

ISSN 0975-0894

The

Child and newborn

The Journal of West Bengal Academy of Pediatrics

RNI Registration No. : RNI/68911/97



West Bengal
Academy of Pediatrics

Volume 26 No.1, January – March 2022

In Memoriam



Dr Umasankar Sarkar was the President of the then IAP West Bengal in 1984 and served as the Secretary of the organization in 1976-77. He was the first Editor-in-Chief of the journal *The Child and Newborn*.

He joined Institute of Child Health, Calcutta in June 1957. Subsequently he joined the laboratory for research work in hematology.

Dr Sarkar left Calcutta for UK in October 1961 and returned to India almost after one decade in June 1971. He also served as the Director of the Institute Child Health.

The Child and Newborn

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E-version of this journal available at website.

ISSN 0975-0894

RNI Registration No.:RNI/68911/97



West Bengal
Academy of Pediatrics

Vol.26, No.1 January - March 2022

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Tackling the Media in COVID Times

Since WHO announced 'mystery pneumonia' on 31 December 2019, the media have been following every step of COVID-19 till the vaccine development and beyond with multiple stories, innumerable discussions, incessant headlines and continuous updates. The constant barrage of new information, new cases, new developments and recommendations has been challenging to keep up with. A news piece one day could be entirely out-of-date by the next morning, and this has meant there have been many questions from the public surrounding the outbreak and the virus. As more information has emerged, experts and public health officials have revised their opinions, advice and recommendations.

Journalists and various media should do their utmost to keep up to date using reliable information from respective health departments and the WHO, and that they should both fact- and reality-check information in order to remain a trusted source.

More than a science story

The COVID-19 is not only far-reaching in terms of cases spreading globally, the disease has impacted so many sectors it has become far more than a health and science story.

Misinformation, stigma and fake news

A pressing problem with modern day online media is the spread of misinformation. Theories have been floating around that the virus was engineered in a lab as a bioterrorism agent, or that the symptoms are actually caused by the 5G mobile network. Thousands of listings promoting fake COVID-19 cures have been reported, and the prices of some sanitizers and facemasks have increased by over 2000%, despite in many cases not being fit for purpose.

Building stigma is incredibly bad for outbreak control – it can drive individuals to hide illness in order to avoid discrimination, it can prevent people from seeking healthcare and it can discourage people from seeking healthy behaviors, all of which aids viral spread.

General techniques for media interviews

Whenever a journalist contacts for expert opinion or briefing, it is better to avoid responding straight away. Ask them to provide information on the exact issue on which they would like you to comment, along with their deadline.

Before the interview:

- Know the purpose. Prepare two or three essential points that you want to get across during the interview.
- Support your points with facts or anecdotes from experience.
- There is no substitute for preparation. Study your subject and ask your friends, family, and colleagues to conduct mock interviews as practice.
- Consider your interview an "enlarged conversation" and speak as naturally as you would to another person.

During the Interview:

- A good rapport with the interviewer is important.
- Voice and delivery should be very clear.
- Maintain eye contact throughout the interview and keep an "open," friendly face.
- Enthusiasm and involvement in the subject should be evident.

Getting your point across:

- Be assertive in a pleasant way so that the conversation centers on subjects you want to talk about.
- Listen carefully to the question. If you don't understand a question, ask that it be repeated.
- Be careful not to repeat an interviewer's words, unless they reinforce what you wish to say. If an interviewer poses false premises in asking a question, correct him/her firmly but politely.
- Don't try to answer hypothetical questions; they tend to obscure your true position. Turn the tables by clearly stating your general position and then offering your own example.
- Use short words and simple, declarative sentences. Avoid scientific terminology. Be descriptive, using images that the listener can picture.

If you don't know the answer to a question simply say, "I don't know, but I'll find out the answer and get back to you." If you have a legitimate reason for withholding certain information then politely say it's confidential or proprietary.

Use the Inverse Pyramid in structuring responses –

Start with a general statement that sums up your position or philosophy succinctly and accurately. In the second part of your answer you should narrow down your response by giving the specifics of why you feel the way you do. This approach is particularly valuable for radio and television. If a producer decides to cut your five minute taped interview down to one minute for the evening news, chances are he/she will use your general statement.

Tips for television and radio:

- Treat your host and the audience as you would friends. Be friendly, spontaneous, and responsive.
- Know the length of your interview before you go on. If you have only a brief interview condense your answers citing your main points quickly. Think in terms of outline rather than exposition.
- Most interview programs will have the host or someone from the production staff "pre-interview" you before you go on, if only for a minute. This will establish what is expected of you, the direction the interviewer intends to take, and how much time you will be allotted. If no one goes over your presentation with you, ask if some time could be made available for this purpose.
- On television, look your interviewer in the eye and call him/her by his/her first name, unless he/she is much older than you. Ignore the technicians on the set and look at the camera only when you want to drive home a special point directly to the viewing audience.
- Defensive body language like wringing hands, folding arms across the chest, clenching fists, or narrowing eyes should be avoided. Gesture naturally, and vary your gestures.

Tips for newspaper interviews:

- Never speak off the record; assume that everything you say will be reported, whether it's before, during, or after an interview. It is always better to send the report in email or WhatsApp text.
- Make sure that what you tell the reporter is what you want to see in print. If you are unhappy with the way you have phrased something, stop and rephrase or clarify your original statement. If you realize after the interview that you misstated a fact or phrased something poorly, call the reporter to correct the error.
- A newspaper reporter generally do not allow you to review copy before it is printed.

Misquoting

Comments may be taken out of context and edited to change their original and intended meaning, to fit the news agenda of the day. The motive is often to create a sensation. If this happens, there are two possible courses of redress – seek an apology and/or a correction, or report the publisher to the Press Ombudsman. In the case of TV or radio, a complaint can be made directly to the broadcaster.

WHO tips for professional reporting on COVID-19 vaccines

The situation is constantly evolving but there are some general guidelines that should be followed whenever possible.

- Don't just report the topline – The findings in a study's summary may not be truly indicative of the full study's findings. Don't report based only on a press release. Always read the full study or research report.
- Don't trust data automatically – Reporting is only as good as its sources. Be sure to use expert and knowledgeable sources to inform stories on COVID-19 and vaccines. When reporting on a new vaccine or study, consult expert evaluations of the latest developments.
- State the source – When reporting on scientific studies, reports, case numbers and vaccines, name the source of the information to show credibility and allow readers to search for more information on the topic.
- Define the terms – Although certain scientific words may be used frequently in reporting on COVID-19 and vaccines, it is important to define scientific terms in every article.
- Use clear language – Some terms can be defined within the article but make an effort to frame explanations in simplified terms so that readers across all levels of comprehension will understand.
- Disclose the side effects – No vaccine in history has progressed through clinical trials and pre-approval as fast as the recent COVID-19 vaccines. Clearly stating the possible side effects of any given vaccine will help inform the public and ease their reservations as will reporting on any side effects experienced by participants in a vaccine trial.
- Don't forget demographics – Not every vaccine will be equally effective across all populations. When reporting on the efficacy of a vaccine in clinical trials, note the demographics of the participants in the trial.
- Remind everyone of the benefits of vaccines – Reporting on potentially effective COVID-19 vaccines is vital for informing those who already plan to be vaccinated, but with misinformation rife during the pandemic, don't forget to inform readers of the importance of all vaccines. Tackle vaccine hesitancy by reporting facts and figures on vaccine efficacy in ending epidemics throughout history.

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Dr Jaydeep Choudhury
Editor-in-Chief

Study to Assess The Clinico-epidemiological Profile of Infants Presenting With Cholestatic Jaundice in A Tertiary Care Pediatric Centre of Eastern India

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Keywords

Mortality in newborns, Neonatal care, Neonatal infection, Newborn

Abstract

Aim

To study the clinico epidemiological profile of infantile cholestasis and to ascertain their etiology.

Methods

This was a hospital based retrospective observational study done on 73 patients documented to have infantile cholestasis presenting to Institute of Child Health, Kolkata between January 2017 and August 2018.

Results

A total of 73 patients were enrolled, of which 46.5% were females and 53.4% were males. The most common presenting symptoms and signs were jaundice in all patients, hepatomegaly in 75%, acholic stool in 35% and splenomegaly in 29%. The most common etiology of cholestasis was biliary atresia (BA) in 37%, followed by idiopathic neonatal hepatitis (INH) in 27%. Other identified causes include choledochal cyst, alpha 1 antitrypsin deficiency, congenital infections, metabolic disorders, progressive familial intrahepatic cholestasis and various syndromes. The average age of onset of symptoms were 18 days. The mean age of presentation to hospital was 85 days.

Conclusion

Extrahepatic etiology accounted for 42% cases and hepatocellular in 58% cases. 27 had BA and 20 had INH. Delay in diagnosis and referral to tertiary care centre for further management affects the prognosis.

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Background

Cholestatic jaundice constitutes 19 to 33% of all chronic liver diseases in children reporting to tertiary care hospitals in India. This results from impairment in bile excretion caused by defects of intrahepatic production or transmembrane transport of bile or due to mechanical ductal obstruction preventing bile flow. Conjugated hyperbilirubinemia is generally defined as a conjugated or direct bilirubin greater than 1 mg/dL when the total bilirubin is less than 5 mg/dL or more than 20% of the total bilirubin if the total bilirubin is greater than 5 mg/dL¹⁻³.

Objectives

The primary objective was to study the clinical and epidemiological profile of infants presenting with cholestatic jaundice to a tertiary care hospital of eastern India. The secondary objective was to ascertain the etiology. Data was collected from 73 patients, aged 0-12 months, documented to have cholestatic jaundice from hospital records. This was a retrospective observational study done on patients admitted from January 2017 to August 2018. Infants with cholestasis due to sepsis or intestinal failure were excluded. Ethical clearance was obtained from the hospital ethics committee.

Statistical Analysis

46.5% (n=34) were females and 53.4% (n=39) were males. Clinical features included jaundice in all patients, hepatomegaly in 75%, splenomegaly in 29% and acholic stools in 31.5% (Table 1). Extrahepatic etiology accounted for 42% (n=31) cases and hepatocellular in 58%. (n=42) cases. 37%(n=27) had BA and 27% (n= 20) had INH. Other aetiology were choledochal cyst in 3 patients, parental nutrition associated cholestasis (PNAC), cytomegalovirus (CMV), congenital rubella,

progressive familial intrahepatic cholestasis (PFIC), alfa-1-antitrypsin deficiency, galactosemia and tyrosinemia. Four patients had Down's syndrome (Table 2).

The mean age of onset of clinical features was 18 days (range – birth to 80 days), with 47% patients presenting after 60 days of life. The mean age of presentation to our hospital was 85 (range 15 to 300 days) days with 38% presenting at 1-2 months age and 46% presenting between 2-6 months age. There were an overall delay of 75 days (range 14 to 299 days) in referral.

Tecnetium 99m Mebrofennin (Hepatobiliary scintigraphy, HBS) scan was done on 53% (n=39) patients and it was confirmatory for 84% of patients with extrahepatic BA. Liver biopsy was done for 77%

(n=56) patients. 44% (n=32) children underwent both HBS and liver biopsy. As extrahepatic BA was the most common cause of infantile cholestasis in our study, they were followed up and 37% (n=10) of them underwent surgical intervention in the form of portoenterostomy.

Out of the 73 children in our study, 14% (n=10) died and 26% (n=19) were lost to follow up. 18 patients were referred to a liver unit for further management.

Discussion

BA represents the major cause of infantile cholestasis and has been reported to occur in 35–41% of the infants¹⁻⁴. In our study as well, the most common etiology was found to be BA followed by INH. The diagnosis of INH in the present study was made after excluding various congenital and acquired

Table 1: Common presenting symptoms and signs of patients presenting with neonatal cholestasis.

Features	All patients	Extra hepatic	Hepatocellular
Jaundice	73/73 (100%)	31/31 (100%)	42/42 (100%)
Hepatomegaly	55/73 (75%)	29/31 (94%)	26/42 (62%)
Acholic stool	23/73 (31.5%)	18/31 (58%)	5/42 (12%)
Splenomegaly	21/73 (29%)	10/31 (32%)	11/42 (26%)
Coagulopathy	9/73 (12%)	6/31 (19%)	3/42 (7%)

Table 2: Etiology of patients admitted with neonatal cholestasis:

Extra hepatic	Hepatocellular
Biliary atresia = 27	Idiopathic neonatal hepatitis = 20
Choledochal cyst = 4	Cytomegalovirus = 3
	Congenital Rubella = 2
	Galactosemia = 2
	Tyrosinemia = 1
	Mitochondrial disorder = 1
	Alpha 1 anti trypsin deficiency = 3
	Progressive familial intra hepatic cholestasis = 2
	Alagille syndrome = 1
	Parenteral nutrition associated cholestasis = 1
	Trisomy 21 = 4
	Syndromic, not diagnosed = 2

infections, metabolic, endocrine and anatomical causes of neonatal cholestasis. However, the lack of availability of all modalities of investigations due to resource and financial constraints of our patients was our major limitation and in 27% of cases we could not determine the exact etiology of infantile cholestasis.

Jaundice was the commonest sign present in all patients at the time of presentation to the hospital which was similar to other studies¹⁻⁵. The other common symptoms and signs were acholic stool, hepatomegaly and splenomegaly. Few of the patients also presented to the hospital with coagulopathy. The average age of onset of symptoms in our study was 18 days and the mean age of presentation to hospital was 85 days which was similar to studies by Yachha SK, *et al*⁵.

Hepatobiliary scintigraphy (HBS) has limited role in evaluation of NC especially if the baby has clearly documented pale or pigmented stools. The time required (5-7 days) for priming the infant before the scan, especially in patients who are referred late, is a limitation. Performing a HBS is optional and one may go for a liver biopsy straightaway¹. However, we did a HBS for 53% cases and it showed non excretion in 84% cases of extrahepatic causes of cholestasis⁶. HBS has been shown to have a diagnostic accuracy of 67% with a low specificity of 37-74% and sensitivity of 98%⁷. Also non excretion in HBS may be due to severe neonatal hepatitis or due to interlobular bile duct paucity and hence needs cautious interpretation⁸.

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Liver biopsy is an essential investigation in the evaluation of neonatal cholestasis having a diagnostic accuracy of 91.6 %⁷. Early exclusion of biliary atresia by liver biopsy can avoid unnecessary laparotomy. The characteristic histopathology features of biliary atresia are bile duct proliferation, bile plugs in ducts, fibrosis and lymphocytic infiltrates in the portal tracts which we saw in our patients. In our study we performed liver biopsy in 77% patients.

There was a significant delay of 2.5 months from the recognition of jaundice to the time of diagnosis and management. The relatively unfavourable overall outcome for biliary atresia is mainly due to this late referral for the appropriate investigations to be conducted; and this has been supported in various other studies also¹.

The major limitation of our study was this being a retrospective study was conducted on a limited number of patients coming to a single tertiary care centre. As we are not a liver unit, we had to refer a few of the patients for further diagnostic tests and management. Due to financial constraint some of the patients were not able to get all the investigations done to arrive at a diagnosis.

The diagnosis of cholestasis should be followed by prompt referral when required, a quick investigative approach and a targeted management, considering the rapid progression of cholestatic jaundice to chronic liver disease.

Digital Learning and Social Media Addiction: Balancing the Boon with the Bane

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Introduction

The COVID-19 pandemic caused by the novel coronavirus SARS CoV 2 has wreaked havoc across the world in the past two years. It has had a significant impact on the lives of people, due to the various Government policies made to curb the transmission of the virus. The entire world went into lockdown and people had no option but to resort to digital social media to maintain connectivity. While there is no denying that the use of social media has brought the world closer and enabled individuals to escape the negative effects of lockdown and social distancing, it has also led to harmful consequences, especially in children and adolescents. According to the American Psychological Association, Internet addiction is defined as a behavioural pattern characterized by excessive or obsessive online and offline computer use that leads to distress and impairment. Social media addiction refers to the uncontrollable urge to use social media such that it impedes growth and leads to physical and mental adverse consequences. A study by Zhao Nan, *et al* in 2021 demonstrated that COVID-19 related stress enhances the risk of addictive social media (SMU) use¹. Altogether 512 Chinese students participated in the study where they provided self-report data on COVID-19 stress and SMU variables like time, active use, flow and addictive behaviour. The study indicated a positive relationship between pandemic stress and SMU variables. Research shows that the use of social media among children of developing countries like India is on the rise², and after the pandemic, it becomes even more pertinent to discuss this issue. The current review attempts to highlight the recent Indian studies that have been done on this topic and also summarizes the recommendations that have been mentioned.

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Methods

A meticulous search was done on electronic databases including PubMed, Medline, Google Scholar etc. to obtain literature on this issue. Indian studies done on or after 2020, which focused predominantly on social media use in children and adolescents were included. There was no restriction based on the study type or design. The following keywords were used : “social media”, “adolescents”, “India”, “pandemic”, “sleep difficulties”, “sleep quality”, “myopia”, “ergonomics”, “obesity”, “cyberbullying”, “anxiety”, “depression”, “self-esteem”, etc.

Results and Discussion

Physical adverse effects of social media addiction in Indian children :

Sleep difficulties – A study by Fernandez B, *et al* in the year 2020 investigated the impact of COVID 19 on internet use by adolescents from four countries including India. The results showed an increased use of social media by participants during the pandemic compared to the pre-pandemic era. Further, those who scored high on online gaming addiction reported poor sleep quality, depression and loneliness³.

Eye problems – Agarwal S, *et al*, in the year 2021, performed a cross-sectional observational study on Indian school going children regarding ocular problems faced by them due to excessive digital screen viewing during the pandemic. 39% of children reported headache, 38% reported rubbing of eyes, 29% of children complained of redness, watering, grittiness, watering of eyes and foreign body sensation and 19% of children reported eye pain⁴. Another study was done by Amit M *et al* in January 2022 to assess the rate of progression of myopia in children before and during the COVID-19 pandemic. 133 children aged 6-18 years were

included in the study. 45.9% of children showed an annual progression of =1 D during the pandemic as compared with 10.5% before the COVID-19 ($p < 0.00001$). History of rapid progression in pre-COVID-19 era ($p = 0.002$) and sun exposure <1 h/day ($p < 0.00001$) were found to be independent risk factors for rapid myopia progression⁵.

Obesity – A study by Surekha BC, *et al* in 2021 compared the Body Mass Index (BMI) of school children between the age of 3-15 years before and after the nationwide lockdown. The study revealed an increase in the mean BMI from 17.32 to 17.80 kg/m² ($p < 0.001$). A major reason for such an increase was the excessive use of social media and online gaming sites by children during the school closure⁶. Another study by Shah N, *et al* in 2020, performed on 77 Indian children between the age of 7-20 years also demonstrated significant weight gain post lockdown⁷.

Chronic neck and back problems – A pilot exploratory study was performed by Choudhary MS, *et al* in 2020 on 186 children between the ages of 10-18 years to determine the impact of ergonomics on children studying online during lockdown. 21% participants reported upper back pain, 18% lower back pain, 11% had headache, 6% reported poor sleep and 6% had behavioural problems. Very few parents understood the importance of ergonomics⁸.

Mental adverse effects of social media addiction in Indian children :

Anxiety, depression and low self-esteem – Previous studies have shown that the compulsive use of social media affects mental health in all age groups. Excessive and problematic social media use has been linked to lower self-esteem and decreased attention span in adolescents. It also leads to impaired cognitive development and speech and language delay in toddlers^{9,10}. A cross-sectional study on 474 Indian adolescents and youth was performed by Nathiya D, *et al* during the pandemic. The study revealed the presence of moderate to severe stress, anxiety and depression among 37%, 30% and 24% of participants respectively. Infodemics refers to the misleading information on digital platforms including social networking sites during a disease outbreak. In this study, contagious COVID infodemics on social media had been found to play a major role as psychological stressors¹¹.

Cyber bullying is a major way of inducing psychological distress like anxiety, depression and

suicidal ideation through social media and adolescents are particularly vulnerable to it. A study by Jain O, *et al* in 2020 attempted to determine the susceptibility to being cyberbullied among adolescents and youth during the pandemic in India. The study had some interesting conclusions. Adolescents of age 17-18 years were found to be significantly more prone to be cyberbullied during the pandemic than before it. Respondents who express their opinion strongly on social media platforms were 82% probable to be cyberbullied during the pandemic. Instagram seems to be particular concern, as 57% of respondents confessed to being cyberbullied on it. Susceptibility to cyberbullying increased with the increase in the degree to which an individual voices their opinion on social media and with their frequency of social media posts. Cyber bullying during online gaming activity also increased significantly during the pandemic. However, pandemic had no impact on the effect of one's perception of others' opinions of them, on their cyber bullying susceptibility¹².

Recommendations and Conclusion

In this digital era, social media has become an inseparable part of our lives. The global lockdown has made us realize what an important role social media play. Hence, children and adolescents should be educated about digital well-being and about the judicious and rational use of social media, so that they can reap its benefits and minimize the risks associated with it. Parents should be educated about the importance of frequent ophthalmic examination, which should include assessment of refractive error, accommodation, dry eye evaluation and ergonomic assessment. Children should be encouraged to follow the 20-20-20 rule of taking 20 seconds break to look at objects 20 feet away from their devices once in 20 minutes. They should be encouraged to view natural light as much as possible, as natural light is a protective factor against myopia progression. Font size of twice the individual's visual acuity is recommended for comfortable digital screen viewing¹³. It is important to practice "digital detox". There are various applications which help monitor the screen time. Children should be encouraged to use such applications and set an upper limit to the number of hours they spend on digital devices in a day. Parents should set family rules like banning device use during mealtimes, in the bathroom, etc¹⁴. Lack of sleep and

insufficient exercise are risk avoiding social media usage at bedtime leads to better sleep quality¹⁵. There are various groups on social networking sites which are dedicated to fitness. Children can be motivated to become part of such groups and follow their exercise routines, to enhance physical activity. Policymakers can incorporate chapters on digital well-being in school textbooks, so that it becomes a part of school curriculum. To prevent mental health problems due to social media addiction, children should be taught the difference between the digital world and the real world. Counselling is the key to promote a healthy sense of self-esteem. Parents and teachers play an important role in prevention of cyberbullying. Open communication with children and adolescents is imperative to enhance a sense of security. Forums should be created to report

cyber bullying and appropriate steps should be taken against the bullies¹⁶.

To conclude, the use of social networking sites among children of both developed and developing countries is only expected to increase in the coming years. Indian policymakers and healthcare professionals must be aware of this increasing trend of social media usage and take appropriate steps to mitigate the harm caused by such websites. More research is needed to explore the amount and type of social media use among Indian children during and after the COVID pandemic in order to create safe online spaces for children to reap the benefits of the internet and at the same time, to avoid the harm.

Conflict of interest – Nil

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Building Self-esteem In Children

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Self-esteem can be defined simply as how one thinks and feels about oneself. But, in real sense it is more than that. Self-esteem is also the sense how well individuals do things that are important to them and how well they can successfully affect their world. Thus it includes not only a sense of self-worth but also the child's self-confidence. It also includes their resilience i.e. their ability to bounce back from negative events quite effectively and choosing to focus on positive aspects i.e, a sense of optimism¹.

Self-esteem is extremely important for child's health and wellbeing and makes social interaction easier (social happiness). It helps children to stay positive and optimistic and to face up to the society with great confidence. It helps them to be more resilient and able to cope with challenges. It is a key to success as an adult.

Children with low self-esteem have difficult time dealing with problems. They are usually self-critical and may become passive, withdrawn and depressed. They may speak negatively about themselves and become pessimistic about their life.

Though self-esteem is in action throughout our lives, its signs in children first become evident to the pediatricians around 4 years of age². At about this age, a pediatrician can find that a child is learning to know herself and can appreciate her own abilities. Initiative and confidence to manage measured responsibility may be seen. Pediatricians may also observe a joy of autonomy in them. An urge to live up to the expectation may also be noted.

The synthesis of self-esteem in children occurs through complex interaction of temperament, developmental stage, family security, the parental

style of discipline, sibling and peer interactions^{2,3}.

Development of Sense of Self

Self-esteem develops gradually throughout life. The appearance of self-esteem requires development of certain cognitive abilities. It is built by accumulation of experiences created by parents and other caregivers. It begins with the responsiveness of the infant's environments. The development of self-esteem is transactional and is built by the responses the children receive to their increasing initiatives and abilities.

Throughout the period of early infancy (2-6 months), infants explore their own bodies – staring intently at their hands, vocalizing, blowing bubbles and touching their ears, cheeks and genitalia. These explorations represent an early stage in understanding cause and effect – the infants learn that voluntary muscle movements generate predictable tactile and visual sensations. All these things have a role in emergence of sense of self and separate from mother.

Infants begin to associate certain sensations through frequent repetition. The proprioceptive sensations of wriggling of fingers always accompany the sight of the fingers. Such “self” sensations are consistently linked and reproducible. The “other” sensations like sound, smell, feelings (which may not be so consistent) are also there. All these things help in emergence of self⁴.

At the age of 3-4 months, infants often smile at all individuals for social interactions and protest when left alone. At the age of 6-9 months, infants display interest in their own mirror image – one of the earliest indications of self-identity. Some infants, at the age of 7-8 months may prefer to grab the cup or spoon rather than accept passive role in eating. Some infants in this age may resist pressure to do

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something that they do not prefer to do⁵.

The sense of self rapidly expands beyond one year of age. By this time the toddlers have developed a specific relation with their caregivers and rest of the environment. They can explore their environment more easily than before and are increasingly able to function independently. At 1-2 years of age they can take pride in their own accomplishments and may clap on their own success⁵.

Preschool children spend more time away from primary caregivers and become much more independent. There is increased awareness of body sensations, increased verbal abilities, modest skill in donning and doffing cloths and also a desire to imitate adults. These newly acquired independences and the demonstration of competence are source of pride when parents take note of it². Preschoolers also enjoy playing alongside other children although not necessarily in co-operative play (ie, helping each other in addition to playing together). At around 4 years of age, children begin to voice judgments about themselves⁶.

In the school years, much of the concept of self-worth and competence is established and reinforced by those around them – the peers and teachers who assume a more influential role in continued development of self-esteem. At around the age of 8 years, children begin to use peer comparison to evaluate their own abilities³. During this period children integrate feelings about themselves from various areas and are able to realize the overall feelings of self-esteem⁷.

Nurturing Self-esteem

Self-esteem is essential to children's health and wellbeing and influence the development of relationship during both childhood and adult. All parents hope that their children will develop a positive self-esteem. Unfortunately, discussions related to self-esteem are usually held as a result of crisis or an observation noted by worried parents or teachers.

The role of pediatrician as a guide to enhance self-esteem in children is very important. The pediatrician may bring the parent's focus in this important matter. They are in a unique position to offer specific recommendations for enhancing self-esteem in their

patients during routine health check-up visits.

Encouragement :

To build positive self-esteem, children need encouragement. Self-esteem is nurtured when adults convey appreciation or encouragement to children. Encouragement should be communicated both verbally and non-verbally. For example, in the initial stage of learning, if a first grade learner spell some word incorrectly, he may not need immediate correction, rather should be praised for his early attempt. An appreciative, interested and positive response to the drawings or paintings by a preschooler can create a potent positive effect rather than criticism or disinterest. In general, the children should be allowed to develop at their own rate and should not be judged too harshly for their earnest early attempts.

Pressure :

The parent should realize the difference between encouragement and pressure. Pressure usually occurs when the parents have unrealistic expectations about their child. Pressure may also come when the parents have a false sense of how little development has occurred in the child. Inadvertent pressure can be detrimental and cause tremendous frustration and has a negative effect on self-esteem. As for example, pressuring a toddler into toilet training when the child shows no sign of readiness or forcing children to participate in rigid structured play is anxiety provoking and has negative effect on self-esteem. Pressuring young children to give up pacifiers or another security objects should not be done. In general, the children should be encouraged to explore and occasionally take risk.

Mistakes :

The parents and teachers should understand that the mistakes are natural part of learning process. The fear of making mistake and feeling embarrassed and humiliated is a strong hurdle in the development of children's self-esteem¹. The mistakes are experiences to learn from rather than to feel defeated. Pressuring children to do things "right" or "perfectly" is discouraging. This will inhibit children to participate in activities in future unless they are certain they can succeed.

The parents and teachers should emphasize what

children are able to do and what they know rather than what they cannot do and what they do not know. The adults may also share some of their own experiences of growing up and what they personally learn from failure².

Overprotection vs. autonomy :

The parents should not indulge in overprotection of their children. They should not control the child's environment so as to reduce any risk of failure or discomfort to their child. It will deprive the child to have the experiences of novel achievement. Also it will not be helpful to develop competence to work through frustrations and disappointments.

Encouraging autonomy is an important element of enhancing self-esteem in children⁸. The parents may show their respect for their children frustrations but should not rush to their aid – "It is hard to write when you are so far from the table. It may help if you push your chair closer".

Communication :

Communication style is an important factor in enhancing a child's self-esteem⁹. Some of the useful ways to build self-esteem in children are active listening, use of positive language, discarding levels, use of encouragement rather than pressure and use of "I" method of communication (i.e. use of reaction statement rather than judgment). The pediatrician should coach the parents and caregivers by setting a correct tone during counseling and should also focus on what parents are doing right.

One of the most important skills in communication is active listening (listening attentively). The parents must be attentive, stop what they are doing and look directly at the children. Non verbal cues like body posture and facial expression should be appreciated. The parents should listen to their opinions and avoid agreement and disagreement with their point of view¹⁰. When parents share their ideas and views with their children, they need to be nonjudgmental.

Children may build parts of their self-esteem by absorbing their parent's comments about them. Children may incorporate repeated judgmental expression (like stupid, clumsy, dull) into overall opinion about themselves. Parents can resist themselves from using judgmental comments by practicing the following suggestions.

- (a) Avoid using labeling words such as, messy, pretty, bad or good to describe a person.
- (b) The parents should be open with their feelings and should describe what they see and feel. Example – "I am angry that your homework is not done." Or "I am very happy that you have colored this picture so nicely".
- (c) Send reaction statement rather than judgment. "I" followed by what the parent sees or feels is a reaction statement (like, I am worried about your grades). Whereas, "You" followed by a noun or adjective describing the child is a judgment (like, you are lazy or you are brilliant).

In the reaction statement the parents explain their feelings to children rather than blame them for their action. Reaction statements identify specific behavior. They describe how the parents feel without attacking children's character. Using reaction statements separates children's performance from their personal worth. Whereas, judgment statements fail to separate children from their performances. Judgment statements lead the children to believe that their personal worth is based on other's opinion of their performance. This approach is believed to be less threatening and demeaning for children, especially in situations requiring discipline.

Discipline and Self-esteem

The relation between discipline and self-esteem is complex. Regarding self-esteem, the best way to discipline children is to provide them with clear and consistent guidelines and set limits (clear-cut rules) for their behavior. Coopersmith observed that children who felt good about themselves came from homes in which limits were clearly defined. Those from homes where limits were unclear and inconsistent felt more anxious and less secure¹¹. The parents should be informed that the limits need to be reasonable and clearly stated. Limits also should be enforced consistently and routinely.

Another positive approach to discipline is problem solving¹². Problem solving takes place when the parents and the child work together to reach a decision. Parents will encourage the child to (a) state the problem (b) express her needs (c) consider alternative solutions and (d) find a solution agreed upon by all.

Parents should be told about the importance of positive language while disciplining their children. For example, when the children are playing kick ball in the house, most of the parents usually yell by saying “No ball playing inside” or “Don’t play ball in the house” or “haven’t I told you before Instead of saying in this way parents can tell the children in a loving context (a) what they can do (b) what the limits are and (c) the reason of this rule. So, they can say “You have to stop this right now. If you kick it inside, you may break a window or hurt yourself or someone else. You may kick the ball outside in the backyard”.

Spanking and hitting are not constructive forms of discipline. They are demeaning to child’s self-esteem. Moreover spanking and hitting can teach children that it is okay to hit when angry or upset. Parents should be encouraged to model appropriate

behavior such as reasoning rather than using spanking or hitting.

Vulnerable Situations

There are certain situations when the children’s self-esteem may be adversely affected. Problems with self-esteem may be found in overweight children. The self-esteem of children who are suffering from enuresis or encopresis may be adversely affected. Negative experiences in school and home may predispose the child to feelings of shame and worthlessness. Marital conflicts, divorce or abuse of a parent may have negative effect on self-esteem of children who may feel responsible for the problems. In these circumstances, parental concern about the problem may provide an opportunity to the pediatrician to work together to minimize the effect to a great extent.

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Fluid in Pediatric Practice

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Introduction

Fluid is an important part of management of critically ill children during hospitalization. Early and appropriate fluid administration may improve the outcome and reduce mortality in sick children. Water is essential for cellular homeostasis. There are two major fluid compartments: the intracellular fluid (ICF) and the extracellular fluid (ECF). Two-thirds of the total body water (TBW) is intracellular. The TBW varies with age; 70% in infants, 65% in children, and 60% in adults. The human body has strict physiologic control to maintain a balance of fluid and electrolytes. However, in disease states, these mechanism may not work properly. IVFs are required if sufficient fluids cannot be provided by using enteral administration for reasons such as gastrointestinal illness, respiratory compromise, neurologic impairment, a peri-operative state, or being moribund from an acute or chronic illness. IVF may have both potential benefits and harms, it should only be administered when clinically indicated. Guidelines for maintenance IVF therapy in children have primarily been opinion based, and evidence-based consensus guidelines are lacking¹⁻³.

Phases of Fluid Therapy

There are four distinct phases of fluid therapy in children.

- (a) *Resuscitation phase* – It is the acute presentation window, when IVFs are needed to restore adequate tissue perfusion and prevent or multiple end-organ injury.
- (b) *Titration phase* – In this phase IVFs are transitioned from boluses to maintenance; this is a critical window to determine what

intravascular repletion has been achieved and the trajectory of fluid gains versus losses in children who are acutely ill.

- (c) *Maintenance phase* – This phase accounts for fluids administered during the previous two stabilization phases and is the time when fluids should be supplied to achieve a precise homeostatic balance between needs and losses.
- (d) *Convalescent phase* – It reflects the period when exogenous fluid administration is stopped, and the patient returns to intrinsic fluid regulation. The dose of fluid during these 4 phases of fluid therapy needs to be adjusted on the basis of the unique physiologic needs of each patient.

Pediatric Maintenance Fluid Calculation

The maintenance fluid volume is calculated on the basis of insensible water loss (IWL) [skin 30% and respiratory 15% does not contain electrolytes]; renal loss (50%); sweat loss (10 %) and stool loss (5%). Historically pediatric maintenance fluid was calculated by Holliday and Segar in 1957⁴. The water requirement was based on the energy expenditure of healthy children. One mL of fluid provided for each kilocalorie (Kcal) expended. But the resting energy expenditure in healthy children is vastly different in those with an acute disease and/or illness or after surgery. So some studies were done using calorimetric methods, energy expenditure in these patients is closer to the basal metabolic rate proposed by Talbot⁵, which averages 50 to 60 kcal/kg per day⁶. But there are disadvantages of this method also as in different illness caloric requirement may not be same and calorimetry is not universally available. So till date due lack of suitable alternative most of the units world wide using

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Holliday Segar formula, though it is over estimating fluid requirements in sick children (Table 1).

The electrolyte concentration of IVFs was estimated based on the composition of human and cow milk. The usual accepted composition consisted of 3 mEq of sodium and 2 mEq of potassium per 100 kcal metabolized⁴.

During initial phases of fluid therapy full amount of estimated maintenance fluid is provided to children if there is no obvious reason for fluid restriction like overt heart failure. Because in most of the cases of acute illnesses like in respiratory distress child remains fluid deprived due to poor oral intake at home. In case of raised intracranial pressure maintenance of cerebral perfusion pressure is very important. To do so we have to maintain good hydration status and provide full maintenance fluid.

After initial resuscitation phase a more fluid restrictive strategy should adopted if the child is hemodynamically stable. Because more liberal fluid approach in this phase may lead to fluid over load. Adult studies demonstrated risks of fluid overload in acute patients like acute kidney injury, acute respiratory distress syndrome, prolonged mechanical ventilation, mortality and intra-abdominal hypertension⁷⁻¹¹. So fluid can be restricted to 60% to 80% depending on the fluid overload, hemodynamic status and primary disease related factors.

Choice of Fluid

Historically pediatric patients are treated with hypotonic fluids. Most hyponatremia in patients who are hospitalized is hospital acquired and related to the administration of hypotonic IVFs in the setting of elevated AVP concentrations^{12,13}. The most serious complication of hospital-acquired hyponatremia is hyponatremic encephalopathy, which is a medical

emergency that can be fatal or lead to irreversible brain injury if inadequately treated^{14,15}.

After the recognition of hospital-acquired hyponatremia in patients receiving hypotonic IVFs and recommendations for avoiding them, the use of 0.2% saline has declined with an increase in the use of 0.45% and 0.9% saline¹⁶. There have been concerns raised about the safety of the proposed use of isotonic maintenance IVFs in sick children. Some believe that this approach could lead to complications such as hypernatremia, fluid overload with edema and hypertension, and hyperchloremic acidosis¹⁷. In the past 15 years, there have been a multitude of clinical trials and systematic reviews to address this dilemma¹⁸⁻²⁰.

Current recommendation by American Academy of Pediatrics of maintenance fluid choice in sick hospitalized children between 28 day to 18 years is isotonic fluid with adequate potassium and glucose²¹.

Dextrose can add osmolarity to a fluid but it has little role in tonicity. It dose not contribute to plasma osmotic pressure or tonicity because it gets rapidly metabolized after entering blood stream.

So DNS with added potassium may be most effective maintenance fluid in sick children.

Monitoring of Fluid Therapy

Patients undergoing fluid therapy should be under strict hemodynamic monitoring. Clinical parameters like blood pressure, CRT, heart rate, respiratory rate should be monitored at regular interval. Urine out put should be noted. Daily fluid balance has to be calculated to avoid unwanted fluid overload. Signs of early fluid overload as well as dehydration to be picked up early. Blood electrolytes specially sodium and potassium should be monitored regularly.

Table 1: Maintenance fluid volume requirement as per Holliday and Segar's formula

Body weight	Energy requirement	Fluid requirement
For the first: 3 - 10 Kg	100 Cal/kg/day	100 ml/kg/day
Plus, for next: 11 - 20 Kg	50 Cal/kg/day	50 ml/kg/day
Plus, for any Wt> 20 Kg	20 Cal/kg/day	20 ml/kg/day

Example: 25 kg child will require $(100 \times 10) + (50 \times 10) + (25 \times 5) = 1750$ ml /day of fluid (inclusive of feeds, IV fluids, drug infusions etc)

Formula to calculate fluid over load :

Daily [fluid intake (L)-total output (L)]/baseline body weight (in kilograms) x 100

Special situations:**Shock²²:**

- (a) In healthcare systems with availability of intensive care, recommendation is to administer up to 40–60mL/kg in bolus fluid (10–20mL/kg per bolus) over the first hour, titrated to clinical markers of cardiac output and discontinued if signs of fluid overload develop.
- (b) In healthcare systems with no availability of intensive care and in the absence of hypotension, recommendation is against bolus fluid administration while starting maintenance fluids
- (c) In healthcare systems with no availability of intensive care, if hypotension is present, recommendation is administer up to 40mL/kg in bolus fluid (10–20mL/kg per bolus) over the first hour with titration to clinical markers of cardiac output and discontinued if signs of fluid overload develop
- (d) As a choice of resuscitation fluid crystalloid is preferred over albumin and balanced fluid is preferred over 0.9% saline.

That resuscitation with crystalloid fluids containing high chloride concentrations (e.g., 0.9% saline) is

associated with hyperchloremic acidosis, systemic inflammation, acute kidney injury (AKI), coagulopathy, and mortality in comparison with resuscitation with more balanced/buffered crystalloids (Chloride concentration is more physiological), like lactated Ringer's, PlasmaLyte (Table 2).

Dehydration:

Features in different degrees of dehydration and fluid requirements are shown in Table 3.

- (a) Patients with mild dehydration may be rehydrated with oral therapy (ORS) if he accepts orally with a volume of 30- 50 mL/kg over 4 hours in small aliquots.
- (b) Patients with moderate dehydration should be given 100 mL/kg ORS over 4 hours.
- (c) Child with severe dehydration needs 100 ml/kg NS or RL IV over 2-3 hours in > 1 yrs of age or 5-6 hours in case of infants or malnourished (SAM) child.
- (d) Dose need to be repeated or inotropes added as per further partial improvement or development of features of cardiac failure.
- (e) Most dehydration is isotonic or hypotonic. For hypertonic dehydration slow correction over 48 hours with hypotonic solution (N/3 or N/4 saline) is needed to avoid cerebral edema.

Table 2: Composition of different IV fluids used in PICU

Fluids	Na+ mmol/L	K+ mmol/L	Cl- mmol/L	Carbohydrate mg/dl	Bicarbonate mmol/L (converted)	Osmolarity mOsm/L
Normal saline	154	0	154	0	0	308
Ringer lactate*	130	4	109	0	28	273
5% Dextrose	0	0	0	5	0	252
Plasmalyte *	140	5	98		27	295

*(balanced salt solution)

Table 3: Features in different degrees of dehydration and fluid requirements

Degree of dehydration	% volume of depletion	Signs and symptoms
Mild	3-5%	Thirst, decrease in urine output, dry mucous membrane
Moderate	6-10%	Postural changes in BP, heart rate, dry mucous membranes, sunken eyes and fontanel, skin tenting, listlessness, tachycardia
Severe	>10%	Poor perfusion, tachycardia, hypotension, lethargy and coma

Ongoing loss replacement :

All ongoing losses to be measured and effort is given to replace volume to volume. Losses include patients with chest tubes in place, uncontrolled vomiting, continuing diarrhea, or externalized CSF shunts. Replacement fluid should be of similar composition as the lost fluid (Table 4).

Renal failure:

Administration of optimal fluid amount is crucial. Patients with a normal intravascular volume should initially be limited to insensible losses (400 mL/m²/d) plus an amount of fluid equal to the urine output and extrarenal loss²³. Noticeable hypervolemic patients require further fluid restriction, omitting the replacement of insensible fluid losses, urine output, and extrarenal losses while considering adequate nutritional support. Usually insensible loss is

replenished with 5% dextrose and urine output is with 1/2 DNS. But fluid composition should be changed depending on the blood sodium level. In renal failure fluid is usually potassium free.

Malnutrition²⁴:

Oral fluid is always preferable in malnutrition over IVF. IV fluid is indicated in case of severe dehydration with shock. Usually 15ml/kg fluid is given over one hour. Choice of fluid is 1/2 DNS. Pulse rate and heart rate should be monitored every 10-15min during fluid therapy to pick up early signs of heart failure. If the child improves after the first bonus it can be repeated at same rate. After that it is changed to low osmolar ORS therapy at rate of 5-10ml/kg/hr by orally or through nasogastric tube depending on the conditions of the child.

Table 4: Electrolytes composition of different body fluids and compatible replacement fluids

Fluid	Na+	K+	Cl-	HCO ₃	Replacement fluid
Gastric	20-80	5-20	100-150	0	½ NS
Small gut	100-140	5-15	90-130	40	NS
Bile	120-140	5-15	80-120		NS
Diarrhea	10-90	10-80	10-110	40	½ NS
Burn	140	5	110		NS or RL

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Therapeutic Plasma Exchange

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Introduction

Apheresis is a general term meaning 'taking away'. It can either refer to plasmapheresis (plasma) or cytapheresis (cells). It is an extracorporeal process for selective removal of abnormal cells or substances in the blood that are associated with certain diseases. It can also be used to administer cells or constituents that are present in plasma in subtherapeutic concentrations. Therapeutic plasmapheresis or therapeutic plasma exchange refers to removal of patient plasma and replacement with autologous or allogenic plasma.

The pathologic substances include circulating immune complexes and autoantibodies (thrombotic thrombocytopenic purpura, systemic lupus erythematosus, systemic vasculitis), immunoglobulins (hyperviscosity syndrome), leukocytes in hyperleukaemic leucocytosis, platelets in severe thrombocytosis, abnormal red cells in sickle cell disease with vaso-occlusive crisis, toxins (mushroom poisoning) and hyperparasitemia (malaria, babesiosis).

History

Evolving from the historical practices of blood letting for hyperviscosity syndrome described as early as 1914, therapeutic plasma change has found a place in evidence-based medicine after the initial case reports of dramatic response in patients of myasthenia gravis. Thereafter TPE became a subject of various clinical trials as an intervention of last resort in a variety of serious immune-mediated diseases.

Introduced in 1986, The American society for Apheresis (AFSA) has published practice guidelines

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which are periodically reviewed every 3 years to provide a scenario of the current evidence-based apheresis practice. AFSA celebrates Apheresis Awareness Day annually on the third Tuesday in September.

Indications

For a substance to be removed by TPE the following criteria has to be fulfilled:

1. The substance must have a long half-life, so that extracorporeal removal is faster than the intrinsic elimination pathways of the body.
2. It must be acutely toxic or resistant to conventional therapy which warrants the need for rapid removal from the extracellular fluid
3. It must have a large molecular weight (>15,000 daltons), thereby restricting removal by techniques like hemodialysis.

ASFA guidelines are summarised in the 2019 guidelines (8th edition) which provides an extensive list based on the following categories

- Category I includes diseases where apheresis is accepted as first line therapy, either as primary standalone treatment or in conjunction with other modes of treatment.
- Category II includes diseases where apheresis is accepted as second line therapy wither as a standalone treatment or in conjunction with other treatments.
- Category III includes diseases in which optimum role if apheresis has not been established, here decision making should be individualised.
- Category IV includes diseases for which published evidence demonstrates apheresis may be ineffective or harmful.

Certain diseases included in Category I are as follows:

- Neurological
- Primary treatment in acute inflammatory demyelinating polyradiculoneuropathy (Guillain Barre syndrome)
- Catastrophic antiphospholipid syndrome (CAPS)
- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
- Paraproteinemic demyelinating neuropathies, chronic acquired demyelinating polyneuropathies
- Acute and short-term treatment in Myasthenia gravis
- N-methyl d aspartate receptor antibody encephalitis
- Renal
- Diffuse alveolar hemorrhage and dialysis independent antiglomerular basement membrane disease (Goodpasture syndrome)
- Focal segmental glomerulosclerosis: Recurrent in kidney transplant
- Renal transplantation (antibody mediated rejection, desensitisation, ABOi living donor)
- Hematological
- Erythrodermic cutaneous T cell lymphoma
- Hereditary hemochromatosis
- Acute stroke in sickle cell disease, stroke prophylaxis
- Thrombotic microangiopathy: Thrombotic thrombocytopenic purpura, Factor H autoantibody mediated, Ticlopidine associated
- Symptomatic hyperviscosity syndrome in hypergammaglobulinemia or with prophylaxis for rituximab
- Miscellaneous
- ANCA associated vasculitis
- Liver transplantation (desensitisation, ABOi living donor)
- Acute liver failure
- Fulminant Wilson disease

Certain diseases are included in Category II are as follows:

- Neurological
- Acute disseminated encephalomyelitis (ADEM) Steroid Refractory
- Lambert-Eaton myasthenic syndrome
- Acute attack or relapse multiple sclerosis
- Long term treatment of myasthenia gravis
- Acute attack or relapse of Neuromyelitis optica spectrum disorders (NMOSD)
- Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS); exacerbation
- Hematological
- Autoimmune hemolytic anaemia, severe cold agglutinin disease
- Severe or symptomatic cryoglobulinemia
- Symptomatic hyperleukocytosis
- Vasculitis
- Hepatitis B polyarteritis nodosa
- Severe complications in Systemic Lupus erythematosus
- Miscellaneous
- Dialysis-related Amyloidosis
- Severe Babesiosis
- Idiopathic dilated cardiomyopathy (NYHS II-IV)
- Heterozygous/ Homozygous familial hypercholesterolemia
- Graft versus host diseases
- Mushroom poisoning
- Phytanic acid storage disease (Refsum's Disease)
- Transplantation, hematopoietic stem cell, ABO incompatible (ABOi)
- Lung transplantation Bronchiolitis obliterans syndrome

Procedure

TPE requires centrifugation devices. Standard haemodialysis or CRRT hemofiltration equipment with a highly permeable filter can be used for this purpose. Two large reliable peripheral vascular

access or a central dual lumen catheter, appropriate apheresis/ dialysis catheters with proper radiologic confirmation of placement are vital. Most TPE procedures exchange 1-1.5 plasma volumes to remove the greatest concentration of the targeted substance.

Estimated plasma volume in litres = $0.07 \times \text{weight (kg)} \times (1 - \text{hematocrit})$

The replacement fluid is used to prevent volume depletion during the procedure. 5% albumin, normal saline or a combination of both is used in most conditions. It markedly reduces pathogen transmission and anaphylactic reactions. Fresh frozen plasma can be used as replacement fluid especially in TTP associated with ADAMTS13 deficiency. Complications are more common with plasma than albumin. Laboratory endpoint is based on desired endpoint of therapy, number of planned procedures and type of replacement fluid.

Filtration of blood through a highly permeable membrane separates the blood into its cellular and noncellular components and allow the plasma proteins to pass but retain the larger cellular elements within the blood path. Pore sizes of these membranes are usually 0.5 μm or less, thus easily rejecting the smallest cellular component, the platelets (3 μm). Blood is drawn from a central venous access and passed through the plasma filter before it is returned to the patient. Effluent produced in this manner contains all of the noncellular components of the patient's plasma. As plasma is filtered out, it is replaced simultaneously with appropriate fluids in equal volume to the plasma removed to prevent hemodynamic compromise. The removal rate of any given plasma component depends on the plasma filtration rate and its sieving coefficient (ratio of a given plasma protein or solute concentration between the filtrate and the blood side of the membrane). Unfractionated heparin is commonly used for systemic anticoagulation in membrane separation plasma exchange and Citrate (anticoagulant citrate dextrose-A solution) is

commonly used in centrifugal exchange devices.

In most cases, TPE serves as an adjunct role, as the patients receive chemotherapy or immunosuppressive therapy.

Comlications

1. Due to any replacement fluid: Citrate induced hypocalcemia presenting with paresthesia, nausea, vomiting, muscle cramps, hypotension, tetany or cardiac arrhythmia may occur. ECG monitoring is required and it is treated with intravenous 10% calcium gluconate. Metabolic alkalosis may occur due to generation of excess bicarbonate by citrate.
2. Vascular catheter complications like infection and thrombosis.
3. Due to non-plasma replacement fluid: hypokalaemia due to dilution, hypocalcemia due to infusion of large volumes of albumin, reduction in coagulation factors or immunoglobulin and inadvertent removal of drug (like IVIG, Rituximab). IVIG should be given after plasma exchange procedure.
4. Donor plasma or RBC exposure: may lead to Hemolytic transfusion reaction, Severe anaphylactic reactions, Transfusion related acute lung injury and Transfusion transmitted diseases. Allergic reactions are treated by intravenous glucocorticoid or diphenhydramine.

Patient must be monitored for the vital signs including heart rate, blood pressure, oxygen saturation and shortness of breath at all times during and post-procedure. Overall mortality of TPE is 0.03-0.05 % mostly due to respiratory and cardiac complications.

Conclusion

Therapeutic plasma exchange (TPE) has proved to be an increasingly popular, effective and live saving therapy for many immunological diseases, however evidence to support specific indications for plasma exchange is variable in quality.

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Infant Colic

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Infant colic has been described as a behavioral syndrome occurring in 1 to 4 month old otherwise healthy infants characterized by long periods of crying and hard to soothe behavior.

The word “colic” is derived from the ancient Greek word for intestine, “Colon”¹. Colic affects 10-40% of children occurring at the same rate in boys and girls².

Symptoms

Fussing and crying are normal for infants especially during the first 3 months of life to communicate the demands to the caregiver. The range of normal crying varies so much, it is difficult to pin down the exact cause. In general colic was described as crying for 3 or more hours a day, 3 days a week, for 3 or more weeks.

Infant colic begins by 2 to 3 weeks and peaks by 6 weeks and then steadily diminishes by 12 weeks and it is uncommon to have colic beyond 6 months³. The 3 hour-cut off for crying or fussing was arbitrary and there is no evidence that the infants who cry more than 3 hours per day are different from infants who cry 2 hours and 50 minutes per day. Care givers are reluctant to keep the behavior diaries for 7 days.

Rome IV Diagnostic Criteria for Infant Colic for clinical purposes, must include all the following⁴.

1. An infant who is <5 months of age when the symptoms start and stop
2. Recurrent and prolonged periods of infant crying, fussing, or irritability reported by caregivers that occur without obvious cause and cannot be prevented or resolved by caregivers.

No evidence of failure to thrive, fever or illness. “Fussing” refers to intermittent distressed vocalization that is not quite crying and contents either.

Features of colic may include the following

1. Intense crying that may seem more like screaming, piercing or an expression of pain
2. Crying for no apparent reason, not like hunger cry or need to change the wet diaper
3. Extreme fussiness even after crying is diminished
4. Predictable timing with episodes occurring in the evening when parents are already tired
5. Facial discoloration such as reddening of the face or paler skin around the mouth
6. Bodily tension such as pulled up or stiffened arms, legs pulled up towards the abdomen clenched fists, arched back or tense abdomen. Sometimes there is relief of symptoms after infant passes flatus or a bowel movement

Red Flag Signs⁵

1. Vomiting (vomit is green, yellow, blood streaked or occurring more than 5 times a day)
2. Change in stool (constipation or diarrhea, especially with blood or mucus)
3. Abnormal temperature (a rectal temperature less than 97°F or over 100.4°F)
4. Irritability
5. Lethargy
6. Poor weight gain

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Causes of Colic

Exact cause is unknown but there may be a number of contributing factors

1. Digestive system that is not fully developed
2. Imbalance or dysbiosis of the bacteria habituating in the gut
3. Lactose intolerance⁶.
4. Overfeeding, underfeeding or inadequate burping
5. Family stress or anxious mother

Treatment

It has been an age old practice to drug the crying infants. Galen, the Greek physician in the second century AD, prescribed opium to the fussy babies and during the Middle Ages in Europe, mothers and wet nurses smeared their nipples with opium lotions before each feeding.

In the past decades there was a practice to treat colicky babies with sedatives (phenobarbitone, diazepam, alcohol etc), analgesics or antispasmodic drugs (scopolamine, dicyclomine) but all these are no longer recommended because of their potential toxic effects⁷.

In >90% cases, the ideal management is not of curing the colic but helping the mother or caregiver to overcome the challenging period in their baby's development⁸.

It is important to assess the baby at a referral point which will help to reassure the mother and take help of diagnostic tools if at all necessary. Pediatricians need to evaluate the stress and anxiety of the mother, lack of family or social support and lack of co-operation at the working place in case of working mothers.

It is also important to discuss with the caregivers, the normal babies' crying pattern and to convince them that babies cry due to many reasons other than hunger so that she should not have a guilty feeling that her breast milk is insufficient for the baby. She must be reassured that this is a short term problem and most of the babies grow out of it by 5 to 6 months of age.

Calming measures including soothing motions, limiting stimulation, pacifier use and carrying the baby around in a carrier, although it is not clear if these actions have any beneficial effects beyond placebo⁹. Dietary changes in the infant in generally not needed.

A systematic review was conducted to examine whether dietary change provides an effective therapy for infant colic. Six databases were searched in 1960, and 24 studies selected for inclusion. In breastfed infants evidence suggests that a hypoallergenic maternal diet may be beneficial for reducing infant colic. In formula-fed infants, colic may improve after changing from a standard cow's milk formula to either a hydrolyzed protein formula or a soy-based formula. Additional clinical studies must be conducted before a recommendation can be made¹⁰.

There are several randomized controlled trials, that Probiotics, specially *Lactobacillus reuteri* DSM 17938, can reduce infant crying relative to controls¹¹. However no benefits were found in a large scale fully blinded trial¹². Simethicone is safe but does not work. Dicyclomine works but is not safe. Little clinical evidence supports efficacy of "gripe water" and caution in use is needed especially in formulations that include alcohol and sugar¹³.

Complications

1. If attempts to control a baby's crying are unsuccessful, anxiety and frustration may develop and lead to caregiver's frustration.
2. Early cessation of breastfeeding
3. Feeling of guilt, exhaustion, helplessness or anger
4. Shaken baby syndrome – the stress of calming a crying baby has prompted the parents to shake the child which can cause serious damage to the brain and death. The risk of this uncontrolled reactions is greater if parents don't have information about soothing a crying child, education about colic and support needed for caring a infant with colic.

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Role of Precision Medicine in Pediatrics

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Introduction

Grouping patients by presenting symptoms or clinical diagnosis is a necessary but flawed approach to contemporary care delivery. Quality of care and patient safety issues arise from the marked inter-individual variability in clinical presentations, disease courses, and responses to standard-of-care interventions. New technologies are enabling increased precision in classifying diseases and identifying at-risk states for adverse outcomes. The development of standardized procedures and protocols has been a key component of many successful quality and safety initiatives. The next frontier of medicine is to better understand the origins of atypical idiosyncratic outcomes in relation to these protocols¹.

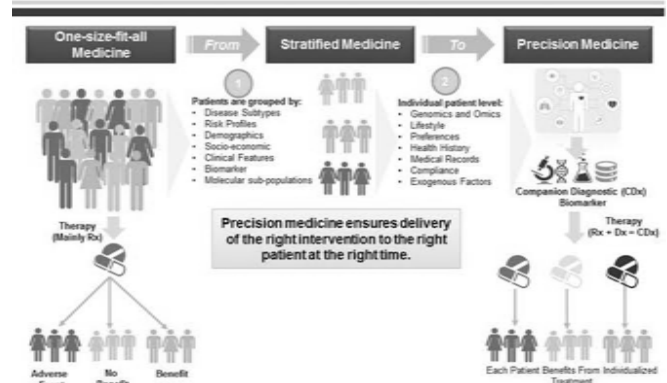
Precision medicine refers to the goal of leveraging extensive patient-level phenotypic and genotypic data to tailor care recommendations, and thereby improve health outcomes. Precision child health (PCH), focuses on the unique needs of the pediatric population. These include the differing physiologic and social determinants of health, disease landscape, and genetic architecture: interrogating data from the genetic code to the postal code. PCH necessitates the integration of large datasets, including but not limited to genomic data. Artificial intelligence and machine learning approaches suggest that operationalizing PCH is increasingly tractable. The aim is a more predictive and preventative approach to medicine that builds on established standardized care protocols by identifying the individuals for whom we should divert from these protocols².

In this commentary, we will discuss how a PCH

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approach can enhance quality and safety. Complex pediatric morbidity and mortality are often associated with a known or suspected genetic condition³. Many contemporary clinical examples illustrating the power and the promise of PCH are the result of translational genomics. Genomic medicine as a priority area has been identified. Centers are participating in multiple large-scale sequencing initiatives, ranging from constitutional (“germline”) DNA to tumours to microbiomes. We will therefore focus on genome-wide sequencing as a specific exemplar, to showcase current opportunities and forecast future developments⁴. New paradigm shift in treatment is shown in figure 1.

Fig 1. New Paradigm Shift in Treatment



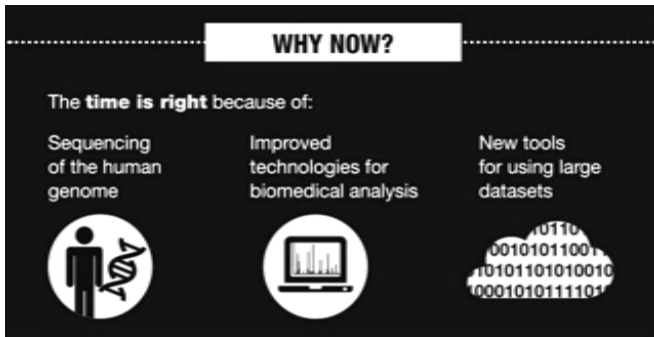
What is Personalized Medicine?

- The provision of right treatment to the right patient at the right dose at the right time.
- The use of new methods of molecular analysis for a better management of a patient’s disease or predisposition to disease⁵.
- Health care that is informed by each person’s unique clinical, genetic and environmental information⁶.

(d) A form of a person's genes, proteins and environment to prevent, diagnose and treat disease⁷.

Figure 2 shown right time for shift, figure 3 shows longer term goals and figure 4 shows biomarkers being used across diseases, figure 5 shows the various aspects and factors of precision public health.

Fig 2. Right Time for Shift



Requirements of PMs

- (a) Diagnostic: to stratify the disease
- (b) Therapeutic

Benefits of PM

- (a) Shift the emphasis in medicine from treatment to prevention
- (b) Guide the correct selection of treatment: avoid the trial and error approach

Fig 3. Longer Term Goals

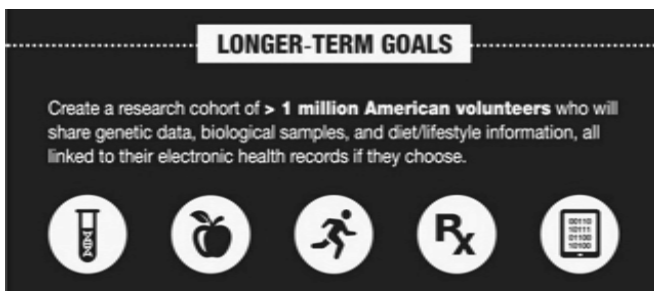
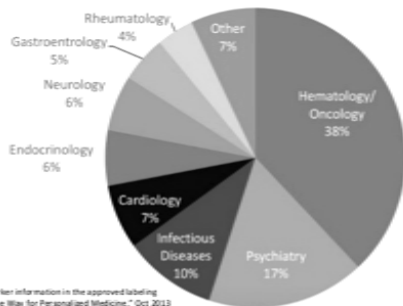
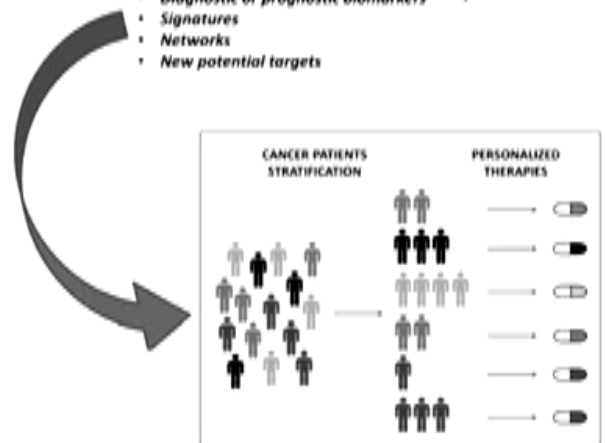
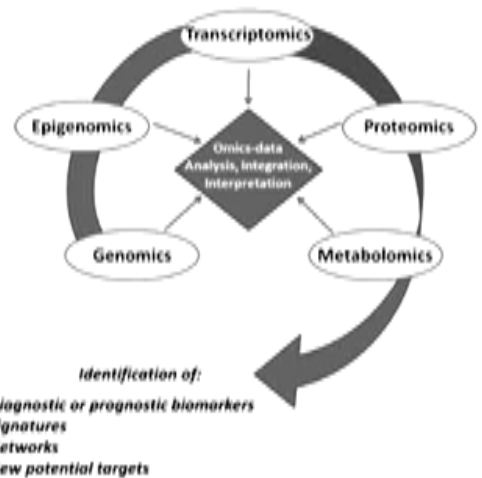
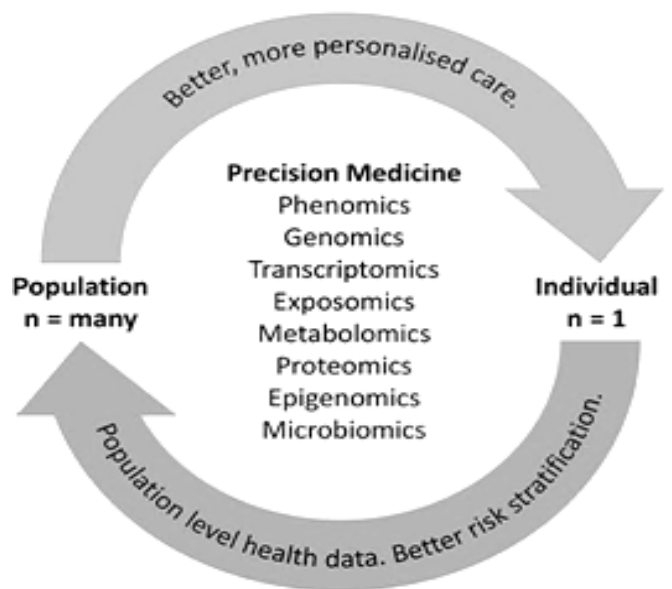


Fig 3. Biomarkers Being Used Across Diseases - But Most Frequent Application in Cancer.



*FDA approvals with biomarker information in the approved labeling. Source: U.S. FDA, "Paving the Way for Personalized Medicine," Oct 2013

Fig 5. Precision Public Health



- (c) Prevent treatment delays
- (d) Providing cost effective treatment

Transcriptomics

- (a) Transcriptome is the complete set of transcripts in a cell and their quantity, for a specific

development stage or physiological condition.

- (b) Transcriptomics, the study of RNA in any of its forms⁸.
- (c) Study of transcriptomics, also referred to as expression profiling, examines the expression level of messenger RNA in given cell population, using techniques like DNA microarray technology.

Proteomics

- (a) Proteome refers to the total set of proteins expressed in given cell at a given time.
- (b) Proteomics is the study of proteome; it uses technologies ranging from genetic analysis to mass spectrometry.
- (c) Genomics -> Transcriptomics -> Proteomics⁹.
- (d) With the advent of highly sensitive proteomic technologies, we can now identify proteins associated with development of diseases well before any clinically identifiable alteration.

Metabolomics

- (a) Metabolome refers to complete set of small molecule metabolites to be found within a biological sample, such as a single organism.
- (b) Genome-> Transcriptomics-> Proteomics-> Metabolomics
- (c) Metabolomics assessment can be pursued both in vitro and in vivo using cells, fluids or tissues¹⁰.
- (d) Basic workflow: Sample collection-> Separation technique-> Detection technique-> Data Analysis using Multivariate analysis

PM and Newborn Health

- (a) Identification of the genetic basis of a large number of single gene disorders.
- (b) Ability to detect genetic variations rapidly and inexpensively in small samples has opened a range of possible genomics applications relevant to newborn health.
- (c) Preconception tests are commercially available to detect mutations.
- (d) For couples at increased risk of having an affected child, costly assisted reproductive technologies including pre-conception genetic diagnosis.

- (e) Embryo selection and implantation are options for increasing the likelihood of a healthy pregnancy outcome.

PM and Pediatric Neurology

- (a) Lysosomal storage disorders (LSD)
- (b) Prospective Avenue for application of PM as most LSD are single gene defects.
- (c) In LSD there is reduced enzyme activity and gradual accumulation of various metabolites with time.
- (d) PM helps to realize which patient will need enzyme replacement therapy (ERT) and which patients will benefit from bone marrow transplantation(BMT).
- (e) Zolgensma (Onasemnogene AAVp) an AAV – delivered gene therapy used to treat Spinal Muscular Atrophy (SMA) , has been approved for clinical use in the US by the FDA
- (f) Golodirsen is an antisense oligonucleotide that results in exon 53 skipping in patients with amenable pathogenic variants of the dystrophin gene, which accounts for approximately 8 percent of the causes of DMD¹¹.
- (g) After the approval of Eteplersen and Ataluren , the US FDA granted accelerated approval to golodirsen in December 2019.
- (h) Milasen , an antisense oligonucleotide was rationally designed , tested and deployed as a novel individualized therapeutic agent for the treatment of Batten disease(Neuronal Ceroid lipofuscinoses , NCL)

PM in Pediatric Respiratory Diseases

- (a) IVACAFTOR is a drug benefitting patients with CFTR class III mutation(G551D mutation).
- (b) Two RCTs in children with G551D-CFTR MUTATION (ENVISION and STRIVE Studies) over 48 weeks period showed great benefits of this new medicine.
- (c) VX-lumacaftor is a new medicine being developed for Cystic Fibrosis patients with homozygous F508del¹².

Asthma treatment :

Basu et al in a study published in Journal of Allergy and Clinical Immunology showed that patients with

a certain type of beta-2 adrenergic receptor gene are unresponsive to Salmeterol and instead showed beneficial response to montelukast¹³.

PM in GI disease

- (a) Azathioprine (AZA) is a drug frequently used in Crohn’s disease.
- (b) It is metabolized by thiopurine methyl transferase(TPMT). Absence or low levels of TPMT could lead to dose dependent side effects or even toxic reactions.
- (c) It is now required to check the TPMT levels and genotype before starting this medicine.

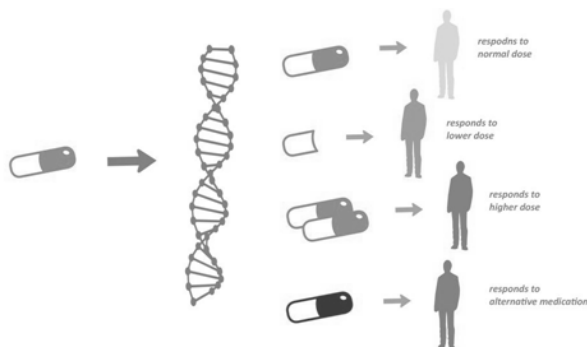
Celiac disease:

- (a) Gut microbiota differs in patients with celiac disease from that of normal subjects.
- (b) Understanding this microbiota in the presence or absence of certain molecules can help in the diagnosis or prognosis or even complete cure of celiac disease.

Principles of Cancer Therapy by PM

Figure shows cancer treatment using precision medicine approach.

Fig 6. Cancer Treatment using Precision Medicine Approach



PM in Acute Lymphoblastic Leukemia :

- (a) Febrile neutropenia in patients with ALL is frequently treated with gentamycin.
- (b) Patients with m1555A mutation (inherited completely from maternal side) causes 50 % of aminoglycoside related hearing loss. ALL

patients found to carry this mutation are not treated with gentamicin.

- (c) TPMT studies are also helpful in ALL patients needing Azathioprine therapy.

PM and Childhood Diabetes

- (a) Pearson et al reported the use of Sulphonylureas (SU) in infants with KCNJ11 mutations, which encode Kir6 ATP sensitive potassium channel.
- (b) Ninety percent of patients were successfully weaned from insulin to SU and the effect was persistent for 1 year with good glycemic control and symptom improvement with a low normal HbA1c.

PM in Pediatric Sepsis

- (a) Whole blood messenger RNA was used to identify genes that are up regulated and down regulated in a cohort of patients with septic shock as compared to normal controls.
- (b) 100 genes with the strongest predictive value were used to identify subclasses of pediatric septic shock(subclass A,B,C). Subclass A had glucocorticoid receptor pathway repressed and had an increased risk of a complicated course.
- (c) Walley and colleagues studied PCSK9(Proprotein convertase subtilisin/kexin 9), a regulator of lipid metabolism¹⁴.
- (d) Patients with atleast one loss of function mutation variant of PCSK9 had survival benefits over others¹⁵.

PM in Hemophilia Treatment

Figure 7 depicts approach to hemophilia treatment.

Fig 7. Approach to Hemophilia Treatment

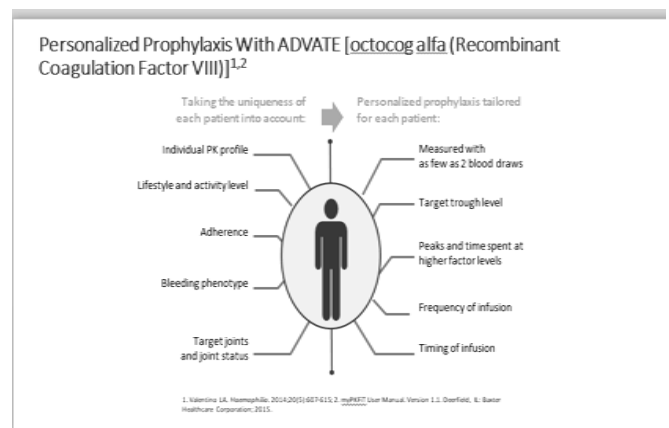


Fig 8. Undesignated Diseases

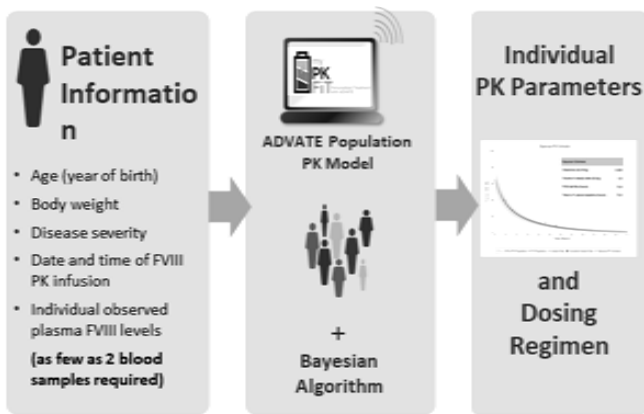


Fig 9. PM in Modern Practice at a Glance

Medical Field	Disease	Biomarker	Intervention
Cancer	Chronic myeloid leukemia	BCR-ABL	Imatinib ⁴
	Lung cancer	EML4-ALK	Crizotinib ⁵
Hematology	Thrombosis	Factor V Leiden	Avoid prothrombotic drugs ⁶
Infectious disease	HIV/AIDS	CD4+ T cells, HIV viral load	Highly active antiretroviral therapy ⁶
Cardiovascular disease	Coronary artery disease	CYP2C19	Clopidogrel ⁷
Pulmonary disease	Cystic fibrosis	G551D	Ivacaftor ⁸
Renal disease	Transplant rejection	Urinary gene signature	Antinejection drugs ⁹
Hepatology	Hepatitis C	Hepatitis C viral load	Direct-acting antiviral agents ¹⁰
Endocrine disease	Multiple endocrine neoplasia type 2	RET	Prophylactic thyroidectomy ¹¹
Metabolic disease	Hyperlipidemia	LDL cholesterol	Statins ¹²
Neurology	Autoimmune encephalitis	CXCL13	Immunotherapy ¹³
Psychiatry	Alcohol-use disorder	GRIK1	Topiramate ¹⁴
Pharmacogenomics	Smoking cessation	CYP2A6	Varenicline ¹⁵
Ophthalmology	Leber's congenital amaurosis	RPE65	Gene therapy ¹⁶

PM in Undiagnosed Diseases

Approach to undiagnosed diseases is shown in figure 8 and figure 9 shows PM in modern practice.

- (a) Exome and whole genome sequencing may have a role in managing a broad array of conditions, both common and rare¹⁶.
- (b) The genetic bases for approximately 40% of over 7000 Mendelian disorders are now known, though clinical testing is not available for all.
- (c) For conditions with known or suspected causal variants, advances in genotyping and sequencing targeted genomics region have led to increasingly routine use of these technologies as diagnostic aids¹⁷.

Generation of PM data and hurdles in generating PM data are shown in figure 10 and 11 respectively.

Discussion

Early trials of precision oncology have improved our understanding of chemoresistance during the course of therapy, and have highlighted cancer

Fig 10. Generation of PM Data

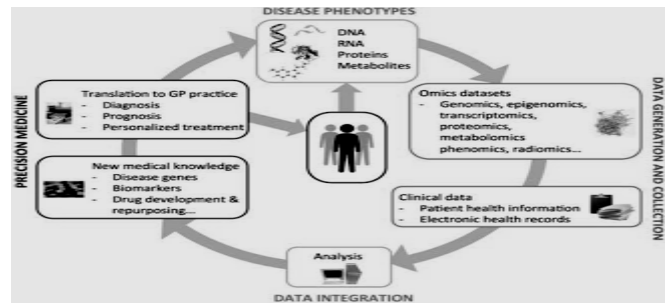
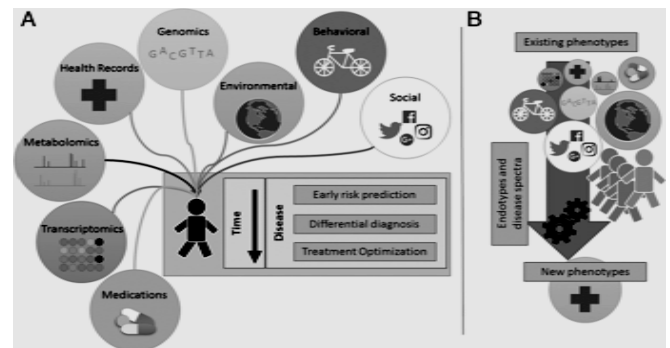


Fig 11. Hurdle in Generation PM Data



heterogeneity and genomic complexity, including the role(s) of epigenetic modifiers in determining disease outcome. NGS has revealed many cancers carry mutations in genes encoding for transcriptional control. Epigenetic dysfunction and transcriptional dysregulation is frequent in many pediatric cancers, particularly leukemias. Inhibition of transcriptional programs and epigenetic modification are potential areas of opportunity in precision medicine. Combination therapy with simultaneous disruption of two genes, termed synthetic lethality, is emerging as a new avenue of targeted precision. This is based on the hypothesis that poor prognosis cancers with loss-of-function mutations become “treatable” when two otherwise discrete and unrelated genes are targeted simultaneously. Epigenetic regulators and genes involved in DNA repair are particularly attractive targets for cancer therapy because of their altered gene expression patterns in cancer cells, compared with normal cells. Targeting of these regulatory genes can selectively kill cancer cells.

Another potential and novel area of precision medicine is the use of nanotechnology to overcome treatment resistance of cancer cells. Delivery systems based on nanoparticles enhance antitumor drug uptake and selective intracellular accumulation in the cancer cell. Multifunctional nanoparticles can

deliver drug combinations for synergistic therapy, and facilitate personalization of therapeutic regimens¹⁸. Superparamagnetic iron oxide nanoparticles (SPIONs) have magnetic properties, show excellent tumor-targeting efficiency, and are thus more effective in personalized cancer treatment¹⁹. Thus, the use of nanotechnology with combination therapy, whether traditional or targeted, is an ideal model for personalized medicine and may hopefully result in cancer cure and eradication²⁰.

The use of antibodies against tumor antigens and stimulation of the patient's own immune system to attack cancer cells are new forms of immunotherapy that have recently been used in patient treatments. A number of immunotherapy agents are in use or under investigation in pediatric cancer. Gemtuzumabozogamicin has become part of the standard of care for pediatric patients with AML. Dinutuximab is an anti-GD2 antibody that is used in the treatment of neuroblastoma. Other immunotherapies under investigation include monoclonal antibodies (e.g., ganitumab), antibody-drug conjugates (e.g., brentuximab vedotin), bispecific T-cell engagers (e.g., blinatumomab), immune modulators (e.g., nivolumab, pembrolizumab, ipilimumab), and anti-cancer vaccines. Cellular therapies using modified T-cells

have also been successfully employed. Based on their extraordinary ability to distinguish foreign peptides from self-antigens through their receptors, T cells are engineered with chimeric antigen receptors (CAR) designed for sustained proliferation and specific targeting of tumor cells. CAR-T cell therapy has been remarkably successful in treating patients with advanced refractory B cell malignancies through chimeric receptors targeting CD19. The success of CAR-T cell therapy in leukemia has been extrapolated to solid tumors where partial success has been demonstrated in sporadic case reports. A few clinical trials have reported using GD2-specific CAR-T cells for neuroblastoma and human epidermal growth factor receptor 2 (HER2) in medulloblastomas with non-dramatic results. A major challenge in CAR design is ensuring specificity for targeting tumor cells, while sparing healthy tissue and minimizing toxicity. Other major barriers need to be overcome for more successful CAR-T therapy. Reducing physical barriers in the extracellular matrix and eliminating the effect of an immunosuppressive microenvironment are some of the measures that ensure successful delivery of engineered T-cells to the tumor cells²¹. Although the outlook for CAR-T therapy promises superior benefits in the treatment of solid tumors, further progress is needed to overcome these challenges.

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Menstrual Health for the Community

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Menstruation or commonly called as “Menses”, is a natural and physiological process which by nature has been coded in our system till eternity. But as natural as it is, it's treated very unnaturally and stigmatized with biases. As physiological as it seems, it is associated with many difficulties and abnormalities.

MHH (Menstrual Health and Hygiene) encompasses MHM (Menstrual Hygiene Management) and the broader systemic factors that link menstruation to health, well-being, gender-equality, education, equity, empowerment and rights. But gender inequality, discriminatory social norms, cultural taboos, poverty and lack of basic services lead to unmet needs of menstrual health. This has a gross negative impact on adolescent health and psychology, which goes unnoticed and unattended.

The very common issue suffered by the society as a whole is the social stigma linked to menses. This is about the way we treat menses and a menstruator. These stigmas are common to all, irrespective of the education or socioeconomic status. Women have to face exclusion from kitchen, temple and festivals during menses. They have to stay, wash clothes and dishes separately. They are treated as dirty during menses. Social norms and stigmas create a pattern which link something that defines one biologically as a woman, as being dirty and shameful. People believe that menstrual blood is a dirty blood containing harmful substances and menses is something that should not be talked about openly. Across the country, women grow up ignorant of why menses occurs and why it is delicate to maintain menstrual hygiene. This passes off generation to generation, from a mother to the daughter and so

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on, with physical as well as psychological impact at large.

Glimpses of the scenario with regard to menstrual health:

- In India, 23 million girls drop out of school early when they start menstruating. (28/05/2018, published in swachhindia.ndtv.com)
- Menstruation is a rarely discussed topic in homes and schools in India. A survey conducted by the Ministry of Education in 2015 found that in 63% of village's schools, teachers never discussed menstruation and how to deal with it in a hygienic manner.
- ICMR 2011-12 report stated that only 38% menstruating girls in India spoke to their mothers about menstruation.
- NFHS 4th survey in 2015-16 showed that half of the women in rural India do not use hygienic methods of protection during periods. They use old rags, re-use same clothes, even share clothes.
- Young people do not have access to reliable and correct information about their reproductive health and risk.
- The 2016 landscape analysis titled Menstrual Health in India observed that of nearly 355 million females in India who have reached menarche, 71% reported no information about menstruation before their 1st periods.
- Menstrual Hygiene Day 2020 (28/05/2020) revealed that only 57.6% women in India use sanitary napkins.
- Hygiene related diseases like fungal infections, urogenital infections and cervical cancer incidence higher in neglected population, all of which are preventable by easy means.

Adolescent girls at their menarche need someone by their side to guide them through periods, teach them about normal menses and when they should seek consult, make them comfortable through PMS and calmly deal with the bodily and psychological changes that come with menses. But instead, we put illogical restrictions in their daily activities and also refrain them from attending school or work. The right to a quality education entitled to every child includes access to drinking water, sanitation and hygiene (WASH) services while at school. But being deprived of the basic knowledge and access to sanitary and a facilitating environment makes it difficult for the adolescent girls to even continue school. Information, education, communication, accessible sanitary products, pain relief and adequate disposing facilities at school would improve the schooling experience of adolescent girls in India. National and International concerns about menstrual hygiene are being propagated through WASH programs in school. If MHH is well managed from the start at a critical stage of a girl's life, it will have a surprisingly favorable outcome in leading female empowerment. MHH is important for the fulfilment of girl's and women's rights which is a key objective of SDG (Sustainable Development Goals). UNICEF envisions a world where every girl can learn, play and safeguard her own health without experiencing stress, shame and unnecessary barriers to information or supplies during menstruation. UNICEF's support to menstrual health and hygiene is aimed at a larger goal of improving education, health and gender equality for girls and women.

India has come a long way from not whispering menses and giving shady nicknames to the menses, to promoting and appreciating a full-fledged feature film, padman, on a low-cost sanitary napkin entrepreneur in 2018. GOI has recognized the

importance of menstrual hygiene to the health and well-being of girls and women. Few examples are production of low-cost sanitary pads, government subsidized sanitary pads in rural areas, school and airport vending machines, pad incinerators and increasing gender separated toilet facilities. Glimpses of efforts in this regard:

- In 2010, MOHFW launched the Free-day Pad scheme, a pilot scheme to provide sanitary napkins at subsidized rates for rural girls.
- SABLA scheme by Union Government aimed at improving health conditions for adolescent girls with menstrual hygiene as important component.
- Nirmal Bharat Abhiyan focuses on menstrual hygiene as a key component of the sanitation mission.
- KSK (Kishor Swasthya Karyakram) aimed at improving the health and hygiene of an estimated 243 million adolescents has Menstrual hygiene as an integral part.
- Ongoing Swachh Bharat Abhiyan pays importance to menstrual hygiene. Adequate knowledge of menstrual hygiene and development of local sanitary napkin manufacturing units is encouraged by Swachh Bharat Mission and self-help groups are to help in propagating such efforts.

We still have a long way to go. It is every individual's responsibility to speak up and help their friends and family through this. Do not hesitate in using words like periods and menses. To understand that menstruation is a fact of life and menstrual health is a global opportunity. Sanitary napkin is a right of every woman. IEC can help hugely with the negative impact of menstruation. For rightly said, "SWACHH BETI, SWASTH BETI."

Suggested Reading

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- 2) dnaindia.com on Menstrual Hygiene Day 2021
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Multiple Serositis and Generalised Anasarca in Severe COVID

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This is a case report of a four and half year old girl child with severe COVID-19 infection presenting unusually with generalised anasarca, right sided pleural effusion and persistent elevation of liver enzymes. Though the patient could fit in MISC criteria as well, after the tropical infections and autoimmune serositis was ruled out the patient improved dramatically after being treated with injection dexamethasone, injection Furosemide and enoxaparin. Treatment as per MISC guidelines was not required in the patient. Even when the patient was discharged after 10 days of hospital stay the liver enzymes were still elevated.

Introduction

Severe COVID-19 infection usually presents as signs of severe pneumonia, acute respiratory distress syndrome, septic shock, multi-organ dysfunction syndrome, pneumonia with cyanosis, grunting, severe retraction of chest, lethargy, somnolence, seizure, SpO₂ < 90 % in room air.

A patient of severe COVID-19 presenting with sudden onset generalised anasarca which initially started with facial puffiness then involving the trunk and limbs within one day, rapid onset right sided pleural effusion, and persistent elevation of liver enzymes is rarely reported in literature.

Case Report

A four and half year-old female girl, was admitted with complaints of fever since last 3 days, high grade, intermittent in nature, accompanied with chills, generalised anasarca which started with facial puffiness and gradually involving the trunk and limbs since 2 days, cough for 2 days and respiratory distress for one day, periumbilical and right hypochondriac pain accompanied with non-bilious, non-projectile vomiting, 2-3 times per day, mainly post feed.

There was no history of diarrhea, no history of decreased urination, joint pain, rash, convulsion, or any history of similar episodes in past. Mother also denied any history of COVID-19 infection in past.

Initial physical examination showed that patient had tachypnea (42/min), tachycardia (144/min), surface temperature was raised, maintained a saturation of 92-93% in room air, generalised anasarca was present, air entry was decreased on the right inframammary part of chest, severe chest retraction was present.

Abdomen was soft but distended, liver was enlarged, 8cm span, tender. Heart sounds were audible, there was no murmur present.

The patient was initially managed with moist oxygen, the bed was kept propped up, and a baseline antibiotic ceftriaxone was given.

Routine investigations showed decreased hemoglobin, decreased leucocyte count, platelet count was slightly low. CRP 195mg/dL. Liver enzymes were 3-fold raised.

RAT for COVID-19 came negative, so COVID-19 RTPCR was sent.

Cholesterol and albumin were within normal limits, urine dipstick showed 2+ proteinuria, so we could rule out nephrotic syndrome, which we had kept as a differential.

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As there were features of heart failure, Trop-T was done which came negative and an ECG showed no abnormality. ECHO was also normal.

Chest X-ray on day 1 showed blurring of right costophrenic angle. Pleural effusion increased on the next day. Pleural fluid aspiration was done, pleural fluid study showed a transudative picture.

Blood reports so far showed, dengue NS1 report to be negative, malaria negative, scrub typhus IgM were negative.

COVID-19 RTPCR report came positive.

Keeping the possibility of MISC in mind, blood for COVID 19 antibody was sent, which also came positive in very high titre (more than 40 times raised).

Considering the patient to have severe COVID infection, the patient was started on injection furosemide, injection dexamethasone D dimer report came 3.75mg/L (≤ 0.5 mg/L is the normal range), so low molecular weight heparin was started at a prophylactic dose.

On day 3 blood culture report came negative, patient had started improving clinically. Chest x-ray showed improvement. Tachypnea and tachycardia got corrected, patient became afebrile.

Inflammatory markers and D dimer were still raised. Liver enzymes were raised (SGPT 1098U/L, SGOT 540U/L). Blood for IgM HAV was negative, PT-INR was normal.

Literature was searched, and it was seen that, there was a report of retrospective cohort study which showed hepatitis is common in children with MISC, and is associated with more severe presentation and persistent elevation of liver enzymes.

Gradually, patient became playful, appetite improved. Repeat D dimer came within normal range, so injection enoxaparin was stopped.

Liver enzymes were raised, anasarca had subsided. ANA profile report which we had sent earlier came negative, we could rule out autoimmune serositis.

So the patient successfully discharged after 10 days. On discharge, there was no anasarca but liver enzymes were still elevated.

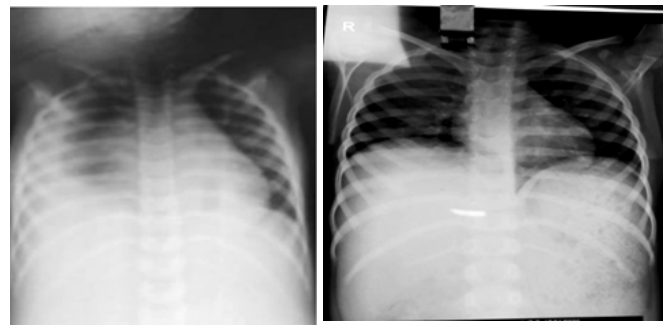


Fig 1. Showing the improvement in chest x-ray, within one day, after treating the patient as per severe Covid guidelines.

The first x-ray was done on day 1 and the second x-ray was done on day 4 of hospital stay.

Discussion

After COVID-19 report came positive, the patient matched MISC criteria as she was a four and half years old child with fever for more than three days, with acute gastrointestinal problems (pain abdomen and vomiting), and evidence of coagulopathy (as the D dimer levels were elevated), and there was very high rise in CRP and other tropical infections and obvious causes of inflammation were ruled out.

But the patient responded after being treated as per the severe COVID guidelines with injection dexamethasone, enoxaparin and furosemide within one day. So, plan of treatment as per MISC protocol with methyl prednisolone and Ivlg was halted.

Severe COVID usually presents with signs of severe pneumonia, acute respiratory distress syndrome, seizures, grunting, lethargy, somnolence, decreased saturation. But COVID infection presenting as generalised anasarca starting with facial puffiness and gradually spreading to trunk and involving the limbs within one day, right sided pleural effusion, and persistent elevation of liver enzymes is a very unusual presentation.

COVID-19 IgG antibody positive in a very high titre with also antigen positivity is not very often seen.

Though the strain causing COVID in this child remains unknown, but this surge of omicron is known to cause relatively less severe disease.

So, whatever might be the initial presentation in this pandemic era COVID-19 infection should be ruled out.

Conclusion

Severe COVID-19 presenting with generalised anasarca and multiple serositis right sided pleural effusion and persistent elevation of liver enzymes is a very uncommon presentation. There are previous reports of MISC associated with hepatitis and MISC

presenting with right sided pleural effusion but dramatic improvement of anasarca and pleural effusion of the patient after being treated with injection dexamethasone (as per COVID guidelines) is very unusual, and has not been reported in literature.

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A Case of Acute Abducens Nerve Palsy Following Covaxin Administration in a Child

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Introduction

Following introduction of COVID-19 vaccination, few adverse effects have been reported, all of which are so far been in adult population. This reported case is from pediatric age group.

Case Report

A 14 years 7 months old female patient, height 5 feet 2 inches and weighing 70 kg, who was absolutely well, received her first dose of Covaxin on 10 January 22, developed acute onset squint of left eye from 13 January 22 and that persisted since then and as shown in figure 1 presented to us on 2 February 22. On clinical examination, she had isolated right sided lateral rectus palsy with no eye tenderness, preserved pupillary (both direct and consensual) and corneal reflexes, visual acuity of 6/6 in both eyes with diplopia. Field of vision was restricted towards right lateral side. Systemic examination was unremarkable with no other focal neuro deficit and no meningeal sign. MRI brain revealed no abnormality, and other routine investigations including CBC, fasting blood sugar, urea culture, creatinin, LFT, lipid profile, chest X-ray-PA, all came out to be normal. Although no direct cause and effect relationship could be established, but assessing the temporal relation between Covaxin administration and onset of squint, and absence of any other possible pathology, it was thought to be due to Covaxin injection. Literature review suggested an inflammatory effect on 6th cranial nerve due to vaccine and hence oral prednisolone 20 mg TDS was started. She showed some improvement after 7 days with better movement of right eye towards lateral side. She has been discharged now and steroid continued with tapering dose for another 7

days. Relevant clinical images before and after prednisolone is submitted herein.

Discussion

From review of literature¹⁻³ few cases of acute 6th cranial nerve palsy following COVID-19 vaccination were found, but all of them occurred in adults with minimum age recorded being 23 years, and none of them was from Covaxin brand. Hence this case is unique in character due to affection of a pediatric patient.



Fig. 1. Squint in left eye

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A Clue in the Blood Smear

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This 3 years old girl, born out of consanguineous marriage (2nd degree), presented with failure to thrive, global developmental delay along with loose, bulky, offensive, occasionally oily stool at a frequency of 10-12 times per day since 1 month of age. Loose stools were aggravated by fatty food and there was history of nocturnal stools. Family history of similar illness was documented. All children of maternal uncle had the same disease; 2 died and 1 living.

Anthropometry revealed Ht 71 cm, Wt 6kg, HC 43cm. (HFA / WFA / WFH <3 S.D). She had noticeable palor, rickety changes over limbs and ribs and protruded abdomen but no organomegaly. Deep tendon reflex was absent in all 4 limbs. Other systems were apparently normal. Ophthalmological evaluation was normal.

Investigation revealed Hb 6.2 gm/dL, WBC 13,540 (N39 L50 M7 E4 B0), peripheral smear showed acanthocytes in fair number, along with poikilocytosis, tear drop cell, schistocytes and microcytic hypochromic RBC. TIBC was 573 mcg/100ml (increased), with RPI 0.5. Lipid profile revealed low serum cholesterol (35 mg/dL), low triglyceride (16 mg/dL) and absent chylomicron.

Vitamin E level was < 0.4 mg/L (Ref 3-9 mg/L) and 25 – OH vitamin D level was 5.3 ng/mL (Ref. 30-50 ng/mL). ABG, liver and renal function tests, thyroid profile, sweat chloride, Anti TTG were normal.

She was diagnosed as a case of abetalipoproteinemia, a rare autosomal recessive disorder, with mutation in MTP gene, also known as Bassen-Kornzweig syndrome. It is characterized by fat malabsorption, acanthocytosis and hypocholesterolemia. Later in life, deficiency of fat-soluble vitamins is associated with development of atypical retinitis pigmentosa, coagulopathy, posterior column neuropathy and myopathy. Hypobetalipoproteinemia was ruled out by a normal LDL levels in parents. Low hemoglobin, Low RPI (0.5), increased TIBC, suggests co-existing iron deficiency anemia.

Treatment included fat restricted diet, high dose of Vitamin E, vitamin D (6, 00,000 IU, IM), MCT oil and coconut oil along with other vitamins, macro and micronutrients. She started gaining weight improvement in motor milestone. Her stool became less frequent and less oily. Follow up was continued at the neuro-developmental clinic.

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Figure in the facing page

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Fig. 1. 3 year old girl with failure to thrive, developmental delay and malabsorption

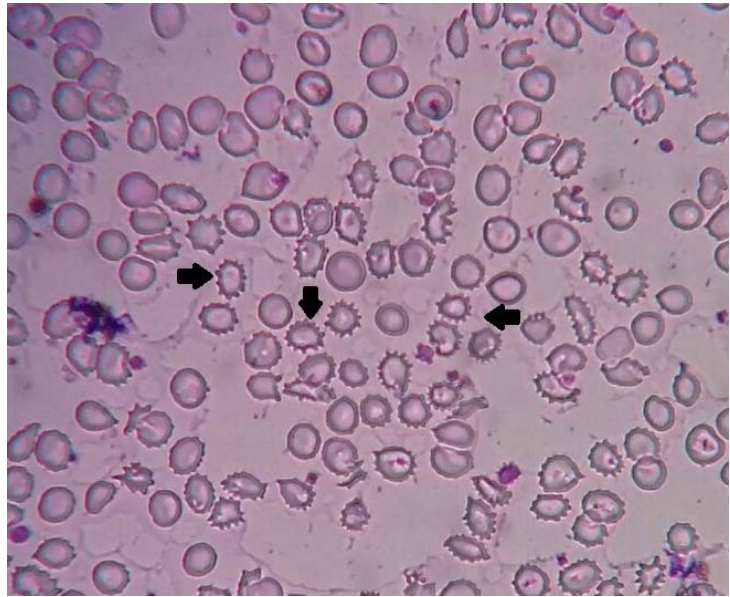


Fig. 2 Characteristic acanthocytes in the peripheral blood smear

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