea and evaluate its compliance to the WHO and IAP guidelines from time to time. Thus monitoring the extent to which our health care providers follow established guidelines in India at the grass root level is of paramount importance.

Material & Methods

This is a cross sectional descriptive observational study to determine the pattern of drug use in treatment of acute diarrhea in children at the Pediatric unit of MGM Medical College, Kalamboli, Navi Mumbai. The study was approved by the Institutional Ethics Committee and was performed over a 10 month period between September 2011 and June 2012. Permission of the competent authority was obtained. The data were collected prospectively from the out patients visiting the OPD as well as in patients admitted to the hospital. Prescriptions of 102 patients who were treated during the course of the study were audited prospectively by using a pre- designed proforma.

Once the consultation with the pediatricians was over, the prescriptions were copied as it is, and the patients and / or their parents / attendants were interviewed in order to ascertain whether they were explained about the management plan and nutrition in diarrhea, after obtaining their informed consent to participate in the study. The data included name, age, sex, indications
(diagnosis), name of the drug(s), dose, route of administration, frequency and duration of treatment advised. After noting down the required parameters prescription was returned to the patients.

All the prescriptions were analyzed for nature of the anti diarrheal drug medication, use of antibiotics if any, ORS, probiotic and zinc therapy in children having diarrhea. Each parameter was expressed in percentage in terms of total number of prescriptions audited.

**Pattern of drug usage**

1. Percentage of patients receiving antibiotic for diarrhea.
2. Percentage of patient receiving injectable drugs, including intravenous fluids.
3. Percentage of patient receiving zinc therapy and the average daily dose.
4. Percentage of patients receiving ORS and nutritional advice.
5. Encounters with concomitant medications used e.g. - antiemetics, antisecretory and antimotility drugs if any, for symptoms like fever, vomiting and abdominal pain during the course of diarrhea

**Prescribing indicators**

The following prescribing indicators were used in this study:-

1. Average number of drugs prescribed:
   It is the total number of drugs prescribed, divided by the number of encounters surveyed. The purpose of this indicator is to describe the pattern of poly pharmacy, where more than 2 drugs are prescribed (Often unnecessary) for the same condition.

2. Frequency of using drug(s) having brand name(s).

**Cost indicators**

In this study the following economic indicators were used.

1. Average cost of Prescription for OPD cases
2. Average cost of Prescription for IPD cases

**Results**

During the study, 102 cases were recorded from MGM Medical College Hospital for Women and Children, Kalamboli, Navi Mumbai, India. In all, 455 drugs were prescribed in 102 prescriptions.

**Patient Demography**

A total of 102 prescriptions and case files (70% OPD and 30% IPD) of acute childhood diarrhea were analyzed. Maximum children (47.4%) were of age group 6 months to 1 year {Male (60%) and female (40%)}. The average number of stools/day at the time of presentation was 4. Of these, 80 % had watery diarrhea and 20 % had presence of mucus in stool. Tenesmus was reported in 25 % cases. 60% had some dehydration and 15 % had severe dehydration, warranting hospitalization. Nutritional advice was given to 92 % cases and 72% were advised to continue breast feeding in writing on the prescription (Table 1).

**Pattern of drug usage**

The percentage of cases where ORS was prescribed was 98 % (Including those after correction of severe dehydration by intravenous fluids in wards), Zinc in 98 %, and
antibiotics in 22% cases (Most common antibiotic being Cefixime for OPD cases and concomitant medication prescribed was paracetamol, domperidone for fever and vomiting respectively (Table 2).

### Prescribing indicators

The percentage of generic prescribing was observed in 99 % cases. Parenteral preparations were prescribed to 30 patients (IV fluids and injectable antibiotics) who were hospitalized for the purpose. 22 of these 30 IPD patients (73.3% of IPD and 22% of all diarrhea cases) received parenteral antibiotics (Ceftriaxone). The average number of drugs per prescription was 4. Poly pharmacy was observed in the most cases (Table 2).

### Table 1: Demographic data of childhood diarrhea at the department of Pediatrics, MGM Medical College Hospital for Women & children, Navi Mumbai

<table>
<thead>
<tr>
<th>S.N.</th>
<th>Parameters</th>
<th>Results (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Average Drugs/prescription</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>Poly-pharmacy practice</td>
<td>99%</td>
</tr>
<tr>
<td>3</td>
<td>Encounters with brand names</td>
<td>99%</td>
</tr>
<tr>
<td>4</td>
<td>Encounters with parenteral preparations</td>
<td>35%</td>
</tr>
<tr>
<td>5</td>
<td>Average cost/prescription (OPD cases)</td>
<td>RS 66/-</td>
</tr>
<tr>
<td>6</td>
<td>Average cost/prescription (IPD cases)</td>
<td>RS 214/-</td>
</tr>
<tr>
<td>7</td>
<td>Encounters with antibiotics</td>
<td>22%</td>
</tr>
<tr>
<td>8</td>
<td>Most commonly</td>
<td>Taxim-O (Cefixime) in OPD; Inj. Taxim</td>
</tr>
<tr>
<td>Prescribed Antibiotic</td>
<td>(Ceftriaxone) in IPD</td>
<td></td>
</tr>
<tr>
<td>----------------------</td>
<td>---------------------</td>
<td></td>
</tr>
<tr>
<td>9 Encounters with ORS</td>
<td>98%</td>
<td></td>
</tr>
<tr>
<td>10 Nutritional advice</td>
<td>92%</td>
<td></td>
</tr>
<tr>
<td>11 Breast feeding / feeding continued</td>
<td>72%</td>
<td></td>
</tr>
<tr>
<td>12 Encounters with Zinc</td>
<td>98%</td>
<td></td>
</tr>
<tr>
<td>13 Encounters with Probiotic</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>14 Encounters with Antisecretory agents</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>15 Encounters with Antimotility agents</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>16 Common Concomitant medications (Other than anti-diarrheal drugs)</td>
<td>Paracetamol and domperidone</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Prescribing and cost Indicators in childhood diarrhea cases at department of Pediatrics, MGM Medical College Hospital for Women & Children, Navi Mumbai.

**Cost indicators**

Total average cost of therapy per prescription worked out to be INR 66 for OPD patients and INR 264 for hospitalized cases (Table 2).

**Discussion**

Acute gastroenteritis continues to be a leading cause of mortality and morbidity in the pediatric population globally, responsible for death of 2.5 million under-five children every year. In India, diarrheal diseases are the second leading cause of child mortality (16%). With good management of dehydration in the hospital setting, higher mortality is particularly observed if diarrhea is associated with under-nutrition (6). The latest HungaMa (Hunger and Malnutrition) report revealing 43% of our children being under-nourished, effective management of childhood diarrhea, including proper nutritional advice, is the need of the hour.

![Sunken Eyes in dehydration](image)

**Fig.-1: Sunken Eyes in dehydration**

There have been few published studies to determine the extent to which health care providers follow treatment guidelines in India (7). The IAP guidelines for management of acute diarrhea in 2004 as well as WHO focused on use of low osmolarity ORS, Zinc in acute diarrhea; limiting antibiotic use in dysentery only where indicated, such as- child under 1 year of age, high grade fever and under nutrition (8). These guidelines were further revised in 2006. However, it is important to study the extent to which such guidelines are being complied with in prescriptions, besides evaluating their cost effectiveness.
The drug utilization study for childhood diarrhea was carried out in the department of Pediatrics of MGM Medical College Hospital for Women & Children, Navi Mumbai, using validated questionnaires, having closed ended questions on the demographical profile of the patient, brief history, symptoms and signs at the time of presentation, prescription pattern, cost analysis and nutritional advice. The prescribing indicators analyzed the average number of drug(s) prescribed, average cost per prescription, frequency of using antibiotics, Zinc, probiotics, antimotility, antisecretory drugs, their use by brand names and parenteral preparations used.

A. Concept of Reduced Osmolarity ORS in the treatment of Acute Diarrhea

The earlier standard WHO ORS had a sodium concentration of 90 mEq/L (glucose 110 mmol/L, osmolarity 311 mOsm/L), which was primarily designed to tackle dehydration in cholera. Several considerations lead to clinical evaluation of reduced osmolarity ORS solutions by WHO (9). One main concern was the potential risk of hypernatremia with earlier WHO ORS in children with non-cholera diarrhea, particularly Rotavirus diarrhea where the stool sodium loss happened to be about 56 mEq Na as compared to cholera stool having about 90 meq/L sodium. It was also recognized that previous WHO ORS provided too much sodium to edematous children having Kwashiorkor (Fig-3 compared with Fig-2) where total body sodium content is high. Finally, laboratory experiments showed that reduced osmolarity solutions (Sodium 75 mmol/L, glucose 75 mmol/L, osmolarity 245 mosmol/L) promote water and sodium absorption more efficiently than earlier WHO-ORS. Based on the WHO/UNICEF and the IAP recommendations a National

![Image](https://example.com/image1)

Fig-2: Assessing dehydration by skin turgor

Expert Group formulated by the Ministry of Health, Government of India recommended that ORS should be prescribed by all physicians for all ages in all types of diarrhea, including cholera (5,8).

In the present study, ORS was prescribed in 98 % cases in compliance to the recommendations. Improvement in ORS prescription rate may be due to increasing awareness amongst practitioners and the community about treating and preventing diarrhea. As a matter of fact, ORS was
adjudged as the biggest invention of 20th century, apart from mass media campaigns about its importance (5). However the need to continue feeding or increased breastfeeding during and after the diarrheal episodes needs to be further emphasized.

**B. Zinc as an adjuvant in the treatment of Acute Diarrhea**

The rationale for use of specific nutrients as treatment of acute diarrhea is based on their effects on immune function or on intestinal structure or function and on the epithelial recovery process during diarrhea. Zinc deficiency has been found to be widespread among children in developing countries, and occurs in most of Latin America, Africa, the Middle East and South Asia. Zinc has been identified to play a critical role in metalloenzymes, polyribosomes, the cell membrane, and cellular function, leading to the belief that it also plays a central role in cellular growth and in the function of the immune system. Intestinal zinc losses during diarrhea aggravate the pre-existing zinc deficiency. Based on the WHO/UNICEF and the IAP recommendations, the Ministry of Health, Government of India has recommended that 20 mg of elemental zinc should be given to all children with diarrhea, older than 6 months, and should be started as soon as diarrhea starts, to be continued for a total period of 14 days. Children aged 2 months to 6 months are advised 10 mg per day of elemental zinc for same duration (10).

In the present study, it was observed that zinc was prescribed in 98 % cases. However, the duration of treatment was not specified as 14 days in 22 % cases. This suggests the need for educating the benefits of adherence to the complete duration of zinc therapy in acute diarrhea for decreasing its duration and severity.

![Fig. 3: Difficult to assess skin turgor for dehydration in PEM (Kwashiorkor)](image)

**C. Nutrition in Diarrhea**

The WHO insists caregivers to continue feeding children during illness (including diarrhea), and to increase intake thereafter (11). Despite this, with-holding of food is
wide-spread in the community contributing to deterioration in patient’s nutritional status. Controversy still persists at several care centers on relative risk of giving cow’s milk in acute diarrhea. Each episode of acute diarrhea causes weight loss and growth faltering. It is proportionate to the number of diarrhea days in a year. If frequent, there remains little time for “Catch-up growth” between diarrhea episodes. Identified as a primary goal in management i.e. to continue feeding with extra plain water, prevents dehydration while maintaining nutrition (12). Diet supplementation resulted in rapid catch-up growth after childhood acute diarrhea. Continued feeding neither increases stool volume, nor diarrheal duration. Withholding food delays repair of brush border and ability to produce enzymes (13). Small, frequent or continuous feed is better than bolus. Enteral feed resulted in faster recovery than I.V. therapy. Feeding also depends on care-givers’ attitude, faith, belief, knowledge, work load, compulsions, time, stress, self confidence. Food should be energy dense, clean and safe, soft, easy to eat, easy to cook, cheap, indigenous and culturally acceptable. To prevent micronutrient deficiency, diet should be enriched with Carotene rich food – Vegetables, butter, ghee, cheese, liver, fish and full cream milk. Poor-man’s dietary source of vitamin-A are curry leaves (25 grams of Curry leaves provide 7560 μgm of Carotene), drum-sticks, carrot and Banana etc. Studies have shown that all sick children having diarrhea and fever are able to accept and retain normal diet in terms of calorie and lipid based nutrition supplementation (14). Moreover, early nutrition supplementation leads to a faster return to baseline weight than in late supplementation group. The optimum approach should be that vast majority of diarrhea can be successfully managed with continued feeding of undiluted non-human milk. Oral rehydration therapy and early feeding along with milk form the basic approach. Lactose intolerance does not merit dietary alteration. Feeding must be continued. Animal milk protein intolerance is not common hence milk may be allowed in full strength.

If exclusively breast-fed, but have no dehydration, the child with diarrhea must continue breastfeeding frequently, that too for longer duration. If not exclusively breastfed or on complementary feed, usual diet with ORS or home based food and fluid (Soup, rice water, coconut water, yogurt) be given with sufficient water. Full diet, including lactose needs to be resumed. Energy-dense, least bulk food more often, every 2-3 hrs is advised. Full strength milk, curd, butter-milk; enrich feeds with fats, sugar (Khichri-curd, amylase rich food, rice gruel) be advised. Only few are likely to have complications from early feeding with undiluted milk. Few infants (Under 1 year of age) having diarrhea with co-existing malnutrition, need to be closely assessed whether to continue milk or receive a special formulation (Cereal-milk mix or with yoghurt). Some advocate specifically designed lactose-free formula. But breastfeeding must continue. Special attention is required for cases with severe malnutrition (Fig-3). Naso-gastric tube feeding may be necessary. Diet must offer 80-100 Cal / Kg / day, fluids 130 ml / Kg / day, proteins 1- 1.5 gm / Kg / Day,
potassium 5mEq / Kg / Day, folic Acid: 5mg on day –1; then: 1mg / day, copper 0.3mg / Kg / day, Zinc 2 mg / Kg / day, Iron 3 mg / Kg / day from day-7 onwards, along with vitamins such as A and D. Unless proper nutrition advice is explained to the caregivers, keeping in view of the above factors, the battle against diarrhea in a under nourished country like ours, will remain half won.

However, in the present study in the teaching hospital setting, nutrition advice was rendered in 92 % cases. Still detailed instruction to parents about diet for individual patient was lacking. Advice to continue breastfeeding was given in 72 % cases of infants, as reflected in prescriptions.

D. Probiotics, Antisecretory and Antimotility Agents:

There is insufficient evidence to recommend probiotics in acute diarrhea in our settings in India. Almost all the studies until now done in developed countries. It may not be right to extrapolate the findings of these studies to our setting where breast feeding rates are high and microbial colonization of the gut is different. The effect of probiotics is strain and dose related. There is paucity of data to establish the efficacy of the probiotic species (L. acidophilus). To recommend a particular species it will have to be first evaluated in double-blind, randomized controlled trials on Indian children who have different and varied spectrum of gut microbiota as that of their western counterparts. Earlier studies have documented a beneficial effect on rotavirus diarrhea which was present in more than 75% of cases in studies from the west. Rotavirus constitutes about 25% of diarrhea in hospitalized children and 15% in outpatient practice in India.

Reduction of total duration of diarrhea has been reported from 26 to 13 hours (15,16). Frequency wise, probiotics claimed to reduce only one stool per day of therapy. Hence it is not cost effective in a resource scarce country scenario, looking at high cost of these products currently available in market, their recommended dose and duration of therapy (Comes to nearly INR 500 alone for one week therapy). Effectiveness of probiotics only in antibiotic-associated diarrhea has however been documented (17,18).

**Racecadotril**: Presently enough evidence is not available on safety and efficacy of anti-secretory drugs e.g.- Racecadotril for recommending its routine use for treating diarrhea. There is no data from Indian setting. Methodologies of most of published studies are in variance, questionable and show conflict of interest on the part of industries.(19)

In the present study, there was no deviation from guidelines on probiotics, antisecretory and antimotility drugs. Working in an academic institution with access to updated information might have helped absence of probiotics, antisecretory and antimotility drug in prescriptions in a teaching hospital setting.

**Antibiotics in Acute Diarrhea**

Most acute diarrhea in children are caused by virus, e.g.- Rotavirus (10-35%), Adenovirus (2-10%), Norwalk virus (2-20%) where there is no role for antibiotics. In other 45-60% cases, no agent is detected, presumably due to untypable viruses. But
indiscriminate use of antibiotics in diarrhea to the tune of 59% has been observed, besides increasing incidence of antibiotic resistance. In contrast, ORS was advised in mere 26% cases of diarrhea (NFHS-III, 2005) whereas it is required in almost all the cases. Antibiotics are indicated for acute bloody diarrhea with specific indications only such as - infancy, immune-compromised state, under-nutrition etc.

Mere presence of RBCs or few pus cells on stool microscopy have poor specificity and should not form the basis to start antibiotics (20).

There was no deviation from these guidelines observed in the present study with regard to antibiotic use. Antibiotics were prescribed for 21% of patients having diarrhea on specific indications, in line with WHO recommendations (21). Mostly oral Cefixime was used in cases of dysentery for OPD and injectable Ceftriaxone for IPD cases, although WHO recommended Ciprofloxacin as the first line drug, keeping 3rd generation Cephalosporins at 2nd line, subject to sensitivity pattern of the offending organism in the region. However, liquid preparations of Ciprofloxacin are not freely available in India and this drug is not preferred by pediatricians for use among children owing to its taste and safety in smaller children. In another study, prescription of cotrimoxazole was found to be the highest at district hospitals (43.9%). Other antibiotics prescribed included Oxytetracycline (11.3%), Ciprofloxacin (8.7%), Nalidixic acid (8.2%) and tetracycline (7.9%) in acute diarrhea elsewhere. (22)

Antiemetics

Most children with vomiting can be managed with frequent small sips (5-10 ml) of ORS. Na citrate or bi-carbonate in it gets mild acidosis corrected slowly which induced vomiting. Antiemetics should be reserved for children in whom vomiting is severe, recurrent interfering ORS intake. Domperidone is the safest with no central nervous system side effects (Extrapyramidal symptoms). A single dose 0.1-0.3 mg / kg in children with severe vomiting recommended, continued use is not recommended. In view of serious side effects, metoclopramide is not recommended for vomiting in acute gastro-enteritis (23,24). In the present study, concomitant use of antiemetic was found to be in concurrence with recommendations.

Prescribing indices

The average number of drugs prescribed per prescription was found to be four. Generic prescribing was recorded in 99% cases. Parenteral preparations, including IV fluids were prescribed in 30 patients who were all admitted to the hospital (29.5% of total) as per guideline. Out of these 30 hospitalized patients, 22 (73%) received parenteral antibiotics (Mostly, Ceftriaxone). These included 12 cases where evidence of bacterial infection was not forthcoming. Poly-pharmacy, prescription by brand names and high average cost per prescription are matters of concern. This requires stricter pharmaco-vigilance and constant reviewing. We recommend establishing an efficient local prescribing policy through an effective practice-based Pharmacy and Therapeutic Committee. Besides, proper training in
ethical prescription policy to be introduced in medical schools and lending supports to continuous education programs, targeting such skills.

Cost of Therapy
In the present study, the average total cost of therapy for OPD cases was found to be INR 66 per child. In a study from Kerala, the estimated cost of drugs per patient came to be between Rs. 37.86 and Rs. 80.00 where as the total cost, including travel and fees came to be from INR 60.57 to INR 129.50 for OPD treatment. Increase in cost of treatment by frequent change of doctors among for under-five children was reported in a study conducted in Uttar Pradesh (27).

As regards IPD cases in the present study, the average total cost of therapy was found to be INR 264, much higher than OPD treatment. An analysis of prescriptions collected in the present study revealed that concomitant medications (Injectable antibiotics, IV fluids, antiulcer drugs, antiemetic medications) contributed to the higher cost significantly.

A study on patients admitted to Infectious Diseases Hospital in Pune City estimated average cost to be borne by the hospital as INR 164.87 and that borne by the patients as INR 111.36. The total cost per patient came to INR 276.23 (25, 26). A study reported that the average cost of therapy in Bangladesh District hospital was found to be TAKA 317.87 and at Thana Health Complex to be INR 406.90 (28).

Conclusion
This study showed a good adherence to standard treatment guidelines of ORS, probiotics, antisecretory, antimotility and antibiotic prescribing practices for acute diarrhea management in children. However, poly pharmacy, prescription by brand names, high average cost/ prescription for IPD cases and inadequate duration of zinc prescription are matters of concern. Further, the current practice scenario in community based non-teaching hospitals need to be explored and compared.

References


Case Reports:
Non respiratory presentation of childhood Sarcoidosis

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Key Words: Sarcoidosis, granulomatous diseases, lymphadenopathy

Abstract

Pediatric sarcoidosis is a rare multisystem disease with varied presentation mimicking a number of common chronic granulomatous diseases like tuberculosis. Herein, a case of pediatric sarcoidosis is presented with failure to thrive, profound anorexia, uveitis and multisystem involvement treated successfully with corticosteroids.

Introduction

Sarcoidosis is a chronic, multisystem, granulomatous disorder of unknown cause. Pediatric sarcoidosis is rare with incidence of 0.22-0.27 per 100,000 children per year (1). In developing countries like India, sarcoidosis is under reported probably due to lack of awareness and the presence of other more prevalent granulomatous diseases, especially tuberculosis. Literature search revealed 14 cases of reported pediatric sarcoidosis in India.

Case report

An 8 year old girl presented with complaints of occasional low grade fever, gross anorexia, pain abdomen, multiple joint pain with decreased range of movement of concerned joints and gradual loss of vision for last 6 months. There was no history of contact with tuberculosis or expose to organic dust, drugs or recurrent aspiration.

**Fig 1: Opacification of lower part of both cornea.**

**Fig 2: Chest xray- bilateral few reticular opacities**

Other history was uneventful. On examination pallor was present, weight 14.5kgs (< 3rd percentile on WHO chart),
height 117cms (< 15th percentile), no signs of vitamin deficiency, no lymphadenopathy.

Liver was enlarged 6 cms below costal margin, non tender, smooth surface, firm with rounded edge. Spleen was not palpable. Opacities were noted on lower part of both the cornea with distortion of both the pupils (fig no.1).

Respiratory rate was within normal limit, normal auscultatory findings. Joint examination was normal except mild restriction of range of movement of bilateral knee and elbow joints. Her hemoglobin was 10.2gms/dl, ESR-72mm, TLC, Platelets, LFT, RFT was normal. Chest x-ray (fig no. 2) was normal except little bilateral reticular opacity. Hepatotrophic viral profile, screening for Wilsons, ANA, Anti DNA, HIV1&2 were negative. Tuberculosis was ruled out by sputum for AFB, Mantoux test, augmented sputum examination. Barium meal follow through and colonoscopy didn’t reveal anything. CT scan abdomen (fig no.3) was done which showed small granulomatous lesions in the liver and retroperitoneal lymphadenopathy. Slit lamp and ultrasonography of both eyes confirmed bilateral chronic granulomatous iridocyclitis with anterior synachiae. Bilateral corneal diameter was 11cms. Acuity of vision – left eye finger count at 1ft and right eye 6 ft. Intraocular pressure was normal in both eyes. Bone marrow examination showed reactive marrow with no abnormal storage cell/ granuloma/ Hemoparasite. The chronic course, clinical features, ophthalmological examinations, CT scan findings and inability to find any mycobacterial or fungal infection directed us towards considering pediatric sarcoidosis as a provisional diagnosis. Liver biopsy (fig no.4) revealed non caseating epitheloid granuloma with Langerhans and foreign body giant cells surrounded by chronic inflammatory cells suggestive of Granulomatous hepatitis. Serum Calcium level was increased (12.2), CRP was 4.8-6 times normal, ACE level 151 (Normal 8-65).

Serum Amylase- 220u/L, serum Lipase-75u/L both was higher than reference range. Xray of concerned joints were normal. She was started on prednisolone 2mg/kg/day for 4 weeks than slowly reduced to a dose of 1 mg/kg/day on alternate days. Her appetite, general wellbeing, nutritional wellbeing has improved. Her vision has not deteriorated any further, and planning of keratoplasty was done.

**Discussion**

Sarcoidosis is a multisystem granulomatous disease of unknown etiology. The disease is relatively rare in the pediatric population (1,2). Infants and younger children (<
5 years) usually present with the triad of skin, joint, and eye involvement, without typical lung disease. However, older children have involvement of the lungs, lymph nodes, and eyes more frequently, as seen in adults (3,4). In a recent international study of childhood sarcoidosis, the mean age at onset was 10.6 years (range, 0.1–16 years) (5). Early-onset childhood sarcoidosis (onset in the first 4 y of life) is rare but well described (3,4).

The respiratory symptoms most commonly observed include cough and dyspnea. The most common radiographic findings in children are hilar lymph node enlargement, with or without lung changes. In the recent Danish report, chest imaging results were normal in 10% of cases (stage 0); 71% of the patients exhibited hilar lymphadenopathy (stage I), 8.3% parenchymal involvement (stage II), and only one parenchymal involvement alone (stage III) (2). But in our case there was no respiratory symptoms only some reticular patterns was noted in x ray.

The most common physical sign of reticuloendothelial involvement is peripheral lymph node enlargement noted in 40% to 70% of cases (9). Herein there was no peripheral lymph node involvement though there was retroperitoneal lymphadenopathy evident in abdominal CT scan.

Hepatomegaly occurs in up to 43% of patients with childhood sarcoidosis (9) and was present in this case. Liver involvement in sarcoidosis can be documented at biopsy in 24–94% of patients.

It is believed that bone involvement is rare in children with approximately 15% to 58% of people have involvement in their bone and joint system. Symptoms are usually joint pain, firmness, and deficiency of movement and it can affect virtually any joint (9).

![Liver biopsy](image)

**Fig 4:** High power view of Liver biopsy revealed non caseating epithelioid granuloma with Langerhans’ and foreign body giant cells surrounded by chronic inflammatory cells

Ocular symptoms are common, and may be the initial manifestation of the disease.

Anterior segment disease consisting of uveitis or iritis is the most common manifestation occurring in 24% to 58% of the children with sarcoidosis (4,9) Uveitis of sarcoidosis is characterized by keratic precipitates, most commonly in the lower part of the cornea. Anterior segment diseases are most frequent. Posterior segment diseases are less common (periphlebitis and chorioretinal granuloma).

Sarcoid involvement of the pancreas is uncommon. Clinically evident disease is rare and results from either direct infiltration of the gland or compression of pancreatic
structures by enlarged peripancreatic nodes (10) Pancreatitis was present here with presence of pain abdomen and elevation of serum Amylase and Lipase.

An erythematous rash is commonly noted in childhood sarcoidosis and occurs in 77% of young children and 24 – 40% in older children (3,9).

The basic histo-pathological lesion is the noncaseating epithelioid cell granuloma. The granuloma consists of epithelioid and giant cells and lymphocytes. The biological markers commonly measured are ACE, calcium metabolism parameters and biochemical liver function. Serum ACE levels are elevated in 40–90% of patients. The sources of this enzyme most probably include the epithelioid cells and macrophages at the site of inflammation.

Depending on disease severity, the steroid treatment is either oral steroid alone or in combination with intravenous pulse methyl prednisolone therapy. Oral prednisone is generally started at a dose of 2 mg/kg body weight/day, and tapered over 2–3 months to the lowest dose. In severe situations, steroid pulses are started using 300 mg/m² methyl prednisolone daily for 3 days, repeated once every 4–6 weeks. Alternative drugs alone or in association with steroids can be proposed in children, based on reports on management of adult sarcoidosis. These include mainly cytotoxic agents and the antimalarial drugs chloroquine and hydroxychloroquine.

**Unique characteristics-**

All the 14 previously published cases of childhood sarcoidosis from India presented with respiratory symptoms, but in our case there was no respiratory symptom.

**References**


Case Reports:
Air Leak Syndrome - Life threatening complication following manual Ventilation
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Key Words: Ventilation, Subcutaneous emphysema, pneumothorax, pneumomediastinum

Pulmonary air-leak syndromes involve dissection of air out of the normal pulmonary airspaces. It can occur due to alveolar rupture or tracheal laceration. Air-leak syndromes include pulmonary interstitial emphysema, pneumomediastinum, pneumothorax, pneumopericardium, pneumoperitoneum, and subcutaneous emphysema.

Pneumothorax and pneumomediastinum occur in 1 to 2% of normal neonates, probably because large negative intrathoracic forces created when the neonate starts breathing occasionally disrupt alveolar epithelium, which allows air to move from the alveoli to the extra-alveolar soft tissues or spaces. The perivascular connective tissue sheath that the air dissects along is more adherent and abundant in preterm infants as compared to term infants. As a result, air leak is more likely to become trapped in the perivascular space created by a partial dissection, which results in pulmonary interstitial emphysema. Pulmonary interstitial emphysema can completely regress or decompress into adjacent spaces, causing pneumomediastinum, pneumothorax, pneumopericardium, pneumoperitoneum, or subcutaneous emphysema. (1) Tracheal laceration after orotracheal intubation in children is a rare but potentially devastating complication resulting in major air leak.(2,3) There are several anatomical reasons why tracheal injuries can occur more frequently in children than in adults (4,5). Mature lungs contain pores of Kohn which are interalveolar pores that allow equilibration of alveolar pressures. Neonatal lungs do not contain these pores yet, which contributes to elevated alveolar pressures, rupture, and air leak.

Air leak is more common and severe among neonates with lung disease, who are at risk because of poor lung compliance and the
need for high airway pressures (eg, in respiratory distress) or because of air trapping (eg, meconium aspiration syndrome), which leads to alveolar over distention. It can be life threatening and sometime may be iatrogenic in neonates needing emergency management in the form of positive pressure ventilation in case of cardiac arrest and apnea. The authors report a neonate with meconium aspiration syndrome developing lethal pulmonary air leak following emergency resuscitation in the form of manual ventilation with endotracheal (E.T) tube and resuscitation bag.

An outside born male neonate was brought to our hospital in gasping condition. History revealed baby was born through meconium stained liquor, and was nonvigorous following the resuscitation steps baby was kept under warmer and suctioning was done under direct view with laryngoscope, and through E.T tube from lower airway. Even after the initial steps baby was not breathing well, with heart rate below 100 per minute, so positive pressure ventilation was done with bag and endotracheal tube. (6,7)

Within minutes of the intubation and ventilation procedure, cervical and facial subcutaneous emphysema, cyanosis and pneumoperitoneum were noted. Within few seconds subcutaneous emphysema progressively involved the whole body starting from head to toe. All attempts after this episode to resuscitate the baby were in vain, and within few minutes the baby expired.

This was a case of massive air leak syndrome following intubation and positive pressure ventilation in a case of meconium aspiration syndrome. Probable cause in this case can be massive alveolar rupture or tracheal perforation. As this was a term baby with meconium aspiration with no prior intubation or trauma sustained during intubation so probability of alveolar rupture remains high.

**References**


Case Report: 
Excessive intracranial calcification due to Hypoparathyroidism
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Key Words: Intracranial Calcification, Hypoparathyroidism, Calcium Metabolism

Abstract
Physiological intracranial calcification noted in 0.3-1.5% of cases, is asymptomatic, incidentally detected by neuroimaging. Pathological basal ganglia calcification is due to various causes, such as: metabolic disorders, infectious and genetic diseases. Hypoparathyroidism and pseudo-hypoparathyroidism are one of the most common causes of pathological basal ganglia calcification, adequate treatment of hypoparathyroidism may lead to marked clinical improvement, serum Ca, P and PTH is to be determined in all cases of basal ganglia calcification to rule out hypoparathyroidism.

Introduction
Hypoparathyroidism, an endocrinial disorder due to various causes like congenital disorders, iatrogenic causes (eg, drugs, surgical removal of the parathyroid glands during thyroid or parathyroid surgery, radiation), infiltration of the parathyroid glands (eg, metastatic carcinoma, Wilson’s disease, sarcoidosis), suppression of parathyroid function such as in hypomagnesemia, HIV, or idiopathic mechanisms. Hypoparathyroidism by any cause is well known for basal ganglia (BG) calcification in most of the patients. It is also well known that extensive intracranial calcification caused by hypoparathyroidism is rare. The case series presented here is of idiopathic hypoparathyroidism which presented with extensive intracranial calcification.

Case: 3mo old male child, admitted in our unit with intractable convulsion since birth. Already visited different doctors and was on Phenobarbitone and phenytoin. Birth wt-2.2 kg, Ht 48 cm (< 3 percentile), present Wt-3.7 kg, U/L- 1.66, OFC-30.5(<3 SD), Pulse 104/min, BP-86/54mm of Hg, not able to control eyes, not able to follow sound, microcephaly with closed fontanel & sutures, planter N/flexor, Jerk- increased, active jerky movement of right side of body, Liver 2 cm, fundus- no cataract, Disc (N). Another 5 yr old male sibling was apparently healthy.

O +ve blood group, Increased CRP, Serum total Ca- 6.3 mg/dl, ionic Ca-3.4 mg/dl, Serum P- 5.7mg/dl, Serum ALK P-191mg/dl (normal 150-470 mg%), PTH- 0.9 pmol/l ( normal 1.3 to 7.6 pmol/l). After ruling out other causes of hypoparathyroidism the possibility of idiopathic hypoparathyroidism was considered. The patient was started on IV Ca gluconate, oral Ca carbonate and alfalcacidol daily, and was asked for follow up.
Fig 1: CT Brain-Calcification in both cerebral hemisphere, mainly in Dentate nuclei, mid brain, caudate nuclei, thalami, putamina, globus pallidi & periventricular region B/L. Both lateral & 3rd ventricles were dilated, with wide extra axial CSF space.

Discussion

Hypoparathyroidism is caused by congenital disorders, iatrogenically induced, infiltration of the parathyroid glands, suppression of parathyroid function, or idiopathic mechanisms.(1) In these cases either there is apparent deficiency of PTH secretion or end-organ failure.(2) Idiopathic hypoparathyroidism is an uncommon condition of unknown etiology. (2) A literature review of the clinical presentations of BG calcification revealed that there are diverse presentations, commonly seizures, mental deterioration, and disorders of cerebellar or extra-pyramidal function. Radiologically hypoparathyroidism causes calcification most often in B/L BG.(4) The most common site is often globus pallidus.(5) Calcification can also occur in the cerebellum, sub cortical white matter, corona radiata and the thalamus. Cerebral deposition of calcium occurs in many pathological brain processes. Calcification, particularly of the BG, is associated with hypoparathyroidism of any type and, rarely, with other metabolic diseases; as a familial trait; and sporadically, without abnormal calcium metabolism. Frequent CT Brain led to the finding that sporadic calcification is the most common form, present in up to 1.5% of all brain scans.(6) Brain calcinosis syndrome (BCS) is defined as B/L calcium accumulation in the brain parenchyma, mainly within the BG. Various terms have been used to describe intracranial calcification including BG calcification(s), Fahr syndrome, intracranial calcification, pallidal calcification, and striopallidodentate calcinosis. More than 50 reported clinical conditions have been associated with BCS, including sporadic entities and the familial conditions. Before CT, 70% to 80% of brain calcification detected on plain skull radiography was associated with hypoparathyroidism.(7) However, about 80% of patients with BCS have no disturbances of calcium or phosphorus metabolism, and most patients with BCS have no clinical symptoms. Therefore, physiological calcinosis, probably related to ageing, is the most common cause of BCS.

* The immediate treatment for all types is calcium supplement with supplementation of PTH in cases of acquired hypoparathyroidism. Also one has to treat symptomatically for the seizures and other
changes, early detection and treatment has good prognosis.

Since adequate treatment of hypoparathyroidism may lead to marked clinical improvement, determination of serum Ca, P, and PTH is mandatory in all individuals with calcification of the basal ganglia to rule out hypoparathyroidism.

Conclusion

Since adequate treatment of hypoparathyroidism may lead to marked clinical improvement and due to its rarity, it is warranted to do serum Ca, P and PTH in all cases with calcification of BG to rule out hypoparathyroidism.

Acknowledgements

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References


Case Report:
Crigler Najjar Syndrome Type II a case report with brief review
Dr. Anjali Edbor, Dr Pradeep Pazare, Dr V.P Dandge, Dr S Nimbhorkar, Dr Sarosh Khan

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Keywords: Crigler Najjar syndrome, Indirect Hyperbilirubinemia, UDP Glucuronyl Transferase

Abstract

Crigler-Najjar syndrome type II (CN-II) is caused by a severely reduced hepatic activity of bilirubin UDP-glucuronyl transferase (UGT). Recently, by the analysis of the genetic background of CN-II patients, it has been clarified that the patients carry homozygous missense mutations or nonsense plus missense mutations on the gene for UGT, and CN-II was inherited as an autosomal recessive trait. We present an 8 month old female baby with waxing waning neonatal hyperbilirubinemia which responded well to oral phenobarbitone therapy.

Introduction

In 1962 Arias described a marked unconjugated hyperbilirubinemia different from Crigler-Najjar type I (CN-I), in which the serum bilirubin level ranges between 60 to 340 µmol/l and the bilirubin UDP-glucuronyl transferase (UGT) activity is <10% of normal levels (1, 2). Therefore also goes by the name of Arias syndrome (type II Crigler-Najjar), the condition is named after John Fielding Crigler (1919), an American Pediatrician and Victor Assad Najjar (1914), a Lebanese-American Pediatrician.

Incidence is less than 1 case per 1,000,000 births. Only a few hundred cases have been described in the world literature, and the real prevalence is unknown.

In this syndrome, Crigler-Najjar type II (CN-II), a slight increase in levels of bilirubin monoconjugates (>30% of total conjugates) are detected in the bile compared to normal controls (27%). Crigler-Najjar syndrome occurs when the enzyme that normally converts bilirubin into a form that can easily be removed from the body does not work correctly. Without this enzyme, bilirubin can build up in the body and lead to jaundice (yellow discoloration of skin and eyes) and damage to the brain, muscles, and nerves.(3)

Crigler-Najjar (type 1) is the early-onset form of the disease. Arias syndrome (type 2) is a later-onset condition.

The syndrome runs in families (inherited). A child must receive a copy of the defective gene from both parents to develop the severe form of the condition. Parents who are carriers (with just one defective gene) have about half the enzyme activity of a normal adult.(3)

Treatment with phenobarbitone causes an increase in the enzymatic activity and reduces at least 25% of the serum bilirubin level in these patients (4).
Case Report

An 8 months old female child was admitted with the complaints of waxing, waning jaundice since birth. There was a history of repeated admissions at other hospitals for this complaint at 1, 5 and 7 months of ages. The available reports suggested that it was a waxing and waning type of indirect hyperbilirubinemia.

There was no history of passing clay colored stools or high colored urine or vomiting or blood transfusion. On examination anthropometry was normal, vitals were stable, and child had mild icterus with hepato-splenomegaly. There was no cataract and facial dysmorphism and no signs of liver cell failure. Her neurodevelopment was normal.

Her investigations revealed normal complete blood count with normal reticulocyte index, RBC on peripheral smear were normal, hemoglobin electrophoresis was normal, G6PD was within normal limits and thyroid function test were normal which ruled out hypothyroidism and hemolytic anemia as a cause of persisting indirect hyperbilirubinemia. It was least likely that breast milk jaundice would persist till this age and Gilbert’s syndrome to present at this age. Hence the strong possibility of Crigler Najjar syndrome type II was kept in mind and the baby was started treatment with oral phenobarbitone 5 mg/kg/day. After 1 week of starting of treatment, serum bilirubin levels started falling down and came down to almost normal levels on discharge. The child is under follow up and is now anicteric with daily oral phenobarbitone 5 mg/kg/day.

<table>
<thead>
<tr>
<th>Age</th>
<th>Total serum bilirubin (mg/dl)</th>
<th>Direct serum bilirubin (mg/dl)</th>
<th>Indirect serum bilirubin (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>17.76</td>
<td>1.76</td>
<td>16.0</td>
</tr>
<tr>
<td>5 months</td>
<td>4.76</td>
<td>1.06</td>
<td>3.70</td>
</tr>
<tr>
<td>7 months</td>
<td>12.53</td>
<td>0.75</td>
<td>11.78</td>
</tr>
<tr>
<td>On admission</td>
<td>6.8</td>
<td>0.8</td>
<td>6.0</td>
</tr>
<tr>
<td>One week after therapy</td>
<td>4.2</td>
<td>0.2</td>
<td>4.0</td>
</tr>
<tr>
<td>On Discharge</td>
<td>1.8</td>
<td>0.2</td>
<td>1.6</td>
</tr>
</tbody>
</table>

Discussion

Crigler-Najjar syndrome type II is an autosomal recessive disorder. It is caused by homozygous missense mutation in UGT1A1 resulting in reduced (partial) enzymatic activity. It is a rare disorder and till now only few hundred cases have been reported. As the UGT1A1 activity is abolished in this condition, it causes Neonatal Hyperbilirubinemia & kernicterus in neonatal period. Unconjugated hyperbilirubinemia in the presence of normal liver function test findings is characteristic of Crigler-Najjar syndrome (5) as was found in our patient.

Type II differs from type I in several aspects: The usual bilirubin level is 17-50 mg/dL in type 1 Crigler-Najjar syndrome and 6-22 mg/dL in type 2. Higher bilirubin levels may be seen in type 2 Crigler-Najjar.
syndrome if coexisting hemolysis or inter-current illness is present.

Fig 1: Photograph showing the patient suffering from Crigler–Najjar syndrome.

Transferase activity measurements and the response to phenobarbitone treatment distinguish type 1 Crigler-Najjar syndrome from type 2. Phenobarbital has no effect in type 1 Crigler-Najjar syndrome but causes an approximately 25% reduction in plasma bilirubin level in most patients with type 2 Crigler-Najjar syndrome.

Because of lower serum bilirubin, kernicterus is rare in type II.

Bile is pigmented, instead of pale in type I or dark as normal, and monoconjugates constitute the largest fraction of bile conjugates.

UGT1A1 is present at reduced but detectable levels (typically <10% of normal), because of single base pair mutations.

Therefore, treatment with phenobarbitone is effective, generally with a decrease of at least 25% in serum bilirubin. In fact, this can be used, along with these other factors, to differentiate type I and II. (5,6)

Our patient also had a very good respond to oral phenobarbitone.

The inheritance pattern of Crigler–Najjar syndrome type II has been difficult to determine but is generally considered to be autosomal recessive. We could not ascertain the hereditary pattern as parents were unwilling for their investigations.

Treatment

Light treatment (phototherapy) is needed on a regular basis throughout life. In infants this is done using bilirubin lights (bili or 'blue' lights). Phototherapy becomes less successful after age 4, because thickened skin blocks the light.

Liver transplantation has been used successfully in some people with type 1 disease. (7)

Blood transfusions may help control the amount of bilirubin in blood plasma. Calcium compounds are sometimes used to bind with and remove bilirubin in the gut.

The drug phenobarbitone is sometimes used to treat Arias syndrome (type 2).

Complications

Possible complications include:

- Kernicterus
- Chronic yellow skin/eyes

Prognosis

Milder forms of the disease (type 2) do not cause severe toxicity, liver damage or other changes during childhood. People affected
still have jaundice, but they have fewer symptoms and less organ damage.

Infants with the severe form of the disease (type 1) may continue to have jaundice into adulthood, and may need daily treatment. If left untreated, this severe form of the disease will lead to death in childhood.

People with this condition who reach adulthood will develop brain damage due to jaundice (kernicterus), even with regular treatment. The life expectancy for type 1 disease is 30 years.

**Conclusion**

In our case the baby had persistent neonatal unconjugated Hyperbilirubinemia. The baby had received oral Phenobarbitone in private clinic that was discontinued by parents on their own that explains partial regression in bilirubin levels in past. This condition responds very well to Phenobarbitone in the dose 5 mg/kg/day which have to be given lifelong.

**References**


3. Osamu Koiwai et. Crigler-Najjar Syndrome Type II is inherited both as a Dominant and as a Recessive Trait. Human Molecular Genetics 1996, 5: 645-647.


Comparative effectiveness of Proton Pump Inhibitor versus H2-Receptor Antagonist therapy for Gastroesophageal Reflux disease.

Proton pump inhibitors (PPIs) are reported to be more effective than H2-receptor antagonists (H2RAs) for the treatment of gastroesophageal reflux disease (GERD) in adults. The aim of this study was to assess the comparative effectiveness of PPI versus H2RA therapy for the treatment of GERD in infants.

Records of infants 1 to 12 mo. of age with GERD were reviewed. Treatment outcome was assessed by the GERD Assessment Symptom Questionnaire (GASQ) (JPGN 2005;41:178-185). Baseline GERD symptoms at visit 1 were assessed after 1-month of H2RA therapy. Ranitidine was stopped and a PPI was prescribed. GERD symptoms were re-assessed after 4 weeks of PPI therapy. The difference in GASQ scores from H2RA and PPI therapy in the treatment group was compared to a control group of 16 infants who were treated with ranitidine over a similar length of time. Outcomes were compared using paired t-test. Results: 57 infants (25 males, age 3.1 ± 2.0 mo., mean ± SD, 69% Caucasian, 26% Hispanic, 5% African-American) with GERD diagnosed by GASQ scoring were studied.

Dietary history showed: breast milk (37%), protein hydrolysate formula (26%), cow milk formula (18%), commercially thickened formula (12%), and amino acid-based formula (7%). There were no significant differences in the rates of breastfeeding or the type of formula feedings in the PPI treatment or H2RA control groups. The GASQ scores after 4 weeks of ranitidine therapy at visit 1 were compared to GASQ scores after 4 weeks of PPI therapy on visit 2. The GASQ score results are shown in the table.

The results showed that GERD symptoms in patients 1 month to 1 year of age significantly decreased after PPI therapy compared to the GERD symptoms observed during treatment with ranitidine. We conclude that acid suppression therapy with PPIs yields a greater reduction in GERD symptoms than ranitidine therapy in infants.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>GASQ Score-Visit1 (H2RA)</th>
<th>GASQ Score-Visit 2 (H2RA or PPI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>H2RA vs. PPI (n=41)</td>
<td>287.1 ± 204.1</td>
<td>90.1 ± 86.7</td>
<td>0.00000 002</td>
</tr>
<tr>
<td>H2RA vs. H2RA (n=16)</td>
<td>114.8 ± 90.8</td>
<td>95.4 ± 111.5</td>
<td>0.50</td>
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</table>
Oral Ibuprofen versus Intravenous Indomethacin for closure of Patent Ductus Arteriosus in Very Low Birth Weight Infants

The purpose of this study is to compare the effects and complications of pharmacologic closure of patent ductus arteriosus (PDA) by intravenous indomethacin or oral ibuprofen in neonates weighing <1500 g at birth [very low birth weight (VLBW) infants].

This is a retrospective study of infants treated with intravenous indomethacin (0.2 mg/kg initially followed by two doses at 24-hour intervals) or oral ibuprofen (10 mg/kg initially followed an interval of 24 hours by two doses of 5 mg/kg) for symptomatic PDA in a neonatal intensive care unit at a medical center in Taiwan during the period of January 2005 to December 2010.

A total of 88 infants received indomethacin and 52 received oral ibuprofen. Among the survivors, the closure rate without surgical ductal ligation was 70.5% (62/88) in the indomethacin group and 61.5% (32/52) in the ibuprofen group (p = 0.342). The incidence rates of oliguria and elevated serum creatinine were significantly lower in the ibuprofen group (p =0.002 and p =0.022, respectively). There was no significant difference in incidence of upper gastrointestinal hemorrhage or necrotizing enterocolitis between the ibuprofen and indomethacin groups (17.3% versus 23.9%; 3.8% versus 11.3%).

In infants with VLBW, oral ibuprofen is as effective as intravenous indomethacin for closure of PDA and is associated with significantly fewer cases of necrotizing enterocolitis among infants with birth body weights <1250 g and significantly lower rates of elevated creatinine levels among neonates with birth body weights ranging from 1000 to 1500 g.

Comments: Oral medication is always the most preferable route of administration in pediatrics. If more studies favor these results, oral ibuprofen is the most effective drug.

Rheumatic fever in children younger than 5 years: is the presentation different?

To review our experience with children who presented with rheumatic fever (RF) before 5 years of age and to compare their presentation with that of older children.

The cardiology database was reviewed to identify patients who were younger than 5 years and had a diagnosis RF using the Jones criteria from January 1985 through March 2000. Patient age, sex, date and age at presentation, and the major Jones criteria fulfilled were noted. When carditis was present, its severity was judged to be moderate to severe when there was radiographic cardiomegaly and/or clinical congestive heart failure. The clinical presentation of patients who presented in the first 5 years of life were compared with the presentation of those whose RF was diagnosed after 5 years of age. Clinical findings at follow-up evaluation and echocardiographic findings both at presentation and at follow-up were noted for the children who were younger than 5 years at presentation.

Of 541 cases of RF seen from January 1985 through March 2000, 27 (5%) were in children who were younger than 5 years
(median: 4.0 years; range: 1.9-4.9 years). Major Jones criteria at presentation were arthritis in 17, carditis in 14, chorea in 3 and erythema marginatum in 3. The carditis was mild in 4 and moderate to severe in 10 patients. Compared with older children, younger children were more likely to present with moderate to severe carditis, arthritis without carditis or chorea, or the rash of erythema marginatum and were less likely to have chorea. The incidence of carditis was similar in the 2 groups as was the ratio of boys to girls. At follow-up (9.6 +/- 5.6 years), 69% of younger children who presented with carditis have clinical rheumatic heart disease. Subclinical, echocardiographically detected valvular abnormalities were detected both at presentation (33% of all children with RF before 5 years of age) and at follow-up (55% of those who initially had carditis).

Approximately 5% of children with RF were younger than 5 years at diagnosis. Compared with older patients, children who presented before 5 years of age were more likely to have moderate to severe carditis and to present with arthritis or the rash of erythema marginatum and were less likely to have chorea. Chronic rheumatic heart disease was common in young children who presented with carditis. Long-term follow-up is necessary to determine the outcome for young children with subclinical echocardiographic evidence of valvular disease.

**Safely ruling out inflammatory bowel disease in children and teenagers without referral for endoscopy**

Up to 70% of children and teenagers referred to a pediatric gastroenterology centre with suspected inflammatory bowel disease (IBD) do not have the disease.

To evaluate whether fecal calprotectin as an ‘add-on test’ improves the specificity of the clinical case definition for suspected IBD in a general pediatric practice. Prospective diagnostic accuracy study conducted. Six outpatient clinics for general pediatrics and one tertiary care hospital in the Netherlands.117 children and teenagers with a clinical suspicion of IBD selected.

Fecal calprotectin was measured (index test) in all patients. Patients with a high index of suspicion on the basis of the pediatrician's global assessment, physical examination and blood results were referred for endoscopy (reference standard). Children and teenagers who were not selected for endoscopy initially were followed for half a year for the appearance of possible additional symptoms (delayed type reference standard).

Primary outcome is proportion of referred patients with confirmed IBD.

The mean age of patients was 14 years (range 6–18). A total of 42 (36%) had confirmed IBD. The pediatricians, who were blinded to the fecal calprotectin result, referred 68 children and teenagers for endoscopy. If they had referred only those patients with a positive fecal calprotectin result (>50μg/g), 54 patients would have undergone endoscopy.

Limitation of the study is relied on clinical follow-up to detect missed IBD.

A diagnostic strategy in general pediatric practice of using a simple clinical case
definition for suspected IBD in combination with a positive fecal calprotectin result increases the specificity to detect IBD and reduces the need for referral to a pediatric gastroenterology centre with a very low risk of missing cases.

Comments: With the development of high yielding specific non invasive investigation, the referral for invasive procedures may be lowered.

Short-term Results of Vagus Nerve Stimulation in Pediatric patients with Refractory Epilepsy

Vagus nerve stimulation (VNS), an alternative method to manage patients with medically intractable epilepsy, has shown favorable results in reducing seizure relapse and improvements in quality of life. In 1997, the U.S. Food and Drug Administration approved the use of this device as an adjunctive therapy for intractable seizure in adults and adolescents older than 12 years of age.

We present a preliminary study of pediatric patients, who suffered from medically intractable seizure and underwent VNS implantation after observation of the baseline seizure frequency.

Classification of epileptic syndrome, seizure patterns and age of onset, seizure frequency reduction and adverse effects were recorded. Patients who underwent VNS implantation included four adolescents and four children. The follow-up duration ranged from 9–33 months. All the patients were responders after the beginning of the stimulation. Five of the eight patients responded to VNS with a seizure frequency reduction rate > 50%, and four of the eight patients experienced a ≥ 90% seizure reduction. No significant adverse effects were noted in all patients during the observation period.

The effective management of medically intractable seizure remains challenging to most clinical physicians. In addition to ketogenic diet and epilepsy surgery, VNS provides an alternative way to manage this issue. Our results suggest that VNS is well tolerated in pediatric patients, and is a favorable and safe method of treating intractable seizure in common clinical practice.

Comments: If more studies confirm the utility of VNS implants, it may prove an excellent adjunctive therapy for intractable seizures.
Dear Colleagues, Warm regards

Please accept the seasons greeting on behalf of we all. The practice of medicine has changed drastically in the twenty first century. There have been many positive as well as negative changes in medical sciences. The good age-old doctor-patient relationship is in doldrums. The communication skills have almost been forgotten. Commercialization is the obvious agenda especially with the development of corporate culture in the health sector. The concept of privatization has added fuel to the fire. The patient, who are willing to pay feel that the life can also be purchased with money. This has resulted in soaring expectations. Because of all these doctors are not only affected by medico-legal cases but many other legal problems arising out of other related issues of staff, instruments & infrastructure. The Government is coming up with newer and newer laws and restrictions on medical fraternity and hospitals. We have experienced this on many occasions, which prompted us along with some other colleagues & friends to form a medico-legal & ethics association.

In last few years, we found various problems, which as a medical consultants / medico-legal experts we were trying to solve single handedly. It was then, that we realized the need of a fleet of experts to work in co-ordination. The association has thus being formed to help you in preventing a disaster in your practice. We hope that we will succeed in achieving the aims and objects of guiding the medical practitioners in their difficult times. The various membership benefits include:
1) Personal / individual professional indemnity cover for upto five years (Amount and terms decided by Executive Board) included in life membership.
2) Hospital insurance at concessional rate (as compared to other insurance / risk management companies).
3) Free med-legal guidance in hours of crisis.
4) Services of crisis management committee at city / district level.
5) Free expert opinion if there are cases in court of law.
6) Services of legal experts at concessional rates (wherever available).
7) Participation in academic activities related to med-legal issues.

All this can’t be achieved without the help of dedicated, hard working, sincere members of the association. Hence, we would like you to become the member of this association. We hope that with active & enthusiastic members like you, our association will attain greater heights as we progress further. Please send your constructive criticism, suggestions, and programs for the future.

Yours truly
Dr. Balraj Singh Yadav
(Secretary)

Address for correspondence:
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9, Friends Colny, Jharsa Rd Gurgaon 122001
Phone: 0124-2339244; 09811108230 E-mail: kmcggn_2006@yahoo.co.in
INDIAN MEDICO-LEGAL & ETHICS ASSOCIATION
Membership Form

Name of the applicant: .................................................................
   (Surname)          (First name)        (Middle name)
Date of Birth: ........................................... Sex: ......................
Address for Correspondence: .................................................................
Telephone No: - Resi. ,........................................Hosp:..............................................
   Mobile:..................................................Other:..........................................
Fax:................................................E-mail ..........................................................
Registration no. ........................................ Date of Reg. ......................
Name of the Council (MCI/Dental/Homeo/Ayurvedic/ Others: ----------

Medical/legal qualification University Year

Experience in legal field (if any) -----------------------------
Name, membership no. & signature of proposer:-----------------
Name, membership no & signature of seconder:-----------------
A) Was / Is there any med-legal case against you /your Hospital: Yes / No
   If, Yes (Give details) -----------------------------------------------
   (Attach separate sheet)-----------------------------------------------
B) Do you have a Professional Indemnity Policy:       Yes / No
   Name of the Company:                                              Amount:
C) Do you have Hospital Insurance:    Yes / No
   Name of the Company:                                              Amount:
D) Do you have Risk Management Policy: Yes / No
   Name of the company:                                               Amount:
E) Is your relative / friend practicing Law: Yes / No
   If Yes, Name:                                                     Qualification:
   Place of Practice:                                                  Specialization:
F) Any other information you would like to share: (Please attach the details)
   I hereby declare that above information is correct. I shall be responsible for any incorrect / fraudulent declarations.
   Place: 
   Date:  (signature of applicant)

Enclosures: Degree & Registration Certificates
Life Membership fee (individual 2500/-, couple 4000/-) by CBS (At Par, Multicity Cheque) or DD, in the name of Indian medico-legal & ethics association (IMLEA) payable at Amravati. Please send the Cheque/DD to Dr. Satish Tiwari, Yashodanagar No.2 Amravati 444606.
MEMBERSHIP FORM
PEDIATRICS ASSOCIATION OF INDIA (PAI)
THE CHILD, B.K. ROAD, RANIHAT CUTTACK-753001, ODISHA

Name of the Applicant: ________________________________
Date of Birth: DD/MM/YYYY
Sex: Male / Female
Communication Address: ____________________________________________________________
________________________________________________________________________________
State: ______________________ Nationality: ____________________________
Telephones: (STD Code) __________________________________________________________
Mobile: ________________________________________________________________________
Email ID: _______________________________________________________________________

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<th>Medical / Pediatric Qualification</th>
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MBBS Registration No. & Registering Authority (e.g. MCI or State Medical Council):- 
________________________________________________________________________________

Short Curriculum Vitae with area of interest (within 10 lines):-
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________________________________________________________________________________
________________________________________________________________________________

Place: ____________________________
Date: ____________________________

Signature of the Applicant
(In hardcopy)

Recommendation of the Nodal Person:-

The statements above are true to best of my knowledge. His/her membership may be accepted.

Name of the Nodal Person: ________________________________