The Child and newborn

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CONTENTS

Special Correspondance
The Child and Newborn
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In Memoriam

Dr Lakshmi Kanta Mitra

Dr Lakshmi Kanta Mitra *was born on 31/07/1939 . He completed his MBBS from NRS Medical College, Calcutta in the year 1963 and subsequently did his DCH from University of Calcutta in the year 1966.*

Dr Mitra served the people of Rishra as a general pediatrician in a career spanning for more than five decades. Generations of people still fondly remember "Lakshmi dactar" as a benevolent child specialist who was always there in times of need. Dr Mitra also helped in the development of academics. He was the founder President of IAP Hooghly Branch. He was the Organizing Chairperson of the 14th WBAP State Conference held in Rishra, Hooghly. Later on he went on to become the Vice President of West Bengal Academy of Pediatrics for two terms, in 1995 and 2007.

Dr L K Mitra breathed his last on 06/04/2024 after a prolonged illness. He is survived by his wife and two sons. May his soul rest in eternal peace.

In Memoriam

Dr Banani Sen Gupta

Dr Banani Sengupta was born on 21.9.1948. Date of death--17.9.2024.

She was life member of IAP. She did MBBS from R.G.Kar Medical college in 1969. DCH from CSS and MD Pediatrics from ICH in the year 1986.

She was Professor of Pediatrics and worked as teacher in different Medical colleges in Wèst Bengal. She was teacher in N RS, Bankura Sammilani Medical College and retired from R. Kar Medical College where she was HOD of Pediatrics. She was teacher in MGM Medical College in Kishanganj for ten years, where was Professor and HOD of Pediatrics for ten years. She was teacher of many Teacher's. May her soul rest in peace.

President's Address

Dear Esteemed Colleagues, It is my privilege and honour, as the President of the West Bengal Academy of Pediatrics, to present a brief overview of our recent academic activities and initiatives that continue to advance pediatric healthcare in our region.

The Journal The Child and Newborn has been an integral platform in sharing vital knowledge and scientific progress, and I would like to take this opportunity to acknowledge the relentless eEorts of its contributors, researchers, and editorial team in upholding the highest standards of medical publication.

Academic Initiatives and Conferences Over the past year, the Academy has organized a series of successful academic programs, including CME (Continuing Medical Education) workshops, regional pediatric meets, and national-level conferences, all aimed at promoting up-to-date clinical practices in pediatric care. Some key events include:

1. **Annual Pediatric Summit 2023:** This flagship event brought together eminent paediatricians, researchers, and healthcare professionals from across India and beyond. With sessions covering emerging pediatric diseases, advancements in neonatology, and the latest in childhood immunization strategies, the summit provided a rich platform for exchange and learning.
2. **Specialized Workshops on Pediatric Subspecialties:** Recognizing the importance of sub specialization in pediatric care, we organized workshops on neonatology, pediatric endocrinology, and adolescent medicine. These workshops were designed to bridge the gap between academia and practical care, helping paediatricians enhance their clinical acumen.
3. **Four Rewards:** In our eEort to foster research in Pediatrics, the Academy launched several reward programs aimed at young researchers and healthcare practitioners. These rewards have encouraged young paediatricians .

Community Outreach and Public Health Awareness: Along with our academic endeavours, the Academy has been active in raising public awareness through health camps, vaccination drives, and educational seminars aimed at parents and caregivers. Our focus on community health ensures that advancements in pediatric care translate into real-world impact. Publications and Scientific Contributions.

Our collaboration with The Child and Newborn continues to flourish, with an increasing number of high-quality research papers, case reports, and review articles being published. I am proud to note that the journal has garnered recognition for its rigorous peer-review process and its dedication to pediatric and neonatal research. The journal serves as a critical resource for

clinicians, educators, and students alike, providing them with valuable insights and evidence-based approaches to child healthcare. Looking Ahead

As we move forward, the Academy remains committed to its mission of advancing pediatric healthcare through education, research, and collaboration. The upcoming year will see the introduction of newer training modules, a strengthened research agenda focusing on digital health in Paediatrics, and international partnerships aimed at bringing global pediatric expertise to our local context. In conclusion, I extend my deepest gratitude to all members, colleagues, and the editorial team of The Child and Newborn for their continued dedication to pediatric healthcare. It is through our collective eEort that we can shape a healthier future for our children.

Asok Kumar Datta
President
West Bengal Academy of Pediatrics

Respiratory Tract Infections in Children, Upper vs Lower, Acute vs Recurrent, with Respect to Their Relation with Vitamin D Deficiency: A Study from Eastern India

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**Ex Pgt, **Ex -Professor and HOD, **Assistant Professor*
Department oif Pediatric Medicine, IPGME&R and SSKM Hospital.

Abstract :

Introduction: Respiratory tract infections (RTIs) are common worldwide and are responsible for significant morbidity and mortality. Vitamin D deficiency has been linked to RTI in children in various studies.

Objectives: To determine the association of vitamin D deficiency with Upper and lower respiratory tract infection, recurrent RTI in children as well as severity of RTI in a tertiary care centre in Eastern India.

Study design: A hospital based observational and analytical case control study.

Materials And Methods: Total 196 children of age group 2 months to 12 years were taken, of which 105 children with RTI were cases and 86 healthy age and sex matched children were controls. RESULTS: Mean age of cases was 40.88±37.57 months and controls was 37.66±35.25months. Infants were the most vitamin D deficient (40.5%). The mean serum vitamin D level in LRTI was (19.01±5.72ng/ml) and in URTI is (22.98±4.47ng/ml) Vitamin D deficiency was associated with LRTI(p=0.0003). The mean vitamin D level in discharged patient is (21.50±4.85ng/ml) and in ICU admitted patient is (15.16±6.71ng/ml)) which was significantly lower.

Conclusion: Cases outnumbered controls in being more Vitamin D deficient. Mean serum vitamin D level was significantly lower in cases compared to controls, which could imply that vitamin D deficiency predisposes to RTI in children. Infants were the most vitamin D deficient (40.5%) . Vitamin D deficiency was more commonly associated with Lower RTI than Upper RTI and in recurrent RTI compared to acute RTI. Mean serum vitamin D levels were lesser in children requiring PICU admissions.

Key words: Upper RTI; Lower RTI; Recurrent RTI; Vitamin D deficiency; children

Introduction:

Respiratory tract infections are very frequent all throughout the world, and they cause a lot of morbidity and mortality. Vitamin D appears to have an impact on a number of immunological pathways, according to new research. Vitamin D status has been linked to respiratory tract infections in children in a few studies conducted in Western countries. Due to a lack of data from Indian research, we conducted a case-control study to assess the link between vitamin D insufficiency and respiratory tract infection in children. A total of 105 children aged 2 months to 144 months were enrolled in the study over the course of 18 months.

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Materials And Methods

Study setting:

In-patients (IPD) and out-patients department (OPD) of Paediatrics department in a tertiary care centre Study population:

Children between age group 2 months to 12 years suffering from respiratory tract infection from both IPD and OPD of Department of Paediatrics between February 2016 and July 2017 were taken as cases. Age and sex matched healthy children were taken as control.

Study period:

1 and 1/2 years (February 2016-July 2017).

Study design:

A hospital based Observational ,case control study.

Sample size:

In this study total 105 cases of age group 2 months to 12 years from both IPD and OPD of Department of Pediatrics. All cases were suffering from respiratory tract infection. 86 disease free age and sex matched children were taken as control.

Inclusion criteria:

All children between 2 months to 12 years of age attending the Department of Paediatrics having respiratory tract infection.

Exclusion criteria-

1. Children having congenital heart disease.
2. Cases of childhood asthma and allergy.
3. Cases of tuberculosis
4. Children getting prophylactic vitamin D3 supplementation.
5. Children having immune-deficiency or getting immuno-suppressive therapy.

The purpose of the study and detail of protocol was discussed with the parents and consent from the parents or assent from the children above 7 years of age was taken after taking Ethical approval.

Detailed history was taken in every child with ARI to find the participant for study. The pre-structured proforma were filled up. The children were classified into upper respiratory infection (URTI) and lower respiratory tract infections (LRTI) on the basis of clinical examination. A child with URTI of at least 6 times per year or LRTI of at least 2 times per year was defined as a patient with recurrent respiratory tract infection (RRI). The interval between every two infection was at least 7 days [40].

From the children of study group 2ml EDTA blood was taken for complete blood count and ESR. From the study and control group 3ml clotted blood were taken for estimation of serum 25(OH) vitamin D3 level. Assessment of serum 25(OH) Vitamin D3 was done by the method of ELISA by EUROIMMUN kits at the Department of Rheumatology. Mantoux test was done to exclude tuberculosis. Chest X-ray was done for diagnosis of lower respiratory tract infection.

Data interpretation and Analysis:

Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate.

Once a t value was found, a p-value was determined value = 0.05 was considered as statistically significant.

Results:

The present study consists of total 191 children of age group 2 months to 144 months, out of which 105 were cases who are suffering from respiratory tract infection and 86 were healthy. Distribution of age in two groups shown in table no. 1(A) was not statistically significant (p=0.8854). Thus age was matched in two groups. In cases 58 (55.2%) patient belonged to male gender and 47 (44.8%) belonged to female gender, whereas in control group 33 (38.4%) belonged to female and 53 (61.6%) belonged to male. Distribution of gender in two groups were not statistically significant (p=0.3731). Thus male and female were matched in two groups

Higher percentage of cases belonged to deficient (40.0%) and insufficient (55.2%) status as compared to sufficient (4.8%) status, whereas in control group higher percentage belonged to sufficient (27.9%) status as compared to deficient (4.7%) and

Table 1: Distribution of cases and control according to Age

	GROUP		
Age group	Case	Control	TOTAL
2 Months to 12 Months	35	30	65
Row %	53.8	46.2	100.0
Col %	33.3	34.9	34.0
12 Months to 60 Months	39	29	68
Row %	57.4	42.6	100.0
Col %	37.1	33.7	35.6
60 Months to 144 Months	31	27	58
Row %	53.4	46.6	100.0
Col %	29.5	31.4	30.4
TOTAL	105	86	191
Row %	55.0	45.0	100.0
Col %	100.0	100.0	100.0

insufficient (67.4%) status [Figure no .1]. Distribution of Vitamin D in two groups is statistically significant (p<0.0001).

The mean serum vitamin D level in LRTI is (19.01±5.72ng/ml) and in URTI is (22.98±4.47ng/ml) with a statistically significant (p=0.0003) value, showing vitamin D deficiency is associated with LRTI.

The mean vitamin D level in discharged patient is (21.50±4.85ng/ml) and in ICU admitted patient is (15.16±6.71ng/ml)) which is significantly lower. Difference of mean vitamin D level in two groups is

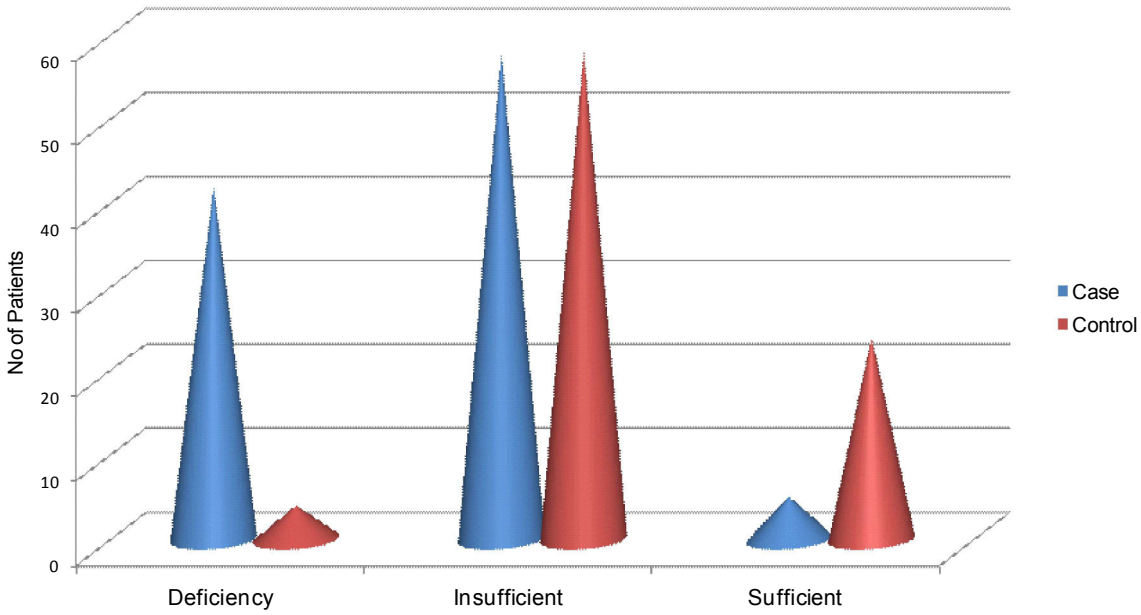

Fig 1: Distribution of vitamin D status in cases and control

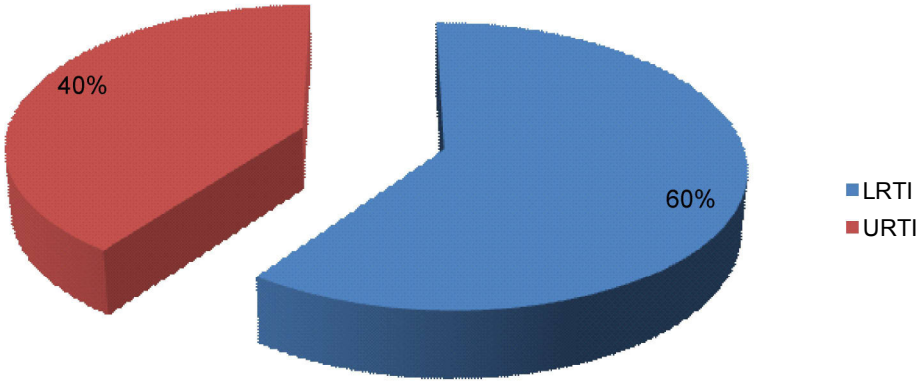

Fig 2: Distribution of cases according to type of RTIs

statistically significant (p<0.0001). Hence lower serum vitamin D is associated with disease severity.

The mean serum vitamin D level in cases across all age groups was found to be considerably lower than controls and was statically significant [Table no.2]. The mean serum vitamin D level in cases as a whole was (20.60±5.59) where as in control group was (26.38±4.58) with a statically significant p value of <0.0001, hence cases were associated with vitamin D deficiency.

The mean serum vitamin D level in exclusive breast fed child was (19.90±6.33ng/ml) and in non breast fed child was (20.90±5.25ng/ml). Difference of mean vitamin D level in two groups is not statistically significant (p=0.4015). No association is found with breast feeding status.

Discussion

Among the all age group in cases, vitamin D was more deficient in infancy (40.5%) which confirms the increased requirements of Vitamin D in infancy. Thus it may be concluded, sunlight exposure or dietary vitamin D supplementation is required from birth to meet their requirements. Vitamin D is naturally deficient in both human and cow's milk. Vitamin D deficiency is rampant in infants who are exclusively breastfed. Subclinical vitamin D deficiency and nonexclusive breastfeeding in the first 4 months were found to be a significant risk factors for severe acute lower respiratory infection (ALRI) in Indian children in the study by Wayse V et al [3]. In our study the mean serum vitamin D level in exclusive breast fed children (19.90±6.33ng/ml) and in non breast fed children (20.90±5.25ng/ml) were statistically insignificant.(p=0.4015). Thus our study was contrary to that of Wayse V et al [3] study. Vitamin D deficiency and insufficiency are serious health issues in children, with varying prevalences documented in studies across the globe. [4-7]. In a study conducted in Greece by Lapatsanis D et al, vitamin D deficiency was found at a rate of 14% in children aged between three and 18 years [4]. Mansbach JM et al. conducted a study on blood 25-hydroxyvitamin D levels in US children aged 1 to 11 years in the United States. In this study vitamin D deficiency was found to be 14% and vitamin D insufficiency was found to be 63% in 1799 children aged between one and five years [5]. In our study Vitamin D deficiency was found in 40.0% of cases while 55.2 % had insufficient vitamin D level, only 4.8 % had sufficient vitamin D status. In control group 27.9% had sufficient vitamin D status where as insufficient vitamin D level and deficient vitamin D level was found in 67.4% and 4.7 % respectively with a statistical significance (p<0.0001). Vitamin D deficiency is becoming more common as a result of inadequate solar exposure, social and cultural taboos, and a diet that does not meet the daily vitamin D need.

Vitamin D contributes to immunity by restoring immunological function and lowering cytokine levels. Vitamin D deficiency, on the other hand, stimulates the release of pro-inflammatory cytokines like IL-6 and TNF-alpha. In our study the mean serum vitamin D level was significantly lower (p<0.0001) in cases

Table 2: Distribution of mean vitamin D level in different age groups in case and control

		Number	Mean (ng/ml)	SD (ng/ml)	Minimum (ng/ml)	Maximum (ng/ml)	Median (ng/ml)	p-value
Age Group (2-12 months)	Case	35	18.9094	5.7097	5.1000	28.0000	20.1000	<0.0001
	Control	30	26.2867	4.3738	20.1000	34.5000	24.7000	
Age Group (12-60 months)	Case	39	21.2177	6.1325	5.8000	34.0000	22.1000	0.0001
	Control	29	26.7586	4.8189	17.9000	35.2000	27.1000	
Age Group (60-144 months)	Case	31	21.7397	4.3121	14.2000	30.6000	21.2000	0.0005
	Control	27	26.0944	4.6946	18.7000	35.0000	25.9000	

(20.60±5.59) than in controls (26.38±4.58), which implies that vitamin D deficiency predisposes to respiratory tract infection in children. Our study is almost similar to the findings in other studies by Velarde Lopez AA et al [8], Roth DE et al [9], Wayse V et al [3], Larkin A et al [10]. In all this studies they compared acute LRTI and mean vitamin D level and found a significant association of vitamin D deficiency with ALRI. However in none of the studies comparison of vitamin D levels of both URTI and LRTI cases and controls was done.

The final activation of vitamin D occurs in the respiratory tract as well, because CYP27B1 is expressed in bronchial epithelial cells and is induced by inflammatory stimuli. In this study the mean serum vitamin D level in LRTI group was 19.01±5.72ng/ml and that of URTI group was 22.98±4.47ng/ml with a statistically significant (p=0.0003) value, showing vitamin D deficiency predisposes more towards LRTI. This is a significant finding comparing LRTI and URTI in my study. No such study was found on literature review comparing mean vitamin D level with the subgroup URTI and LRTI.

In 105 cases, the number of acute cases was 74(70.5%) and recurrent cases were 31(29.5%). Maximum no. of recurrent cases (71%) belonged to age group 12-60 months and vitamin D deficiency and insufficiency were more in this age group. So vitamin D deficiency may be an additional contributing factor for recurrent RTI, both URTI and LRTI. Vitamin D increases the conversion of immature monocyte to mature macrophages and increases its other function. Also Recurrent RTI is more common in 12-60 age group and vitamin D deficiency and insufficiency were more in this age group. So vitamin D deficiency may be an additional contributing factor for recurrent RTI. Vitamin D supplementation may help in prevention of RRTI. This study is similar to study of Ozdemir B et al [11]. significant (p=0.1076). So there was no association of vitamin D with severity of pneumonia.

In our study group, case severity was assessed by requirement of paediatric intensive care admission versus direct discharge from general paediatric ward. Out of 105 cases, 15(14.3%) cases were admitted in PICU and 90 (85.7%) were discharged. The mean vitamin D level in discharged patient from general ward was 21.50±4.85ng/ml while that of PICU admitted patient is 15.16±6.71ng/ml. This significant difference in mean ($p < 0.0001$) strongly suggests correlation of vitamin D deficiency with severity of respiratory illness in our study population. These data imply that vitamin D's immunomodulatory characteristics may have an impact on the severity of ALRI. Only a few research have found a link between vitamin D deficiency and severity. Lobey Lopez M et al [12] found 25-OHD level of children admitted because of a LT-ARI were <30 ng/ml. and lower levels of 25-OHD were found to be correlated with severity of the disease. Inamo Y et al [13] observed that significantly more children with ALRI who required supplemental oxygen and ventilator management were vitamin D deficient in his study.Our study is similar to Lobey Lopez M et al [12] and Inamo Y et al [13]. The possible role of diminished serum level of vitamin D as a facilitator or consequence of the infection needs further evaluation.

Sismanlar T, Aslan AT, Gülbahar Ö, Özkan S [14] found no significant correlation between vitamin D levels and lower respiratory tract infection in terms of disease and its severity. However, it was found that vitamin D deficiency/ insufficiency was observed with a high rate in all children included in his study. My study is similar to Sismanlar T et al [13] study in terms of disease severity.

Conclusion

(a) Deficiency of serum level of 25(OH) Vitamin D3 is significantly associated with RTI, both URTI and LRTI

(b) Deficiency of serum level of 25(OH) Vitamin D3 is more associated with LRTI as compared to URTI

(c) Though there was significantly low level of serum 25(OH) Vitamin D3 was in children admitted to PICU it may be attributed to other co-morbidities.

(d) To conclude supplementation of vitamin D may be useful in prevention of RTIs, specially the LRTI group and to decrease the number of PICU admission. However more studies are needed to be performed in this field to assess further

correlation with frequency, severity and the types of RTIs.

Limitations Of The Study

(a) Small sample size.

(b) Shorter duration of the study led to fewer samples being collected and fewer follow up in recurrent RTI cases.

(c) Due to a lack of data being collected, regarding the duration of sun exposure and food habits in infants and older children, nothing is known about the cause.

(d) Serum 25(OH) Vitamin D3 assessment by ELISA is not considered the gold standard, HPLC and TMS are the gold standard.

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Hereditary Angioedema- A Brief Overview

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Abstract : Hereditary angioedema (HAE) is an uncommon disorder with autosomal dominant mode of inheritance, characterized by recurrent episodic swelling of face, limbs, genitals, airway and gastrointestinal tract. Most patients with HAE remain undiagnosed and untreated due to lack of awareness. Swelling episodes in patients with HAE are mediated by bradykinin. Excess bradykinin due to defective C1 inhibitor (C1-INH) protein is the basic fault. While in type 1 HAE C1-INH levels are low, HAE type 2 is diagnosed by normal levels of C1-INH that is functionally defective. C1-INH levels and function are normal in type 3 HAE (nl-C1INH-HAE). Treatment of acute attacks, short term prophylaxis and long-term prophylaxis are the main forms of management. C1-INH concentrate is the preferred treatment for patients with HAE. Alternative options are fresh frozen plasma, attenuated androgens and tranexamic acid. In this review, we update on the pathogenesis, clinical features, diagnosis and management of HAE.

Keywords- Hereditary angioedema, bradykinin, C1 inhibitor, acute attacks, short term prophylaxis, long term prophylaxis, attenuated androgens, tranexamic acid

Introduction

- Angioedema is characterized by swellingof subcutaneous and/or submucosal tissue because of increased vascular permeability.
- Angioedema may be broadly categorized intohistamine and bradykinin mediated. (1)
- Most cases of hereditary angioedema (HAE)have onset in childhood.
- HAE is an uncommon, potentially life-threatening diseaseand has an autosomal dominant mode of inheritance. (2)
- HAE is characterized by episodes of subcutaneous and/orsubmucosal swelling typically affecting extremities, face,genitals, airway and gastrointestinal mucosa. (3)

Epidemiology

- The global prevalence of HAE is 1:10,000 to 1:50,000. (4)
- It is expected that there are more than 50,000 patientswith HAE in India at present.
- HAE is grossly underrecognized in India.
- Because of lack of awareness, most patients with HAE remain undiagnosed and untreated.

The basic abnormality in HAE patients i.e., deficiency of C1-INHprotein was identified more than 60 years ago. C1-INH is a protease inhibitor in the serpin superfamily.(5) HAE is divided into various subtypes based on the level and functional activity of C1-INH protein: (4)

(1) HAE-1 is the most common type (~85% of all patients) and is diagnosed by low C1-INH levels.

(2) HAE-2 is the second most common type (~15% of all patients) and is diagnosed by normal C1-INH levels but low C1-INH functional activity.

Both type 1 and type 2 HAE are caused by pathogenic variants in the SERPING1 gene.

(3) HAE with normal C1-INH (nl-C1INH-HAE) is a rare subtype of HAE (<5%) wherein the levels and functional activity of C1-INH protein is normal. nl-C1INH-HAE may be caused by mutations in FXII gene, ANGPTI (Angiopoietin-1) gene, Plasminogen gene, Kininogen gene and heparan sulfate 3-O-sulfotransferase 6 gene. (4)

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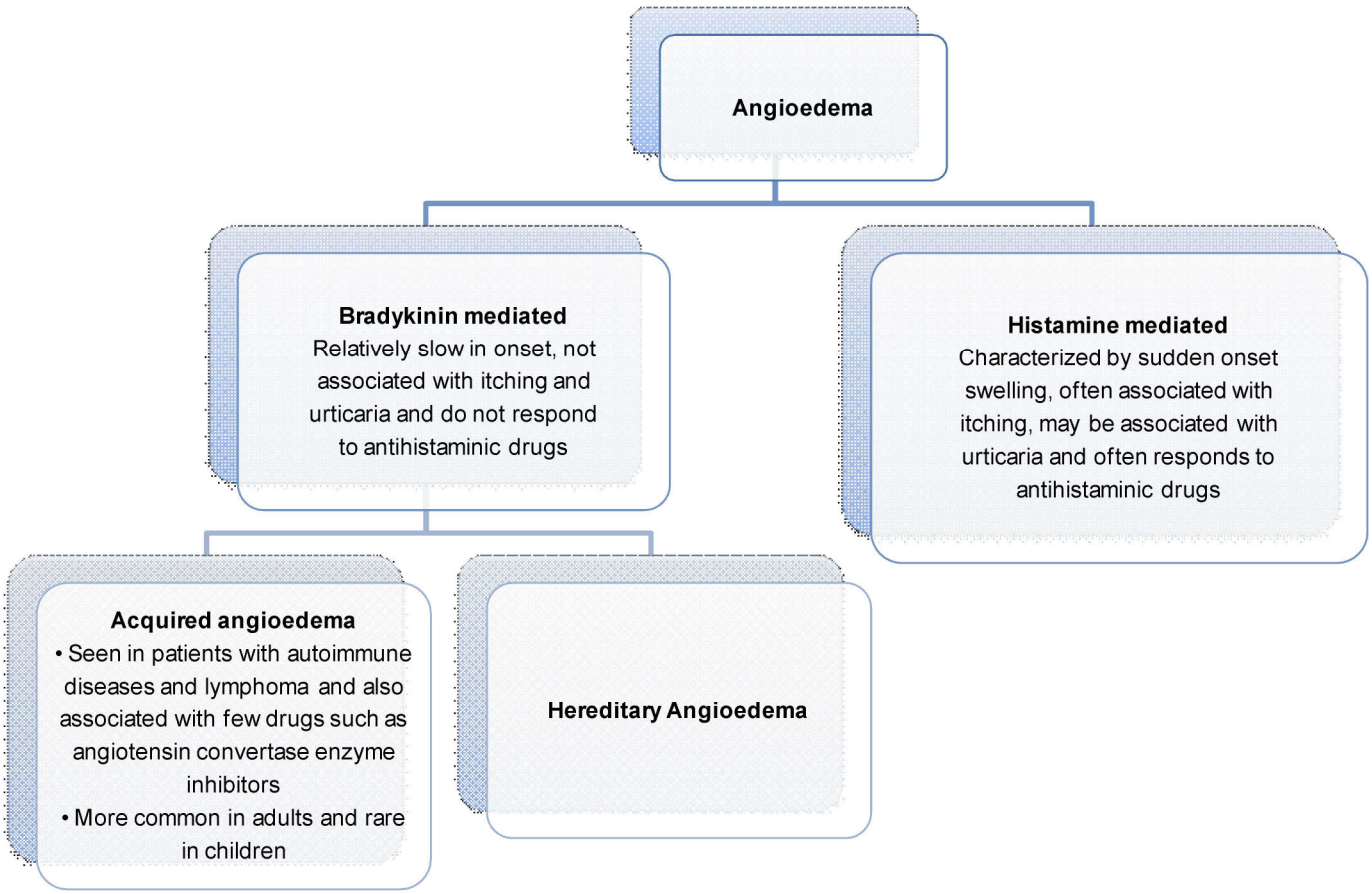

Fig 1: Angioedema- Different types

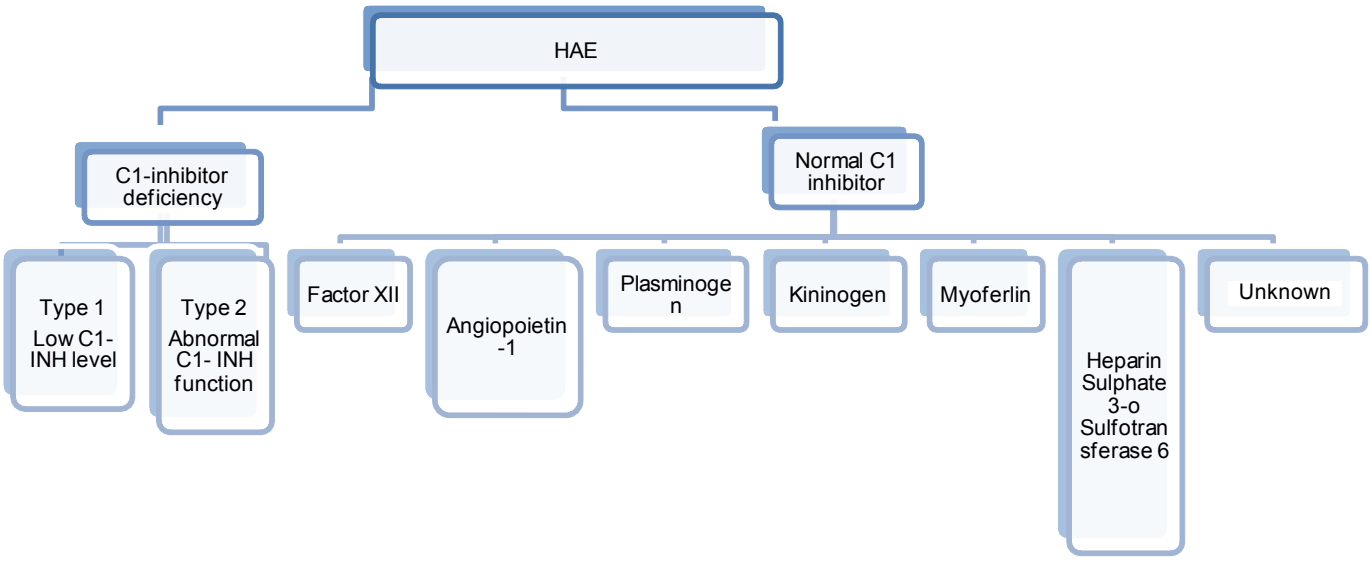

Fig 2: Classification of HAE

Pathophysiology (Figure 3)

The figure 3 shows the pathway for production of bradykininand angioedema. C1-INH protein is an inhibitor of variouscomplement proteases, contact system proteases(FXIIa, Plasma kallikrein), intrinsic coagulation pathwayand fibrinolytic pathway. (6)

Deficiency of C1-INH protein or impaired function of C1-INHprotein as is seen in patients with type 1 and type 2 HAErespectively, leads to uncontrolled activation of FXII, plasmakallikrein and over production of bradykinin. Bradykininstimulates its receptor to cause vasodilatation, increasedvascular permeability and angioedema. (7, 8)

Pathophysiology of normal C1-INH-HAE is more complex.There is role of bradykinin and vascular endothelium inmediating episodes of angioedema in these patients. (9, 10)

Clinical features

- Non-pitting, non-urticarial, non-pruritic subcutaneousand/or submucosal swelling. (11, 12)
- Typically lasts for 3 - 5 days. (11, 12)
- Most attacks are spontaneous. A trigger such as physicalor mental trauma, infection, surgical or dental procedure maybe identified in few cases. (11-16)
- Limbs, face, eyes, lips and genitals are the most commonlyinvolved sites. (11-16)
- Bowel wall edema may lead to abdominal pain, vomitingand occasionally diarrhea. (11-16)

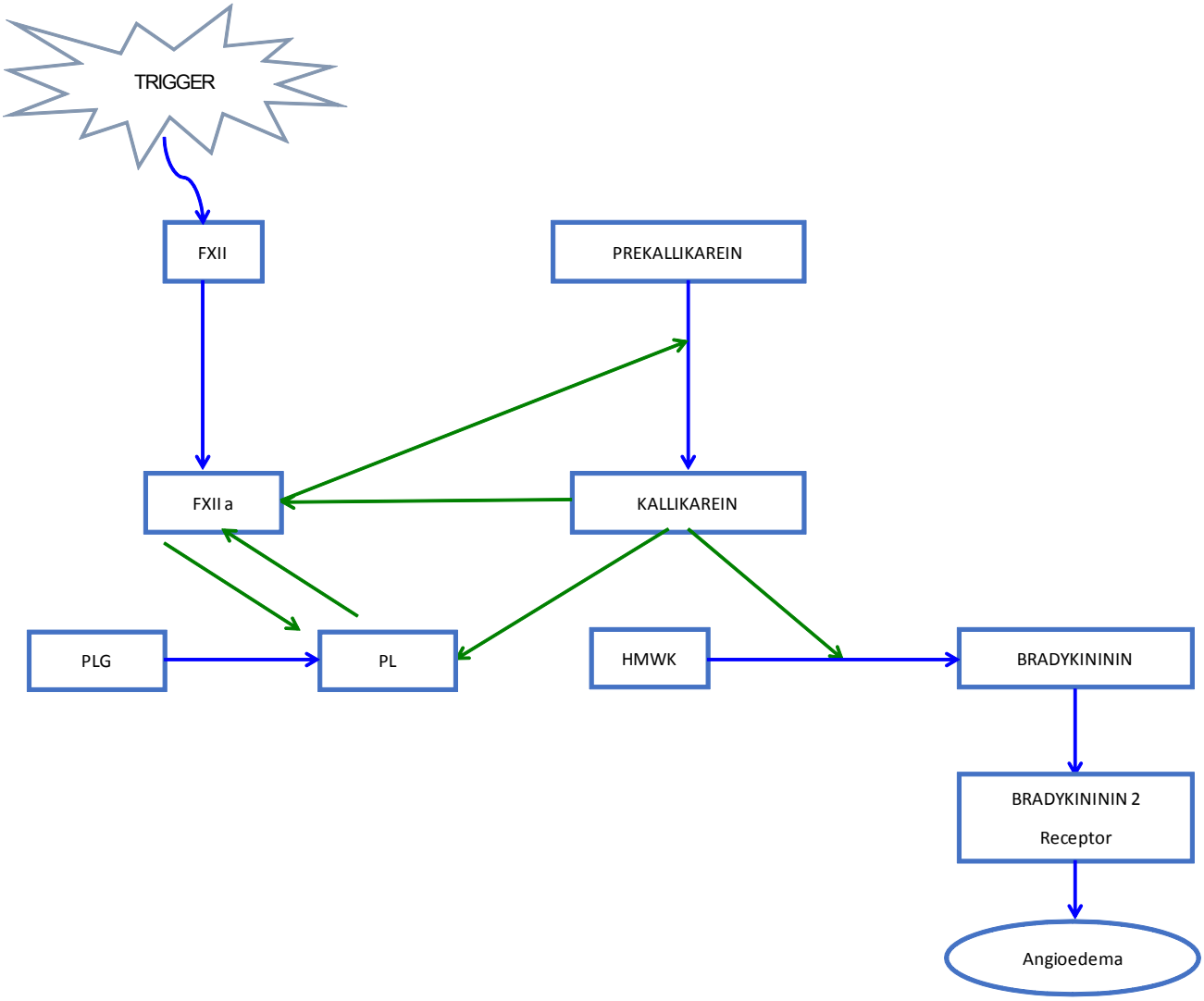

Fig 3: Pathophysiology of HAE

- Laryngeal edema is a potentially life-threateningcomplication of HAE and more than 50% patients will haveat least one episode of laryngeal edema in their life time. (14)
- Prodromal symptoms (such as numbness, tingling sensation,pain and formation of faint erythematous serpiginous toannular non pruritic rash resembling erythema marginatum)may be seen in up to 50% of all patients. (13-16)

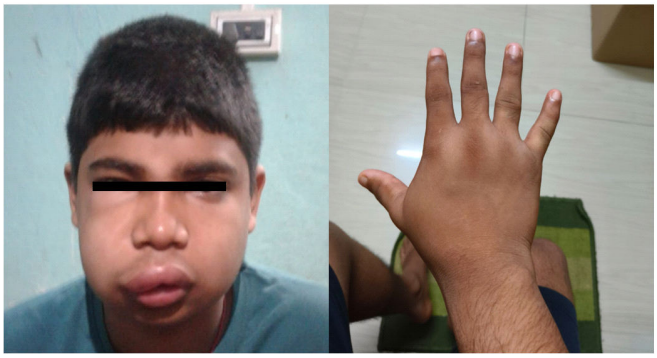

Fig 4: Face and hand swelling of a patient with HAE

Laboratory diagnosis (Figure 5)

- Measuring C4 levels alone for screening test is only 80% effective. So, screening test should include C4 level assessment, C1 INH levels and C1 INH function.
- C4 and C1-INH levels are assessed by nephelometry and C1-INH functions are assessed by ELISA (Enzyme linked immunosorbent assay).
- In Type 1 HAE all 3 values are low, in Type 2 HAE, C4 values and C1-INH functional levels are low but C1-INH levels are normal. All 3 values are normal in normal C1-INH HAE due to mutation in plasminogen, angiopoeitin, factor XII genes. Further diagnosis is confirmed by genetic analysis. Once diagnosis is confirmed, family member should be screened.

Treatment

It is not possible to cure HAE permanently because of its genetic etiology. Treatment is initiated to

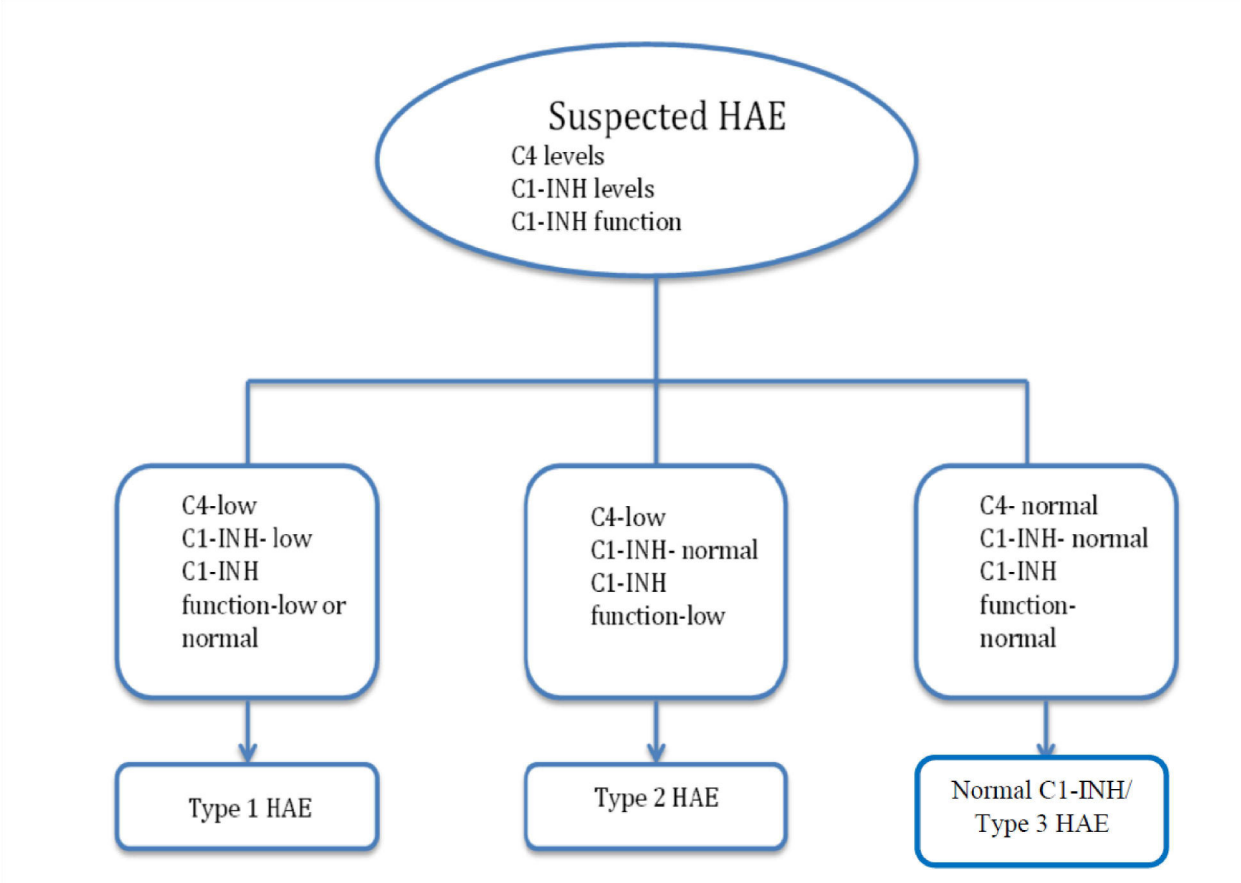

Fig 5: Laboratory diagnosis of HAE

minimise episodes of angioedema, prevent any disease related mortality and improve quality of life of patients. Treatment of HAE may be categorized into termination of acute episodes (on-demand treatment), long term prophylaxis (for prevention of attacks) and short-term prophylaxis(to be given in situations where an attack is expected to occur such as during the dental procedures or endotracheal intubation). (17,18)

(1) On-demand treatment (Table I)-

Ideally all acute episodes of angioedema should be treated.

- Plasma derived C1-INH concentrate is now available in India for on-demand treatment of HAE. (19-21)
- It is the treatment of choice for termination of all acute attacks of HAE. (20, 21)
- Plasma derived C1-inhibitor concentrate can be used in a dose of 20 units per kg body weight, maximum dose 1000 units (intravenous).(20, 21)
- The other option (in case of non-availability or non-affordability of C1-INH) for acute/on demand treatment is fresh frozen plasma (FFP). (21-23)
- FFP contains 1 unit of C1-INH protein in each ml. In someobservational studies it has been found to be effective interminating acute episodes of HAE including laryngealedema [Dose: 10-20 ml/kg (4-5 units in adults)]. (22, 23)
- The dose can be repeated after 12 hours if there is noappreciable improvement.
- Considering the potential adverse effects associated withfrequent use of FFP, it is advisable to use FFP during alife-threatening episode of angioedema such as involvement of

Table I- Drugs used for on-demand treatment(21-23)

Drug	Regulatory status	Dosage	Mechanism of action	Side effects
Plasma derived C1-INH	Licensed for use in adolescents and adults of more than 12 years in USA and for patients of all ages in Europe. **Now available in India.**	20U/kg intravenous	Inhibition of plasma kallikrein and coagulation factor Xlla	Chances of anaphylaxis, transmission of infectious agents
Ecallantide	Licensed for use inpatients of more than16 years in USA. **Not available in India**	30 mg subcutaneous	Inhibition of plasma kallikrein	Uncommon- anti drug antibodies, risk of anaphylaxis
Icatibant	Licensed for use in USA and Europe for patients of more than 18 years. **Not available in India.**	30 mg subcutaneous	Antagonism of bradykinin B2 receptor	Common- injection site reactions
Recombinant human C1-INH	Licensed for use in adults in Europe. Not available in India.	50U/kg or 4200 U (whichever is higher) intravenous	Inhibition of plasma kallikrein and coagulation factor Xlla	Uncommon- risk of anaphylaxis
Fresh frozen plasma	Not approved	10-20 ml/kg or 2-4 units	Replaces C1-INH protein	Infusion reactions, transmission of viral agents, volume overload

larynx and tongue and severe abdominalattack. (22, 23)

- It has been observed that attenuated androgens [danazol(200-400 mg) or stanozolol (2-4 mg)] used at the onsetof attack may abort an ongoing episode of angioedema.

  These drugs are not effective in an established episode ofangioedema.
- Early use of high dose intravenous or oral tranexamic acid(1000 mg every 3-4 hrs for 12-18 hrs) may also lead toresolution of symptoms in milder episodes.
- In these contexts, it is important to identify a prodrome(such as erythema marginatum, severe fatigue or prickingsensation).
- Corticosteroids, antihistamines and epinephrine are noteffective for the management of acute episodes of HAEand must not be used.

(2) Prophylactic treatment

(a) Short-term prophylaxis-

Short term prophylaxis is recommended before a surgicalor dental procedures or any invasive medical interventions(such as endoscopy) as these procedures may trigger anacute attack.

- Risk of developing angioedema is very high in the first 24-48hours after the procedure.
- Plasma derived C1-INH concentrate, when available, is aneffective treatment option for short term prophylaxis.
- Attenuated androgens [danazol 200-400 mg orstanozolol 2-4 mg or doubling the dose of these drugs if apatient is already taking them as long-term prophylaxis],FFP (10-20 ml/kg) or tranexamic acid [30-50 mg/kg/day(maximum 3-4.5 gm/ day) or doubling the dose if a patientis already taking tranexamic acid as long-term prophylaxis]may be used for short term prophylaxis.
- Prophylaxis should be initiated 2 days prior to theanticipated date of procedure and should be continued5 days later. (24-26)

(b) Long-term prophylaxis (Table II)

- There are no strict guidelines on indications for initiatinglong-term prophylaxis. However, it may be reasonable tostart long-term prophylaxis in patients who experienceat least more than one episode of angioedema everymonth or who has life threatening laryngeal attacks. (24)
- It is better to keep a low threshold for initiating long termprophylaxis till better on demand treatment options areavailable in India.
- Commonly reported side effects of androgens are weightgain, acne, virilization, menstrual irregularities, hirsutism,hepatic abnormalities, growth retardation, behavioural andmood alterations, headache and cardiovascular risk. (27)
- Monitoring should be done once every 6 months(blood pressure, weight, height, liver function tests, lipidprofile, alpha fetoprotein, liver ultrasonography). (27)
- Tranexamic acid is less effective but safer as compared toattenuated androgens.
- Tranexamic acid is a safe and preferred option for long termprophylaxis in children, during pubertal age group, duringpregnancy and while breastfeeding.

There is preliminary experience that a combination oftranexamic acid and attenuated androgens may be moreefficacious than either of the 2 drugs used alone.

Drugs available for long-term prophylaxisin India at present:

Danazol:

50 mg 2-3 times a week to 600 mg per day

Stanozolol:

0.5 mg 2-3 times a week to 4 mg per day

Tranexamic acid:

30-50 mg/kg/day (Maximum 3 gm per day)

Please note

- Androgens are contraindicated during pregnancyand breast feeding.
- Avoid triggers: such as trauma, exertion, stress,oral contraceptive pills, angiotensin convertaseenzyme (ACE) inhibitors. Triggers are usuallypatient specific. These must be identified andavoided.

Table II- Drugs used for long-term prophylaxis

Drug*	Regulatory Status	Dosage	Mechanism of action
Plasma derived C1 INH	Licensed in United States and Europe for patients =12 years.	1000 U intravenous every 3-4 days	Inhibits plasma kallikrein, coagulation factor Xlla
Lanadelumab*	Licensed for long-term prophylaxis by FDA for patients aged 12 years or older in 2017. Not available inIndia.	300 mg every 2 weekly	Fully humanized IgG1 monoclonal antibody directed against plasma kallikrein
Berotralstat#	FDA approved for prophylaxis in adults and children more than 12 years old. Not available in India.	150 mg OD with food	Selective kallikrein inhibitor
Danazol	Approved in United States for adults. Available in India.	100 mg alternate days to 600 mg/day	17-a alkylated androgen acts as an inducer of C1-INH synthesis in liver, causes more expression of C1-INH mRNA in mononuclear cells in the peripheral blood, increases catabolism of bradykinin by inducing aminopeptidase P activity
Stanozolol	Approved in United States for adults and children. Available in India.	0.5mg alternate days to 4 mg/day	17-a alkylated androgen acts as an inducer of C1-INH synthesis in liver, increases catabolism of bradykinin by inducing aminopeptidase P activity
Tranexamic acid	Not approved for HAE. Available in India.	30–50 mg/kg/day in 2–3 divided doses (maximum dose3 g/day)	Antifibrinolytic, acts as a competitive inhibitor of plasminogen, reduces conversion of plasminogen to plasmin, prevents plasminogen mediated activation of FXII

Conclusion

Hereditary angioedema (HAE) is an uncommon disorder characterized by episodic edema. The disease remains undiagnosed for several years because of lack of awareness.HAE should be suspected in all patients who present with episodic edema without urticaria, and C4, C1-INH levels and C1-INH function should be assessed. Most patients have diseases onset in childhood. Hence, pediatricians have an important role to play in the early diagnosis of HAE. First line treatment for HAE is C1-INH concentrate. Patients with HAE can also be managed using fresh frozen plasma, attenuated androgens and tranexamic acid.

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Malignant Autosomal Recessive Osteopetrosis Type 1 with TCIRG 1 Gene Mutation

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Abstract:2yr old boy born out of a 2nd degree consanguineous marriage presented with failure tothrive and increasing head size. There was squint and setting sun sign. He had marked pallor and hepatosplenomegaly. Skiagram of skull showed unusually thickened calvarium. Chest X Ray showed densethickened ribs. Limb X rays showed dense, abnormally shaped femur, tibia and fibula.These Skiagrams matched the classical bone in bone or marble bone appearance.Whole exome sequencing confirmed the diagnosis of Autosomal recessive Osteopetrosis (ARO) type 1 pathogenic variant caused by mutation of TCIRG1 (T cell immune regulator) gene.Osteopetrosis is a rare genetic disease due to abnormal osteoclast function orsynthesis. It can be inherited by Autosomal dominant, Autosomal recessive or X linkedinheritance. AR Osteopetrosis is the malignant infantile or severe form. Life expectancy is less than 10 years. It is rare with an incidence of 1 in 2,50,000 live births Early genetic diagnosis of this complex condition is needed as beyond 10 months age severely reduced marrow space leads to greater failure rates of HSCT. Gene therapy and in utero HSCT are some of the futuristic interventions. Our case was managed with regular blood transfusions and a ventriculoperitoneal shunt surgery.

Keywords: dense bones; Autosomal recessive osteopetrosis type 1; TCIRG 1gene mutation; HSCT

2yr old boy born out of a 2nd degree consanguineous marriage presented with failure to thrive and increasing head size. He had a birthweight of 2.5kg and otherwise uneventful birth history.He had delayed milestones with dolichocephalic head, frontal bossing, prominent superficial veins. There was squint and setting sun sign. He had marked pallor and hepatosplenomegaly. His elder sibling was normal and there was no family history of similar illness.

Complete blood count showed Hb 6.3gm%, Retic count 0.75%, TLC 6100, platelet count of 50,000. Hb electrophoresis was normal. Liver function tests and kidney function tests were within normal limits.Skiagram of skull showed unusually thickened calvarium. Chest X Ray showed dense thickened ribs. Limb X rays showed dense, abnormally shaped femur, tibia and fibula. These Skiagrams matched the classical bone in bone or marble bone appearance. Echocardiography showed a small peri membranous VSD. Non contrast CT brain showed obstructive hydrocephalus due to aqueductal stenosis with exceptionally thickened calvarium. MRI Brain showed obstructive hydrocephalus with extensive venous collaterals along scalp.The patient was clinically diagnosed as osteopetrosis.

Whole exome sequencing further confirmed the diagnosis of Autosomal recessive Osteopetrosis (ARO) type 1.This was a pathogenic variant caused by mutation of TCIRG1 (T cell immune regulator) gene.

Osteopetrosis is a rare genetic disease due to abnormal osteoclast function or synthesis. It can be inherited by Autosomal dominant(AD), Autosomal recessive(AR) or X linked inheritance. AR Osteopetrosis is the malignant infantile or severe form. mutations in TCIRG1, CLCN7, OSTM1, SNX10 and PLEKHM1 lead to osteoclast-rich ARO (in which osteoclasts are abundant but have severely impaired

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resorptive function), whereas mutations in TNFSF11 and TNFRSF11A lead to osteoclast-poor ARO. In osteoclast-rich ARO,as in our case, majority are due to TCIRG1 mutation[1,2,3,4,5]. Here, abnormal osteoclast ruffled-border development due to poor endosomal and lysosomal transportation prevents bone and mineralized cartilage from being reabsorbed. Life expectancy is less than 10 years. It is rare with an incidence of 1 in 2,50,000 live births[1]. It is characterized by dense, abnormally shaped bones. The “Erlenmeyer flask” deformity is evident at the ends of long bones; A “bone-in-bone” appearance most frequently is noted in the hand phalanges; “Rugger jersey spine” where alternating sclerotic and lucent bands give a striped appearance[2,3,4].There is narrowing of marrow spaces and skull foramina. This leads to bone marrow failure, compression of cranial nerves, breathing and feeding difficulties. Loss of vision, hearing and facial palsy is common. Extramedullary hematopoiesis leads to hepatosplenomegaly. Loss of function mutations in TNFSF11 and TNFRSF11A lead to disrupted osteoclast development and a condition of osteoclast poor osteopetrosis[5].

Intermediate autosomal recessive osteopetrosis is the result of a loss of function mutation in CAII, the gene responsible for the production of the carbonic anhydrase II protein.[3]

Autosomal dominant osteopetrosis is the result of the dysfunction of chloride channel 7 secondary to a dominant-negative mutation of CLCN7[4]. The autosomal dominant form is of variable severity and presents later in life. It is also known as Albers Schonberg disease or type 2 Osteopetrosis and is more common [2]. It is milder with an incidence of 1 in 20,000 live births. It may be asymptomatic or present with bony fractures and scoliosiswith a normal life expectancy.

Hematopoietic stem cell transplantation (HSCT) is curative with better results if done in early infancy[1,3]. Early genetic diagnosis of this complex condition is needed tooffer better treatment options and prevent complications. Beyond 10 months of age severely reduced marrow space leads to greater failure rates of HSCT [1]. Interferon gamma-1b is an injected drug designed to delay disease progression and is the only therapy specifically approved by the U.S. Food and Drug Administration (FDA) for the severe infantile form of the disease. It is not currently approved for the treatment of the noninfantile form of osteopetrosis and does not appear to help in adults.

Corticosteroids in low doses are prescribed to help with blood countsand stimulate bone resorption.

Physical and occupational therapy can help children develop motor and other skills.

Bone care may include casts, splints, or surgery to correct fractures and misshapen bones.Gene therapy and In utero HSCT are some of the futuristic interventions[1]. Our case was managed with regular blood transfusions and a ventriculoperitoneal shunt surgery. He was also given prednisolone 1mg/kg/day.

Fig 1a : 2yr old boy with dolichocephalic head with protuberant abdomen;Fig 1b setting sun sign

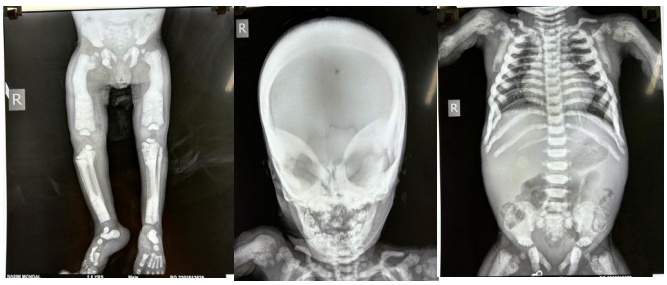

Fig. 2a : Skiagram of pelvis and lower limbs showing dense abnormally shaped bones, Erlenmeyer flask deformity in long bones , bone in bone appearance of metatarsals ; Fig 2b showing Skiagram chest with dense thickened ribs, bone in bone appearance in b/l humerus; Fig 2c showing abnormally thickened calvarium

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Impact of Simulation Based Training (SBT) on Healthcare Quality, Safety and Patient Outcome in a Subdistrict Hospital

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Abstract

Background: Lack of knowledge and training of health care providers (HCPs) in managing paediatric emergencies often lead to increased referral from subdistrict hospitals, even without proper stabilisation.

Methods: A quasi-experimental study donein a subdistrict hospital, to identify the gaps in health care quality and safety as per National Quality Assurance Standards (NQAS), arrange simulation-based training (SBT)for health care providers and analyse the effects of SBT on confidence, knowledge, attitude of health care providers and patient outcome.36 doctors and nurses were included in this study following convenience sampling. Multidisciplinary teams of six participants were trained every second weekly, from January to June in 2024 on management of common paediatric emergencies.

Results: SBT led to significant improvement in confidence, knowledge and attitude of HCPs in managing common paediatric emergencies [KP2]. Several system changes were implemented [KP3]. There has been 15% improvement in NQAS Hospital Score, p value <0.001 [KP4], decrease in hospital referral rate (9.43% to 6.61%) and mortality rate (2.46% to 1.23%) from January to June 2024 [KP4].

Keywords: Simulation based training, healthcare quality, safety, outcome, referral

Introduction:

Simulation-based training has been widely recognized for its effectiveness with regard to enhancing the knowledge, skills, attitudes and confidence of healthcare providers in managing high-stress situations across a variety of disciplines [1-4]. Beyond the level of individual development, in situ simulation-based approaches have also been identified as invaluable tools for assessing and optimizing the operational readiness of healthcare facilities. While human factors and ergonomics has gained recognition for its importance in healthcare quality and patient safety, existing evidence underscores its potential to enhance the quality of care and patient safety through healthcare system redesign. [5,6]

Aims:

1. Implement a SBT curriculum for HCPs to manage common paediatric emergencies
2. Assess the effectiveness of SBT in quality of patient care
3. Appraise the reduction in referral and mortality rates

Methods:

Study design: Quasi-experimental study

Period of Study: 6 months (January – June'24)

Needs assessment (December 2023): To identify gaps and plan activities as per National Quality Assurance Standards (NQAS)

Sampling: Convenience sampling

Inclusion criteria: Doctors and nurses available throughout the study period

Exclusion criteria: Not giving consent to participate

Setting: Labour room, Emergency room, ward

Ethical clearance: December 2023

Intervention: In situ immersive SBT for multidisciplinary teams with six participants was conducted every second weekly for two hours duration (two sessions per day), from January – June

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2024. Total 24 sessions were conducted. HCPs were trained to manage common paediatric emergencies encountered in a subdistrict hospital - Birth asphyxia, Supraventricular Tachycardia (SVT), Cardiac arrest, Septic Shock, Acute Severe Asthma,Transportation of sick child, Snake envenomation and breaking bad news.

Manikins: Little Anne, Baby Anne, Resusci Anne, Prestan Adult torso and infant with appropriate props, moulage, software and equipment to improve the realism of the simulation scenarios

Sample size: 36 learners, 16 doctors and 20 nurses after taking written consent.

Study tool: Pre & post-test questionnaire were filled up by the participants at the beginning and end of simulation sessions. There were 10 questions in each set assessing the knowledge, attitude and confidence of the learners based on how they manage the common emergencies in their workplace. Cumulative score in percentage was calculated.

NQAS Safety and Quality assessment: Data collected in December 2023 and June 2024 with Self-assessment tool for health facility (SaQushal) 2022 and cumulative score was calculated before and at the end of the study period [7].

Hospital records: Data on admission, discharge, referral and death were analysed.

Statistical analysis:

The categorical variables are presented as frequencies and percentages. Fisher's exact test was used to analyse contingency tables. For all results, p value < 0.05 was considered statistically significant.

Results:

Various system changes have been implemented and alteration in behaviour of HCPs was noted following the SBT [KP3] as shown in Table 1[8].

Significant improvement has been noted in the knowledge, attitude and confidence of the health care providers [KP2] after SBT, depicted in Table 2.

Table 1. : Implementation of System Changes [KP3]

Table 1. Scenarios of SBT	System Changes Implemented (KP3)
1.Birth asphyxia	Newborn resuscitation corner
2.SVT	Defibrillator machine, Crash cart
3. Cardiac arrest	CPR board, Step stool & CPR form
4.Septic shock	Code blue team and Rapid response team
5.Acute Severe Asthma	SBAR handover
6.Transportation of sick child	Transport team and Transport Kit
7.Snake envenomation	AVS, Atropine & Neostigmine available at ER
8.Breaking bad news	Counselling room & Counselling form, SPIKES

Table 2 : Improvement in confidence, knowledge and attitude of healthcare providers [KP2]

Table 2. Cumulative score (%)	Pretest	Post test	1 m Post test	Gain (%)	
Confidence [KP2]	31.6	85	80	53.4	48.4
Knowledge [KP2]	30	86.6	83.3	56.6	53.3
Attitude [KP2]	33.3	83.3	78.3	50	45

There has been 15% improvement in NQAS Hospital Score, p<0.001 [KP4] as shown in Table 3.

Table 3. Improvement in NQAS Hospital score [KP4]

Dec 2023 (Before SBT)	June 2024 (After SBT)	p value
50 %	65 %	<0.001

A gradual decrease in hospital referral rate (9.43% to 6.61%) and mortality rate (2.46% to 1.23%) was noted from January to June 2024 [KP4] as shown in Table 4.

Discussion:

There was a significant improvement in knowledge, attitude and confidence of the doctors and nurses in managing sick patients in the hospital.

There was a significant improvement in their behaviour as indicated by the system changes that were incorporated in their daily practice and reflected by the improvement of NQAS score at an interval of 6 months.

To our knowledge, this was the first study of its kind,done in a subdistrict hospital in India, to implement and utilize SBT for the improvement of quality and safety of health care facility and to assess its impact on knowledge, attitude, practice and behaviour of HCPs and patient outcome.

Conclusion:

SBT led to significant improvement in confidence, knowledge and attitude of HCPs, improvement in healthcare quality and safety scores and decreased referral and mortality rates, though it can be multifactorial.

Table 4 : Decrease in hospital referral and mortality rates [KP4]

Table 4	Jan	Feb	March	April	May	June
Admission	933	1062	1255	1295	1307	1300
Discharge	773	904	1084	1170	1162	1096
Referral (%)	88 (9.43)	81 (7.63)	95 (7.57)	66 (5.1)	82 (6.27)	86 (6.61)
Death (%)	23 (2.46)	20 (1.88)	20 (1.59)	24(1.85)	25 (1.91)	16 (1.23)

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Early Literacy Promotion

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There is a significant relationship between literacy and health. Literacy is a powerful determinantof health and well-being throughout life of an individual. The life-long health of an individual is more strongly correlated with literacy than with occupation or income (1, 2).

Low literacy is associated with chronic illness, low physical and mental health and high rates of acute health services use (1). It has a significant effect on the children as they age. Poor academic skills are consistently correlated with higher dropout rate, unemployment and entrance into juvenile justice system. Adolescents with low reading ability are more likely to smoke, use alcohol, carry a weapon and engage in a physical fight (3). On the other hand, higher level of literacy is associated with positive health outcome like appropriate use of inhaled asthma medication or choosing to breastfed a baby. So, early literacy promotion should be a practical focus for anticipatory guidance in a pediatric health care setting. This article aims to describe what early literacy means and how it can be promoted, and also to help health care providers to assess and incorporate literacy promotion into their everyday practice.

What is early literacy?

Early literacy is what children know about reading and writing before they actually learn to read and write. It is not teaching reading or drilling with using flash-cards. Instead, it is laying foundation, so that the children gain necessary skill when they are developmentally ready to read. Early literacy has been defined as "the skills, understandings and attitudes that young childrendemonstrate before they are able to control conventional forms of reading and writing" (4).

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Basically, babies develop in an environment of relationship. It is the parent-child relationship which most strongly affects emotional and behavioral functioning (5). Foundation of early relationship is built by "serve-and return" interaction – like responding with a smile and encouraging words when babies bubble. It is strengthened through close attention to babies' cues and by speaking, singing and reading with children from birth (4). These same interactions also help to promote early literacy skills.

Language and Literacy

Language is a system of sounds, gesture and experiences that people use to communicate with each other. It is the ability to both use and understand spoken words or signs. It is all about ideas passing from one person to another and also includes the ability to use and understand written words or symbols to communicate. Whereas, early (or emergent) literacy may be described as "those behaviors shown by very young children as they begin to respond to and approximate reading and writing acts".

Development of Language Learning

Language development starts with sounds and gestures and then includes words and sentences. Children learn about language long before they speak. Conventionally, language skill can be divided into receptive (learning and understanding) and expressive (talking) abilities. Receptive language generally precedes expressive language.

The normal newborns demonstrate preferential response to human voice over inanimate sounds. They recognize the mother's voice reacting stronger to it than to a stranger voice. By 4 months of age infant can distinguish their own native language from rhythmically similar ones (6). By 6 months of age, infants can passively follow the adult's line of visual regard, resulting in a joint reference to the same

object and events in the environment (7). By 9 months of age, infants selectively respond to their names and appear to comprehend the word, "no". At about 1 year of age, children begin to understand that pictures represent real objects. From 12 months onwards, children's understanding of language meaning gradually increases. At about 2 years of age, by studying the sounds and words around them, the children can follow a 2-step command and also can utter two-word combination phrases. Thereafter a dramatic increase in the language use occurs. At about 3 years of age the children may retell familiar stories and at 4 to 5 years of age they can start to recognize letters and their sounds (3). Milestones of the language development are the same for children who learn more than one language.

When the children are exposed to more than one language, they may split their time and attention unequally between them. They hear fewer words and sentences in each than monolingual peers. But when combined across languages, the size of their vocabulary is usually equal to or greater than that of children learning one language.

Promotion of early literacy

It is evident from several studies on early brain development that reading aloud, speaking to babies, singing and sharing books can permanently change neuronal connections in the brain. Early literacy development happens when adults are reading, speaking, or singing with babies and children-regardless of the language or skill level of the adult (4).

Recent research has suggested that infant-caregiver relationship alters the expression of the gene responsible for regulating emotions and stress through an epigenetic change. In the similar way, all these early experiences may be embedded in our brains and produce long lasting change in our behavior.

The architecture of developing brain is physically altered by experiences during infancy. At birth, a baby's brain contains 100 billion neurons which make trillions of connections. Those connections that are stimulated by frequent use persist and less used synapses are eliminated as the brain matures.

Benefits of reading :

Reading aloud may help in preservation of neuronal connections associated with skills such as memory, creativity, comprehension and language. Reading aloud exposes children to vocabulary they do not hear in daily conversation. It also stimulates imagination. In time, children learn that the abstract letters on the page represent words, and they become aware of different smaller sounds that make words. All these experiences result in reading readiness.

Benefits of speaking :

Day to day experience with spoken words is important, because the more the infant hears about what they are looking at and attending to; stronger their overall comprehension becomes (8). Until recently, it was believed that the number of words babies hear was key to growing vocabulary. However, newer researches support conversational turn-taking, especially between 18 to 24 months as more important mechanism for language learning. Responsive back-and-forth (serve-and-return) interaction is more important than words quantity (9).

Benefits of story-telling :

Conversation with very young children about shared experiences strongly enhances early literacy. Toddlers learn about stories when a parent or other caring adult describes a shared experience (10). They watch the story teller's face, collaborate with nodding or repeat a word to show interest or to keep the teller engaged, and respond with emotion. For emotional reason, children want to hear the same story over and over again. Repetition allows them to internalize the story and master its pieces.Most children aged 24 to 30 months know the rudiment of storytelling. They can sequence events (in varying degrees), set an action in place and time, and organize a story around a central character (often themselves).

Stories also help the children to become acquainted with their own and other culture. Storytelling enhances the social elements of language (e.g. making polite request, greeting people, giving and receiving compliments, apologizing, using an appropriate tone of voice and volume for different environment etc.). Stories should be told directly and expressively (i.e. with vocal intonation, gestureand facial expression and body movements). Young listeners often better understand a story when it is told than when it is read (11).

Benefits of book-sharing :

Reading aloud together appears to stimulate cognitive development more than other family activities. Shared reading is focused and immersive and involves frequent interactions resulting in rich language exposure which enhances language development (2).

Frequent mother-child book reading at home supports vocabulary and oral comprehension development in young children. Mother tends to talk more with their children while book sharing than in other family contexts. Book sharing with children at any age helps to instill love of reading (12).

By conversing with infants and toddlers while book sharing, parents can enrich learning by adding language-building strategies like-

- Serve and return
- Dialogic reading- asking questions to encourage a child's participation in story reading
- Child-directed speech- exaggerating relevant phonetic differences

Early, routine and quality book sharing has significant relational benefits for both infants and parents.

For infants – Shared reading has been linked to mother-child attachment security (12). Frequent quality book sharing appears to promote secure attachment, sustained infant attention and enhance prosocial behavior.For parents– There are studies to show that shared reading is associated with improved parenting style, reduced maternal depression and stress level, enhanced parentalsense of competence and self-esteem (13).

Bedtime reading –There is strong evidence to suggest that reading at bed time should be incorporated in daily family routine (17). Ideally, bed time reading should begin from birth because of its positive effects for child sleep and child mother relationship (13, 17). Reading to infants from birth also provides bonding opportunities for siblings, non-breast feeding parents and fathers and also positive cognitive outcome (2).

Printed versus e-book – Sharing printed books teaches early literacy and language skills and promotes relational bonding better than e-books (12).

Benefits of singing :

Many parents may not consider shared reading to be a favorite activity in the newborn period but they may enjoy singing to their newborn. Singing appears to increase infant attention via pitch contour and tone. Singing is similar to rhyming. For infants, rhyme and rhythm may resonate even more than speech. Their simple repetitive structure and sound may promote early language development (14). It has been suggested that rhythmical exercises and combining rhythm and song lyrics in children's play help prepare brain to learn to read and write (15).

Communal musical activities (like gathering to sing at a play-school center) encourage attentive listening and holding pattern which helps to develop reading skills. Children's songs can teach language and basic spelling patterns, rhyming, sentence pattern and parts of speech. They also help to develop new vocabulary and a sense of story and sequencing. Using singing and movements together helps to develop pre-reading skill (like letter sound, middle sound of a word). Music can be an entry point to a new language for children, who may be more socially comfortable singing along than speaking out (16).

Can we make a difference?

Early literacy promotion may be included as an essential part in the routine care ofinfants and toddlers. Pediatricians can talk with the parents about the benefits of speaking, reading and singing with their children from birth in any context or situation. It can be done in well child visit, during hospitalization or in office practice. By providing information to families about brain development and serve-and return interaction, pediatrician can reinforce how everyday action by parents can make lasting and positive difference for children and families.

Specific recommendations (4)

1. Promote literacy with the families early, even before the child is born.
2. Inquire regularly about the barriers that may interfere with one-to-one time with young children like digital media exposure, use and access.
3. Describe simply and clearly about the nature and purpose of early literacy (admitting that there are multiple forms of literacy and multiple pathways for promoting early literacy).
4. Incorporate books into well-child visits whenever possible. A developmentally and culturally appropriate book may be gifted to patients and parents. Model how book sharing helps babies

build relationships with both the parents and books.

5. Link literacy milestones to other developmental milestones (e.g. when their babies mouth their first book, use a pincer grasp to turn pages or sit independently to hold a book).
6. Create a language rich-environment in examination/waiting room using books, posters or other tools that promote communications between parents and children.
7. Help families to develop literacy promoting habits by assessing parent's own comfort level with reading aloud, and encourage those who lack confidence or skillto sing, talk and tell stories.
8. Encourage families about daily book sharing – making it a healthy family routine (e.g. at bed time).
9. Encourage families to tell stories, speak and sing in their home language.
10. Advocate availing community resources for literacy support like admitting to early years center (pre-school/play school).

Conclusion

Early literacy promotion in office setting should be an essential part of pediatric primary care. The primary care setting is the ideal venue for literacy promotion. Suggestions in support of literacy promotion may be incorporated into the advices about growth and development which the parents are receiving in routine health visits. Studies show that parents who received one book (from health professionals) were much more likely to read aloud to their children and report reading as a favorite activity of their children. The effect was greatest for poorest families. Medical professionals who promote literacy providing books and advices will build stronger bonds between health professional and family.

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A Case of Kyphoscoliosis And Bilateral 6th Nerve Palsy

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Abstract: Horizontal gaze palsy with progressive scoliosis (HGPPS) is a disorder that affects vision and also causes an abnormal curvature of the spine (scoliosis). People with this condition are unable to move their eyes side-to-side (horizontally). As a result, affected individuals must turn their head instead of moving their eyes to track moving objects. Up-and-down (vertical) eye movements are typically normal. In people with HGPPS, an abnormal side-to-side curvature of the spine develops in infancy or childhood. It tends to be moderate to severe and worsens over time. Because the abnormal spinal alignment can cause disfigurement and interfere with movement, it is often treated with surgery early in life.

Introduction:

Congenital bilateral 6th nerve palsy due to hypoplastic bilateral 6th nerve at pons and associated faulty crossing of pyramidal fibers controlling the trunk leading to kyphoscoliosis is very rare and under the influence of neuronal migration guiding protein ROBO3. We present a similar case on a 14-year-old girl who underwent corrective spine surgery due to kyphoscoliosis at our Hospital.

Case Summary:

A 14-year-old girl born out of consanguinous marriage presented with severe back pain and inability to turn her eye in lateral gaze since birth. She has no impairment of higher function and academic performance in school is average. But outdoor activity is restricted due to her kyphoscoliosis and Back pain.

On examination:

She is conscious, cooperative, alert but her lateral gaze is impaired on both sides (Fig. 1). She can move both eyes upwards and downwards in conjugate fashion(Fig 2). She has preserved near vision and convergence. Higher function is intact. She can walk independently but with low speed. Kyphoscoliosis (Fig. 3) is significant with Cobb angle of 41 degrees (Fig. 4). MRI brain showed butterfly-shaped medulla in axial section (Fig. 5) and hypoplastic pons (Fig. 6).

Genetic test by clinical Exome sequencing showed mutation of ROBO 3 gene in chromosome number 11. (Fig.7)

She was operated for Kyphoscoliosis by orthopedics department, and post op period was uneventful .

Discussion :

A horizontal gaze requires the lateral rectus muscle of one eye, innervated by the abducens nerve, and the medial rectus muscle of the contralateral eye, innervated by the oculomotor nerve, work together. This coordinated activity is controlled by the abducens nucleus and MLF. The absence of the abducens nucleus and non-decussation of MLF fiber leads to the classic clinical finding of bilateral horizontal gaze palsy.

The mechanism of the scoliosis aspect is less clear, but it may result from a lack of normal contralateral pathways to spinal muscles.

Crossing of Corticospinal axons across the midline in the medulla forms the basis of contralateral motor control and formation of medullary hump on medulla. No decussation leads to deformity like butterfly medulla.

ROBO 3 gene is located in chromosome 11q23 responsible for midline crossing of hindbrain axons.

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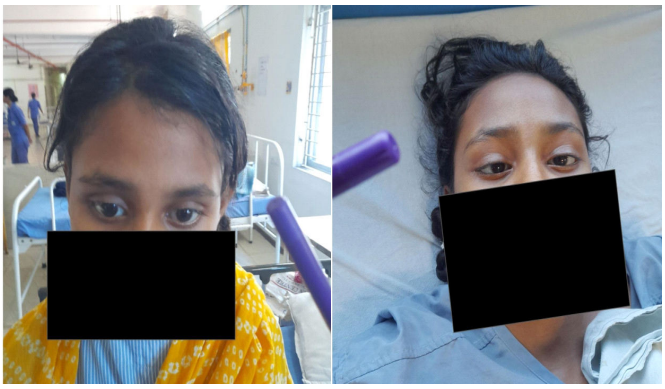


Fig 1- Rt and left gaze impaired

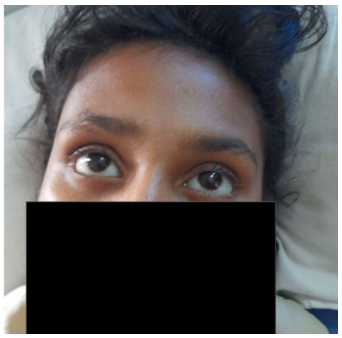


Fig 2- Upward gaze intact

Fig 3- Kyphoscoliosis

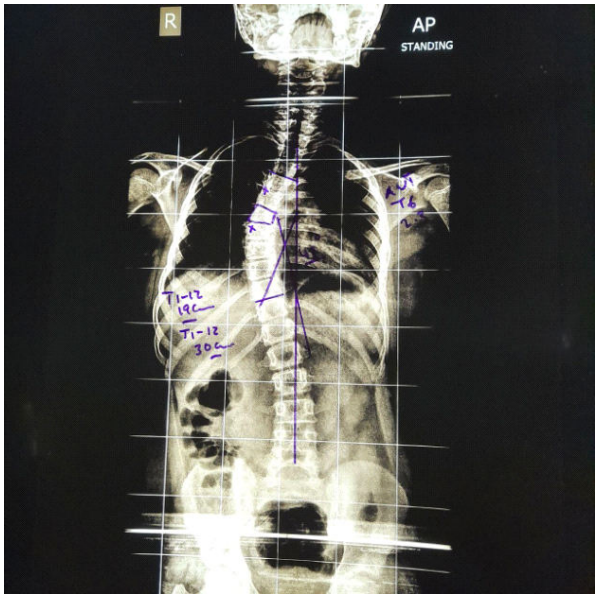


Fig 4: Cobb's angle =41 °

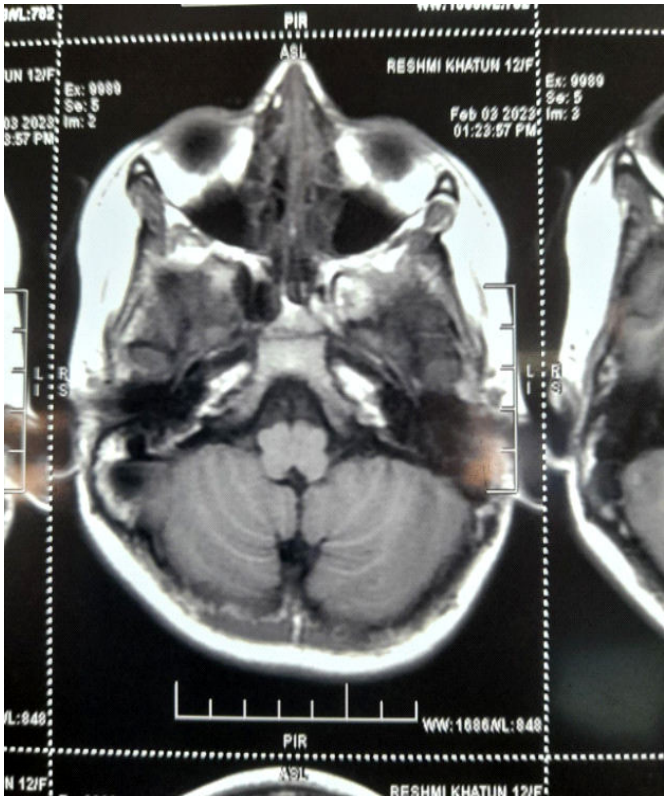


Fig 5: Butterfly medulla

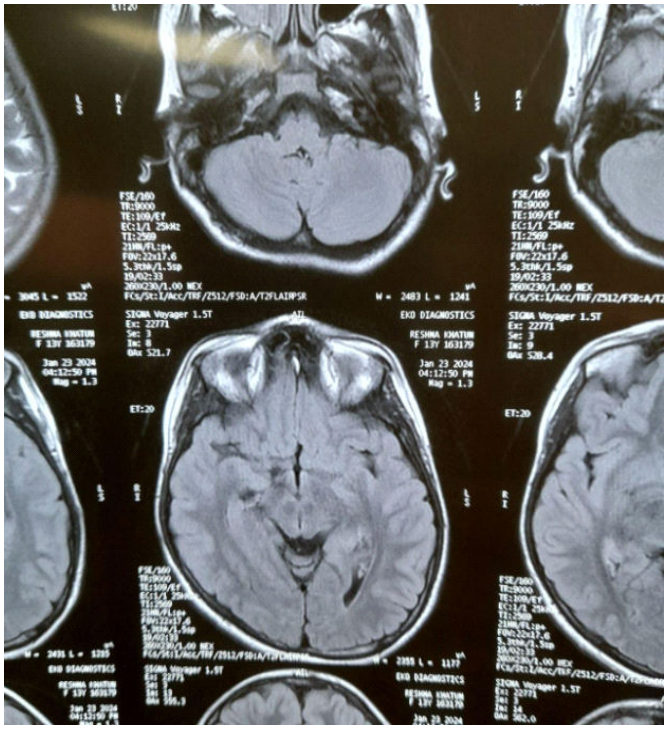
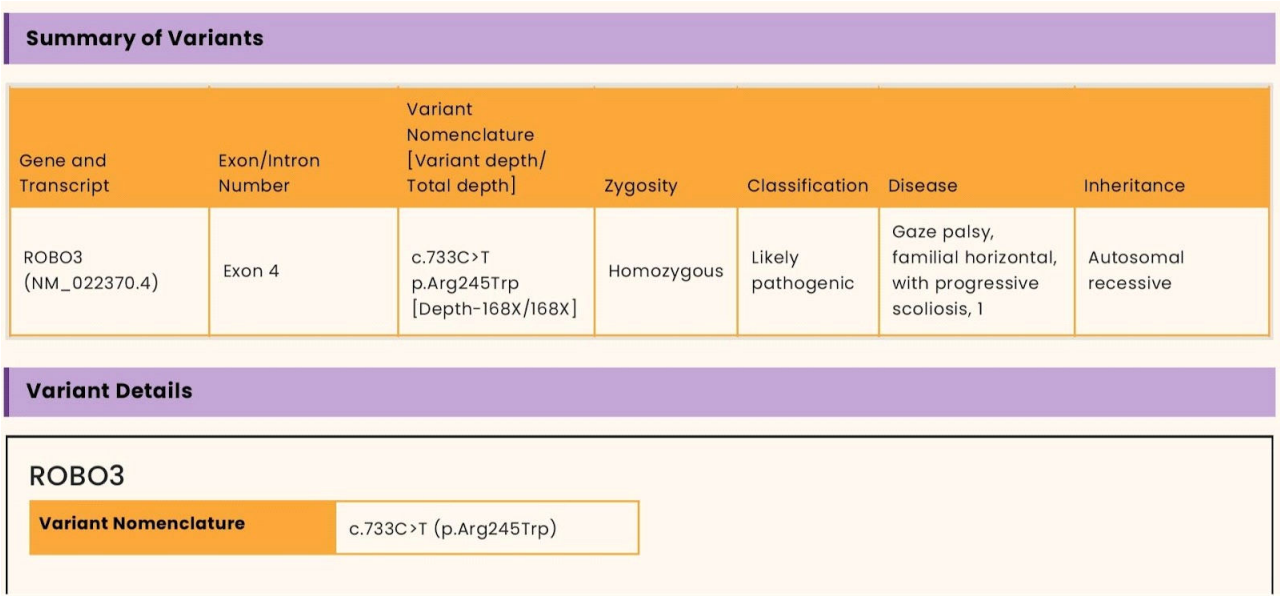


Fig 6: Hypoplastic pons



Summary of Variants

Gene and Transcript	Exon/Intron Number	Variant Nomenclature [Variant depth/ Total depth]	Zygosity	Classification	Disease	Inheritance
ROBO3 (NM_022370.4)	Exon 4	c.733C>T p.Arg245Trp [Depth-168X/168X]	Homozygous	Likely pathogenic	Gaze palsy, familial horizontal, with progressive scoliosis, 1	Autosomal recessive

Variant Details

ROBO3

Variant Nomenclature	c.733C>T (p.Arg245Trp)

Fig 7: Clinical exome sequencing

The ROBO3 gene provides instructions for making a protein that is critical for the normal development of the nervous system. The protein is active in the developing spinal cord and in the brainstem, a region that connects the upper parts of the brain with the spinal cord. In the brainstem, the ROBO3 protein helps direct nerve cells (neurons) to their proper positions in a process called neuronal migration. The protein also helps guide the growth of axons, which are specialized extensions of neurons that transmit nerve impulses throughout the nervous system. Some axons are very long, connecting neurons in the brain with those in the spinal cord and elsewhere in the body.(1,2,3)

For the brain and body to communicate effectively, certain bundles of axons must cross from one side of the body to the other in the brainstem. These include axons of motor neurons, which transmit information about voluntary muscle movement, and axons of sensory neurons, which transmit information about sensory input (such as touch, pain, and temperature). The ROBO3 protein plays a critical role in ensuring this crossing of motor control during brain development. (4,5)

Conclusion: Early diagnosis of HGPPS can prevent development of kyphoscoliosis and its complication.

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Declaration of competing interest: no conflict of interest , **Consent:** Taken

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