The Child and newborn

West Bengal Academy of Pediatrics

The Journal of West Bengal Academy of Pediatrics

RNI Registration No. : RNI/68911/97

ISSN 0975-0894

Volume 27 No.1, January – March 2023

In Memoriam

Dr Bimal Kumar Kundu

Dr Bimal Kumar Kundu *an eminent paediatrician breathed his last on the 1st of January 2023 at the age of 75. He had been treating children for more than five decades.*

He was born on 17th July 1947 at Uttarpara. After passing from Uttarpara Govt High School he joined R.G.Kar Medical College in the year 1966. He completed his graduation in 1972 then he moved to SSKM hospital. He completed his DCH where he obtained gold medal.

Dr Kundu was also closely associated with Institute of Child Health Kolkata. He has been survived by his wife, his two sons.

The Child and Newborn

West Bengal Academy of Pediatrics, Oriental Apartments, Flat H1
15C, Canal Street, Kolkata 700 014
Phone : 033 2265 4072, Email : wbap2013@gmail.com, Website : www.wbap.in
E-version of this journal available at website.

ISSN 0975-0894 RNI Registration No.:RNI/68911/97

West Bengal Academy of Pediatrics

Vol.27, No.1 January - March 2023

CONTENTS

Special Correspondance
Dr Kaustav Nayek
Editor-in-Chief, The Child and Newborn
"Oriental Apartments" Flat H1
15C, Canal Street, Kolkata 700 014
Email : kaustav25@yahoo.co.in

Editorial

It is indeed a great honour to be selected as the ediditor of Child and Newborn of West Bengal Academy of Pediatrics.I am humbled and I would like express my gratitude to all the office bearers and Executive body members for having faith in me to carry forward this journal. This is indeed a great responsibility and will be chalanging to take this journal to greater heights.It is going to be a dream project of WBAP and I am confident the dream will be a reality as we have a very academic and learned editorial board. We plan to achieve small targets and work towards making this journal a peer reviewed indexed journal in the coming days. We should reach our goal by successfully achieving the milestones. This first issue is rolling of the ball. This will be an excellent platform for pediatricians and acdemicians not only from India but globally to publish and share their scientific work. I am sure this journal is going to enrich all of us satisfy our hunger for knowledge. Regular publication is a promise and we will also having special issues in between."We will have letters to the editor section in future issues. Your valuable inputs towards betterment of this jurnal and of course constructive critisim is welcome. With the co operation of the editorial board, the office bearers of WBAP and the global Pediatric fraternity Child and Newborn is destined for bright future. Let us all work towards making this journal the face of WBAP.

Dr Kaustav Nayek
Editor-in-Chief

Prevalence of Human Rotavirus A Among Children with Acute Diarrhoea in Burdwan District: A Hospital-Based Cross-sectional Study

***Dr Arghya Nath, **Dr Nivedita Mukherjee, ***Dr Suraj Mondal, ***Dr Kuntal Das, ****Prof. Kaustav Nayek**

Research Scientist-B, **Research Assistant, * Medical Lab Technologist, Department of Microbiology*
***** Principal and Professor, Dept. Of Paediatrics , Burdwan Medical College and Hospital.*

The Reoviridae family includes the segmented, undeveloped RNA virus known as Rotavirus. Rotavirus is a major contributor to severe gastroenteritis disease (GID) in young children all around the world. Studies show that by the age of two, almost all children are at risk of acquiring the Rotavirus; nevertheless, children in developed countries tend to have their first infection earlier than children in industrialized countries. India contains data on Rotavirus disease and strain characterization; however, the studies that produced these data were conducted in different eras and with different methodologies. Despite these limitations, a 2001 evaluation revealed the large range of viruses that were prevalent in India at the time. In this investigation, RT-PCR was used to analyses all samples (n = 64), and the results showed that 5 people had a human RotavirusA infection. In the district of Burdwan, human RotavirusA incidence is 7.04%. GID, vomiting, and decrease urination were found common among our study groups in different age groups.In our study, the high infectivity rate of human Rotavirus A was discovered below the age group of 10 months. Some mothers of children were TORCH positive as well as SARS-CoV-2 positive. This study is a hospital-based cross-sectional study in the Burdwan district at the time period of one year, 2022-2023 The limitations of our study relate to the molecular identification of Adenovirus 40 & 41 types as both of these enteric viruses also cause diarrheal illness.

***Keywords**: Human Rotavirus A, RT-PCR, Children, GID, Burdwan District*

Introduction

Rotavirus is a segmented, undeveloped RNA virus that belongs to the Reoviridae family. Around the world, Rotavirus is a prominent factor in severe gastroenteritis in young children [1-3]. According to studies, by the age of two, virtually all children run the risk of contracting the Rotavirus; however, children in industrialized nations tend to have their first infection at a younger age than children in developing nations [4, 5].

One of the primary causes of sickness and mortality in children under five, particularly in low-income nations, are diarrheal illnesses accounting for more than 500,000 fatalities annually [6]. In many cases of infantile gastroenteritis, the etiologic agent remained unknown prior to the 1970s, but a breakthrough came in 1973 with the discovery of viral particles in duodenal biopsy samples from kids who had severe Diarrhoea [7] and in faeces samples from kids who had acute Diarrhoea [8]. The newly found virus was given the name "Rotavirus" (derived from the Latin word "rota," which means "wheel") due to its distinctive morphological form (Fig. 1a). Rotaviruses were quickly identified as a leading cause of serious Diarrhoea in children under the age of five both globally and in the United States. Rotaviruses were quickly identified as a leading cause of life-threatening Diarrhoea in young children and babies under the age of five around the world and in the young of several mammalian and avian species [9].

In 2003, 114 million cases of Rotavirus infection were reported in children <5 years of age globally, of which 24 million cases required outpatient visits and 2.3 million needed hospitalizations. In 2013, Rotaviruses were associated with an estimated 200,000 deaths in children under the age of five. Rotavirus prevalence is higher in low-income countries because of access to health care and a greater prevalence of comorbid conditions (such as

Correspondance : Arghya Nath, *Research Scientist-B,Department of Microbiology, Burdwan Medical College and Hospital. Email : arghyanath.biotech@gmail.com*

malnutrition) [11]. For instance, 43% of all Rotavirushospitalizations in children under the age of five occur in newborns by the time they are 8 months old in Africa, whereas just 27% do so in Europe[12]. Additionally, a country's income level and seasonality are correlated, with high-income nations experiencing more seasonal sickness than low-income nations[13].

Figure 1 : The WHO projected in April 2016 that Rotavirus infection caused the deaths of 215,000 children under the age of five globally in 2013. World Health Organization clearance was obtained to reprint this figure. Rate of Rotavirus mortality in children under the age of five, 2013 [14].

On the basis of the antigenic specificity of the capsid proteins in the virus and the pattern of the electrophoretic mobility of the 11 RNA segments of the viral genome, Rotaviruses are divided into 7 distinct serogroups (A-G). Only groups A–C of the seven Rotavirus serogroups are known to infect humans, and group A Rotaviruses are viruses that cause serious, life-threatening illnesses in children worldwide. The majority of the mass of the particle is made up of the inner capsid protein VP6, which carries the subgroup (SG) specificities that allow group A viruses to be classified as belonging to SG I, SG II, SG I and II, or neither SG, based on their reactivity with the SG-specific monoclonal antibodies (MAbs) 255/60 and 631/9. For group A viruses, additional typing systems were added based on antigenic epitopes on the proteins that make up the inner capsid (for VP6, SGs I and II) and on proteins of the outer capsid, namely the glycoprotein VP7 (G serotypes) and the spike protein VP4 (P serotypes). Antibodies that neutralize VP7 and VP4 are produced. In epidemiological studies, neutralizing mouse MAbs for typing VP7 has been widely utilized since they are simple to make [10]. Nevertheless, other G types have been found to be prevalent in different areas of the world; of note, G9 strains were reported in India before they spread to other geographic regions [15]. All known G serotypes have been correlated with genotypes; however, more P genotypes than serotypes have been identified, which has led to the development of a serotype/ genotype dual nomenclature for P types [16].

India has data on Rotavirus illness and strain characterization, however, the research from which this data came out was done at various eras and using diverse approaches. Despite these restrictions, a 2001 assessment showed the wide variety of viruses present in India at the time [15].

Materials & Methods

Study Design:

This was a cross-sectional based study carried out in the Microbiology department of Burdwan Medical College, Burdwan, and West Bengal. The study period was June 2021 to June 2022

Study Population:

Includes all neonatal patients whose Diarrhoeal disease has been confirmed.

Inclusion & Exclusion Criteria:

Neonatal individuals with the acute Diarrhoeal disease are included in this study. Unknown fever and rota vaccine-taken individuals are not participating in this study.

Sample size and sampling:

The desired samples were chosen using a purposive sampling strategy in accordance with the inclusion criteria. The department of microbiology collected all the rectal swabs&faeces samples from neonatal patients who had an acute Diarrhoeal disease.

Ethical:

The study was approved by the Institutional Ethics Committee (IEC) of Burdwan Medical College, Burdwan. Informed consent was obtained from all patients during rectal swab &faeces sample collection.

Sample Collection:

The rectal swabs were collected in, VTM (viral transport media) with the help of flocked non-toxic synthetic fibers such as polyester as well as synthetic nylon-handled swabs sticks. The faeces samples were collected in a sterile container with 10ml normal saline water.

Viral RNA Extraction:

The children's RNA from the serum sample was isolated by using the HiPurA Viral Automated RNA Purification Kit. RNA concentration was measured by measuring OD values using a fluorimeter (Qubit).

C-DNA Synthesis:

The extracted clinical RNA samples then convert into C-DNA by Prime Script™ 1st strand cDNA Synthesis Kit 6110A (Takara Bio) as per the manufacturer's protocol.

Primers:

The primers Beg9 & End9 of VP7 gene sequences of Human Rotavirus A strains were retrieved from a reputed published article in J. Clin. Microbial. (PMID:10325310) The Forward primer was Beg9, 5'-GGCTTTAAAAGAGAGAATTTCCGTCTGG-3, and the reverse primer was End9, 5'-GGTCACATCATACAATTCTAATCTAAG-3'. [17].

Molecular Detection of Rotavirus by Real-Time PCR:

The SyBr green qualitative Real Time-PCR reactions that target the region of the VP7 gene of Human Rotavirus A were performed using TB Green Premix Ex Taq II (Ti RNase H Plus) manufactured by TAKARA Bio. Each reaction consisted of 1X TB Green Premix master mix, designed primers of a short sequence of H1N1 HA gene in a 25µl reaction. Bio-Rad CFX 96 real-time PCR conditions consisted of initial denaturation incubation at 95°C for 2 minutes followed by 38 cycles of alternating 95°C incubations for 5 seconds, 56°C incubations for 30 seconds, and 72°C incubations for 10 seconds. Fluorescence was detected after every 72°C extension incubation. A total of 64 clinical samples were screened by this method where we can confirm the Human Rotavirus A to assess each specimen & DNA suitability for PCR amplification, the presence of the housekeeping gene Beta Actin was employed as an internal control. Here in this study, Beta Actin was used to validate the SyBr Green-based RT-PCR test run, which acts as an internal test run control.

Results

In this study, all samples (n=64) were examined using RT-PCR, which revealed that 5 individuals were infected with Human Rotavirus A. The prevalence rate of Human Rotavirus A in the Burdwan district is 7.04%. Among the mother of those 64 children 2 mothers (3.125%) were found SARS-CoV-2 positive and one mother (1.56%) shows TORCH positive shown in the table.1

Among 5 Human Rotavirus A positive children, the highest prevalence shows in within 10 years age group i.e. 18.75% and in between 11-24 and 25-36 months shows an equal positivity rate of 2.85%. Moderate Diarrhoea (MD) & severe Diarrhoea (SD) were found in less than 10 months of children highest than others (MD-81.25%; SD-75%). On the basis of sex ratio male children were prone to more infections than females. 3 males are infected witha total of 5 positive. Among 31 male children 3 (9.68%) individuals are positive on the other hand 2 (6.06%) female children are positive among 33 individuals (table 2)

Among 64 childrenGastrointestinaldisorderswere found in 56 individuals, and Vomiting and Decreased Urination were found in 50 and 16 children respectively. Less than 10 months of age group 93.75% of individualshave been affectedby GID as well as vomiting (87.5%) and urination problems (37.5%). The tabulated forms of signs and symptoms are represented in table 3.

Discussion

Rotavirus continues to remain the primary cause of diarrhea-related mortality in children under the age of five, accounting for close to 130 000 fatalities yearly, despite the Rotavirus burden declining over the previous ten years. In 2016, Rotavirus ranked third among the pathogens that contributed to mortality in children under the age of five, after malaria (517 000 fatalities) and streptococcus pneumoniae (359 000 deaths). One of the most frequent causes of death in children in impoverished nations is a diarrheal illness, and Rotavirus has

Table 1:Prevalence of other infections among mothers of suspected children.

Individuals	SARS-CoV-2 Positive	SARS-CoV-2 Negative	TORCH Positive	TORCH Negative
Mother (n=64)	2 (3.12%)	62 (96.88%)	1 (1.56%)	63 (98.44%)

Table 2: Characteristics of the children with moderate & severe Diarrhoea.

Characteristics	Rotavirus Positive (n=5)	Moderate Diarrhoea (n=28)	Severe Diarrhoea (n=36)
Age Groups			
=10 months (n=16)	3 (18.75%)	12 (75%)	13 (81.25%)
11 – 24 months (n=35)	1 (2.85%)	11 (31.43%)	17 (48.57%)
25 – 36 months (n=13)	1 (2.85%)	5 (38.46%)	6 (46.15%)
Sex			
Male Neonates (n=31)	3 (9.68%)	15 (48.38%)	21 (67.74%)
Female Neonates (n=33)	2 (6.06%)	13 (39.39%)	15 (45.45%)

Table 3:Sign Symptoms of Children admitted in SNCU ward

Age Groups	G.I.D (n=56)	Vomiting (n=52)	Decreased Urination (n=16)
=10 months (n=16)	15 (93.75%)	14(87.5%)	6 (37.5%)
11 – 24 months (n=35)	32 (91.42%)	28 (80%)	5 (14.28%)
25 – 36 months (n=13)	9 (16.07%)	10 (76.92%)	5 (14.28%)

repeatedly been identified as the most prevalent infection linked to severe Diarrhoea. In our investigation of 64 new-borns who presented with Diarrhoea, 7.04% of the stool samples tested positive for Human Rotavirus A. Numerous investigations on RotavirusDiarrhoea carried out in India were hospital-based and revealed positive rates of up to 34%. In studies conducted outside of a hospital environment and in the community, Rotavirus-related Diarrhoea cases are far less common. In one investigation, the frequencies of Rotavirus positive in various contexts, including hospitalizations for Diarrhoea (20%), newborn infections (35%), symptomatic and asymptomatic infections in the community (15.1% and 6.3%, respectively), and nosocomial enteric infections (22.5%), varied substantially [19].

The present study showed that the vaccine has already alleviated the burden of Diarrhoea among those younger than 5 years in several countries that have introduced it. There is a lack of information on the frequency of Diarrhoea and its causes, a problem that is frequently particularly severe in areas with large burdens. As a result, estimates in these areas depend more on models with predictive validity. In our study, the high infectivity rate of Human Rotavirus A was found on below the age groups of 10 months whereas other studies said the highest prevalence rate shows in the age groups between 12 to 24 months [21]. The limitations of our study are to molecular detection of Adenovirus 40 & 41 type because it also causes diarrheal disease and it both are enteric viruses. Due to limitations of funding support, we could not go with this study forward.

Our data should encourage others to look more diligently for nosocomial neonatal Rotavirus infections to characterize carefully the strains that are found and to consider as a clinical corollary, not the absence of symptoms of these infections in new-borns but they'relikely to protect children against subsequent severe disease. Further studies and a wide range of sample sizesare required for predicting a precise and accurate prevalence rate of Human Rotavirus A in our community, which will be helpful for mankind.

Conclusion

In conclusion, a high prevalence rate (7.04%) of moderate (75%) and severe (81.25%) diarrheal sickness has occurred in age groups under 10 months. Additionally, those age groups have high vomiting and low urine frequency patterns. Additionally, a Rotavirus vaccine for India will need to be cost-effective for the health system and address the unique epidemiological characteristics of Rotavirus since all new-borns were unvaccinated. The enormous illness burden caused by Rotavirus

in Indian children might be significantly reduced with the appropriate adoption of safe and effective Rotavirus vaccination. There is a scope for clinicians and researchers to do further study with the help of our study.

Acknowledgment

Grateful to the Principal, Dean, and Medical Superintendent of Burdwan Medical College for allowing us to conduct the study; to all the staff of the Microbiology laboratory for cooperating with us to carry out the study; to all the participants of this study for their full-hearted support and co-operations.

Conflict of Interest

None

References

1. A. Z. Kapikian and R. M. Chanock, “Rotaviruses,” in Fields Virology, B. N. Fields, D. M. Knipe, P. M. Howley et al., Eds., vol. 2, pp. 1657–1708, Lippincostt-Raven, Philadelphia, Pa, USA, 3rd edition, 1996
2. V. Martella, N. Decaro, A. Pratelli, M. Tempesta, and C. Buonavoglia, “Variation of rotavirus antigenic specificity in a dairy herd over a long-term survey,” in Genomic Diversity and Molecular Epidemiology of Rotaviruses, N. Kobayashi, Ed., Research Signpost, Trivandrum, India, 2003
3. E. A. Palombo, “Genomic diversity and interspecies transmission of rotaviruses,” in Genomic Diversity and Molecular Epidemiology of Rotaviruses, N. Kobayashi, Ed., Research Signpost, Trivandrum, India, 2003.
4. N. A. Cunliffe, P. E. Kilgore, J. S. Bresee et al., “Epidemiology of rotavirus Diarrhoea in Africa: a review to assess the need for rotavirus immunization,” Bulletin of the World Health Organization, vol. 76, no. 5, pp. 525–537, 1998.
5. J. S. Bresee, R. I. Glass, B. Ivanoff, and J. R. Gentsch, “Current status and future priorities for rotavirus vaccine development, evaluation and implementation in developing countries,” Vaccine, vol. 17, no. 18, pp. 2207–2222, 1999
6. GBD Diarrhoeal Disease Collaborators. Estimates of global, regional, and national morbidity, mortality, and aetiologies of Diarrhoeal diseases: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Infect. Dis. 17, 909–948 (2017).
7. Bishop, R. F. et al. Virus particles in epithelial cells of duodenal mucosa from children with acute non-bacterial gastroenteritis. Lancet 2, 1281–1283 (1973). This study shows visualization of rotavirus as the causative agent of viral gastroenteritis and the associated histopathology.
8. Flewett, T. H. et al. Letter: Virus particles in gastroenteritis. Lancet 2, 1497 (1973).
9. Estes, M. K. & Greenberg, H. B. in Field's Virology (eds Knipe, D. M. & Howley, P. M.) 1347–1401 (Lippincott Williams & Wilkins, 2013).
10. Hoshino Y, Kapikian AZ. Classification of rotavirus VP4 and VP7 serotypes. Arch Virol Suppl. 1996;12:99–111.
11. Crawford, S., Ramani, S., Tate, J. et al. Rotavirus infection. Nat Rev Dis Primers 3, 17083 (2017). https://doi.org/10.1038/nrdp.2017.83
12. Sanderson, C., Clark, A., Taylor, D. & Bolanos, B. Global review of rotavirus morbidity and mortality data by age and region. WHOhttp://www.who.int/immunization/sage/meetings/2012/april/Sanderson_et_al_SAGE_April_rotavirus.pdf (2011).
13. Patel, M. M. et al. Global seasonality of rotavirus disease. Pediatr. Infect. Dis. J. 32, e134–e147 (2013).
14. World Health Organization. Rotavirus mortality rate in children younger than 5 years, 2013. World Health Organizationhttp://www.who.int/immunization/monitoring_surveillance/burden/estimates/rotavirus/rotavirus_deaths_map_b.jpg?ua=1 (2017).
15. Estes MK. Rotaviruses and their replication. In: Knipe DM, Howley PM, Griffin DE, et al., editors. Fields' virology. 4th ed. Philadelphia: Lippincott, Williams and Wilkins; 2001. pp. 1747–85.
16. O'Mahony J, Foley B, Morgan S, Morgan JG, Hill C. VP4 and VP7 genotyping of rotavirus samples recovered from infected children in Ireland over a 3-year period. J Clin Microbiol. 1999 Jun;37(6):1699-703. doi: 10.1128/JCM.37.6.1699-1703.1999. PMID: 10325310; PMCID: PMC84927.
17. GBD 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1151-1210. doi:10.1016/S0140-6736(17)32152-9
18. Ramani S, Kang G. Burden of disease & molecular epidemiology of group A rotavirus infections in India. Indian J Med Res. 2007;125:619e632.
19. John J, Sarkar R, Muliyil J, Bhandari N, Bhan MK, Kang G. Rotavirus gastroenteritis in India, 2011-2013: revised estimates of disease burden and potential impact of vaccines. Vaccine. 2014;32(suppl 1):A5-A9. doi:10.1016/j.vaccine.2014.03.004
20. Mandal, Shyamapada. (2014). Is Rotavirus Gastroenteritis a Global Emerging/Re-Emerging Problem?. Translational Medicine. 04. 10.4172/2161-1025.1000143.

Adolescent Care In Office Practice

Prof Sukanta Chatterjee
Ex HOD Pediatrics&Adol Clinic in charge, MCH Kolkata
Chairperson AHA 2023

Objectives

After studying this document the reader should be able to understand;

- The concept of adolescent care in office practice
- Steps in organizing adolescent care in office practice
- Steps in adolescent interview and physical examination
- HEADS – Psychosocial interview schedule
- Management of common adolescent issues

Introduction

In 1999, Indian Academy of Pediatrics made a hallmark decision of extending the age of pediatric care upto and including 18 years. This was followed by various national training programs culminating in Post Graduate Diploma in Adolescent Pediatrics of Kerala University. Currently only a few pediatricians are taking care of adolescents in office practice. This document shall highlight practical practice points that shall help a pediatrician to provide adolescent care in a systematic manner.

Like a 'well baby clinic' offers health promotion, disease prevention, screening for physical and psychosocial problems and parental guidance, an adolescent clinic does the same for adolescents and their parents. Most professional bodies recommend an annual health visit for adolescents or atleast once in early, middle and late adolescence.

Professional Attitude

One should be fond of adolescents, to take care of them. Incase one does not like adolescents, it is better to refer them to a professional who does. In contrast to the younger pediatric age group, where the history is taken only from the parents or the accompanying caregiver, due to developing autonomy and independence, it is mandatory to take history from the adolescent in a confidential setting. Ideally, it is good practice to set up an adolescent clinic and schedule a convenient day and time to see adolescents as they prefer to be with their own age group.

Aims of Setting-up an Adolescent Clinic

1. To reinforce & encourage health promoting lifestyles.
2. To detect and intervene physical, emotional & behavioral problems.
3. To provide anticipatory guidance against risk taking behavior.
4. To provide parental guidance
5. To immunize
6. To take care of reproductive and mental health issues

Steps in organizing Adolescent Health Services

Step.1: The available adolescent services in the neighborhood are first surveyed.

Step.2: Health needs of the adolescents are determined by conducting a survey in the existing Pediatric clinic.

Step.3: Training of the paediatrician in Adolescent Medicine would enable him to offer appropriate services .The ancillary staff is also trained in handling delicate adolescent issues.

Step.4: School and community referral networks are identified to increase the scope and reach of the services.

Step.5: Finally, the Adolescent Clinic is set up.

Correspondance : Sukanta Chatterjee, *Ex HOD Pediatrics&Adol Clinic in charge, MCH Kolkata. Email :sukantachatterjee@hotmail.com*

Although this unit would mainly focus on establishing an Adolescent Clinic in a private setting, the basic principles remain the same.

Hoffman's Principles

An adolescent clinic and its services are set up according to the following principles called Hoffman's principles:

1. Availability –Adolescent services should be available in the local neighborhood.
2. Accessibility-The services should be easily accessible by public andprivate transport.
3. Approachability-The services should be adolescent friendly.
4. Appropriateness-They should be appropriate according to the socioeconomic status, culture and value system of the population.
5. Acceptability-They should be acceptable to the community.
6. Affordability-The consultation fees should be kept flexible to cater to the needs of the underprivileged adolescent.

Structure of the Adolescent Clinic

While establishing an adolescent clinic, the important points to be kept in mind include:

- ***Venue:*** The clinic should ideally be set up in a Government or Corporate set up where all referral services & other medical facilities are available under one roof. A super specialty adolescent practice can also be set up in an already existing Pediatric clinic in the private set up. In the rural area, it can be set up in the Aganwadi in collaboration with the village Panchayath.
- ***Receptionist & Waiting Area:*** The clinic should be adolescent friendly. The receptionist should be sensitive towards adolescent issues. Baby posters and toys should be removed from the waiting area. Health education material and pamphlets and magazines without advertisements of cigarettes and alcohol could be kept in the waiting area.
- ***Consultation room & Examination room:*** The consultation and examination room should preferably be separate to allow for privacy.
- ***Medical Personnel:*** Ideally, a multidisciplinary team should manage an adolescent clinic. Pediatrician, clinical psychologist, counsellor and dietician would be the important members of this team.
- ***Laboratory:*** It is needed to perform screening and diagnostic tests.
- ***Seminar Room:*** Seminar room could be used to conduct health awareness programs, group discussions, life skill and counselling sessions with the adolescents.
- ***Equipment and Materials:*** The essentials needed in the clinic before one ventures into adolescent care are:
    1. Adult size stethoscope and blood pressure cuff
    2. Adult size examination cot (around 7 feet long)
    3. Adult weighing machine, stadiometer
    4. Height, weight, body mass index, blood pressure centile charts
    5. Tanner charts
    6. Snellen chart
    7. Orchidometer

Scheduling

The clinic should preferably be scheduled on a Saturday evening or Sunday morning when both the adolescent and parents are free. As adolescents prefer to be with others of the same age, it is advisable not to see younger patients at the same time. Once everything is in place, a notice could be put up in the clinic addressed to the adolescents and their parents explaining the rationale behind setting up the Adolescent Clinic at least 2-3 weeks in advance .All adolescent patients attending the pediatric OPD could be registered. They could be later called to the Adolescent Clinic for a detailed evaluation. This is what we do to begin from the exiting general pediatric OPD.

Services Available

The services provided by the Adolescent Clinic should be prominently displayed on the notice board. These would include:

- Annual health checkup & issue of the Adolescent

Health Card.

- Immunisation
- Family Life Education & Life Skill Classes
- Counselling services
- Sports Pre participation Evaluation
- Premarital counseling for 18+ years

Adolescent Interview

It is one way of gathering information from the adolescent, the other is through a screening questionnaire .A questionnaire saves time and is good for keeping records but it is not a substitute for a personal interview.

Objectives of the interview are:

- To determine the health problem and to monitor it.
- To develop a rapport with the adolescent.
- To motivate the patient to carry out the treatment plan.

Key points: To be remembered while conducting the interview are;

- Confidentiality should be assured to the patient and its limits should be clearly stated.
- The Pediatrician should adopt a non-judgmental attitude.
- During the interview only open-ended questions should be asked so that the communication is bi-directional.

Total time: Required for the interview is usually 30-45minutes.This could be split in the following way

- First 5-10minutes could be spent with the adolescent and his parents together. Conventionally parent might start narrating when service provider assures adolescent that he/she will be heard separately
- The next 20minutes can be spent with the adolescent alone eliciting a history and doing a physical examination.
- The last 10minutes could be spent with the patient and his parents reviewing the treatment plan.

History taking

An usual Pediatric history can be taken. The focus points would be h/o low birth weight, h/o allergy, h/o serious disease in the past & any h/o premature coronary artery disease, mental disease, suicide, diabetes mellitus & neoplasia in the family.

Building Rapport: Taking a psychosocial history from the adolescent forms an extremely important part of the otherwise routine pediatric history taking. To obtain the co-operation of an adolescent, it is essential the clinician makes eye contact with the adolescent as soon as the boy or girl enters the chamber. The adolescent should be greeted and in fact he or she should be given the opportunity to introduce the accompanying adults. It is also necessary that the clinician should introduce himself or herself to the adolescent and explain how he or she can help the adolescent. While taking a history, the pediatrician should listen actively, reflect and summarise appropriately to develop a good rapport with the adolescent.

HEEADSSS acronym is used worldwide to take a psychosocial history that includes details regarding the following:

- H- Home: Family members, relationship with each, disciplinary methods
- E- Education: School/ college performance, ambition, teachers, peers
- E- Eating habits: Dietary habits, body image issues
- A- Activities: Play, hobbies, media usage, leisure time activities with peers
- D- Depression: Change in mood or behaviour for >2 wks, suicidal ideation
- S- Substance Abuse: Drug use in adolescent or peers, attitude about drug use
- S- Sexuality: Menstrual history, sexual activity, pregnancy, contraception, intimate relationships, sexual abuse, orientation
- S- Safety: Violent acts, possession of arms, traffic rules

To make history taking adolescent friendly the HEEADSSS screening starts with non-sensitive topics like home, education then gradually passing towards more personal and private issues like depression, substance use, sexuality etc.Details of the questions that can be asked for taking a psychosocial history are given in the annexure. A

good psychosocial history gives a wealth of information about the adolescent's emotional wellbeing, determines strengths, screens for high risk behaviour and psychiatric disorders and indicates the areas of therapeutic intervention. For example, a 15 year old girl presenting with abdominal pain off and on to the clinic on a HEEADSSS screen revealed that she had a foul smelling vaginal discharge, dysmenorrhea, experimented with alcohol once and had attempted suicide twice. On further interviewing, she confided that her stepfather was sexually abusing her. The HEEADSSS screen in this case helped the clinician to plan his management in terms of treating the pelvic inflammatory disease, substance use, depression and ensuring the adolescent's safety.

Examination

A male pediatrician should ensure the presence of a female health professional while examining a female adolescent and vice versa for a female pediatrician. Presence of mother during physical examination is particularly comforting to adolescent girls. A detailed head to toe and systemic examination is to be conducted including body mass index, waist circumference and blood pressure. Common adolescent physical problems that should be looked for include anemia, dandruff, lice, acne, hirsuitism, caries, myopia, goitre, scoliosis, gynecomastia. Sexual maturity rating should be done for adolescents especially those with pubertal and endocrinal problems after getting informed consent from the adolescent.Getting consent for such sensitive clinical examination is a skill by itself. The clinician may introduce the consent issue by saying `I may do a checkup how you have matured in your genital organs, if you permit'. For routine checkup a standard SMR clinical examinationcould only be done after getting informed consent, otherwise a picture card of standard SMR may be used for self-reporting. Adolescents should also be taught the technique of breast and testicular self-examination.

Anticipatory Guidance

Adolescence is an age for autonomy, bids and identity crisis with great peer affiliation and sometimes conflicts with family. It is also an age for experimentation. So at every visit the clinician should screen for high risk behaviour (using the HEEADSSS screen) like inappropriate nutrition and physical activity, substance abuse, violence, suicide, media abuse, risky sexual behaviour and rash driving. Incase the adolescent is not indulging in any such activity; he/ she should be appreciated. The risks of indulging in such activities should also be discussed and tips to remain 'risk free' like handling negative peer pressure should be discussed. This is called anticipatory guidance, here the clinician anticipates a problem before it occurs and gives appropriate health promotive and disease preventing advice. Similarly at every visit, adolescents and their parents should be counselled and given tips about handling various developmental issues to minimise conflicts and enhance communication and bonding.

Immunisation status should be also checked at every adolescent visit. IAP recommends Tdap, Hepatitis-B, Typhoid, MMR, Chicken pox, Hepatitis A, Human Papilloma Virus vaccine and influenza vaccines for adolescents.

Management

All adolescent concerns must be addressed and the treatment plan should be outlined. The treatment and management are discussed first with the adolescents and later with parents after obtaining consent from adolescent . The adolescent should understand the management plan fully and its relevance. The risks and rewards should be highlighted,these would in turn motivate the adolescent to adhere to the treatment. All roadblocks to the treatment should be addressed. For example, a 13 yr old obese adolescent boy on being explained the management plan of dietary restriction of fats and sweets, increased physical activity and decreased TV viewing, expressed that his mother loaded the fridge with colas, ice creams and chocolates which he could not resist. This roadblock was discussed with the mother. She agreed to keep plenty of fruits instead of junk food in the fridge. This helped the adolescent in adhering to the management plan.

Most adolescent physicians form a network of 'adolescent friendly' specialists. The primary care physician in a few cases may need to play the role

of the 'gatekeeper' and collaborator amongst various specialities. For example an adolescent with learning disability and attention deficit disorder with nicotine addiction will need the services of a psychiatrist, clinical psychologist, special educator and a deaddiction specialist. The pediatrician in charge of this case has to ensure appropriate referrals, management and follow up of the case in the best interest of the adolescent. At community level local IMA branches (various specialists available) could take the initiative in starting adolescent clinics as being done in Kerala.

Conclusion

This unit has discussed in brief practical tips to establish an adolescent clinic and to manage adolescent patients in office practice. Though adolescents form 23% of our population, they are mainly a neglected lot as until lately they neither fell into the realm of a physician nor the pediatrician. Currently they are facing immense challenges in the form of increasing health problems of malnutrition, drug and media abuse, road traffic accidents, violence, HIV/ AIDS, stress, depression and suicide to list a few. They are in need of counselling and guidance from a knowledgeable, trustworthy and nonjudgmental adult – a pediatrician with whom they have a rapport since childhood fits into this role perfectly. Pediatricians should empower adolescents to make healthy choices regarding their lifestyle and thereby ensure that they grow into responsible healthy adults of tomorrow!

Wilson's Disease(OMIM277900)

***Dr Soumita Sarkar, *Dr Debanjana Dasgupta, **Prof Kalpana Datta**
**Resident, **Professor*
Department of Pediatrics , Medical College, Kolkata

Introduction

This disease was first described in 1890 (Gowers, Strumpel),1912- Dr SAK Wilson. This is anautosomal recessive(AR) disorder and is characterised by hepatolenticular degeneration. It is mainly attributed to mutation in ATP7B gene (chrm13q14.3).

Dr Samuel Alexander Kinnier Wilson

Other copper overload states:

1. MEDNIK syndrome-Rare multisystem disorder of copper metabolism, AP1S1gene defect,characterised by Mental Retardation, Enteropathy, Deafness,Neuropathy,Ichthyosis and Keratoderma.
2. INDIAN CHILDHOOD CIRRHOSIS-1980s,Maharashtra,Rural Hindu middle income families,cow milk contaminated with copper from untinned brass utensils,High mortality (92% without chelator)
3. Normal neonate (high liver copper – becomes normal by 6months age)
4. Chronic cholestasis(biliary atresia)

Correspondance : Kalpana Datta, *Professor, Medical College, Kolkata. Email:drkalpanadatta@gmail.com*

Epidemiology of Wilson Disease

Globally incidence is 1/30,000 to 1/10000 births worldwide (1/90 carriers). India is a geographical hotspot for Wilsons disease.Incidence is around 7.6% cases in a study of Liver disorders in North India.(1) WD clinic from South India reports 15-20 new cases every year(1). Lowest age affected in India - 3 years (Kalra 1999)(2)There is a 25% recurrence risk.Male:Female ratio : 2.7:1 in India(2) (may be due to protective effect of estrogens in females).

Ref: 1. Nagral A, Sarma MS, Matthai J, Kukkle PL, Devarbhavi H, Sinha Set al. Wilson's Disease: Clinical Practice Guidelines of the Indian National Association for Study of the Liver, the Indian Society of Pediatric Gastroenterology, Hepatology and Nutrition, and the Movement Disorders Society of India. J Clin Exp Hepatol 2019;9:74 98.

2.Wilson's Disease Update: An Indian Perspective by Niraj Kumar, Prashant LK, Vinay Goyal

Genetics

More than 750 mutations worldwide, 36 of them are found in India.High degree of homozygosity in India due to intra-caste marriages.P.His1069glu (exon 14) most common in Europe; p.arg778leu most common in Asians. p.C271X and p.G1101R most common in India, associated with earlier age of onset.Genetic mutation cannot predict clinical severity and vice versa – Incomplete penetrance.

Copper – Double Edged Sword

Total body copper-100mg

Sources-liver, fish, meat, lentils, nuts, chocolate.

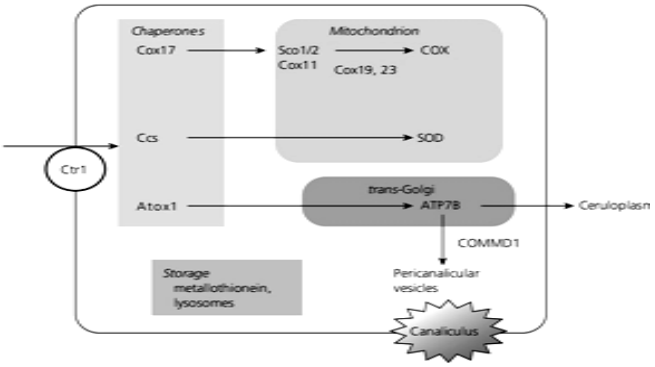
RDA-200 to 440 mcg/ day.

Cu is essential for:A) Mobilisation of iron Fe2+ to Fe3+ with the help of CeruloplasminB)Formation of enzymes/proteins: cytochrome c oxidase, ALA synthase, monoamine oxidase, tyrosinase, hepcidin, superoxide dismutase, factor V, VIII.

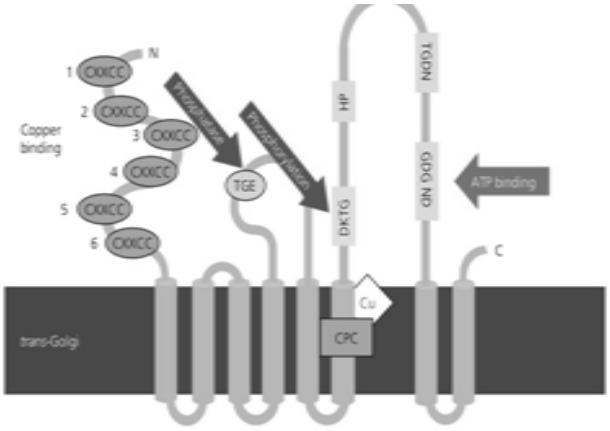
Copper deficiency: associated with chronic peritoneal dialysis, Total Parenteral Nutrition, Zinc excess, chronic malabsorption, gastrectomy. Clinical findings are depigmentation, fragile hair, myeloneuropathy, hepatosplenomegaly, osteoporosis, anemia.This is known as Menkes disease, which is an X-linked recessive disorder.

Cu Absorption- from duodenum (via CTR1) → Enterocyte → bound to metallothionein for desquamation) or to portal blood via ATP7A → uptake to hepatocyte by CTR1 for usage /excretion. Phytates, zinc (induces metallothionein), molybdenum decreases copper uptake.

Excretion of copper- 90% in bile and 10% in urine.



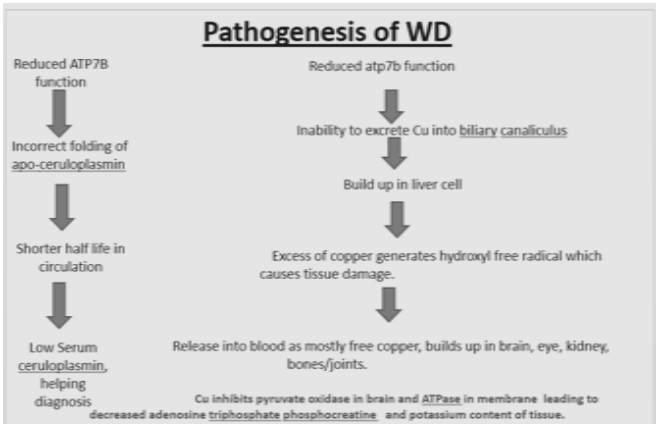
This above image shows how ceruloplasmin deals with copper inside a canaliculus and how copper is transported within organelles.



The above image depicts ATP7B which is membrane bound copper transporting ATPase and shows how copper is being transported into vesicles.

ATP7B-

- Encodes a membrane bound copper transporting P type ATPase.
- Binds Copper to apo-ceruloplasmin (serum transport)
- Packages copper into vesicles for exocytosis in bile (via trans Golgi)



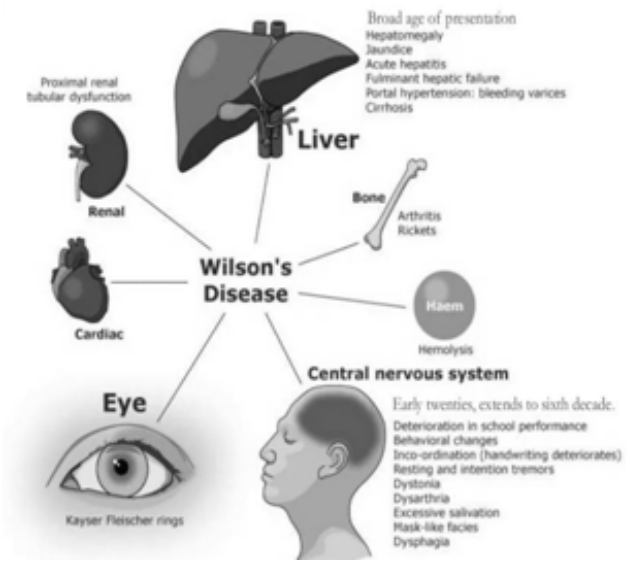
CERULOPLASMIN

- Copper bound Ferroxidase
- Acute phase reactant (delivers Cu to macrophages)

ACERULOPLASMINEMIA:Autosomal Recessive disorder, iron deposition in liver, pancreas, brain ?leading to Dementia, Dysarthria, Dystonia, Diabetes Mellitus.Age of onset – 40 years.

Clinical features

Multiple systems are affected with copper deposition in them.



Hepatic Wilson Disease

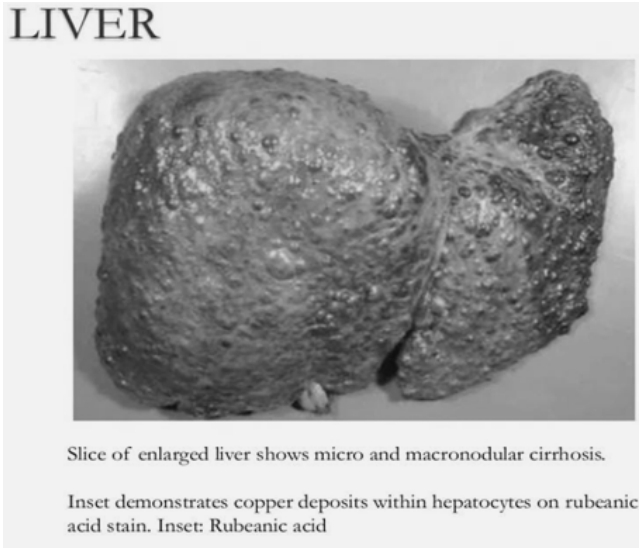
Most commonly seen in children (India –1st decade with varied presentation).

Asymptomatic hepatomegaly/abnormal LFT with low Ceruloplasmin level. May present as seronegative acute hepatitis, subacute/chronic hepatitis, acute liver failure (5%), cryptogenic cirrhosis, portal hypertension. Other effects of hepatic dysfunction like delayed puberty, amenorrhea, coagulation defects may also be present.

Chronic Wilson disease can have low titres of autoantibodies thus mimicking autoimmune hepatitis.

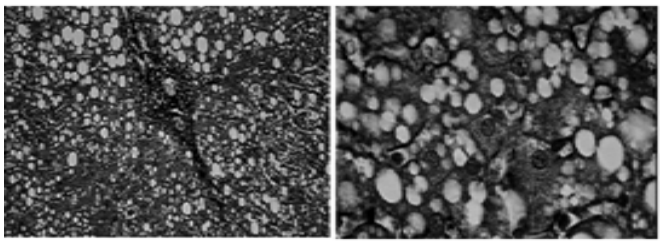
Always suspect Wilson's disease in any child with undiagnosed liver disease.

Histopathological Changes in liver



Slice of enlarged liver shows micro and macronodular cirrhosis.

Inset demonstrates copper deposits within hepatocytes on rubeanic acid stain. Inset: Rubeanic acid



All grades of hepatic injury seen- steatosis, Hepatocellular ballooning, Degeneration, Glycogen granules,Enlarged Kupffer cells.

Neuro Wilson

Most commonly begins from 2nd decade of life.

Initial symptom – gait (30-75%) and speech disturbance (goes on for years). Movement disorders(intention tremors, involuntary movements) are frequently present.

Dysarthria is seen in 85 -97% cases. (dystonia of bulbar muscles, high pitched whining).Other neurological features include drooling of saliva, dystonia (11-69%), parkinsonism, motor incoordination, deterioration in school performances and psychosis or behavioural changes (20%).

Chorea, Athetosis, Cognitive impairment/dementia, Seizures, Hyperreflexia, Myoclonic seizure, Urinary incontinence, Autonomic dysfunction are also frequently attributed to neuro-Wilson.

Image shows 'vaccuous smile'-masked facies with open mouth caused by dystonia of facial and mandibular muscles, seen in Neuro-wilson.

Tremor types in WD:

- resembles essential tremors, but asymmetric.
- Cerebellar intention tremor
- Postural tremor: classic tremor for WD ?wing-beating tremor, holding.

Cognitive impairment in WD:

- Exclude hepatic encephalopathy.
- Frontal lobe syndrome: impulsivity, promiscuity, impaired judgement, apathy, executive dysfunction decreased attention, and emotional lability, pseudobulbar features (sudden outbursts of inappropriate laughter or tearfulness)

Subcortical dementia: slowed thinking, memory loss, and executive dysfunction.

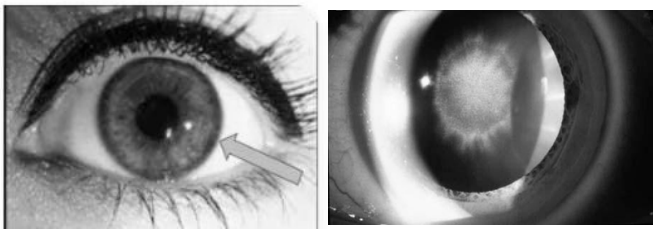
Psychiatric changes in WD:

Most common:depression (20 to 30%), personality

change, incongruous behavior, and irritability. Diagnosis may be delayed significantly in these individual.

Ocular Signs

KayserFleischer Ring: Clinical hallmark but also seen in 3% of normal population.Seen in 50% of hepatic WD; 95% of Neuro WD.Caused due to deposition of copper in Descemet's membrane. Visible by naked eye at times/requires slit lamp.Greenish brown discoloration appearing first at upper cornea, then lower cornea.Disappears with treatment.Not specific for Wilson's disease,also seen in chronic cholestatic disease such as primary biliary cirrhosis or neonatal cholestasis. Other ocular findings include saccadic pursuits, loss of accommodation, eyelid apraxia or sunflower cataract.



SUNFLOWER CATARACT – 2-17% CASES

Haematological changes

Coombs negative hemolytic anemia--Maybe the initial feature.

Decay of liver cells may result in release of large amounts of stored copper → inhibits RBC transketolase and thus leads to haemolytic anaemia.

Associated with Acute liver failure of WD, poor prognostic factor.

Osseo-muscular features

More common in India, upto 14% cases. Radiological osteoporosis, spontaneous fracture, large joint polyarthritis, low back pain, refractory rickets, myopathy may be the presenting symptoms.

Maybe related to kidney problems also.

Others

Kidney: Proximal RTA > Distal RTA leading to nephron-calcinosis, refractory rickets

CVS: Cardiomyopathy, arrhythmias

Pancreatitis

Hypoparathyroidism

Infertility and recurrent abortion

Skin: blue lunulae, acanthosis nigricans, pretibial hyperpigmentation.

Management Of Wilson's Disease

When to suspect Wilson's disease???

As a differential diagnosis in children and teenagers with:

(i) Unexplained acute or chronic liver disease

(ii) Fulminant hepatic failure

(iii) Neuropsychiatric illness of unknown cause

(iv) Unexplained behavioral changes

(v) Unexplained Coombs negative hemolytic anemia

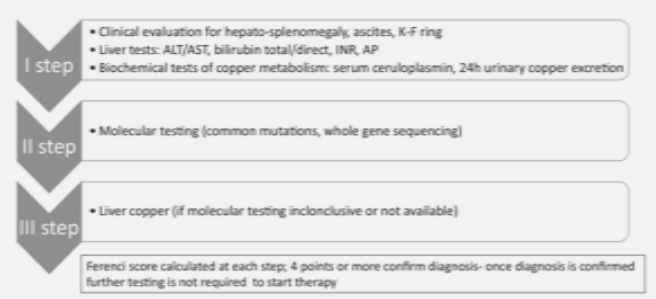
(vi) Fanconi syndrome

(vii)Unexplained elevation of transaminases

Investigations:

Early diagnosis of WD is of utmost importance for prompt initiation of treatment and a favourable outcome.No single test is diagnostic of WD

Diagnostic approach:



Serum Ceruloplasmin :

132 kd alpha globulin, synthesized by hepatocytes and secreted in circulation.Carries 90% of copper in blood in bound form.Normal values of s. ceruloplasmin is >20 mg/dl.It decreases by 50% of lower normal value in 90% of patients with WD

Extremely low ceruloplasmin level (<5mg/dl) is taken as a strong evidence in diagnosis

However a normal serum ceruloplasmin level does not exclude diagnosis

False positive results in:

Neonates

Protein energy malnutrition(PEM)

Marked renal or enteric protein loss – Nephrotic syndrome or protein losing enteropathy

Fulminant hepatitis

End stage liver disease

Rarely with Menkes disease or hereditary aceruloplasminemia

Condition with copper deficiency like TPN, after gastric bypass surgery, excess zinc administration

10% heterozygotes for WD

False negative: associated infection/inflammation

Serum Copper:

Serum total copper may be low, normal or high in Wilson's disease

Serum free copper estimation is useful in diagnosis of WD

Serum free copper is determined indirectly by

Free Copper(microgm/dl)

= Serum total copper(microgm/dl) – (3.15 x Serum ceruloplasmin[mg/dl])

Normal serum free copper is 8-12 microgm/dl.In children with WD its above 20-25 microgm/dl

It may be 10 times high in patients with fulminant hepatic failure or intravascular hemolysis.Also indicator of compliance with treatment

24 Our Urine Copper Estimation:

Normal value is <40 microgm/day.

In Wilson's Disease usually it is >100microgm/day

Penicillamine Challenge test:In WD urine cu excretion may go upto>1000microgm/day

False positive reports:

Any copper chelation therapy

Contamination

Rarely in chronic hepatitis, cholestatic cirrhosis or nephrotic syndrome

Renal failure is a contraindication for this test

Liver Copper:

Determined from liver biopsy samples.Normal hepatic copper content is <55microgm/gm dry liver tissue. In untreated WD usually it is >250microgm/gm dry liver tissue

Limitations of this test :

Unreliable in advanced liver disease

Biopsy not feasible in child with severe liver dysfunction

Negative biochemical stain for copper in liver biopsy never rules out WD

Other Tests:

Liver function tests: AST/ALT ratio>2, ALP/bilirubin ratio<4

Features of Hemolysis - Coombs negative hemolytic anemia present

Serum uric acid – May be decreased

Ophthalmological examination – KF ring, Sunflower cataract

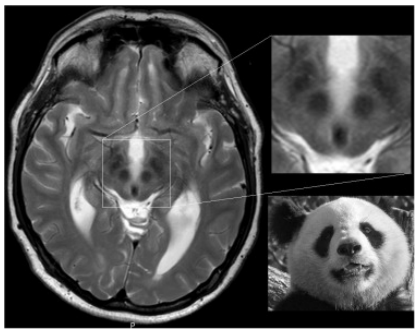
Neuroimaging:

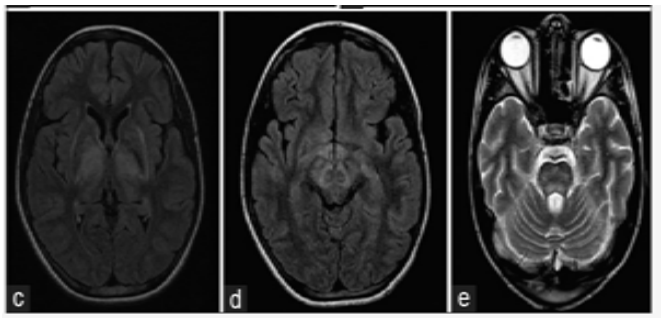
CT Brain - Cortical atrophy and ventricular dilatation are the most common finding in CT brain, each involving up to 45% Indian WD cases

MRI brain:

T2 hyperintensities involving bilateral basal ganglia (72%), thalamus (58%) and midbrain (49%) along with atrophy involving cerebrum(70%), brainstem(66%) and cerebellum (52%)3

Characteristic findings including the "face of giant panda" in midbrain and the "face of miniature panda" in pons.Extensive involvement in severe disease.





Molecular Genetic Testing:

Mutational Analysis:

(i) Specific mutations in ATP7B gene is identified

based on various ethnic groups

(ii) The common mutations in Indian scenario include C813A, G3182A, C2975A.

This is the basis of screening of WD in India

Haplotype Analysis: Analysis of alleles

Entire ATP7B gene sequencing: Not available commonly

Modified Leipzig score:Diagnostic scoring for WD…

Table 2: Modified Leipzig Score for Diagnosing Wilson's Disease (Modified from Nagral *et al.*, 2019)[21]

	Features	Score
1	Kayser-Fleischer corneal rings	Present=2; Absent=0
2	Serum ceruloplasmin	Normal (>20 mg/dl) = 0; 0-5 mg/dl=3; 6-11 mg/dl=2; 12-20 mg/dl=1
3	24-hour urinary copper (in absence of acute hepatitis)	>100 mcg/day=2; 40-100 mcg/day=1; <40 mcg/day=0
4	Coomb's negative hemolytic anemia with liver disorder	Present=1; Absent=0
5	Genetic mutation	Detected on both chromosome=4/One chromosome=1/Not detected/test not done=0
6	Liver biopsy	Orcein or Rhodamine-positive granules=1
7	Neurobehavioral symptoms	Present=2; Absent=0
8	MRI brain	Typical features suggestive of WD present=1; absent=0
9	Family history of WD	Sibling death from liver or neurological features suggestive of WD=1
	Total score	4 or more=Definitive diagnosis of WD 3=Possible WD and further evaluation needed 2 or less=WD unlikely

Treatment:

Treatment modalities in WD can be categorized into:

(i) Anti copper therapy: Copper chelators and zinc

(ii) Symptomatic therapy: Medical & Surgical

(iii) Definitive therapy : Liver transplantation

(iv) Dietary management: Avoid high copper containing foods including shellfish, nuts, chocolate, mushrooms, and liver

(v) Antioxidants:Alpha tocopherol

Lifelong medical therapy is needed in all patients with WD

D- Penicillamine(DPM):

Cornerstone of therapy in WD

Mechanism of Action:

Moblization of copper from hepatocytes

Induction of metallothionein in liver

Augmenting thiol pool

Direct anti-inflammatory action

Reducing hepatic fibrosis

Dose = 20mg/kg/day before meals(Max=1g/day)

Pyridoxine must be given with it in dose of 25mg/day

In Neuro WD:

There is Paradoxical neurological worsening (PNW) with Pencillamine. A "start low and go slow" de coppering policy is advocated.

Adverse Effects of D-penicillamine:

Urticaria, agranulocytosis, aplastic anemia

Rarely SLE, nephrotic syndrome, Goodpasture syndrome

Dermatological toxicities

Regular monitoring of CBC must be done in patients receiving DPM

Monitoring: CBC, urinalysis, creatinine after the first week monthly during the first 3months, 3 monthly intervals until stable target values are achieved, then twice per year, urine copper for compliance (can increase upto 2000)

Treatment withdrawn if WBC < 3000, ANC<2000, TPC< 120,000 per mm3, protein 2+ on a dipstick, >10RBCs/hpf. Replace with Zinc.

Zinc:

Introduced for WD treatment in 1961

Mechanism of Action:

Induces metallothionein synthesis = Cu entering portal in enterocytes circulation

Induces metallothionein in hepatocytes

Interferes with lipid peroxidation

Enhance glutathione in liver ie, Oxidative Damage

Advantages:

No neurological deterioration and can be used 1st line in neuro WD

Additive effect with penicillamine

Switch-over to Zn can be done after initial treatment with DPM

Very cheap and easily available

Not teratogenic

Disadvantages: Maximum action after 3weeks of initiation

Side effects: Gastritis, Amylase & lipase increases

Dose: 75mg in children and 150mg in adolescents in 3 divided doses. Formulation: Zn acetate with least side effects

Other Copper Chelators:

Symptomatic therapy:

Levodopa carbidopa & dopamine agonists for parkinsonism-like features

Drugs	Route of administration & Dose	Adverse effects	Special remarks
Dimercaprol (British anti-Lewisite)[68]	Deep intramuscular 5 mg/kg bolus f/b 2.5 mg/kg 1.5 ml (10% suspension in peanut oil) twice a day	Painful Hematoma & sterile abscess at injection site HT & tachycardia (dose dependent) Nausea, vomiting, abdominal pain Headache, paresthesia	BAL is lipid-soluble with best blood-brain barrier permeability amongst all copper-chelators Tachyphylaxis-efficacy reduces with continuous use Not preferred now – May be tried as a 1-month course in combination of DPM in refractory cases
Trientine[68,71]	Oral (in 3 divided doses) - Start low-go slow policy Adults: 750 mg – 2 g/day Children: 20 mg/kg/day	Paradoxical neurological worsening (up to 26% cases) Late-onset HSE: lupus, nephritis Sideroblastic anemia Skin rash; ageusia Pancolitis; hemorrhagic gastritis	Safe in pregnancy but avoid breast-feeding Take away from meals Monitor for iron deficiency
Unithiol (Dimercapto Propane sulfonate)[68]	Oral 200 mg twice daily	Early HSE: fever, leucopenia Nausea, dysgeusia	A sulfonic acid derivative of dimercaprol Only few reports in literature; no reports from India to date
Tetrathiomolybdate (Undergoing clinical trials – not commercially available)[71]	Oral 20 mg 3 times per day with meals and 3 times without meals	Bone-marrow suppression (reversible) Acute hepatitis Elevated aminotransferases, triglycerides and cholesterol Seizures Paradoxical neurological worsening (less common)	Damage epiphyseal bone-growth in animal studies – dangerous to use in children and adolescents

Anticholinergics and Benzodiazepines for dystonic features & tremor

Botulinum toxin injection may help focal dystonia, related tremor

Seizures - antiepileptics, preferably avoiding drugs with primary hepatic metabolism

Psychiatric symptoms - behavioural therapy or antipsychotics, preferably the atypical ones to minimize the extrapyramidal side effects

Lesioning surgery and deep brain stimulation - in refractory cases

Liver transplantation: Hepatic failure is the primary indication for liver transplantation (LT) in WD

No risk of recurrence in WD after liver transplantation

PROGNOSIS:

Untreated WD is progressive & fatal

Special Scenarios:

Pregnant Adolescent:

Zn continued at same dose

Penicillamine and trientine continued with upto 25-50% dose reduction

Frequent monitoring of copper status

Surgery: DPM interferes with wound healing and should be reduced for 10-14 days post-op period

Monitoring of Treament:

H/O and clinical examination to detect progression of disease process

TABLE 6. Wilson's disease scoring system to predict the outcome of children with hepatic decompensation (King's Wilson index) by Dhawan et al (8)

Score	Bilirubin, μmol/L	INR	AST	Leukocytes, 10^9/L	Albumin, g/L
0	0–100	0–1.29	0–100	0–6.7	>45
1	101–150	1.3–1.6	101–150	6.8–8.3	34–44
2	151–200	1.7–1.9	151–200	8.4–10.3	25–33
3	201–300	2.0–2.4	201–300	10.4–15.3	21–24
4	>300	>2.5	>300	>15.3	0–20

AST = aspartate aminotransferase.
11 points and above - urgent listing for liver transplantation.

Periodic slit lamp examination

Biochemical investigations

Response to treatment:

(a) 24hr urine Cu excretion – In Cu chelator therapies

(b) Urinary and plasma Zn levels – in Zn therapy

Global Assessment Scale for Wilson's Disease (GAS for WD)-Assessment including neuropsychiatric, hepatic and osseomuscular features along with their effect on quality of life

Family Screening:

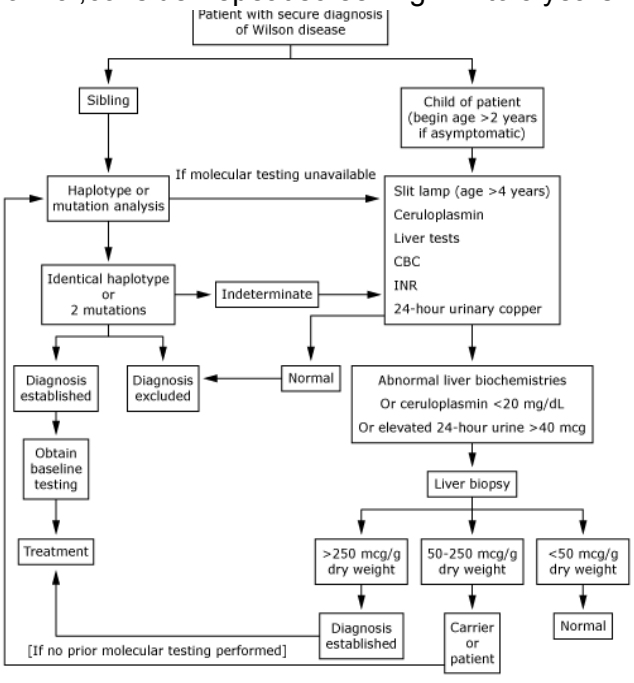
Siblings of a proband carries 25% risk, offspring and parents have 0.5% risk of developing WD

1st& 2nd degree relatives including siblings, parents and offspring of a WD patient should undergo assessment for KF ring along with serum ceruloplasmin and 24 hour urinary copper.(If genetic testing unavailable)

Monitoring for WD symptoms every 6 12 months even if diagnosis has been ruled out during first screening

Screening algorithm for 1st degree relatives

If initial screening by blood and urine testing is normal,consider repeat screening in 2 to 5 years.



Novel Therapies In Wd:

Pharmacologic inhibition of p38 and INK MAPK signaling pathways in vitro are potential new therapeutic targets for rescue therapy

Animal tested gene therapies: lentiviral gene transfer, or adenovirus mediated transfer.

Key Message:

Keeping a very low threshold for clinical suspicion to avoid missing the diagnosis of WD

Early recognition and adequate anti copper therapy

Adequate monitoring of patients

Genetic counselling and screening of relatives of index case.

References

1. Nelson Textbook of Pediatrics, 21st edition
2. A Riyaz Pediatric Gastroenterology &Hepatology , 4th edition
3. "Wilson's Disease update: An Indian perspective" , Niraj Kumar, Prasahnt LK, Vinay Goyal; AIAN review
4. Martins da Costa C, Baldwin D, Portmann B et al. Value of urinary copper excretion after penicillamine challenge in the diagnosis of Wilson's disease. Hepatology. 1992 Apr;15(4):609-15. doi: 10.1002/hep.1840150410. PMID: 1551638.
5. Ferenci P, Steindl-Munda P, Vogel W, Jessner W, Gschwantler M, Stauber R, Datz C, Hackl F, Wrba F, Bauer P, Lorenz O. Diagnostic value of quantitative hepatic copper determination in patients with Wilson's Disease. Clin Gastroenterol Hepatol. 2005 Aug;3(8):811-8. doi: 10.1016/s1542-3565(05)00181-3. PMID: 16234011.
6. Roberts EA, Schilsky ML. Diagnosis and treatment of Wilson disease: an update. Hepatology 2008; 47:2089.
7. Linn FH, Houwen RH, van Hattum J, van der Kleij S, van Erpecum KJ. Long-term exclusive zinc monotherapy in symptomatic Wilson disease: experience in 17 patients. Hepatology. 2009 Nov;50(5):1442-52. doi: 10.1002/hep.23182. PMID: 19731238.
8. Weiss KH, Gotthardt DN, Klemm D, Merle U, Ferenci-Foerster D, Schaefer M, Ferenci P, Stremmel W. Zinc monotherapy is not as effective as chelating agents in treatment of Wilson disease. Gastroenterology. 2011 Apr;140(4):1189-1198.e1. doi: 10.1053/j.gastro.2010.12.034. Epub 2010 Dec 24. PMID: 21185835.
9. "Wilson's Disease in children: A Position Paper by the Hepatology committee of the European Society for Pediatric Gastroenterology, Hepatology and Nutrition", Piotr socha, Wojciech Janczyk, Anil Dhawan et al
10. Piyush Gupta Textbook of Pediatrics, 2nd edition

Multiple Exchange Transfusions in Neonates with Antenatally Detected Fetal Anemia. Is Delivering Early the Way Forward?

***Devdeep Mukherjee, **Pruthvi Raj, ***Prasanna Roy, ****Dipanwita Sen**

**Consultant neonatologist, The Mission Hospital, Durgapur.*

***Consultant transfusion medicine, The Mission Hospital, Durgapur.*

****Fetal consultant, Ultra Clinic, Asansol and obstetrician, Kamala Nursing Home, Asansol.*

*****consultant obstetrician and gynaecologist, The Mission Hospital, Durgapur*

Background: *The recommended treatment for rhesus disease in neonates involve phototherapy and exchange transfusion. Medical management involves the use of immunoglobulin, albumin and phenobarbitone. We had 3 pre term neonates who were diagnosed to have fetal anemia from the 31 week ante natal scan along with a sudden rise in titres of the indirect coomb's test (ICT). Initial anomaly scan at 20 weeks was normal. 2 fetuses had received intra uterine transfusions prior to delivery.*

Clinical description: *Neonates were electively delivered prematurely after being detected with fetal anemia and were noted to have elevated cord blood and serum bilirubin levels. Mother had O negative blood group. She had received anti D prophylactically. Mother was a 2nd or 3rd gravida for all the cases.*

Management: *Babies received triple surface phototherapy soon after delivery. They needed multiple double volume exchange transfusions on successive days. Immunoglobulin at 1 gram/kg was given on 2 consecutive days. Albumin infusion and phenobarbitone was also given. Babies also needed respiratory support for respiratory distress syndrome and other supportive management for prematurity.*

Conclusion:*In a resource limited setting, where intra uterine fetal transfusion is not possible or difficult to be performed repetitively, severely affected fetuses can be delivered prematurely and treated with repeated exchange transfusion and phototherapy as we did for our cases. Ante natal scans help in early diagnosis and should be used to monitor these pregnancies closely.*

Keywords: *fetohemolytic disease, exchange transfusion, intra uterine fetal transfusion, jaundice,*

Introduction

Rhesus disease in neonates is seen when maternal ant-D antibodies cause hemolysis of rhesus positive fetal red blood cells after crossing the placenta. This commonly occurs as a result of a prior Rh positive fetal maternal transplacental haemorrhage in atleast 75% of pregnancies [1].

Case report

Case 1:

A 3rd gravida mother with one living child delivered a baby by emergency caesarean section at 33 weeks, as ante natal scan was suggestive of fetal anemia.

Mother's blood group was O Rh "D" negative. She had previously received anti D prophylactically. Anomaly scan, in this pregnancy at 20 weeks was normal and indirect coomb's test (ICT) was negative. At 31 weeks, fetus was noted to have middle cerebral artery (MCA) peak systolic velocity (PSV) of 79.25 cm/second (median PSV for age42.43) with measurement being 1.86 multiples of median (MOM). Polyhydramnios was documented. ICT was 1:256 at 32 weeks. 33 weeks scan showed rising MCA PSV- 91.24 cm/second (median PSV for age 48.56) and 1.95 multiples of median. With rising ICT titres, MCA PSVand polyhydramnios, baby was electively delivered at 33 weeks. Cord blood haemoglobin at birth was 9.8 mg/dl and total cord bilirubin (TB) was 8.2 mg/dl (140 micromol/L) [Figure 1]. Baby received triple surface phototherapy (with LED phototherapy unit) immediately after birth. Total serum bilirubin at 1 hour of age was 11.1 mg/dl (190umol/L) and direct coomb's test (DCT) was strongly positive. Baby underwent double volume (180 ml/kg) exchange

Correspondance : Devdeep Mukherjee, Consultant neonatologist, The Mission Hospital Email : dr.devdeep.mukherjee@gmail.com

transfusion (ET) at 3 hours of age with leucofiltered reconstituted whole blood (fresh O negative packed red blood cells and AB plasma), following which bilirubin was 6.8 mg/dl (116umol/L). Immunoglobulin was administered at 1 gram/kg after 1st ET. At 26 hours of age, baby had TB of 12.7 mg/dl (217umol/L) following which 2nd ET was done. Immunoglobulin (1 gram/kg) was repeated on day 2 after discussion with hematology. Post 2nd ET, bilirubin was 9.2 mg/dl (157 umol/L) at 36 hours of age. At 48 hours, bilirubin increased to 21.2 mg/dl (362 umol/L) and baby underwent a 3rd ET, following which bilirubin was noted to be in a decreasing trend and baby gradually came off phototherapy on day 5 [Figure 1]. Albumin infusion (1 gram/kg/day) was given on day 2 and day 3. Phenobarbitone (5mg/kg/day) was also started on day 2 with rising bilirubin and continued for 5 days. On day 10, with hemoglobin of 8.6 mg/dl, baby received a packed red blood cell transfusion with O negative blood. DCT was negative prior to discharge on day 12(Fig 1).

Case 2 :

2nd gravida mother with O negative blood group had a history of previous unexplained neonatal death. She was not administered anti D previously. 29 weeks scan showed MCA PSV 60.5 cm/sec (1.54 multiples of median). ICT was 1:256. Baby received single intra uterine transfusion (IUT). However subsequent MCA PSV was in a rising trend – 78.5 cm/sec. Baby was electively delivered at 32 weeks. Cord blood hemoglobin was 10 gm/dl after birth and cord bilirubin was 8 mg/dl (136.8 umolL). Baby was given triple surface phototherapy. Baby subsequently underwent 2 exchange transfusions on consecutive days (Day 1 at 3 hours of life and day 2 at 27 hours of life) along with 2 doses of immunoglobulin at 1 gram/kg, and albumin 1gram/kg/day on successive days. She also received phenobarbitone for 5 days, similar to case 1.

Case 3:

4th gravida mother with 3 previous pregnancy losses was noted to have fetal anemia at 33 weeks scan. MCA PSV was 75 cm/sec (1.7 multiple of median). ICT was 1:256. Baby received 2 IUT. MCA PSV was in a rising trend. Baby was delivered electively at 35 weeks. Cod blood hemoglobin was 8.5 gm/dl and cord bilirubin was 10 mg/dl (171 umol/L). Baby received triple surface phototherapy and an initial exchange transfusion at 4 hours of age followed by immunoglobulin 1 gram/kg. Baby underwent a 2nd exchange transfusion at 30 hours of age and a 3rd exchange transfusion at 54 hours of age. Baby also received a 2nd dose of immunoglobulin, 2 doses of

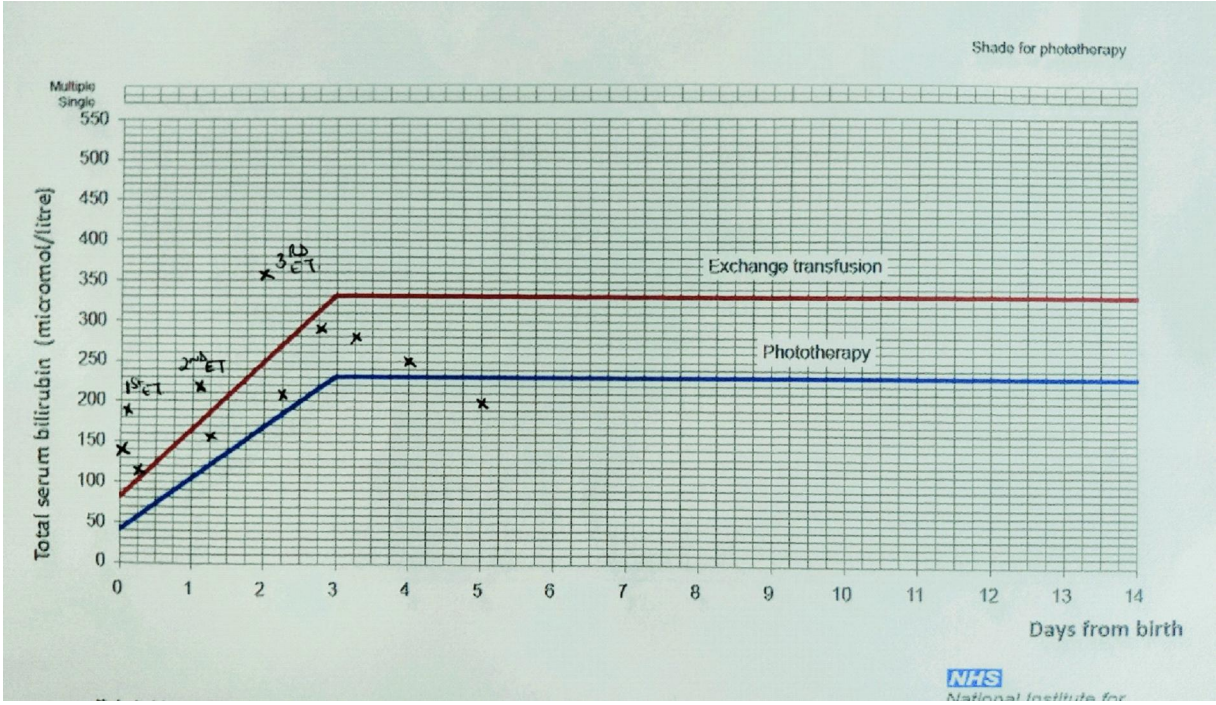


Fig 1: NHS jaundice graph for the 33 weeker. 'x' marks the bilirubin level. 'ET' signifies exchange transfusion

albumin infusion and phenobarbitone similar to the 1st case.

All babies were delivered in bilirubin stained amniotic fluid and cried immediately at birth. Case 1 and 2 needed continuous positive airway pressure (CPAP), initially due to mild respiratory distress syndrome. They received caffeine citrate. Case 3 did not need any respiratory support.

Babies remained hemodynamically stable during hospital stay and had umbilical lines (umbilical artery and umbilical venous catheters) placed for exchange transfusion. Nasogastric tube feeds were started from day 4 and they went on to full feeds by day 7. Sepsis markers were in normal range. Thyroid stimulating hormone, glucose 6 phosphate dehydrogenase and liver function test were in normal range. Reflexes were normal as per gestation and magnetic resonance imaging (MRI) brain at term gestation (40 weeks) did not reveal any abnormality. Otoacoustic emission (OAE) at 6 weeks was also reported as normal. Babies have been achieving milestones as per age. No neurological sequalae has been noted.

Discussion

Sensitisation of a rhesus negative mother commonly occurs when fetal rhesus positive red cells spontaneously leak in to their circulation which usually happens when the placenta separates at delivery for which anti -D administration is recommended within 72 hours. Apart from anti-D, other antibodies like Rh C, D, E, c, e, Kell, Kidd and Duffy are also known to produce IgG mediated hemolysis in the neonate. These antibodies are capable of crossing the placental barrier and the hemolytic ability is related to their avidity and not on their absolute concentration as a result of which even low concentration of antibodies may cause severe disease in the newborn[1-2].Hence screening for RBC irregular antibodies by IAT method (indirect antiglobulin test) should be performed in every pregnancy and clinically significant antibodies should be followed up closely[3]. Neonates if undiagnosed may present with severe anemia as we saw in our index case.

Extra medullary erythropoiesis may cause hepatosplenomegaly. Hydrops, metabolic acidosis, high output cardiac failure and death are seen in severe cases if undiagnosed. Neonates may develop kernicterus[1-2, 4].These events usually happen after 16 weeks, as antibodies do not usually cross the placenta prior to that[1]. For our case series this was noted after 30 weeks.

Prior history of hemolytic disease and elevated maternal antibody titres increase clinical suspicion.In these case, the initial ICT was negative with normal fetal anomaly scan. In vitro cell-mediated maternal antibody functional assays, amniotic fluid spectrophotometry, ultrasound fetal assessment, and fetal blood sampling help in early diagnosis[2]. Our patients were diagnosed early on the basis of fetal scans. Increased MCA PSV is an indicator of fetal anemia. Anemia decreases blood viscosity which thereby increases venous return and preload, leading to an increase in cardiac output[5].

Intrauterine fetal transfusion (IUFT) is beneficial for fetohemolytic disease. Survival ranges from 41-66%[6]. In a resource limited setting like ours, IUFT is challenging due to the paucity of blood irradiator.Severely affected fetus can be delivered prematurely and treated with exchange transfusion and phototherapy as we did for our cases[2]. Immunoglobulin also helps in Rh hemolytic disease as has been established in several previous studies[4]. Our patients also received immuno-globulin, albumin and phenobarbitone[8-9]. Our patient needed multiple consecutive exchange transfusions. Case reports of babies needing more than 2 exchange transfusion are mainly anecdotal and have been rarely reported. Most neonates respond to a single double-volume exchange transfusion[10]. 2 or more exchange transfusions are rarely needed.Serum bilirubin levels normalised after 3 double volume exchange transfusions for 2 our patients and the other baby needed 2 exchange transfusions.

We intend to highlight the importance of delivering early, followed by phototherapy, pharmacotherapy and repeated exchange transfusion for neonates with severe Rh hemolytic disease and fetalanemia in a low-cost health care setting where ultra sound guided IUFT is difficult to avail.

Conclusion:

In a resource limited setting, intra uterine fetal transfusion is difficult. Babies may need to be delivered early to initiate appropriate treatment.

Pregnancies with risk of severe fetal anemia need to be followed up closely with anomaly scans. Early detection in 3rd trimester helped in initiating timely treatment.

Repeated double volume exchange transfusions (>2) may be considered if bilirubin is rising despite maximum phototherapy and other pharmacotherapy

Acknowledgements:

Dr Rahul Prasad, senior clinical fellow, neonatology, The Royal Hospital for Women, Dr Ju Lee Oi, consultant neonatologist, Royal Hospital for women, Sydney, Australia, Dr Tejas Hambhir, consultant neonatologist, Rainbow children's hospital, Secunderabad, India, were involved in extensive discussion related to managing this baby.

Dr Aritra Sengupta, Dr Krishanu Mondal, Dr Joshi Anand Kerketta – consultants of pediatric medicine, The Mission Hospital, Durgapur, India, shared their opinion regarding treatment.

References

1. Whittle MJ. Rhesus haemolytic disease. Arch Dis Child. 1992 Jan;67(1 Spec No):65-8.
2. Bowman J. The management of hemolytic disease in the fetus and newborn. Semin Perinatol. 1997 Feb;21(1):39-44.
3. White J, Qureshi H, Massey E, Needs M, Byrne G, Daniels G, et al; British Committee for Standards in Haematology. Guideline for blood grouping and red cell antibody testing in pregnancy. Transfus Med. 2016 Aug;26(4):246-63.
4. Mundy CA. Intravenous immunoglobulin in the management of hemolytic disease of the newborn. Neonatal Netw. 2005 Nov-Dec;24(6):17-24.
5. Andrei C, Vladareanu R. The value of reference ranges for middle cerebral artery peak systolic velocity in the management of rhesus alloimmunized pregnancies. Maedica (Bucur). 2012 Jan;7(1):14-9.
6. Lemery D, Urbain MF, Van Lieferinghen P, Micorek JC, Jacquetin B. Intra-uterine exchange transfusion under ultrasound guidance. Eur J ObsteGynecol Reprod Biol. 1989 Nov;33(2):161-8.
7. Mukhopadhyay K, Murki S, Narang A, Dutta S. Intravenous immunoglobulins in rhesus hemolytic disease. Indian J Pediatr. 2003 Sep;70(9):697-9.
8. Tsao YC, Yu VY. Albumin in management of neonatal hyperbilirubinaemia. Arch Dis Child. 1972 Apr;47(252):250-6.
9. Kumar R, Narang A, Kumar P, Garewal G. Phenobarbitone prophylaxis for neonatal jaundice in babies with birth weight 1000-1499 grams. Indian Pediatr. 2002 Oct;39(10):945-51.
10. Kakkar B, Agrawal S, Chowdhry M, Muthukumaravel PJ, Makroo RN, Thakur UK. Exchange transfusion in neonatal hyperbilirubinemia: A single Centre experience from Northern India. TransfusApher Sci. 2019 Dec;58(6):102655.

Lessons learnt:

1. In a resource limited setting, intra uterine fetal transfusion is difficult. Babies may need to be delivered early to initiate appropriate treatment.
2. Pregnancies with risk of severe fetal anemia need to be followed up closely with anomaly scans. Early detection in 3rd trimester helped in initiating timely treatment.
3. Repeated double volume exchange transfusions (>2) may be considered if bilirubin is rising despite maximum phototherapy and other pharmacotherapy

Multiple Serositis and Generalised Anasarca in Severe COVID- A Case Report.

***Prof.Subhasish Bhattacharyya, **Dr.Sudip Saha, ***Dr.Shreya Mukherjee**
**Professor and Head, **Associate Professor, ***PGT(Pediatrics) Department of Paediatrics, Chittaranjan Seva Sadan, Kolkata*

This is a case report of a four and half year old female 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 be fit in MISC criteria as well, after the tropical infections and Autoimmune serositis was ruled out but the patient improved dramatically after being treated with injection dexamethasone, injection Lasix 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 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 presenting with sudden onset generalised anasarca which initially started with facial puffiness then involving the trunk and limbs within one day, rapidly right sided pleural effusion, and persistent elevation of liver enzymes is rarely reported in literature.

Case Report

A four and half year-old female child,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 diarrhoea,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.

P/A 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 COVID19 came negative,soCOVID 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.

Correspondance : Subhasish Bhattacharyya, *Professor & HOD, CSS, Kolkata. Email : dr_subhasish@hotmail.com*

As there were features of heart failure, a trop T was done which came negative and an ECG which 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,MPDA negative,scrub typhus IgM negative.

COVID19 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 Lasix,injection dexamethasone. D dimer report came 3.75mg/L(<=0.5mg/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 WNL.

Literature was searched, and it was seen that, there is case report of a 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,so we could rule out autoimmune serositis.

So the patient successfully discharged after 10 days.

On discharge ,there was no anasarca present but liver enzymes were still elevated.

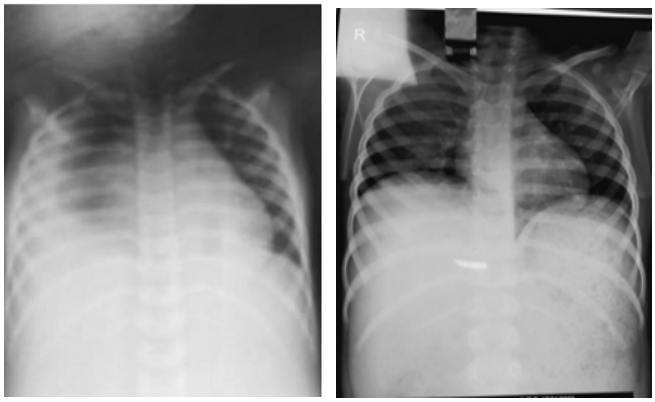


Figure1- showing the improvement in chest xray, within one day, after treating the patient as per severe covid guidelines.

The first xray was done on day 1 and the second xray was done on day 4 of hospital stay.

Discussion

After COVID 19 report came positive,the patient had fit inthe 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 Lasix within one day. So, plan of treatment as per MISC protocol with methyl prednisolone and IvIg was haulted.

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 presenting with generalised anasaraca 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.

References

1. Revised comprehensive guidelines for management of COVID19 in children and adolescents below 18 years.(Government of India guidelines).
2. Amanda Cantor et al.Hepatology.2020Nov.Acute Hepatitis Is Prominent Presentation of the Multisystem Inflammatory Syndrome in Children: A single center report.
3. S Yuliarto et AL.Trop Biomed.2021.Potential severe pediatric SARS-COV-2-induced multisystem inflammatory syndrome resembles dengue infection.

Disseminated Hydatid cysts of liver and lung in a 6 years old girl from rural West Bengal

***Prof. T.N Ghosh, **Prof. Sumanta Laha, ***Dr. Sayan Bera, ***Dr. Nachiketa Dalai**
Professor, ** Associate Professor, * Junir Resident,*
Department of Paediatrics, Burdwan Medical college and Hospital.

Introduction:

Echinococcosis (hydatid disease) is widespread, serious human Cestode infection , caused by ingesting larva of the parasite known as Echinococcus group of species (Echinococcus granulosus and Echinococcus multilocularis).[1]It is of major public health importance especially in sheep farming areas like Central Europe, Africa, South America, New Zealand, Australia, Central Asia and China because sheep is the intermediate host [2]. It is also evident from previous reports that in India, Kurnool, Kadapa and Chittoor districts are more epidemic from Andhra Pradesh .[3].

But disseminated hydatid disease in paediatric population from eastern India specially from rural part of West Bengal is rare.

Hydatid cyst usually affects the liver (50-70%), followed by lungs (15-30%) and rarely in other organs like spleen, kidney, bones and brain.[1] Clinical manifestations vary based on the organ affected and the load and size of cyst affecting the organ. Usually, patient may remain asymptomatic for many years because cyst grows only 1- 3cm per year, due to which many cases may go undiagnosed.

Clinical spectrum of hydatid echinococcosis is based on the size and number of cysts. However, symptoms including fever, chills, nausea, vomiting , dyspnea, dysphagia, pain in the right upper quadrant, chest pain ,chronic cough, hemoptysis increased abdominal girth hepatomegaly ,a palpable mass. Mass effects can be noted in the brain and bone [1]Serious complications result from compression of adjacent structures or spillage of cyst content. Sometimes ,free rupture of the echinococcal cyst may cause anaphylaxis and smaller cysts may be released that can circulate to and lodge in other organs.[2].

The diagnosis of echinococcosis is mainly based on patient's history, clinical findings, haematological and serum biochemical profiles including serum Bilirubin, ALP, leucocytes, eosinophils, serum protein.[4] The confirmation can be made with the help of immunoelectrophoresis that demonstrate antibodies to antigen , whereas ELISA (Enzyme Linked Immuno Sorbent Assay) and indirect hemaggutination test are of initial choices that have 90% sensitivity. It is also evident that USG (Ultrasonography) helps in diagnosis, treatment and follow up of the patients, whereas CT scan can be preferred in cases where USG fails due to patient related difficulties such as obesity, excessive intestinal gas, abdominal wall deformities and previous surgery.

Hence, we present a case of 6 years old girl child, who belonged to rural part of West Bengal in Eastern part of India .

Case Report :

6 years old girl child was apparently well one month back . Then , she developed insidious , gradually progressive cough ,with no diurnal variation, but associated with fever, breathing difficulties, nausea with non projectile vomiting , & gradual onset , non progressive pain abdomen in right upper quadrant for last 1 month . In Negative history , there is no history of any blood in sputum during coughing, any alter sensorium , any bone pain , contact history of TB.

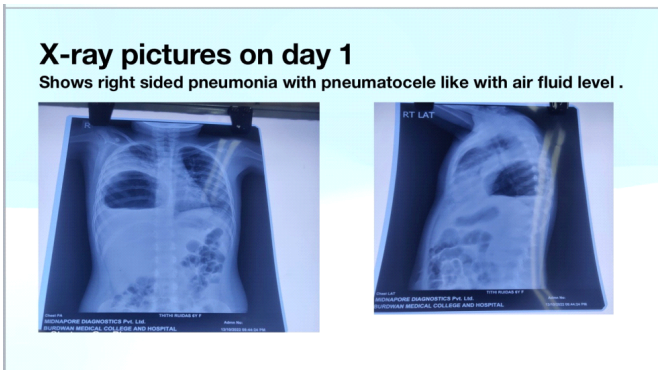
In positive history , she has history of playing with dog in neighbourhood. There is no significant past

Correspondance : T N Ghosh, *Professor, Department of Pediatrics, Burdwan Medical College and Hospital. Email : tnghosh39@gmail.com*

history. She achieved all developmental milestones as per age. Her parents and siblings are healthy. No consanguinity in marriage is present .Immunisation history is upto date as per national immunisation schedule and no calories deficit is found in dietary history. Birth history was term with birth weight of 3kg by normal vaginal delivery . There is no history of SNCU admission. This patient has height of 111cm which is 50 percentile and weight of 16kg which is 10 percentile. In general examination, anaemia, cyanosis clubbing, icterus, oedema were absent . Pulse is 106 /min , Bp =100 /70 mm of Hg .

In respiratory system examination , on palpation apex beat is 5th ICS , 1cm midline to mid clavicular line, and trachea is in central position. And percussion note is impaired resonance upto 4th ics and from 5th ics dullness is heard in right side of chest. On auscultation , there is decreased breath sounds in right side of chest with bronchial and cavernous type of breath sounds .

Other systems examination are within normal limit .



So , Emergency digital chest X-ray shows right sided pneumonia with pneumatocele like with air fluid level So , the provisional diagnosis on admission was pneumonia . Treatment started with Iv antibiotics - injection Coamoxyclav and Amikacin along with other symptomatic treatment.

Blood investigation shows haemoglobin is 11gm/ dl, WBC count is 12,300 /cu,mm , with neutrophil (35%), lymphocytes (53%) , Eosinophils (12%), platelet is 5,20,000 /cumm , ESR is 30mm /1st hour . Urea is 16 mg/litre , creatinine value is 0.6 . And LFT is within normal limit.

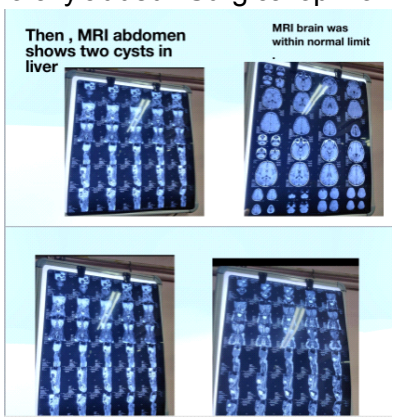
USG thorax shows right sided pleural effusion with right lower lobe consolidation.

After seeing ultrasound reports , diagnosis changed to right sided pleural effusion along with pneumonia. And antibiotics changed to Meropenam along with Vancomycin as child looked sick in day 2 of admission. And alternative diagnosis is made as staphylococcal lung abscess with pneumatocele . So, pleural fluid study for cytology, gram Stain , AFB stain , culture sensitivity, LDH ,protein is sent after USG guided diagnostic pleural tap . No therapeutic intervention is done as child is clinically stable And there is chance of deterioration due to rupture of abscess.

CECT of thorax shows large thick wall cavity (8.6 mm* 8.2 mm) at basal region of right lower lobe , containing air fluid level . Multiple collection with enhancing wall was noted in segment 5 of liver . (Liver Abscess?) . USG of liver shows two cysts, one in (5.6cm x 4.2cm) right lobe and another (4.2cm x 4.3 cm) cyst in left lobe . And then amoebic and Hydatid cysts came into the diagnostic possibilities.MRI of abdomen also shows two cysts in liver where MRI brain is within normal limit.

Child was afebrile for 5days on day 11 before febrile for last 3 days . Mean time, Blood culture sensitivity report shows MSSA positive , sensitive to levofloxacin linezolid. Accordingly antibiotics changed to levofloxacin , linezolid with metronidazole to cover the amoebic liver abscess as diagnostic possibilities in day 13 . Then , pleural fluid study shows no abnormalities. CBNAAT from sputum and pleural fluid is also negative. Then Blood for Echinococcus IgM and IgG reports were positive on day 17 . Again USG liver was done to do staging of cysts . And staging was CE1 (WHO classification) . Now diagnosis is hydatid cyst of liver (stage CE1) and lung .

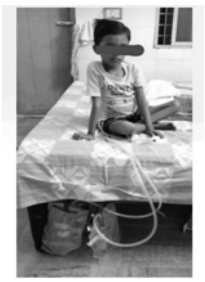
Then Albendazole 15mg /kg /day in divided dose twice daily orally added . Surgical opinion was taken



from dept of CTVS and advised to sent this pt to NRS or SSKM hospital for operative management of lung cysts and liver cysts stage CE 1 (but size is >5cm) . But Patient went to CMC ,vellore for operative management. Thoracoscopic right lung cystectomy, tube pneumonostomy and open drainage with omentoplasty of liver hydatid cyst are done under general anaesthesia and epidural analgesia . Finding was ruptured cyst with pale walls in right lower lobe , filled with air and daughter cyst . In liver , two cyst with hydatid sand and daughter cysts . But no cyst to biliary communication is found

Discussion :

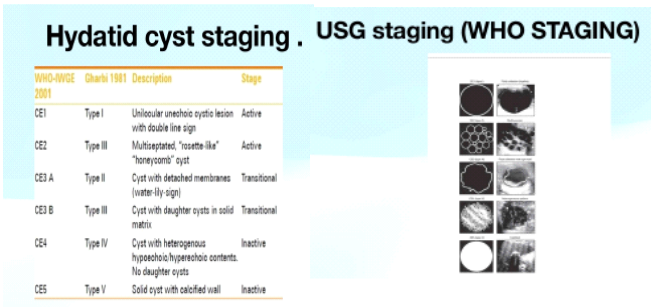
Hydatid cyst is particularly endemic in sheep raising



or cattle-raising rural area and caused by the parasite known as Echinococcus. Dissemination of Echinococcus in the body occurs through the bloodstream. Hydatid cyst can occur anywhere in the body but the two most commonly organs involved are liver and lungs[2].Concurrent involvement of lung and liver accounts for 4% to 25% of patients with hydatid disease as depicted in the case report published by Aghajanzadeh et al.5 Hydatid cyst can be found as solitary or multiple in numbers.[4].The prevalence of multiple pulmonary cysts and bilateral cysts is 30% and 4%[6]. In our case, the patient was found to have multiple hydatid cysts involving both lungs and liver.

Mostly hydatid cysts are found as the incidental finding and remain asymptomatic[7].When these cysts produce symptoms, it is due to growing cyst which encroaches the involved organ as well as nearby structures. It has been noticed that lung cysts grow much faster than cyst in another organ of the body because of negative pleural pressure.[8]. A cough, dyspnoea and haemoptysis can be the typical features of hydatid cyst affecting the lung.[9]

Hepatomegaly and abdominal pain can be the presenting features of hydatid cyst affecting the

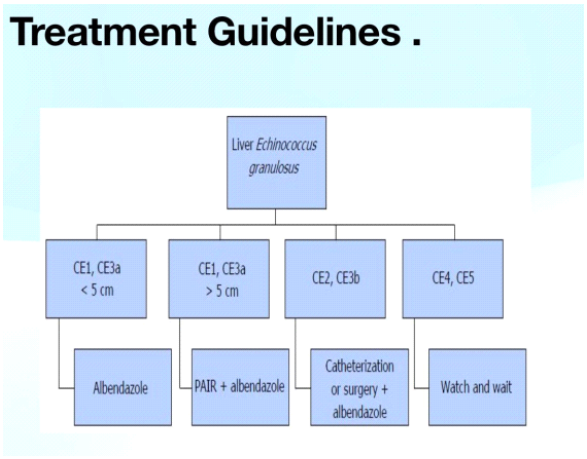


liver.[10]. In our case, the patient presented with a cough and dyspnoea without haemoptysis and abdominal symptoms.Diagnosis of hydatid cyst can be established with a combination of history, physical examination, radiological evaluation, laboratory diagnosis, serological tests and histopathological assessment by using a CT-guided biopsy[11].

The results of routine laboratory works are non-specific. Eosinophilia can be non-spe- cific finding present in patients infected with echinococcosis as seen in our patient. Serological studies play an important role in the diagnosis of echinococcosis. The indirect haemagglutination test and ELISA have a sensitivity of 80% to diagnose hydatid cyst but ELISA test is also useful to detect recurrence. [11]

Hydatid cysts can be treated by surgical or medical intervention. Surgical resection is the cornerstone for the treatment of hydatid cyst of lung and liver[12][13] and is useful for the patient where cysts cause compression due to their large size.

However, medical therapy is indicated in patients with primary liver or lung cysts that are inoperable, patients with cysts in two or more organs and peritoneal cysts. In our case, our patient did undergo surgery due to concurrent involvement of both lungs



and liver. Albendazole and mebendazole are the two effective chemotherapeutic agents approved for the treatment of hydatid cysts[14]. The duration of medical treatment ranges from 3 to 6 month, and it can be prolonged without any risk of side effects.

References

1. Kliegman St geme , Blum , shah , Tasker, Wilson , Nelson Textbook of Pediatrics , 21 1st edition , volume 1, page number,1897 -1900.
2. Solaymani A, Jozani ZB, SeyedAlinaghi SA, Jamali SR. Multi-organ echinococcosis: a case report. Journal of International Medical Publisher. 2011;5(1):1-3.
3. Lee RC, Chou YH, Chiang JH, Chen YK and Hsu HC. Hydatid cyst of the liver: a case report and literature review. Kaohsiung Journal of Medical Sciences. 2005;21(9):418-23.
4. Attef M Elshazly, Manar S Azab, Samar N ElBeshbishi and Hany M Elsheikha. Hepatic hydatid disease - four case reports. Cases Journal. 2009;2(58);1-4.
5. Aghajanzadeh M, Safarpoor F, Amani H, et al. one-stage procedure for lung and liver hydatid cysts. Asian Cardiovasc Thorac Ann 2008;16:392–5.
6. Mehta P, Prakash M, Khandelwal N. radiological manifestations of hydatid disease and its complications. Trop Parasitol 2016;6:103–12.
7. Shehatha J, Alizzi A, Alward M, et al. Thoracic hydatid disease: a review of 763 cases. Heart Lung Circ 2008;17:502–4.
8. Dincer SI, Demir A, Sayar A, et al. Surgical treatment of pulmonary hydatid disease: a comparison of children and adults. J Pediatr Surg 2006;41:1230–6.
9. Toleti S, Subbarao M, Dwarabu P. Hydatid disease of the lung presenting with hemoptysis and simulating a lung abscess. Trop Parasitol 2012;2:69–70.
10. Ezer A, Nursal TZ, Moray G, et al. Surgical treatment of liver hydatid cysts. HPB 2006;8:38–42.
11. Eken H, Isik A, Balci G, et al. A rare case of isolated cystic hydatid of thyroid gland.
12. ramos G, orduña A, García-Yuste M. Hydatid cyst of the lung: diagnosis and treatment. World J Surg 2001;25:46–57. rare disease.
13. Arif SH, Malik AA, Khaja Ar, et al. role of albendazole in the management of hydatid cyst liver. Saudi J Gastroenterol 2011;17:343–7.
14. Imad S, Dandan M. Hydatid cysts treatment and management. Medscape 2016.
3. Sinha DN, Palipudi KM, Rolle I, Asma S, Rinchen S. Tobacco use among youth and adults in member countries of South-East Asia region: review of findings from surveys under the Global Tobacco Surveillance System. Indian J Public Health 2011;55:169-76.

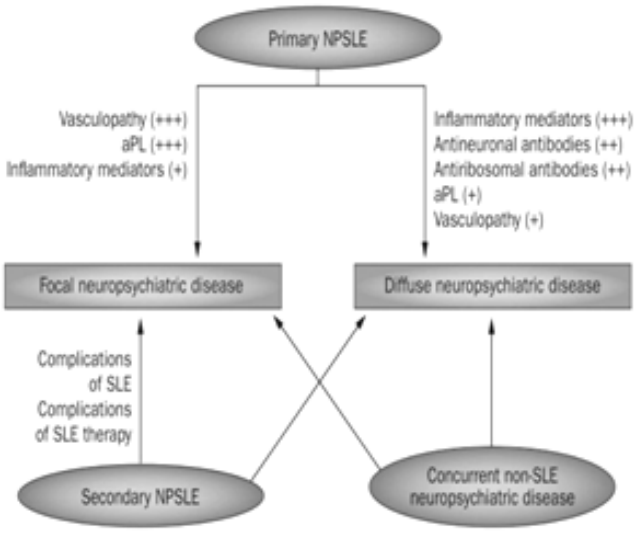
Neuropsychiatric Lupus

***Dr Soumita Sarkar, *Dr Debanjana Dasgupta, **Prof Kalpana Datta**
**Resident, **Professor*
Department of Pediatrics , Medical College, Kolkata

Systemic Lupus Erythematosus(SLE) is a multisystem autoimmune disease. Around 43-95% cases of childhood SLE(cSLE) patients have CNS involvement. CNS lupus in cSLE is more prevalent,more severe and has greater consequences on the developing brain. While neurpsychiatric SLE(NPSLE) can occur independently of active systemic disease and without serologic activity, known risk factors include- concurrent SLE activity, presence of antiphospholipid antibodies and history of NPSLE events in the past.

NPSLE subsets

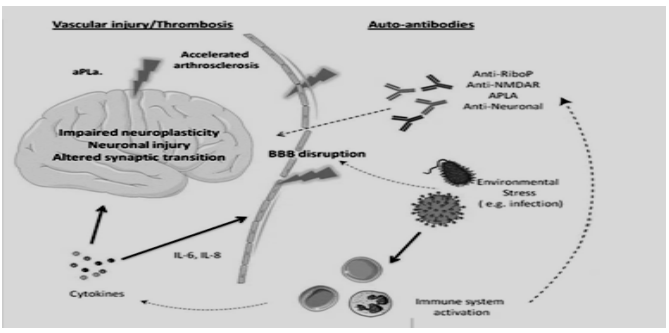
NPSLE can occur as a result of mechanisms related to SLE(primary NPSLE), or due to complications of the disease like high blood pressure, uremia or SLE treatment(eg. Infection) (Secondary NPSLE), or as a coincidental neuropsychiatric event completely unrelated to SLE.



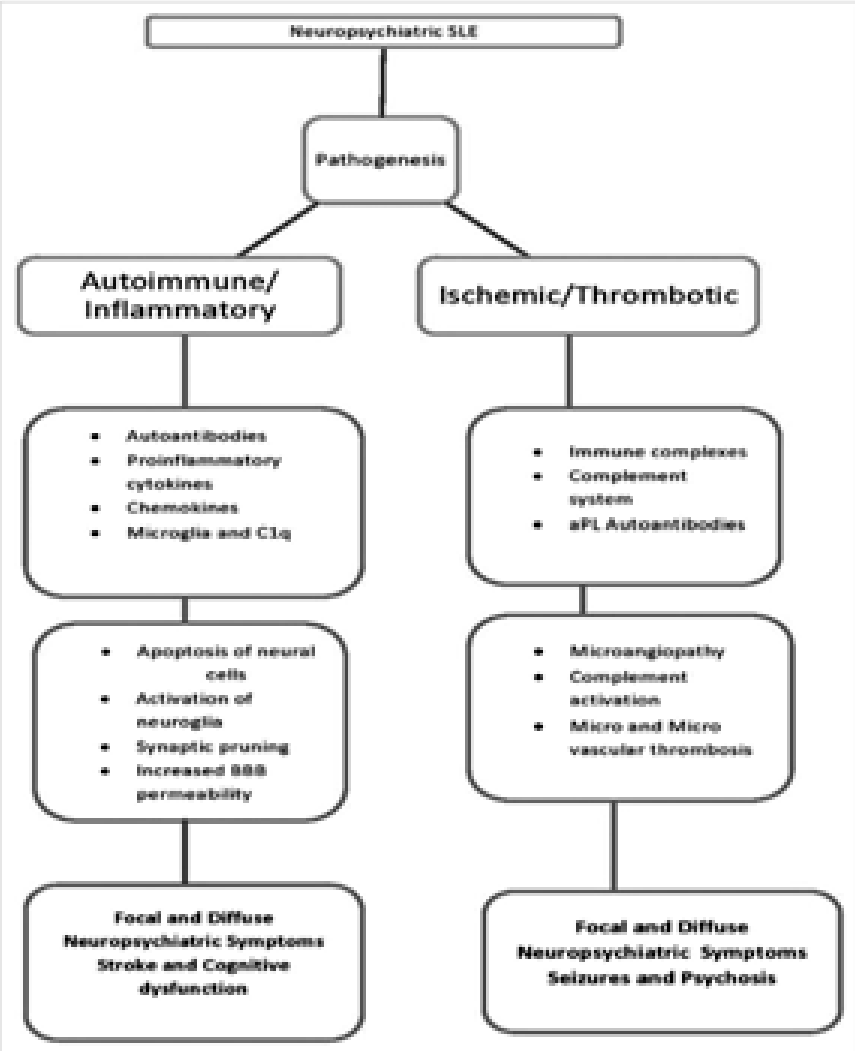
Correspondance : Kalpana Datta, *Professor, Medical College, Kolkata. Email:drkalpanadatta@gmail.com*

Pathogenesis

Multiple autoimmune and inflammatory mechanisms play a role in the pathogenesis of NPSLE Proinflammatory cytokines and chemokines in CSF along with autoantibodies are responsible for NPSLE manifestations. Autoantibodies cause neurotoxicity by holding a gated ion channel in. open position,thus, altering synaptic transmission and subsequently causing neuronal death. The majority of autoantibody mediated damage is due to cross-reactivity between anti-dsDNA with other antigens like N-methyl-D-aspartate receptor(NMDAR). The antibodies gain access to neuronal cells due to increased permeability of blood brain barrier or maybe produced locally via intrathecal production. Antiphospholipid antibodies cause focal neuropsychiatric symptoms like cerebrovascular accidents(CVA) and seizures by promoting intravascular thrombosis while anti-P and anti-NR2 antibodies cause diffuse neuropsychiatric events like depression,psychosis, cognitive impairment through a direct effect on neuronal cells. There is increased production of proinflammatory cytokines like IL-6, IL-8 via activation of nuclear factor kappa B(NFkB).



Broadly speaking, the pathogenesis of NPSLE maybe- Autoimmune/ Inflammatory or Ischemic/ Thrombotic



Definition And Diagnostic Criteria For Neuropsychiatric Lupus-

Definition: NPSLE is a group of neurologic syndromes of the central and peripheral nervous system and/or of the psychiatric syndromes observed in patients with SLE in which other causes are excluded by laboratory, clinical, neuropsychological tests and neuroimaging.

Prerequisite for diagnosis:

1. Altered cognitive and/or neuropsychiatric status manifestations or sensorimotor neuropathy
2. Higher SLEDAI score(>10)
3. Antiphospholid, antiribosomal-P, anti-neuronal,anti-ganglioside and anti-Ro antibody, one of the antibodies is positive
4. Complicated with tissue infarction,haemorrhage, or more limited focal neuron injury results from impaired blood flow(thrombosis)
5. Skin lesions

Diagnosis

NPSLE Grade 1(definitive NPSLE): SLE plus at least one altered cognitive and/or neuropsychiatric status manifestations or sensorimotor neuropathy and one of the following: higher SLEDAI, antibody positivity, thromboembolism, or skin lesions.

NPSLE Grade 2(Suspected NPSLE): SLE and at least one altered cognitive and/or neuropsychiatric status manifestations or sensorimotor neuropathy

Exclusions and Provisions

Secondary causes such as medication side effects, thyroid disease, infection, metabolic disturbances, Thrombotic thrombocytopenic purpura, valvular heart disease, depression, sleep apnea, and psychosocial or functional related conditions need to be excluded

Classification Criteria For Npsle-

The American College of Rheumatology(ACR) 1999 criteria established 19 different NPSLE syndromes-12 of which were of central nervous system.

CENTRAL NERVOUS	SYSTEM	Peripheral Nervous system
1.Aseptic meningitis	7.Acute confusional state	1.Guillain-Barre syndrome
2. Cerebrovascular disease	8.Anxiety disorder	2.Autonomic neuropathy
3. Demyelinating syndrome	9.Cognitive dysfunction	3.Mononeuropathy-Polyneuropathy
4. Headache	10.Mood disorder	4.Myasthenia gravis
5.Movement disorder	11.Psychosis	5.Cranial neuropathy
6.Myelopathy	12.Seizure disorder	6.Plexopathy

The disease activity score(SLEDAI) and damage index(SLICC damage index) both have neurologic items in their scores.

Clinical Presentations-

1. Stroke- 19% cases of SLE
2. Seizures- 4-12% cases
3. Mental status- a. Altered confusional state/ delirium, b. Psychosis
4. Inflammatory and demyelinating disease
5. Myelitis- 1-2% cases
6. Aseptic Meningitis- Headache, Stiff Neck

   -CSF: Lymphocytic pleocytosis and elevated protein

   - Focal/multifocal neurological symptoms or seizure +/-

   - MRI: may show leptomeningeal enhancement
7. Chorea- rare(<1%)

Treatment Complications And Associated Complications-

1. Reversible Posterior Leukoencephalopathy syndrome(RPLS)/ Posterior Reversible Encephalopathy Syndrome(PRES)
2. Progressive Multifocal Leukoencephalopathy(PML)
3. Infections- Cryptococcal Meningitis most frequent CNS fungal infection in SLE
4. Medication Side effects

Diagnosis

All SLE patients who present with signs or symptoms of neuropsychiatric disease should be evaluated in a similar way to that of non-SLE patients who present with the same manifestations, to rule out non-SLE related conditions.Since there is a lack of gold standard diagnostic test for CNS lupus, overdiagnosis or underdiagnosis is inevitable.

Diagnostic work up includes:

1) CSF Analysis- mainly to rule out infection,can be completely normal in CNS Lupus. Pleocytosis seen in one-third patients. CSF protein is elevated in 50% patients. CSF IgG synthesis rate may also be elevated. Oligoclonal bands seen in 80% patients, mainly in those with CNS demyelination.
2) Anti-phospholipid Antibody testing- Lupus anticoagulant,Anticardiolipin antibody and anti-beta2 glycoprotein 1 should be tested in all neuro-lupus patients.

   Most common CNS manifestation associated with aPL in cSLE are ischemic stroke and CVT, secondary to thrombosis of cerebral vessels.
3) Imaging in CNS Lupus-Main purpose is to differentiate from other lesions that potentially affect the brain such as abscesses,hematomas or strokes.Current EULAR imaging recommendation for diagnosing CNS lupus is anatomic imaging with MRI(T1,T2,FLAIR,DWI and Gadolinium enhanced T1 sequences).Presence of multiple focal white matter hyperintensities is the most common finding.Few may have cortical gray matter hyperintensities that rarely extend into the underlying white matter.Limitations-do not distinguish between immune mediated demyelination and demyelination due to ischemic injury.

Table showing the diagnostic work up in a child with neuro-lupus

Diagnostic Work Up	Function
Auto-antibodies	Antiphospholipid antibody testing
CSF Analysis	To exclude infections
EEG	Seizure activity
Nerve conduction studies	Peripheral neuropathy
MRI Brain	Anatomic imaging
Neuropsychological assessment	Cognitive dysfunction

Management

Antiplatelet therapy with or without anticoagulation is required in patients with thrombotic cerebrovascular disease with aPL positivity.

Establish diagnosis of CNS Lupus	CSF analysis, autoantibody profiling, neuroimaging
Identify Confounding factors	Hypertension, infection and metabolic abnormalities
Symptomatic therapy	Anticonvulsants, Psychotropic and anxiolytic agents
Immunosuppression	Steroids, Azathioprine, Mycophenolate mofetil, Cyclosporin, Rituximab, IVIg, Plasma exchange
Anticoagulation	Aspirin, Heparin and Warfarin

Specific Clinical Findings And Treatment

1) Lupus headache-Prophylactic treatment for recurrent headache. Always exclude aseptic or septic meningitis, cerebral or subarachnoid haemorrhage and sinus thrombosis in lupus patients with severe headache.
2) Movement disorders-most common in cSLE, particularly chorea.Treatment-dopamine antagonists(for symptomatic relief), immunosuppression(to treat active SLE).
3) Cognitive dysfunction-peak age of cSLE coincides with critical cognitive maturation period, 3-5% children develop severe cognitive dysfunction(m/c domains affected-attention, visual and verbal memory, executive function and psychomotor speed).
4) Myelitis-very rare(1%),but more common in lupus patient than general population, gray matter and white matter myelitis.
5) Seizures in Neuro-Lupus- not so common in childhood SLE.Generalised tonic clonic seizures are most common(75%),followed by simple seizures(18%) and complex partial seizures.Most often occurs during disease flares.Specific indications to start AED:
    1. 2 or more unprovoked seizures occurring with at least 24 hrs apart,
    2. MRI Brain shows structural abnormalities,
    3. Partial seizure,
    4. Epileptiform EEG,
    5. Focal neurological signs,
    6. Serious brain injury.

If seizures represent active lupus, appropriate immunosuppression is needed.

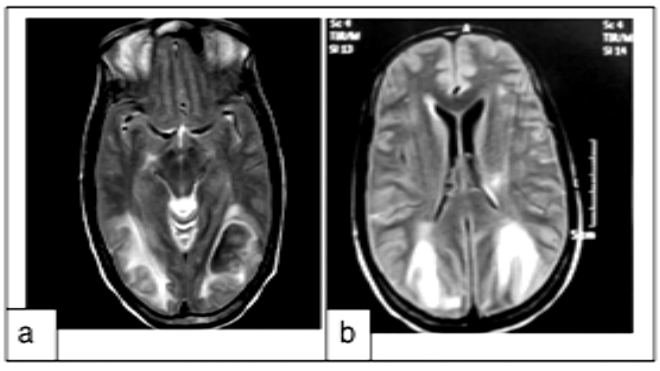
PRES(Posterior Reversible Encephalopathy Syndrome)/RPLS(Reversible Posterior Leucoencephalopathy Syndrome)

Reversible neurological deficits in SLE.Characterised by headache,hypertension,seizures,altered sensorium,b/l cortical blindness and MRI findings(b/l subcortical and cortical hyperintensities of the white and grey matter with predominantly posterior distribution on T2 and FLAIR section).

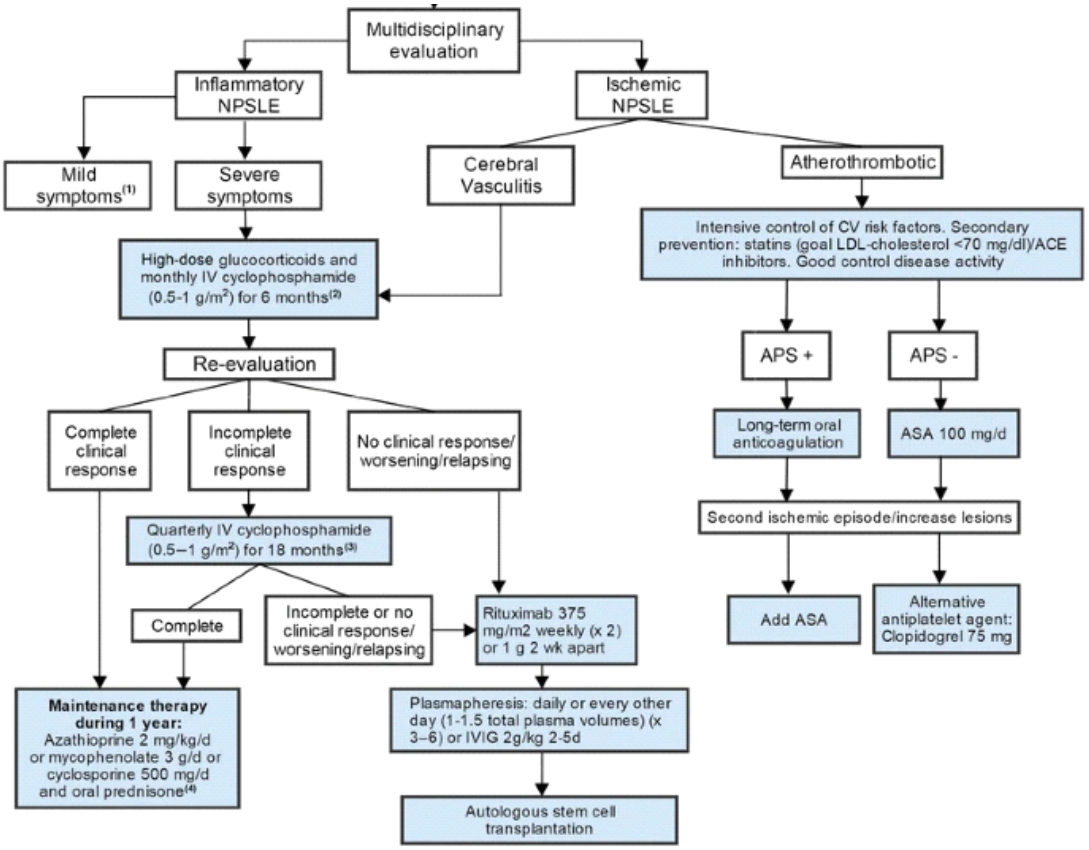
Two types in SLE

1. Hypertensive PRES-occurs in inactive SLE,reversible with antiHTN and anticonvulsants.
2. PRES due to active SLE-needs immunosuppressive therapy.

Pathogenesis-Cerebral edema with diffusion of plasma proteins and cells into extracellular space(cytotoxic and vasogenic theory).



MRI findings (T2 sequence (a), FLAIR (b) showing the diffuse confluent white matter hyperintensities in bilateral parieto-occipital region



Flowchart showing the approach to treat a case of neuropsychiatric SLE(NPSLE)

References

1. Bertsias GK,LoannidisJAP,Aringer M,et al EULAR recommendations for management of systemic lupus eruthematosus with neuropsychiatric manifestations: report of a task force of the EULAR standing committee for clinical affairs.Ann Rheum Dis 2010;69:2074-2082.
2. Hanly JG.Diagnosis and management of neuro-psychiatric SLE.Nat Rev Rheumatol2014;10:338-347.
3. Bertsias GK,Boumpas DT,Pathogenesis diagnosis and management of neuropsychiaytic SLE manifestations. Nat Rev Rheumatol2010;6;358-367.
4. Rubinstein TB, Putterman C, Goilav B. Biomarkers for CNS involvement in pediatric lupus. Biomark Med. 2015;9(6):545-558. doi:10.2217/bmm.15.26
5. Hanly, J. Diagnosis and management of neuropsychiatric SLE. Nat Rev Rheumatol 10, 338–347 (2014). https://doi.org/10.1038/nrrheum.2014.15
6. Kivity, Shaye et al. “Neuropsychiatric lupus: a mosaic of clinical presentations.” BMC medicine vol. 13 43. 4 Mar. 2015, doi:10.1186/s12916-015-0269-8
7. Sarwar S, Mohamed A S, Rogers S, et al. (September 14, 2021) Neuropsychiatric Systemic Lupus Erythematosus: A 2021 Update on Diagnosis, Management, and Current Challenges. Cureus 13(9): e17969. doi:10.7759/cureus.17969.

Hereditary Vitamin B 12 Deficiency Due To Methyl Malonic Aciduria

***Dr. Shreya Mukherjee, ** Prof.Subhasish Bhattacharyya**
**PGT, Paediatrics, **Professor and Head, Department of Paediatrics,*
Chittaranjan Seva Sadan, Kolkata

There are three forms of vitamin B12 -methyl cobalamin, 5-deoxy adenosyl cobalamin and cyanocobalamin. Vitamin B 12 deficiency can have haematological as well as neurological manifestations. Here, we describe a case of a 7year-old male child getting admitted with complaints of vomiting followed by generalised tonic-clonic convulsions. There were 3 such similar episodes in past. Each time hypoglycaemia was associated with the episodes of convulsion. First episode of convulsion began at the age of 8 months of age, followed by similar episode at three years, 5years and then at 7 years of age. Every time there was cessation of seizure on correcting the hypoglycaemia. The child's mother and maternal uncle also had similar history of convulsion since their childhood. However, they had no documented episodes of hypoglycaemia and were being treated with anticonvulsant medications. Mother was also on atypical antipsychotic medication. Due to the repeated episodes of hypoglycaemia in the child, possibility of IEM was considered. Urine for non-glucose reducing substance was absent. Urine ketone was 2+. Blood for TMS and urine for GCMS was sent. Urine GCMS report of the child showed the methyl malonic acid level to be 7.5micromole/mili mole of creatinine suggestive of vitamin B 12 deficiency. GCMS of the child's mother was also sent which showed increased methyl malonic acid level. The child was treated with parenteral vitamin B12 and is now on follow up. This case suggests that inborn errors of metabolism is an important cause of vitamin B 12 deficiency and should be ruled out in patients presenting with hypoglycaemia and neurological abnormalities.

Introduction

Methyl malonic acidemias are a group of metabolic disorders of diverse aetiology characterised by impaired conversion of methyl malonyl-CoA to Succinyl-CoA. The wide variations in severity of clinical course range from very sick new-born infants to apparently asymptomatic adults. Prognosis depends upon the severity of symptoms and the occurrence of complications. All defects causing isolated methylmalonic acidemias are inherited as autosomal recessive traits. A child having raised methyl malonic acid level in GCMS, with similar family history of having multiple episodes of convulsions and neuropsychiatric manifestations, improving after being treated with parenteral vitamin B 12 is an interesting and rare case.

Caser eport

A 7-year-old male child presented to our hospital with generalised tonic clonic convulsion lasting for 10 minutes. Patient had history of vomiting since morning. Blood glucose was 36mg/dl. Blood glucose was corrected and seizure was aborted.

Correspondance : Prof.Subhasish Bhattacharyya, *Professor and Head, Department of Paediatrics, Chittaranjan Seva Sadan Email : dr_subhasish@hotmail.com*

There was past history of three similar episodes of hypoglycaemic convulsions in past and each time the patient had to be admitted in hospital.

There was no developmental delay in the child. But the mother complained that the child was hyperactive and inattentive.

There was a family history of recurrent episodes of convulsions since childhood in the mother and maternal uncle. Mother was on anticonvulsant and atypical antipsychotic.

As there were recurrent episodes of hypoglycaemia in this child urine for non-glucose reducing substance was sent which came negative, urine ketone was 2+ and urine for GCMS showed raised methyl malonic acid level7.5micromol/milimol creatinine (normal range is 0-6), report mentioned vitamin B 12 deficiency.

Analytical Interpretation

Urine metabolic profiling revealed elevated excretion of Methyl malonic acid (MMA).

Mildly elevated levels of MMA may be suggestive of Vitamin B12 deficiency.

GCMS of mother was also sent which was also in higher range.

METABOLIC SCREENING, URINE

DISORDERS	ANALYTES RESULTS BIOLOGICAL REFERENCE INTERVAL	UNITS
METABOLIC PROFILE	Amino Acidopathies	All related analytes within acceptable limits
Fatty Acid Metabolism Disorders		Organic Acidurias All related analytes within acceptable limits
Methyl Malonic Acid	7.5	0 - 6 µmol/mmol of Creatinine
		All other related analytes within acceptable limits

Neuroimaging -MRI and EEG was done which were normal.

The patient was treated with mecobalamin injection 1 mg was given intra muscularly daily for one week during hospital stay, then weekly dose was given for one month, now the patient is on follow up and on monthly injection.

Patient was also advised vitamin B 12 rich diet.

Plan is to give lifelong parenteral vitamin B12 supplementation.

The child has not developed any further episodes of convulsion after the treatment has been started.

Discussion

Vitamin B 12 deficiency has both haematological as well neurological manifestations. Vitamin B 12 is essential of central nervous system development. Deficiency can occur due to low dietary intake, malabsorption, inborn errors of metabolism associated with malabsorption like hereditary intrinsic factor deficiency, Imerslund -Grasbeck syndrome, and drugs like proton pump inhibitors and H2 blockers [1,3].

Methyl malonic aciduria is a disorder of amino acid metabolism which usually presents from 1 month to one year of age. It has an autosomal recessive inheritance. It has predominant neurologic manifestations and presents with seizures, encephalopathy, developmental delay, and stroke.[2]

So, every child presenting with recurrent episodes of hypoglycaemia should be screened for inborn errors of metabolism.

As methylmalonic aciduria is an autosomal-recessive condition family members having similar illness should also be screened and treated accordingly.

Conslusion

A child presenting with recurrent hypoglycaemic convulsions from infancy, being diagnosed with vitamin B 12 deficiency due to methyl malonic aciduria, and having similar illness in family members is an interesting case and has been rarely reported in literature.

Limitation

Vitamin B 12 level estimation could not be done.

Genetic testing could not be done.

References

1. Nelson Textbook of Pediatrics:21st edition.
2. A rare case of familial methylmalonic acidemia presenting with Acrodermatitis Enteropathica type of lesion Wali P. P Parakh H Reddy P Dr. Pradnya P. Wali, Junior Consultant Neonatologist, Dr. Hemant Parakh, Consultant Neonatologist, Dr. Prashant Reddy, Consultant Pediatricians, Sunrise Children Hospital, Hyderabad, AP, India.
3. Acta Clin Croat. 2019 Jun; 58(2): 295302.doi: 10.20471/acc.2019.58.02.13PMCID: PMC6884369 PMID: 31819326Neurological symptoms of vitamin B12 deficiency: analysis of pediatric patients*Hepsen Mine Serin 1 and Elif Acar Arslan2
4. Neurological disorders in vitamin B12 deficiencyCh S Pavlov 1, I V Damulin 1, Yu O Shulpekova 1, E A Andreev Affiliations expandPMID: 31094486DOI: 10.26442/00403660.2019.04.000116.
5. Vitamin B12 deficiency: case report and review of literature Brahim El Hasbaoui 1, Nadia Mebrouk 2, Salahiddine Saghir 1, Abdelhkim El Yajouri 1, Rachid Abilkassem 1, Aomar Agadr 1 Affiliations expand PMID: 34046142PMCID: PMC8140678DOI: 10.11604/pamj.2021.38.237.20967

Determinants of Quitting Tobacco in School-children

***Dr Kamirul Islam, **Dr Nilanjan Ghosh**
Medical Officer,Assistant Professor*
Department of Paediatrics, Burdwan Medical college and Hospital.

Introduction: *Tobacco use is prevalent among Indian school-children. Data regarding predictors of successful quitting are scarce.* ***Aim:*** *To identify the determinants of quitting tobacco in school-children.* ***Materials and Methods:*** *This prospective cohort study was conducted between January 2018 and December 2019 among 2458 school-children selected by complete enumeration. Data were collected by direct interview using pre-designed, pre-tested, semi-structured schedule. Different study variables were compared among children who were able to quit tobacco and who were not able to quit.* ***Results:*** *Six hundred and fifty two (26.5%) school-children were able to quit tobacco successfully. Nicotine dependence (Relative risk=1.67) was the most significant determinant of quitting, followed by daily use of tobacco (Relative risk=1.65).* ***Conclusions:*** *Nicotine dependence of an individual is the most important determinant of quitting tobacco.*

Keywords: *Smoking, Cigarette, Dependence, Nicotine, Adolescent*

Introduction:

Excessive use of tobacco, the foremost cause of preventable morbidity and mortality, and is responsible for 12% of global deaths.[1] Majority of these deaths will occur in developing countries, like India.[1] Asian countries have an additional burden due to excessive popularity of smokeless tobacco.[2] Prevalence of tobacco use among students is highest in Bangladesh (43.3%), followed by India (34.6%).[3] Decreased awareness, risky mind set-up, poor literacy and repeated advertisements by tobacco companies- all are responsible for high prevalence of tobacco use in Indian school-children.[1, 2] Tobacco use is associated with diseases including coronary artery diseases, chronic obstructive airway disease, cancers of oral cavity, upper airway and lungs, fetal growth restrictions etc. Onset of this disease process occurs in late adolescence/ early adulthood. Cessation of smoking is associated with reversibility of disease process, increase in life expectancy and better quality of life.[2] But, successful quitting is difficult to achieve. Nearly 50% of tobacco users were able to quit tobacco permanently with help of modern pharmacotherapy.[4] Detailed information regarding predictors of successful quitting is scarce in Indian context, especially in adolescent population. Available few articles suffer from methodological issues (assessing quit attempts/ intention to quit instead of successful quitting, small sample size, risk ratio was not calculated).[5, 6] Hence, we had undertaken this study to find the determinants of quitting tobacco in school-children.

Correspondance : Dr Kamirul Islam, Medical Officer, *Burdwan Medical College and Hospital. Email kamirul.islam7@gmail.com*

Materials and Methods:

This prospective cohort study was conducted between January 2018 and December 2019, after taking necessary approval from Institutional Ethics Committee. Informed written consents were taken from each participant/ their legal guardians. All the current tobacco-user school-children from 5th to 12th standard were included. Eleven schools (9-government, 2-private) with 18653 children were selected for the study (Source- Office of District Inspector of Schools). Who were severely ill, absent despite 3 visits, denied consent and lost in follow-up were excluded. A pre-designed, pre-tested, semi-structured schedule was used to collect data. They were treated (counseling and/or pharmacotherapy)

and followed-up at out-patient at quarterly interval/ earlier, if clinically indicated. Tobacco smoking was defined as inhaling smoke of burning tobacco into mouth and lung at least once in last week.[7] Smokeless tobacco use was defined as chewing, sniffing or keeping tobacco preparation in mouth at least once in last week.[2] Socioeconomic status was assessed by modified Kuppuswamy scale.[8] Problem families are those which lag behind the rest of community.[9] Nicotine dependence of an individual was measured by Fagerström Test for Nicotine Dependence (FTND). Low, medium and high level of nicotine dependence was defined as FTND score <4, 4-6 & >6, respectively.[10, 11] Two separate scores were calculated for the users who use both smoking and smokeless tobacco products and the higher score was taken for analysis. Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI Kid) was used as a screening tool to identify associated psychiatric disorders.[12] Registered student of school at the time of study was considered as the school-children. Abstinence from tobacco for at least 12 months or more was defined as quitting.[13]

SPSS version 19.0 (Statistical Package for the Social Sciences Inc, Chicago, IL, USA) was used for data analysis. Kolmogorov Smirnov test (as n >2000) was used to check normal distribution. Categorical and continuous variables were expressed in proportion and mean values, respectively. Significance of association between two attributes in contingency table was assessed by Pearson's chi-square (?2) test. Significance of difference between two means was checked by Student's unpaired t test. Risk ratio (RR) with 95% Confidence Interval (CI) was calculated taking quitting tobacco as positive outcome.[14] Binary logistic regression model (stepwise method) was generated to calculate Cox and Neglekarke's R2 to identify individual contribution of different factors in quitting tobacco. P =0.05 was considered as statistically significant.

Results: Two thousand six hundred and seventy nine (2679) tobacco-users were identified and 221 were excluded (3 with serious illness, 26 were absent despite three visits, 16 refused consent and 176 did not complete follow-up). Hence, 2458 school-children (93.2% male) were included with a mean age of 14.8±2.8 years. Majority of them belonged to Hindu religion (1302, 53.0%), lower socioeconomic status (1261, 51.3%) and joint family (1538, 62.6%). Psychiatric co-morbidities and other substance abuse were observed in 218 (8.9%) and 185 (7.5%) children, respectively. Nine hundred and thirty four (934, 38.0%) children were exclusive smokers, 909 (37.0%) were using smokeless tobacco exclusively and 615 (25.0%) were using both. High nicotine dependence was seen among 869 (35.4%) children. After repeated counseling and pharmacotherapy, 652 children (26.5%) were able to quit tobacco. Different variables of two groups of children (who quitted tobacco and who were not able to quit tobacco) are illustrated in table 1.

Nicotine dependence (RR=1.67, 95% CI=1.59-1.73, P<0.0001) emerged as most significant determinant of quitting tobacco, explaining 52.3-52.5% variance of it; followed by daily use of tobacco (RR=1.65, 95% CI=1.57-1.74, P<0.0001) which can explain another 13% variance of quitting tobacco. Risk ratios of different determinants with 95% CI are represented in detail in table 2. Overall, our model could correctly predict75.6%-76.3% variance of quitting tobacco.

Discussion: Nicotine dependence emerged as the most significant determinant of quitting tobacco, followed by habit of tobacco use. We observed that 26.5% school-children were able to quit tobacco. Different studies from abroad reported a successful cessation rate of 7.7-27.8%.[15, 16] Multiple Indian studies estimated intention to quit among tobacco-users, which varies between 39%-63.3%.[5, 6, 17] Heterogeneity of population and differences in operational definitions might lead to this discrepancy. Level of nicotine dependence among school-children corroborates with findings of other researchers from India and abroad.[18, 19] Bernstein, et al and Islam, et al also noted that FTND score is the single most significant factor responsible for quitting.[5, 20] Nicotine alters the mesolimbic pathway and responsible for temporarily pleasing mood enhancement and makes quitting difficult.[21] Similar to the findings of current study, multiple authors reported that different socio-demographic variables (age, sex, type of family, socioeconomic status), type of school, variables related to tobacco use (age of

Table 1: Distribution of the study population according to quitting tobacco and different variables (n=2458).

Variables	Quitted Tobacco (n=652)	Not Quitted Tobacco (n=1806)	Significance
Age (y)*	14.6±2.3	14.9±3.1	t=2.2568, P=0.0241
Sex#			
Male	584 (25.5)	1708 (74.5)	?2=19.0415,P=0.0001
Female	68 (41.0)	98 (59.0)	
Religion#			
Hindu	348 (26.7)	954 (73.3)	?2=0.0582, P=0.8093
Others	304 (26.3)	852 (73.7)	
Type of Family#			
Nuclear	368 (40.0)	552 (60.0)	?2=136.971,P<0.0001
Joint	284 (18.5)	1254 (81.5)	
Socioeconomic Status#			
Upper	179 (39.2)	278 (60.8)	?2=47.9222 P<0.0001
Middle	188 (25.4)	552 (74.6)	
Lower	285 (22.6)	976 (77.4)	
Type of School#			
Government	364 (29.7)	862 (70.3)	?2=12.5675 P=0.0004
Private	288 (23.4)	944 (76.6)	
Belonged to Problem Family#			
Yes	323 (24.5)	997 (75.5)	?2=7.8154, P=0.0052
No	329 (28.9)	809 (71.1)	
Age of Onset of Tobacco Use (y)*	13.9±2.0	12.3±2.9	t=13.0140 P<0.0001
Duration of Tobacco Use (y)*	4.3±0.9	6.1±1.2	t=34.9179 P<0.0001
Nicotine Dependence*			
Low	388 (49.2)	400 (50.8)	?2=513.0442,
Medium	256 (32.0)	545 (68.0)	P<0.0001
High	8 (0.9)	861 (99.1)	
FTND score#	3.1 ±1.2	5.9 ±1.5	t=42.9572, P<0.0001
Habit			
Daily	88 (7.5)	1089 (92.5)	?2=420.4862, P<0.0001
Occasional	564 (44.0)	717 (56.0)	
Psychiatric co-morbidities			
Present	41 (18.8)	177 (81.2)	?2=7.3119,P=0.0068
Absent	611 (27.2)	1629 (72.8)	
Other Substance Abuse			
Yes	22 (11.9)	163 (88.1)	?2=21.9818, P<0.0001
No	630 (27.7)	1643 (72.3)	
Knowledge about injurious effect of tobacco			
Absent	209 (18.2)	938 (81.8)	?2=21.9818, P<0.0001
Present	443 (33.8)	868 (66.2)	

*No (%), # Mean±SD, FTND- Fagerström Test for Nicotine Dependence

Table 2: Relative risk of different determinants taking quitting as good outcome (n=2458).

Risk Factors	Relative Risk	95% Confidence Interval	P Value
Age >15 y	1.18	1.04-1.35	0.0124
Male Sex	1.26	1.11-1.44	0.0004
Hindu Religion	0.99	0.95-1.04	0.8092
Joint Family	1.36	1.28-1.44	<0.0001
Lower Socioeconomic Status	1.12	1.06-1.17	<0.0001
Reading in Private School	1.09	1.04-1.14	0.0004
Belonged to Problem Family	1.06	1.00-1.11	0.0136
Age of onset of tobacco use =12 y	1.34	1.17-1.52	<0.0001
Duration of Tobacco Use =5 y	1.44	1.26-1.64	<0.0001
High Dependence to Nicotine	1.67	1.59-1.73	<0.0001
Daily Use of Tobacco	1.65	1.57-1.74	<0.0001
Presence of Psychiatric co-morbidities	1.12	1.04-1.20	0.0017
Other Substance Abuse	1.22	1.15-1.29	<0.0001
No knowledge about injurious effect of tobacco	1.24	1.17-1.30	<0.0001

FTND- Fagerström Test for Nicotine Dependence

initiation of tobacco use, duration of tobacco us, habit of tobacco use), presence of psychiatric comorbidities and concurrent other substance abuse also influence quitting among tobacco users.[5, 6, 15] They are also important determinants of nicotine dependence.[19, 22] Hence their effect on quitting might be due to interplay of these variables.

This study may be associated with recall bias. Self-reporting of the school-children was main mode of data collection. Thus, concealed information may lead to inaccuracy. Only urban schools were included with a small fraction of girls (approximately 7%). Nearly one-fourth factors responsible for successful quitting remained unknown.

To conclude, the present study identified the predictors of successful quitting of tobacco among school-children. Tobacco use had its origin in early childhood and adolescence;[5] hence, school-children should be targeted and made aware of injurious effect of tobacco.[21] Considering high prevalence of tobacco use in school-children, proper cessation program is the need of hour to decrease future burden of tobacco related morbidity and mortality.[21] Appropriate categorization of school-children depending on their dependence level may be helpful.[21, 23]

References

1. World Health Organization. WHO Report on the Global Tobacco Epidemic, 2008. The MPOWER Package. Geneva: World Health Organization; 2008.
2. Critchley JA, Unal B. Health effects associated with smokeless tobacco: a systematic review. Thorax 2003;58:435-43.
3. Sinha DN, Palipudi KM, Rolle I, Asma S, Rinchen S. Tobacco use among youth and adults in member countries of South-East Asia region: review of findings from surveys under the Global Tobacco Surveillance System. Indian J Public Health 2011;55:169-76.
4. Jorenby DE, Fiore MC, Smith SS, Baker TB. Treating cigarette smoking with smokeless tobacco: a flawed recommendation. Am J Med 1998;104:499-500.
5. Islam K, Saha I, Saha R, Samim Khan SA, Thakur R, Shivam S. Predictors of quitting behaviour with special reference to nicotine dependence among adult tobacco-users in a slum of Burdwan district, West Bengal, India. Indian J Med Res 2014;139:638–42.
6. Patel PM, Rupani MP, Gajera AN. Dependence on smokeless tobacco and willingness to quit among patients of a tertiary care hospital of Bhavnagar, Western India. Indian J Psychiatry 2019;61:472-9.

7. West R, Shiffman S. Smoking cessation. 3rd ed. Abingdon: Health Press;2016.
8. Sharma R. Revised Kuppuswamy's Socioeconomic Status Scale: Explained and Updated. Indian Pediatr 2017;54:867-70.
9. Park K. Park's textbook of preventive and social medicine. 23rd ed. Jabalpur: Bhanot; 2015.
10. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström test for nicotine dependence: A revision of the Fagerström Tolerance Questionnaire. Br J Addict 1991;86:1119-27.
11. Ebbert JO, Patten CA, Schroeder DR. The Fagerström test for nicotine dependence-smokeless tobacco (FTND-ST). Addict Behav 2006;31:1716-21.
12. Sheehan DV, Sheehan KH, Shytle RD, Janavs J, Bannon Y, Rogers JE, et al. Reliability and validity of the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID). J Clin Psychiatry 2010;71:313-26.
13. West R. Tobacco smoking: Health impact, prevalence, correlates and interventions. Psychol Health 2017;32:1018–36.
14. Altman DG. Practical statistics for medical research. 1st ed. London: Chapman & Hall; 1991.
15. Abdolahinia A, Sadr M, Hessami Z. Correlation between the age of smoking initiation and maintaining continuous abstinence for 5 years after quitting. Acta Med Iran 2012;50:755–9.
16. Kim H, Lee KS. Success Factors for Tobacco Smoking Cessation among Korean Female College Student Smokers. J Community Health 2020. [Epub ahead of print].
17. D'Souza G, Rekha DP, Sreedaran P, Srinivasan K, Mony PK. Lung India 2012; 29:137-42.
18. Fagerström K, Furberg H. A comparison of the Fagerström Test for Nicotine Dependence and smoking prevalence across countries. Addiction 2008;103:841-5.
19. Jayakrishnan R, Mathew A, Lekshmi K, Sebastian P, Finne P, Uutela A, et al. Assessment of nicotine dependence among smokers in a selected rural population in Kerala, India. Asian Pac J Cancer Prev 2012;13:2663-7.
20. Bernstein SL, Boudreaux ED, Cabral L, Cydulka RK, Schwegman D, Larkin GL, et al. Nicotine dependence, motivation to quit, and diagnosis among adult emergency department patients who smoke: a national survey. Nicotine Tob Res 2008;10:1277–82.
21. Kaur J, Sinha SK, Srivastava RK. Integration of tobacco cessation in general medical practice: Need of the hour. J Indian Med Assoc 2011;109:925-8.
22. Islam K, Datta AK, Seth S, Roy A, Das R. A study on the prevalence and correlates of nicotine dependence among adolescents of Burdwan Town, West Bengal. Indian J Psychiatry 2019;61:89-93.
23. Singh A, Katyan H. Classification of nicotine-dependent users in India: a decision-tree approach. J Public Health 2019; 27: 453–9.

WBAP EB Member 2023

Name	Post	Email
DR KALPANA DATTA	PRESEDENT,CIAP EB	drkalpanadatta@gmail.com
DR INDRANIL CHOWDHURY	SECRETARY	indranil.chowdhury1234@gmail.com
DR ASOK KUMAR DATTA	PRESIDENT ELECT	asokdatta31@yahoo.com
DR SUSHMITA BANERJEE	IMM. PAST PRESIDENT	sushmitabanerj@gmail.com
DR DIBYENDU RAYCHAUDHURI	VICE PRESDIENT	dr.dibyenduraychaudhuri@yahoo.com
DR MADHUMITA NANDI	IMM PAST SECRETARY	madhumitabanik@rediffmail.com
DR MIHIR SARKAR	JT. SECRETARY	drmihir09@gmail.com
DR PRIYANKAR PAL	TREASURER	mailme.priyankar@gmail.com
DR KALPANA DATTA	CIAP EB	drkalpanadatta@gmail.com
DR KAUSTAV NAYEK	CIAP EB	kaustav25@yahoo.co.in
DR KRIPASINDHU CHATTERJEE	CIAP EB	kschatterjee@gmail.com
DR ABHIJIT SARKAR	EXECUTIVE MEMBER	dr.sarkar@yahoo.com
DR AGNI SEKHAR SAHA	EXECUTIVE MEMBER	agnisekhar@hotmail.com
DR AMITA SINHA	EXECUTIVE MEMBER	amitasinhamandal@gmail.com
DR ASHIM KUMAR GHOSH	EXECUTIVE MEMBER	akgasn@gmail.com
DR BIPLAB BANERJEE	EXECUTIVE MEMBER	biplabjoy19@gmail.com
DR NILANJAN GHOSH	EXECUTIVE MEMBER	niltughosh@gmail.com
DR RUPA BISWAS	EXECUTIVE MEMBER	drrupa.biswas@gmail.com
DR SAMIK HAZRA	EXECUTIVE MEMBER	samik.hazra@gmail.com
DR SHUBHADEEP DAS	EXECUTIVE MEMBER	shubhadeepnrsdoc@gmail.com
DR SUMANTRA KUMAR RAUT	EXECUTIVE MEMBER	drsuman.raut@gmail.com
DR KAUSTAV NAYEK	Editor-in-Chief, CIAP EB	kaustav25@yahoo.co.in
DR SAMIR RANJAN DAS	Chairperson,Constitution Committee	das.samir2006@gmail.com
DR DEBAJYOTI BURMAN RAY	Chairperson, WBAP Board of Trustee	drdebajyotibroy@gmail.com
DR SWAPAN KUMAR RAY	Chairperson, Scientific Committee	drswapanray@gmail.com
DR VINAY ASAWA	Chairperson, Finance Committee	vinayasawa91@gmail.com
DR INDU SURANA	Chairperson, Community Action Plan	Indu.paed@rediffmail.com
DR ASAMANJA HAJRA	Coordinator, WBW Week	ahajra008@rediffmail.com
DR KAUSIK CHAKRABARTI	Coordinator, Immunisation Committee	drkausik.chc@gmail.com
DR ABUL FAZL A RAHAMAN	SPECIAL INVITEE	afardgp54@yahoo.com
DR ATANU BHADRA	SPECIAL INVITEE	atanu4bhadra@gmail.com
DR CHAMPAK DAS	SPECIAL INVITEE	champakdas23@gmail.com
DR SUBROTO CHAKRABARTTY	SPECIAL INVITEE	chakrabartty.subroto@gmail.com
DR SUKANTA CHATTERJEE	SPECIAL INVITEE	sukantachatterjee@hotmail.com

Published by Dr Indranil Chowdhury, Hony Secretary, West Bengal Academy of Pediatrics, 15C, Canal Street, Kolkata 700 014 and Printed by Roshni Enterprise, Kolkata