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JOURNAL COMMITTEE

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From The Editor's Desk...

Orissa Journal of Pediatrics is the official Journal of Indian Academy of Pediatrics, Orissa State Branch. It has seen a lot of ups and downs with the growth and stagnation of the State Branch. The Infant mortality rate as well as the Neonatal mortality rate of the State is decreasing at pace with the national figures but still we are left with the second highest figure next to Jharkhand. Infectious diseases are rampant in Pediatrics. The situation has improved much in the costal districts and industrial townships but the tribal areas have witnessed the worst ravage from cholera last year. Health facilities getting adequate day by day with wide gap in distribution. Health in private sector is ready to provide facilities of National and International standards but watershed areas even do not have the approach to minimum health facilities. Added to the problems is the consumer protection. Law views life with at most respect and to keep it going anything and everything possible over the earth is deemed to be done. In contrast a large segment of our community is unable to spend on edibles. Government is in no way ready to subsidies the total health expenditure of all individuals. This keeps a health professional in tight hands. Knowledge to manage and save life is not deficient but the resource to do the same is not available. The confusion of legal, moral and ethical concerns made our hands tight culminating in unnecessary referrals and over crowding of the referral canters with its ultimate negative out come. Compounding the terrible situation is the apex Govt. institutions where accountability only exits in pen and papers. The culminating effect for a poor man is to land up in a no mans land for medical help. Private areas are so costly that they remain unapproachable.

In this scenario the class of physicians affected most are the Pediatricians who care for an unproductive segment of the society, for whom family budget is at the lowest minimum but emotional overplay is maximum. With each loss of a newborn or child the county also looses maximum mean serving age for life expectancy is going high as on today. Multiple training sessions were undertaken and being undertaken exposing Pediatricians, general practitioners and paramedicals in child survival but the results are not very encouraging. Some where something is not correct. May be we feel the negativity but no word to express it. The very approach of training those who are already trained and repeatedly train them in subjects that they can not reproduce is becoming counter productive. What USA is doing today with its newborns with such an expansive Health network if we try to reproduce it over here may be it is bound to fail. In spite of chasing the care providers if we could have tracked the beneficiaries we might have been more successful. We provide them what we feel to be their need but the ground reality may be something different and with the cumulative experience one can vow for the later.

Let the grass root Pediatrician take his decision as to what best can be done to protect children in his territory. Let him fix his goal. Let all agencies help him in achieving his goal. IAP with its mammoth membership should open the way and leap forward to unify public with Govt. initiatives and other organizations working for children.

Gadadhar Sarangi
The Editor

ANNUAL REPORT IAP ORISSA 2009

Dr. A.B. Nayak, *Secretary*

Dear friends I thank all of you from the core of my heart for your cooperation and timely advice. I am indebted to our President Dr. G.B.Nanda and Treasurer Dr. Prasant Saboth for their timely guidance and help. I am also thankful to all the Executive members, Dr. Gadadhar Sarangi, our ex. President, Dr. Niranjan Mohanty, our central executive body member and the IAP Khurda team for their advice and cooperation throughout the year for organizing all the academic activities. The events organized during the year – 2009 are-

1. **State IAP NNF Conference**:-

   State IAP NNF Conference was held on 11th April 2009 at Hotel Suryansh, Bhubaneswar. Mrs. Manorama Mohapatra, Editor, the Samaja, inaugurated the Conference and urged the pediatricians to treat the children as own. Various topics were discussed in the academic fiesta. My heartfelt thanks to Dr. Sailaja Nandan Parida, President and Dr. Arikhit Swain, Secretary of NNF ,Orissa chapter as well Dr. Arijit Mohapatra, Organising Chairperson and Dr. Biswajit Mishra, Organising Secretary of the conference for successfully conducting the event.

2. **Midterm CME on Basic Pediatrics:** - The CME was conducted under the stewardship of Dr. Gadadhar Sarangi, Prof. Pediatrics, Hi-Tech Medical College, Bhubaneswar on 12th July 2009. 17 topics were discussed by in and out house resource persons. The outhouse resource persons were Dr. Amar Verma, Dr. K.K Ghosh, Dr. Sabitri Bhagat and Dr. Tapan Ghosh.

3. **Workshops**: - Ganjam District branch conducted a workshop on "Childhood Asthma" in MKCG Medical College, Berhampur on 9th June 2009. It is the only branch to conduct a workshop this year. I salute the branch.

4. **ORS Day & Week Celebration: -** All the district branches of IAP celebrated the ORS Week from July 23rd to July 29th in schools and hospitals as well in medical colleges.IAP Orissa State & Khurda branch jointly celebrated the ORS day in Shantipalli slum, Shaheed Nagar, Bhubaneswar. The function was presided by Sj.Ananta Narayan Jena,Mayor, Bhubaneswar Municipality. Dr. Arabinda Mohanty, Secretary, IAP Khurda District Branch spoke on management of diarrhoea and importance of ORS. Dr. Reddys Lab Pharma Company helped IAP, Orissa to celebrate the week. I sincerely thank the organizing personnel of all branches for celebrating the week and Dr. Reddy's lab for its generosity for the cause of children.

5. **World Breast Feeding Week:** - All the district branches celebrated the week in their respective places and stressed the beneficial effects of breast feeding. A joint celebration of the week by IAP Orissa & IAP Khurda branch was organized near Bhagabanpur High School, Patrapara on 1st August 09. Mrs. Anu Garg IAS, the commissioner cum principal Secretary, Health and Family welfare, Govt. of Orissa, Director of Family Welfare, Deputy Director. Nutrition and representatives of NRHM, UNICEF, CARE INDIA and State Council for Child Welfare and State Social Welfare Board attended the function. The Secretary spoke on Govt's commitment to breast feeding. Dr. Arabinda Mohanty, convenor, Orissa IMS act cell discussed on importance of Exclusive Breast feeding and IMS act. Other dignitaries also spoke on the occasion. It was followed by a quiz competition amongst young mothers. Later, local health workers and villagers staged a play on breastfeeding.

6. **PALS COURSE for doctors**: - It was conducted at SVPIPGIP, Sishu Bhawan, Cuttack on 28th & 29th August 2009 under the guidance of Dr. Niranjan Mohanty HOD Pediatrics, SVPIPGIP & SCB Medical College. Dr. Bishwajit Mishra and Dr. Arakhita Swain were the Zonal & local Co-ordinator respectively. Certificates were distributed to successful candidates by the Organising team. I thank the organizers for the event. Dr. G. B. Nanda President IAP Orissa State Branch & Prof. Dr. Chinara, Principal, SCB Medical College, Cuttack inaugurated the PALS course.

7. **PALS COURSE for Nurses-** It was conducted for the first time in Orissa under the co-ordinatorship of Dr. Bishwajit Mishra at Hi-Tech Medical College, Bhubaneswar. 40 Nurses attended it and the successful candidates were given certificates by the Organising team. I congratulate Dr. Bishwajit Mishra for conducting the event for the first time in Orissa & East Zone. President IAP Orissa Dr. G. B. Nanda formally stared the course.

8. **IAP QUIZES**:-IAP Quiz 2009 for Undergraduate & Post Graduates, both college and divisional round were conducted successfully along with NNF Neonatology PG Quiz under the leadership of Prof. Dr. Niranjan Mohanty on 17th September 2009 and 10th October 2009 respectfully at SCB Medical College Cuttack. President Dr. G. B. Nanda, Secretary Dr. A.B. Nyayk & Treasurer Dr. Prasant Saboth of IAP Orissa State Branch, divisional coordinator Dr. JN Behera, Neonatalogy PG Quiz coordinator Dr. Atul Samal, President NNF Orissa, Professors from SCB Medical College, SVPIPGIP, Sishu Bhawan, Hi-tech Medical College, KIMS, IMS were present in the programme. IAP thanks to Prof. Dr. Niranjan Mohanty for conducting it successfully.

9. **Participation of State IAP in activities of Govt. and other organizations-**

- IAP President Participated in two State level meetings of Govt. of Orissa on "Management of Swine Flu infection. The Meetings were presided by Hon`ble Chief Minister of Orissa.
- Prof. Niranjan Mohanty and Dr. G. B. Nanda attended IAP zonal workshop on "Advance Vaccinology "in Kolkata.
- President IAP participated in State level meeting on introduction of MMR Vaccine in National immunization schedule.

10. **IAP Orissa State Branch Secretariat & Guest house**:-A piece of land was purchased at Patia Chhack, Bhubaneswar in February 2009 for IAP.

A memorandum of Understanding was signed with IMA, Bhubaneswar on 29th July 2009 to permanently occupy the 3rd Floor (2400sqft) of IMA house, near Capital Hospital, Bhubaneswar, to use as IAP State branch Secretariat & IAP guest house. The building is expected to complete by the end of 2009. IAP Orissa State branch will have its own Secretariat & guest house.

11. **Growth Development & Behavior Disorder (GDBD) Chapter: -** I congratulate Prof. Dr. S.N. Parida being elected as National President of Growth Development & Behavior Disorders subspecialty chapter of Indian Academy of Pediatrics. It is pride for IAP Orissa State Branch.

12. **IAP Neocon-2009:-** Indian Academy of Pediatrics, Orissa State Branch is hosting the 2nd National Conference of IAP Neocon-2009 from 06.11.2009 to 08.11.2009 with the conference theme **"Every Newborn – Our Responsibility"**. I congratulate Dr. Arjit Mohapatra and Dr. Bishwajit Mishra, the Organizing Chairman and Secretary & their Organising team for successfully conducting it.

Long live IAP. Long live IAP, Orissa State Branch.

AUDITORS REPORT

INDIAN ACADEMY OF PEDIATRICS (IAP)
ORISSA STATE BRANCH
KANAN VIHAR , PHASE - I , BHUBANESWAR

RECEIPT & PAYMENT ACCOUNT FROM
2ND DECEMBER 2008 TO 2ND NOVEMBER 2009

	RECEIPTS	AMOUNT (RS.)		PAYMENTS	AMOUNT(RS.)
To	Opening Balance			Internet Charges	7,153.00
	Cash in Hand	1,720.79		Computer Peripherials	4,250.00
	Cash at Bank	526,233.95		Postage & Courier	11,743.00
	Term Deposit	27,126.00		Printing & Stationery	4,869.00
				Salary	21,000.00
To	Donation from Pharma Co.	79,660.00		Mid-term CME Conference	63,866.00
				EB Meeting Exp	23,921.00
To	New Membership Fees	10,500.00		Gold Medal & Mementos	42,312.00
				Bank Charges	220.00
To	Interest Received	41,514.00		Travelling Expenses	22,330.00
				Telephone Expenses	10,642.00
To	Deligation Fees-12/07/2009	8,400.00		Orissa State Pedicon	29,660.00
				Website Expenses	19,500.00
To	Orissa State Pedicon-2008	25,000.00		Orissa Journal	20,000.00
				Election Expenses-2009	10,000.00
To	Election Fees	4,500.00		IAP Quiz Expenses	12,332.00
			By	Closing Balances :	
				Cash in Hand	446.79
				Cash at Bank	20,409.95
				Term Deposit	400,000.00
		724,654.74			724,654.74

Place : Bhubaneswar
Date : 3rd November 2009

For DWEIPAYAN DAS & CO.
Chartered Accountants
Dweipayan Das
Dweipayan Das
Proprietor

HAIR CHANGES IN MALNUTRITION

Gadadhar Sarangi*, B. K. Mohapatra **, Swarnalata Mohapatra ***

Abstract :

Protein Calorie Malnutrition is rampant in the developing world. The growth and form of hair is affected as a part of the generalized growth retardation. Under scanning election microscope irregularity of the hair tip, niche formation under the crests of wavy nodal lines, linear brakeage in the shaft and herniation of the hair material through the lateral wall are observed.

Key Word :

Protein Calorie Malnutrition (PCM), Marasmic-Kwashiorkor, Scanning Electron Miscoscope.

Introduction:

Hair is a cutaneous appendage typical of human skin. In the evolutional process it has lost most of its protective functions in human beings. The scalp hair and eye-lashes retain the property of protection to some extent. Thus human race becomes the least hairy mammal on earth. Tactile perception is one of the important minor functions it serves because of its rich nerve net-work.[1]

Hair is formed of hard keratin with high sulphur content that is responsible for its extraordinary tensile strength.[2] The Cortex is made up of a low sulphur fibrillar component tightly packed in a sulphur rich matrix. The fibrillar component consist of macrofibrills of 7 nm thick, arranged in a longitudinal laminated form which on cross section gives a thumb print appearance.[3] In Malnutrition the amino acid contents in the hair changes. The cysteine content was reported to be significantly less and correlates with the degree of malnutrition.[4]

Protein Calorie Malnutrition (PCM) is a condition, which results from deprivation of protein and calorie from the diet. Marasmus and Kwashiorkor are two extreme states of PCM, the former resulting from predominant calorie deficiency while the later from protein deficiency. Because of the non-availability of protein or protein getting utilized for calorie the growth and repair of body gets affected and consequently the growth and texture of hair also gets affected in these conditions.

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The slow growth rate of Marasmic Child slows down the hair growth. The main changes are of texture and a lack of pliability, giving rise to rough, lusterless, straight hair that can be easily pluckable and is brittle. [5] In marasmus the hair is fine and dry, the diameter of the hair bulb is reduced to a third of normal and almost all follicles are in telogen. [6] Johnson and his colleagues reported significant difference in shaft diameter, percentage of anogen and telogen between well nourished and severely Malnourished children. As it is not suitable to asses different grades of PCM the method was not recommended for PCM assessment is field conditions. [7]

In Kwashiorkor the hair is sparse, thin, brittle, wavy and silky or shows a mixed picture with rough and standing hair as in marasmus. The degree of hair loss varies from mild to serve. Hairs are easily pluckable but the hair growth rate is adequate. The colour may be golden, blondy, rusty or light brown. The colour changes may be generalized or patchy. Black hair turns brown and brown hair turns blonde. The hair grown during the period of malnutrition is pale, therefore alternate bands of dark and pale hair are seen in a single strand (Flag sign) [5]. The hair may be prematurely gray or show a "pepper and salt" appearance and become sparse, fine and brittle. The hair shafts may show constrictions which increase their vulnerability to trauma. In kwashiorkor the hair follicles are more in anogen although most are atrophic [8].

In moderate to severe PCM the morphological charges in scalp hair include reduction in diameter of the hair shaft, bulb and medulla. The medulla may even be absent. [9,10] In both the forms of PCM hair is brittle and easily shed and partial or complete alopecia may occur. The hair is lusterless and if normally black, may assume a reddish tinge. [11,12]

Material & Methods :

To examine the hair in malnutrition a case of marasmic kwashiorkor was selected. There was partial alopecia. The hairs were light brown, sparse, fine, brittle and easily pluckable. The hairs were examined under Scanning Electron Microscope (SEM) with different magnifications. For this purpose a JEOL model (JSM 35 cf), SEM was used.

Observations :

Under optical microscope no visible difference in the hair shaft or the tip between normal and malnourished hair is observed. When viewed under SEM at low magnification (X-540), the tips look more or less pointed (Pl 1.1 and Pl 2.1). But in magnification more than 1200 times, the tip appears wavy and lamellar (Pl.1.2). In malnutrition the hair tip is irregular and the projections are uneven (Pl.2.2). This finding is observed in most of the hair tips.

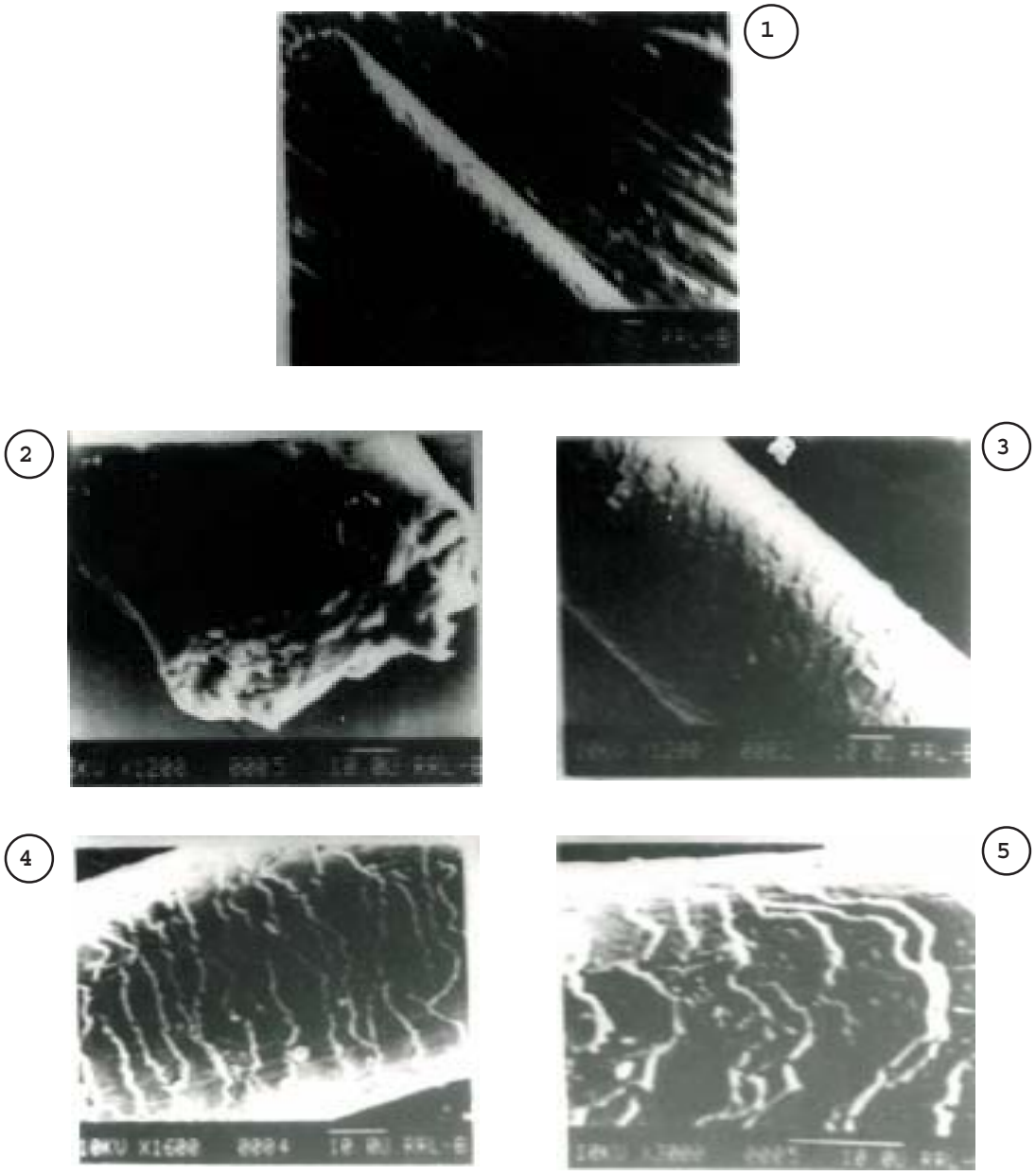

Plate 1: Electron micrograph of Normal Hair

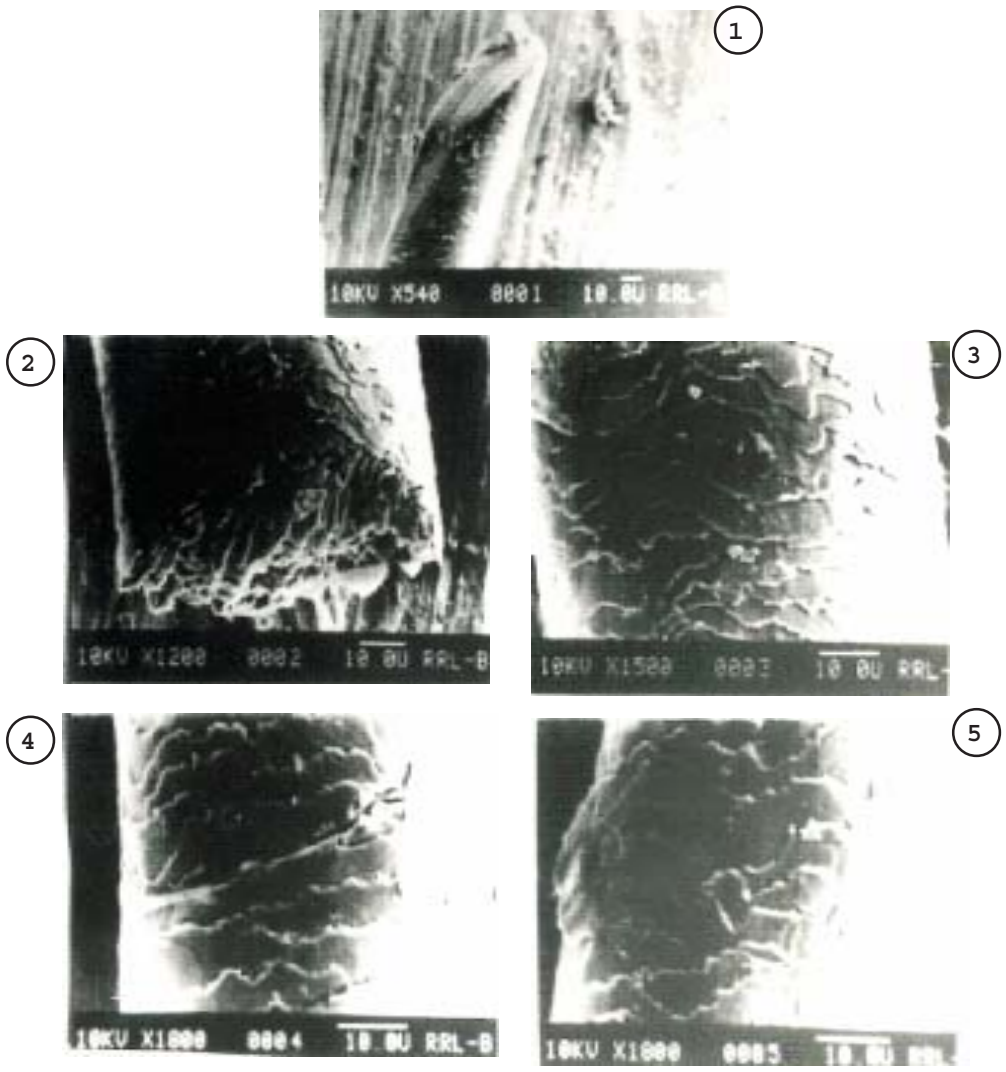

Plate: 2 Electron Micrograph of abnormal hair

EXPLANATION OF FIGURES:

Plate 1: Electron micrograph of Normal Hair

1. Upper Most-Normal hair tip at lower magnification.
2. Upper left-Hair tip, appear uniform.
3. Upper right-Normal hair shaft
4. Lower left-Normal wavy nodal markings
5. Lower right-Enlarged view of wavy nodal markings.

Plate 2: Electron Micrograph of abnormal hair.

1. Upper most-Abnormal hair tip at lower magnification.
2. Left upper-Hair tip, appear irregular non-uniform.
3. Right upper-The notch in the wavy nodal marking.
4. Left lower-The Breakage line.
5. Right lower-Herniation of the hair substance.

There are normal wavy nodal markings interspersed regularly in the hair shaft. They are in one plane. In normal hair the pattern is evident in higher magnifications. The single plane disposition is obvious even in 3000 times magnification (Pl.1.4 &5). In hair of malnutrition the nodal wavy pattern is maintained but the height of the wave is more and they are more acute. There is a niche below the crest of the wave and there is shedding visible in the area indicating that they are in different planes. This observation is met frequently but not invariably (Pl.2.3)

Usually in the malnourished hair there are breakage lines often extending from one side to the other in the shaft. At times it is partial or complete. This is better visible in 1800 times magnification (Pl.2.4). To the naked eye or in lower magnifications this line is not very much appreciated.

One of the rare findings in malnutrition is the protrusion of the hair substance in the lateral aspect of the hair shaft, delineated properly in 1800 magnification. This may be an out-growth or may be herniation of the hair substance out through the weak cortical tissue of the hair.

Summary & Conclusion:

The hair of a case of Marasmic-kwashiorkor was studied under scanning electron microscope. In higher magnification few unusual findings like (a) Irregularity of the hair ends, (b) Increase in crest height along with niche formation, (c) Breakage line in the hair shaft, and (d) Herniation of the substance through lateral wall were observed. These findings briefly describes the ultra structure of malnourished hair which has hither to not been reported in literature so far.

References :

1. Winkelmaan RK. The innervations of a hair follicle. Ann NY Acad Sci. 1959; 83: 400- 407
2. U. Jakubovie HR., Ackerman AB. Structure and function of the skin. In : Moschella S, Hurley H, Edt. Dermatology 2nd ed. Philadelphia : W.B. Saunders, 1985:1-103
3. Breathnach AS. An atlas of ultra structure of human skin. London : Churchill Livingstone 1971
4. Menafee E and Friedman M. Estimation of structural components of abnormal human hair from amino acid analyses. J. Pr. Chem 1985, 5: 333-341
5. Desai SC, Seth RA, Udani PM. Nutrition and hair anomalies. In : Orfanos, Montanga, Stuffgen. Edt Hair research. Berlin : Springer 1981.
6. Bradfield RB, Cordario A, Graham GG. Hair root adaptation to marasmus. Lancet 1969, ii : 1395 – 1396.
7. Johnsons AA, Latham MC, Roe DA. An evaluation of the use of changes in hair root morphology in the assessment of Protein-Calorie Malnutrition.
8. Bradfield RB, Bailey MA. Hair root response to under nutrition. In montanga W, Dobson RL Edt Hair growth. Oxford : Pregamon, 1968 : 109 – 119
9. Visweswara Rao K, Bhatia RYP, Pralhad Rao N. Morphological changes in Scalp hair in mild and moderate forms of protein calorie malnutrition. Indian J Med Res 1978; 68: 631 – 640.
10. Visweswara Rao K. Bhatia RYP, Pralhad Rao N. Morphological changes in scalp hair of children with severe forms of protein calorie malnutrition. Indian J Med. Res. 1978, 67:86-96.
11. EL- Hefnawi H, Shukri AS, Rashed A. Kwashiorkor in United Arab Republic Br. J. Dermatol 1965, 77, 137 – 150.
12. Sims RT. Hair growth in Kwashiorkor. Arch. Dis Child. 1967, 42 : 397 – 400.

CHIKUNGUNYA FEVER

Baldev S. Prajapati*, Rajal B. Prajapati, Panna S. Patel*****

Introduction :

The name "Chikungunya" is derived from the word "Swahili" meaning 'that which bends up' in reference to the stooped posture developing as a result of the arthritic symptoms of the disease. The name is derived from Makonde, one of the African languages. It is also spelt as Chiken Gunea. It is spread by bite of 'Aedes Aegypti' mosquito. Abrupt onset of fever with chills, flushing of skin and joint pain are main characteristics of the disease. It is almost always self limiting and rarely fatal.

Chikungunya virus was first isolated from the serum of a febrile person in Tanzania in 1953. Since then, it has been isolated repeatedly from several countries in Africa. The virus was also identified in many parts of Asia.

Chikungunya Virus :

Viruses in the families of Togaviridae, Flaviviridae and Bunyaviridae are principally arthropod-borne or spread as zoonoses. (Table-1).

Chikungunya virus is a Group IV (+) RNA virus belonging to Togaviridae with genus Alphavirus and species Chikungunya. Ross River, O'nyong-nyong are other viruses belonging to the same family with genus alphavirus. They have been associated with similar syndrome.

Transmission :

Chikungunya virus is most commonly transmitted to humans through the bite of an infected mosquito, specifically mosquitoes of the Aedes genus like Aedes Aegypti. They usually bite during day time (Daylight) hours. Culex and Mansonia mosquitoes can also transmit the disease. Once the mosquitoes are infected, they remain so throughout life.

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Table-1

Arboviruses

Family	Genus	Virus (examples)	Clinical Manifestations
Togaviridae	Alphavirus	• Chikungunya	Fever, Rash, Arthritis
		• Eastern equine encephalitis	Encephalitis
	Rubivirus	• Rubella	Rash,Arthritis
Flaviviviridae	Flavivirus	• Yellow fever	Hepatitis, haemorrhagic fever.
		• St. Louis encephalitis	Febrile illness with headache, encephalitis
		• Dengue	Fever, Rash, Haemorrhagic fever
	Hepatitis C like	• Hepatitis C	Hepatitis
	Pestivirus	• Bovine viral diarrhea	Diarrhoea
Bunyaviridae	Bunyavirus	• La Crosse	Aseptic meningitis Encephalitis
	Phlebovirus	• Sandfly fever	Fever
	Nairovirus	• Congo-Crimean Haemorrhagic fever	Haemorrhagic fever
	Hantavirus	• Hantaan,Seoul, Belgrade, Sin Nombre	Non-Cardiogenic pulmonary oedema.
	Tospovirus	• Tomato spotted wilt	Spotted wilt in plants

Outbreaks of Dengue and Chikungunya usually involve small towns while outbreaks of o'nyong-nyong and West Nile fever usually involve villages.

Vertical Maternal Fetal Transmission :

In March 2005, an epidemic of chikungunya virus began in the southern portion of Reunion Island. There was report of acute chikungunya to 84 pregnant women. 74 mothers had infection quite earlier to the delivery date and their newborns appeared asymptomatic. Conversely, 10 newborns had severe attacks after birth and required prolonged hospitalization. Four babies developed meningo-encephalitis, three disseminated intravascular coagulation. Six babies required NICU care with intubation and assisted ventilation. No infant died. These cases were confirmed by specific serology testing or PCR or both for mothers and newborns. It was noted that all severe cases involved women with viremia and fever in the intrapartum period.

Epidemiology :

Africa : Chikungunya virus is transmitted in the forests of tropical Africa by aedes aegypti mosquito. The vertebrate portion of the cycle is provided by non-human primates such as monkeys and baboons which amplify and maintain virus circulation. It is thought that endemic circulation and moving epidemics in troops of primates are responsible for survival of the virus and local spill over into human population. In Africa villages or rural areas these mosquitoes may then infect humans and substantial viremia measure suggest that humans, in appropriate setting may contribute to mosquito infection, leading to further virus amplification. This becomes particularly important when domestic breeding of Aedes Aegypti is present in large number, a situation that may lead to village and large urban epidemics in Africa. The classical chikungunya epidemic which occurred in Tanzania in 1953, resulted when Aedes Aegypti borne disease moved through multiple villages over an expense exceeding 5,000 Kms. In studies of individual dwellings, there was a highly significant trend for multiple cases to occur once a single case had occurred. This of course, could be a reflection of flight – range of Aedes Aegypti vectors and human habits.

Asia : Transmission in Asia follows a different pattern from that seen in Africa, being primarily transmitted from human to human by Aedes Aegypti. Although Asian monkeys develop significant viremia after chikungunya virus inoculation and have been found to harbour antibodies to it, they have never been shown to participate in any important way in the maintenance or amplification of the virus in the continent.

Chikungunya activity in Asia has been documented since its isolation in Bangkok, Thailand in 1958. Other South-East Asian countries which have experienced chikungunya outbreaks are Cambodia, Vietnam, Burma, Srilanka and India. A series of epidemics usually lasting a single year have been reported from Sri Lanka and India.

India : First out-break of chikungunya in India was in 1963 in Kolkatta. It was responsible for extensive dengue like infection with occasional haemorrhagic manifestations. Chikungunya virus was isolated from cases with severe disease like haemorrhagic manifestations. Serious cases were more common among infants, young children, elderly and immunocompromised patients. Severe manifestations were less common among young adults. In 1964, there was an epidemic of chikungunya in Vellore, Madras and Pondichery. In 1973, a small localized out-break was reported from Barsi, Sholapur district in Maharashtra State. No out-break was reported from India after 1973 till 2005.[13,14]

Again, there was increase in incidence of fever cases in Maharashtra State since December, 2005. 258 villages from 15 districts have reported 34,725 fever cases till April, 2006. Similarly, 18,529 cases of fever with arthritis or arthralgia have been reported from seven districts of Karnataka State since December, 2005. In Andhra Pradesh, 5,671 cases were reported from December, 2005 to February, 2006. Orissa experienced the out-break of the disease with almost 4,900 cases in February and March, 2006. It is estimated that thousands of people suffered from chikungunya during its recent out-break in 2007 in Gujarat.

Clinical Features :

The incubation period is usually 2-3 days with a range of 1-12 days. Chikungunya is an acute viral infection of abrupt onset. Fever, rash and joint involvement are characteristic features of this disease. Fever rises abruptly often reaching to 39 to 40°C (102-104°F) and may be accompanied by chills. This acute phase lasts for 2 to 3 days. The temperature may remit for 1-2 days, resulting in a "Saddle-back" fever curve.

The arthralgias are polyarticular, migratory in type. Small joints of hands, wrists, ankles and feet are commonly affected. Larger joints are less commonly involved. Pain on movement is worse in the morning, improved by mild exercise and exacerbated by strenuous exercise. Joint swelling may occur but collection of fluid is uncommon. Patients with milder articular manifestations

are usually symptom free within a few weeks, while patients with severe joint involvement require months to resolve completely. Generalized myalgias as well as back and shoulder pain is common. Joint involvement is less common and if it is presents, it is of mild degree in children compared to adults. Young children may present with irritability and excessive crying due to myalgia.

Cutaneous manifestations are typical with many patients presenting with flush over the face and trunk. This is usually followed by maculopapular rashes all over the body. The trunks and limbs are commonly involved but face, palms and soles may also show lesions.

Headache, photophobia, retro orbital pain and conjunctival infection are other common manifestations during acute illness. Sore throat due to pharyngitis is also fairly common.

Severe manifestations of the disease like meningo-encephalitis are rare. They may develop in newborns, infants, elderly and immuno-compromised patients. Lymphadenopathy is unusual feature of the disease. Chikungunya outbreaks result in several hundreds or thousands of cases but deaths are rarely encountered. Death may occur due to pre-existing medical disease.

Differential diagnosis of chikungunya include Dengue, Dengue haemorrhagic fever, Rose River and Onyong-nyong viral infections.

Diagnosis :

Though definitive diagnosis can only be made by Laboratory means, Chikungunya should be suspected when epidemic disease occurs with characteristic triad of fever, rash and joint manifestations. The following criterias are suggested for case definition. (Table-2)

Table-2

Case definition of Chikungunya

Suspected case

An acute illness characterized by sudden onset of fever with several of following symptoms - joint pain, headache, backache, photophobia, arthralgia, rash.

Probable case

As above and positive serology (when single serum sample is obtained during acute phase or during convalescence).

Confirmed cases

A probable case with any of the following :

1. Four fold HI antibody difference in paired samples
2. Detection of IgM antibodies
3. Virus isolation in serum
4. Detection of CHIKV nucleic acid in sera by RT-PCR

Suspected Case :

Acute illness characterized by sudden onset of high grade fever maybe with chills, associated with other symptoms such as joint pain, skin rash, headache, photophobia, retro orbital pain, backache, myalgia etc.

Probable Case :

As above and positive serology when single serum sample is obtained during acute phase or during the convalescence.

Confirmed Case :

A probable case with any of the following :

- Four fold haemagglutination inhibition (HI) antibodies difference in paired serum samples.
- Detection of IgM antibodies.
- Virus isolation from serum.
- Detection of Chikungunya virus nucleic acid in sera by RT-PCR.

Laboratory Tests :

The facility for laboratories working on chikungunya available in our country is at National Institute of Virology, Pune and National Institute of Communicable Diseases, Delhi.

Serological Diagnosis :

- Virus specific IgM antibodies are readily detected by Capture ELISA in patients recovering from Chikungunya infection and they persist for about 6 months.
- Haemagglutination Inhibition (HI) antibodies appear with ceasation of Viremia. All patients will be positive by day 5 to 7 of the illness.

Collection, Storage and Transportation of the Sample : (Table-3)

Table-3

Collecting storage and transportation of sample

For serology :

Blood

Acute sample – within 5 day of onset of illness

Convalescent or paired sample – 10-14 days after first sample

Transport :

Transport to laboratory at 2-8°C as soon as possible. Do not freeze.

If more than 24 hours delays is expected, the serum should be separated and stored frozen.

For isolation of virus and RT-PCR :

Blood – Collect within 5 days of illness (transport within 48 hour in cold, preferably frozen).

Laboratory diagnosis depends on the quality of sample, time of collection of sample, its storage and necessary precautions taken during transportation.

For Serology :

First sample should be collected 5 days after the onset of illness. Convalescent or paired sample should be collected 10 to 14 days after the first sample.

For Isolation of the virus and RT-PCR :

Blood for isolation of virus and RT-PCR should be collected within first 5 days of illness. These samples should be sent immediately, within 48 hours to the referral laboratory. It should preferably be frozen.

Transportation :

Specimens should be transported to the laboratory as soon as possible. The temperature should be maintained 2 to 8°C during transport of the specimens. The whole blood should not be frozen as hemolysis may interfere with results of tests.

If more than 24 hours delay for transportation of specimens is expected, the serum should be separated from blood and serum should be stored frozen.

Management :

There is no specific treatment for chikungunya. The illness is usually self limiting and will resolve in due course of time.

Supportive care with rest is indicated during the acute joint symptoms. The antipyretics and analgesic drugs can be used for symptomatic relief. The commonly used drugs are paracetamol 15 mg/kg/dose, Ibuprofen 8 to 10 mg/kg/dose and Diclofenac sodium 1 to 3 mg/kg/day. Aspirin, Nimesulide and other NSAIDs should be avoided to prevent gastric bleeding and other hazards. In unresolved arthritis refractory to NSAID, Chloroquine 250 mg/day is recommended. There is no role of antibiotics. Steroids should not be used. It has been observed that at times it may cause serious complications. Mild exercise tend to improve joint symptoms, but strenuous exercise may exacerbate the symptoms.

Prevention And Control :

There is no specific medicine or vaccine available against chikungunya infection. Vector control is thus very important measure for prevention of the disease transmission. Elimination of mosquito breeding sites or source reduction is an effective method of control of the disease. Aedes Aegypti is typically a container habitat species and breeds primarily in artificial container and receptacles. Aedes Aegypti mosquito does not fly more than 100 meters from its original shelter.

Control of Mosquito Breeding :

- All water tanks, barrels, cisterns, trash containers need to be covered tightly with a lid.
- Remove or empty water in old tyres, tin cans, buckets, drums, bottles or from other places where mosquitoes breed.
- Clogged gutters and flat roofs that may have poor drainage need to be checked regularly.
- Water in bird baths and plant pots or dip trays should be changed at least twice a week.
- Pets water bowls need to be emptied daily.
- In ornamental water tanks and garden, larvivorous fish (Guppy fish) need to be introduced. They eat mosquito larvae.
- Weeds and tall grass should be cut short. Adult mosquitoes look for these shady places to rest during hot day light hours.
- In case water containers can not be emptied regularly, temephos (1 ppm) should be applied.

Protection from Mosquito Bites :

- Use of insecticide (Permethrin) treated mosquito nets or curtains has been found effective. Especially children should sleep under insecticide treated nets during day time.
- Insecticide spray kills the mosquitoes.
- Fogging operations with 2% pyrethrum is also recommended.
- It is very essential that people should be educated for all these measures and scientific information regarding the disease.

Chikungunya Virus Vaccine :

This vaccine has passed through various phases. It was conducted a Phase II, randomized, double-blind, placebo-controlled, safety and immunogenicity study of a serially passaged, plaque-purified live chikungunya (CHLK) vaccine in 73 healthy adult volunteers. It was found promising and highly immunogenic. Certain well-tolerable side effects were noted. It may become available for use in practice in the future.[13]

References :

1. CD Alert Vol.10 : No.2, Chikungunya Fever, February, 2006; 1-8. Monthly Newsletter of National Institute of Communicable Diseases, Directorate General of Health Services, Government of India.
2. Lam SK, Chug KB. Alpha viruses. WHO collaborating centre for Arbovirus Reference and Research, Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Kuala Lumpar. Http://www.vadscorner.com/alphaviruses.html 27.8.2006.
3. Long S.S., Pickering LK, Prober CG (Eds) Principles and Practice of Pediatric Infectious Diseases, 1st edn. New York; Churchill Livingstone 1997.
4. Kliegman RM, Jenson HB, Behrman RE et al. (Eds) Nelson – Textbook of Pediatrics. 18th edn. New Delhi : Elsevier, 2008.
5. Passi GR. Global update. Disease Watch – Chikungunya fever. Indian Pediatr 2006, 43 : 751.
6. Kapse A. Chikungunya – A Re-emerging Disease. IAP Bulletin Academy Today, September, 2006, 25-27.
7. Chikungunya (Internet Information) IMA GSB, New Bulletin, September, 2006.
8. Robillard PY, Boumahni B, Gerardin P et al. Vertical maternal fetal transmission of the chikungunya virus. Ten cases among 84 pregnant women. Press Med 2006, 35 : 785-788.
9. http://www.who.int/csr/don/2006_03_17/en/index.html.
10. http://www.cbwinfo.com/Biological/Pathogens/CHLK.html.
11. http://www.cdc.gov/travel/other2006/chikungunya_india.htm.
12. Edelman R, Tacket Co., Wasserman SS, et al. Phase II safety and immunogenicity study of live chikungunya virus vaccine TSI-GSD-218 American Journal of Tropical Medicine and Hygiene, 2000, 62: 681-685.
13. Bhat S: Chikungunya Fever – A Re-emerging viral disease. In Gupte S (Ed) Recent Advances In Pediatrics-18 : Hot Topics 1st edn. New Delhi. Jaypee Brothers Medical Publishers (P) Ltd. 2009, 229-236.
14. Chhabra M, Mittal V, Bhattacharya D et al. Chikungunya fever : a re-emerging viral infection. Indian J Med Microbiol 2008,26 : 5-12.

ROTA VIRUS GASTROENTERITIS

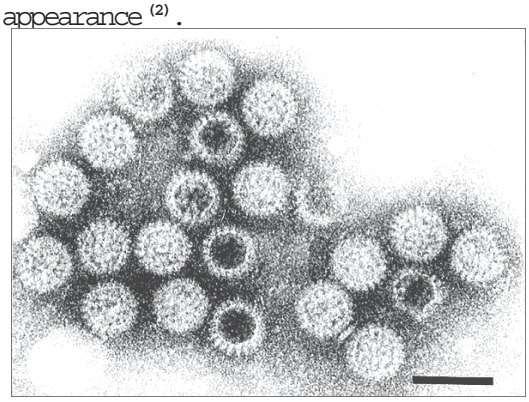
Gadadhar Sarangi*

Abstract :

Rotavirus is one of the commonest causes of severe gastroenteritis in infants and young children. The mortality and severity is high in malnourished children. Laboratory diagnosis is difficult in the field but clinical features well correlates with the laboratory findings. Maintenance of fluid and electrolytes is the cornerstone of therapy. Vaccine remains the answer for this widespread disease. Trials are on to reduce the cost and to make it available to the developing world.

Introduction :

Brener and Horne is 1959 described a novel technique of electron microscopy which ushered a new era in the field of experimental and diagnostic virology. Rota virus in 1963 was first described as an agent of infantile murine diarrhoea. 10 years after in1973 Bishop and his associates observed by electron microscopy, in the duodenal epithelium of children with diarrhea, a 70 nm virus at Royal children's hospital in Melbourne of Australia[1]. Subsequently in 1974 Flewtt and colleagues advanced the name "rotavirus" based on its "wheel-like" appearance [2].



Rotavirus
Reprinted from emerging infectious DiseasesVolume 4 No. 4

Within 5 years of this discovery rotavirus was recognized as the most common cause of diarrhoea in infants and young children world wide, accounting for approximately one third of cases of severe diarrhoea requiring hospitalization.

The Virus :

Rota Viruses are 70nm icosahedral, none enveloped, double stranded RNA virus belongs to the family Reoviridae. Rota Viruses are classified as groups, subgroups and serotypes. The groups do not have any antigenic relations. Group A: Predominantly affect humans and Group B in China and Group C occasionally reported to be pathogenic. Other 4 groups (D, E,F&G) are not seen in humans.

Rota Viruses are subdivided to two subgroups (I & II) depending upon the VP6 protein present in the inner capsid.

The serotypes are determined depending upon the VP4 (Protease cleaved/ P Protein) and VP7 (Glycoprotein / G Protein)

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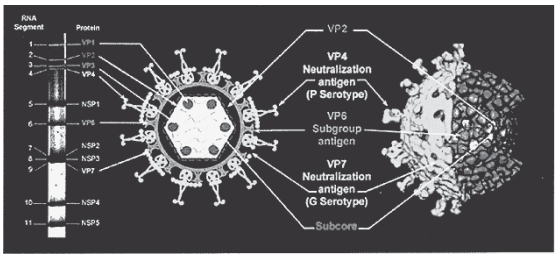
The Virus has three layered capsid. The outer capsid is made up of VP4 (P Protein) encoded by 4th gene and VP7 (G Protein) encoded by 7, 8, 9 genes. They define the serotype of the virus. The inner capsid is made up of VP6 protein encoded in 6th gene which is most abudant and immunogenic in the virion. Anti VP6 antibodies inhibit virus transcytosis through the intestinal epithelium barrier[3] The internal shell surrounds the 11 segment double stranded RNA genome.



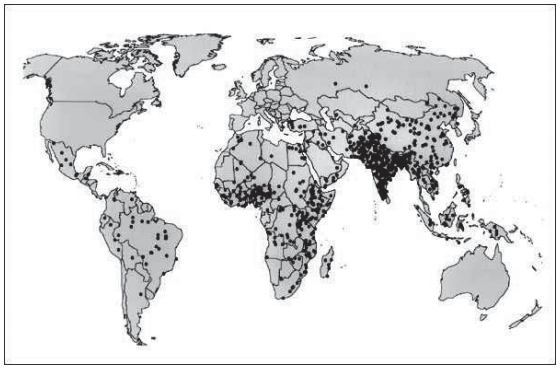
The Three layered capsid of the virus
Reprinted from "Fields virology" 3rd Edt. Vol.2

The individual genomic RNA segment can reassort independently producing a Reassortant particle of mixed parentage which could theoretically lead to the emergence of 110 different G and P combinations. G1, G4, G9 with P4 and P8 serotypes with combinations are predominant world wide causing 90% infection in industrialized countries and 68% infection in Asian countries[4]. GI P [8] is the globally predominant strain followed by G3 P(8), G2 P(4) and G4 (8). G9 strains have emerged in the early 2000s and have become predominant in some regions of the world including Europe and parts of Eastern Asia. Less usual strains like G10P(11) and G12 P(6) are also evolved in India.[5]

Both G & P proteins induce neutralizing antibodies and may be involved in protective immunity.

Epidemiology :

Rotaviruses are the leading cause of severe diarrhoeal diseases and dehydration in infants and children worldwide under the age of 5years. It has been estimated that rotavirus infection is responsible for 111 million episodes of diarrhoea requiring home care and 2 million hospitalization from the same cause with approximate 4, 40,000 deaths in under fives, 82% of which occurs in the developing world [6] almost 100,000 deaths occurs each year in India alone and double the number are lost in African countries [7].



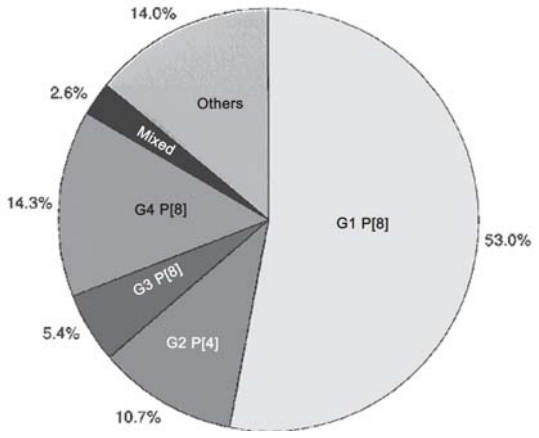
Distribution of Death due to Rotavirus gastroenteritis World Over
Reprinted from Nat Med 1997; 3:10-11

Distribution of Death due to Rotavirus gastroenteritis World Over

Virtually all the children are infected by the time they reach two to three years of age. Most symptomatic episodes occur between 3months and 2years with a peak incidence between 7 and 15months [8]. Neonatal rotavirus infections are mostly asymptomatic and caused by unusual strains as reported from six hospitals from India [9]. The disease has definite winter seasonality in temperate climate and year round exposure in tropical countries. In south India a mean minimum temperature of 24^{O}C predisposed more to rotavirus infection [10].

GIP(8), G3P(8), G4P(8) and G2P(4) strains dominate world over [11]. Unusual strains are common is several developing countries like those with serotype G9 accounted for 9.5% of all rotaviruses from a multicenter collection in India [12].

Strain Distribution World Over



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As rotavirus infects all the children below 5years and the infectivity is very high, it is unlikely to reduce disease burden by improving water, food or sanitation. Vaccination remains the only alternative. Natural immunity is suggested because of infrequent occurrence of more than one episode of rotavirus diarrhoea in a child and decreased incidence of the disease with increasing age [13]. Furthermore protection increased with each infection against moderate to severe disease, less against, mild and least against asymptomatic infection [14].

The global scenario recently getting changed with the advent of new oral rotavirus vaccines [15].

In a study from south India overall Rota virus infection amongst children with acute diarrhoea was 22.55% with no gender specificity. The study revealed 66.1% G2 serotype followed by G4 (13.6%) G1 (9.3%) and G3 (1.7%). Dual infection was present in 9.3% dominated by G1 - G2 (63.6%). The dominantly present serotype was G2 (P4) (10).

In a multicentric analysis from 40 published study from all over India out of 13,000 pediatrics inpatients with diarrhoea, 28% neonates and 18% children had rotavirus infection. G1 and G2 were the common serotypes in children where as G9 (P11) was isolated more frequently from neonates. 50% of infection occurring within 6months and 75% within 9months attracts the feasibility for neonatal vaccination [16].

The study by G. Kang et al from 18 cities of India, among children attending hospital for diarrhoea the rotavirus infection was present in 23.4%. There was marked geographical differences with G1 serotype being common in western India. Group B viruses

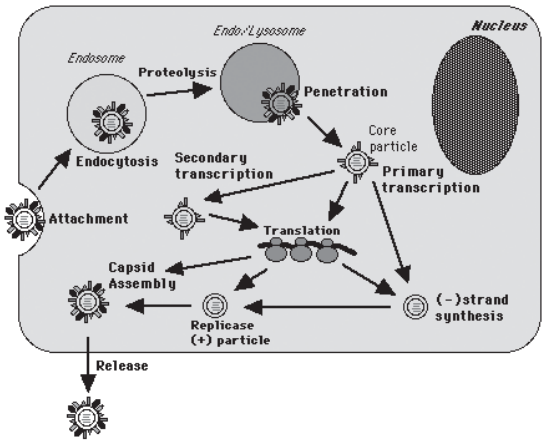
were detected from Kolkata and Pune. G6 G8 G9 and G9(P19) were reported from western, southern and eastern India, may be as a result of zoonotic transmission [17].

Pathophysiology :

Rotavirus infection has a wide spectrum from asymptomatic to sever disease which depends upon both the Virus and Host. In the Virus some alleles of VP4 are not virulent; virus strains got attenuated in the host and are species specific. In host, age and nutritional states are the two variables that modifies response. Malnutrition delays recovery by modifying intestinal inflammatory response. Increase of age elevates the neutralizing antibodies. Rate of epithelial cell replacement and fluid absorption are also age dependent. New born do not possess the age deponent protease expression for cleavage of VP4.

Rotavirus infects the mature absorptive villous epithelium of upper 2/3rds of the small intestine and is confined to the mucosa. Though found in lamina propria and lymphatics, replication in these sites and systemic spread does not occur in immunocompetent host.

The Pathological lesions from Rota virus infection varies from no visible lesions through slight lesions like enterocyte vacuolization and loss to large lesions like villous blunting and crypt hyperplasia but there is no absolute correlation between histological lesions and disease symptoms [18]. Diarrhoea does not follow intestinal cellular damage rather precedes it, as diarrhoea appears on 5th day where as intestinal lesions on 6th day in experiment with rabbits. Rotavirus affects the intestinal brush border membrane Na+ glucose and Na+ leuicine cotransport system [19] to cause diarrhoea.



Replication of Rota Virus

In the course of events rotavirus got attached to the enterocytes. It gets internalized to the cell loosing the outer capsid and activates the virion associated transcriptase. The viral proteins and RNA concentrate in the cytoplasm is called viroplasms. From the viroplasm replication takes place as well as NSP4 (Non structural Protein 4) which has an enterotoxin like activity, is released which in turn releases ca++ from the endoplasmic reticulum. Ca++ in turn disrupts the microvillar cytoskeletal network resulting in cell necrosis and malabsorptive diarrhoea, lowers expression of disacharidages and inhibits Na+ solute transport system resulting in osmotic diarrhoea. A component of secretory diarrhoea was suggested with elevated PGE2 in the cell [18]. Enteric nervous system (ENS) block reduces rotavirus diarrhoea up to 67% suggests a role of activation of ENS resulting in increased intestinal Motility by rotavirus infection [20].

Clinical Manifestations :

The disease spreads among no immune children through person to person contact, feco oral route, air borne droplets or contact with contaminated toys[8]. Children from low socioeconomic back ground and low birth weight infants have an increased risk for hospitalization [21]. Both symptomatic and asymptomatic patients shed rotavirus in their stool for 7 to 10 days. but shedding can happen to last for several weeks. The virus is highly resistant in the environment and can survive for months in stools at room temperature [22].

The incubation period ranges from 1to3days but mostly within 48hours and there is often exposure to other children with diarrhoeal illness. It starts with anorexia and vomiting with low or moderate grade pyrexia, watery bloodless copious diarrhoea and abdominal cramps. Dehydration often is the presenting complaint. Diaper dermatitis, disproportionate tachycardia, weight loss and signs of dehydration are obvious physical findings. Hyperactive bowel sounds are the most common physical finding.

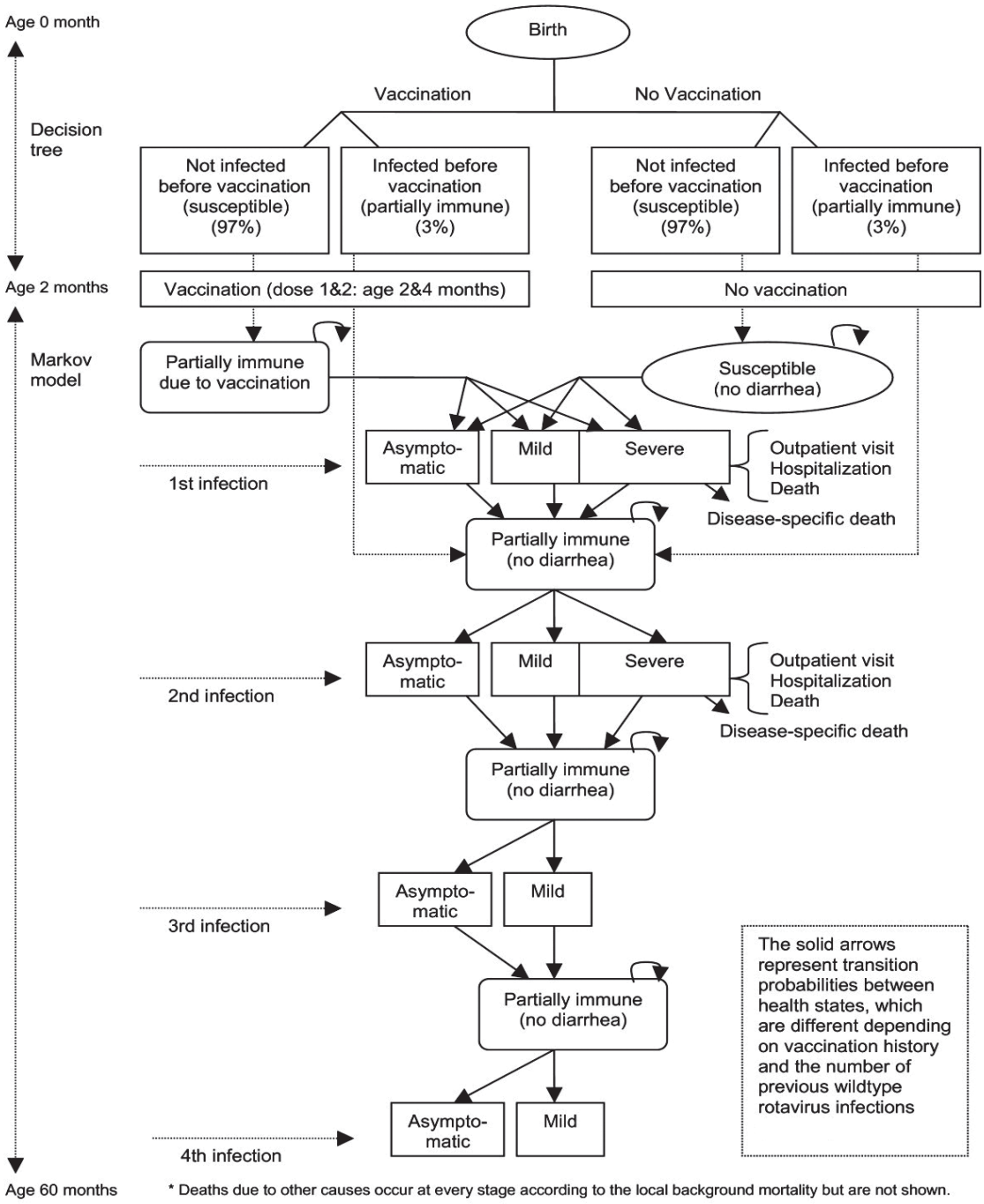
Rotavirus infection is usually localized to the intestine but involvement of extra intestinal sites, including respiratory, liver, kidney, lymph nodes and the central nervous system has been reported. Rota virus has been isolated from blood within 3 days from 64.3% at Rota positive cases from stool. When rotavirus was only isolated from stool children had high fever but no extra intestinal manifestations [23].

Rota virus affected children develop acidosis while passing an acid stool. The presence of reducing substances in the stool suggests of significant carbohydrate malabsorption [24].

Rotavirus infection is frequently associated with respiratory symptoms than with diarrhoeas of other etiology. [25]

Depending upon the duration and severity of diarrhoea, grade of dehydration and mode of therapy, Puuska and Vesikari had devised a point scoring system to classify the severity of diarrhoea. The total score given was 20. Up to 9 was taken as mild, 9 to 17 as severe and beyond 17 was taken as fatal. [26] However more than 10 watery stools a day can be taken as severe gastroenteritis. Rota virus diarrhoeas were more severe with a score of 11.0 ± 3.7 to non Rota virus diarrhoea with median score of 5.6 ± 3.2 [26].

Modification of Markov model delineates the natural infection probabilities. Those none immunized/not infected previously, with first infection either remained asymptomatic, develop mild or severe infection. In the second challenge they remain either asymptomatic or develop mild/severe symptoms. With 3rd infection the clinical scenario changes to no or mild manifestation. The 4th infection gives results like 3rd infection with more cases being asymptomatic. Further infection fails to produce disease.



Mrkovs model

Diagnosis :

It is well known that administration of antibiotics will not be of any help in case of rotavirus diarrhoea or any other viral diarrhoea. Therefore rapid diagnosis of Rota virus infection is the need of the day. A number of diagnostic assays have been developed to detect the virus and/or to demonstrate the serological response induced by the virus in the host.

Electron microscopy, viral culture and Reverse Transcriptase polymerase chain reaction (RT-PCR) are highly sensitive but needs costly equipments, reagents and trained man power which is not possible in field conditions.

Enzyme Immunoassays give 90% specificity and sensitivity and can be performed is the field conditions. ELISA and latex Agglutination are found to be as sensitive and specific as polyacrylamide Gel Electrophoresis in the diagnosis of rotavious diarrhoea[27]. Rapid Immuno-chromatographic tests available as commercial test kits have the same sensitivity and specificity as ELISA.

ELISA Test is taken as the golden standard for diagnosis in the field conditions even though at times it fails to detect viral antigens in the stool with high titer of corresponding antibody. In this test stool is allowed to react with plastic beads washed with guinea pig antirotavirus antibody for 3 hours at 45^{O}C. After washing, the beads are allowed to react with rabbit antirotavirus antibody conjugated with horse-raddish peroxidase for 1 hour at 45^{O}C. After final incubation the beads are kept in a buffer of Hydrogen peroxide and 0 phenyle diamine. The reaction is made to stop with 1N HCL and the concentration of the oxidized product is measured at 492 nm wavelength in a quantum 2 Photo spectrometer[28].

Latex Agglutination test - In this test 1 drop of the buffered stool is added to I drop of detection latex which contains rabbit antirotavirus antibody. A control with inactivated rotavirus is also provided. The mixture is rotated at 90-110 rpm for 5 minutes. If agglutination in the test exceeds than the control, the test in taken as positive[29].

Polyacrilamide Gel Electrophoresis (PAGE) - This procedure detects the RNA of the virus. The stool is treated with sodium dudecyl sulphate to disrupt the virus. Then treated with phenolchloroform to deproteinise the nucleic acid. Homogenized and heated to prevent recoiling of RNA. Electrophoresis is done in a polyacrylamide gel and stained with silver nitrate[28].

Rapid Immunochromatographic Test - The test strip contains a mobile monoclonal mouse origin antirotavirus antibody conjugated to colloidal gold particle. When the rotavirus in the stool migrate to the immobilized antibody area, a positive test band becomes visible[29]. It is easy to perform and is available as single commercial test kits.

Laboratory Findings :

Blood reflects features of isotonic dehydration with acidosis. The stools are free from blood or leukocytes. Often reducing sugars are detected with an acidic stool [30].

Treatment :

Avoidance and treatment of dehydration are the main goals in therapy. ORS for some dehydration and intravenous fluids for severe dehydration are mandatory. Usually cases recover with fluid and electrolyte replacement. The second objective is maintenance of adequate nutrition in the face of vomiting more so when the child is malnourished.

Antibiotics and antiviral drugs have no role in rotavirus diarrhoea. Antiemetics and antidiarrhoeals also do not offer added benefits.

Zinc is involved in epithelial barrier integrity, tissue repair and immune function. Diarrhoea can be associated with increase in fecal Zn loss by blocking enterohepatic circulation. Efficiency of Zn treatment on diarrhoea duration include an improved absorption of water and electrolytes by the intestine and quicker generation of gut epithelium [31].

Zn works better with malnourished children and children with Zn deficiency and in intracellular pathogenic diarrhoea like rotavirus and enterpathogenic Ecoli diarrhoea.

The mean duration of acute diarrhoea is significantly low in those receiving in. Children receiving Zn are reported to have 18.8% reduction in stool frequency, 15% shortening of diarrhoeal duration, 17.9% probability of reduction in acute diarrhoea cases most of whom are due to rotavirus [32].

There is evidence of clinically significant benefit of probiotics in the treatment of acute infectious diarrhoea in infants and children, particularly in rotavirus gastroenteritis. Lactobacillus G G showed the most consistent effect. [33]

The washing of the hand by tap water alone and with soap reduces the viral titers by 72.5% to 83.6%. Alcohol with savlon reduced virus titer by 99%, where as the reductions by proviodine, dettol and hibisol ranged from 95 to 97%. However aqueous solution of chlorhexidine is significantly less effective in virus removal [34].

Single dose of human scrum immunoglobulin given orally with 300mgs/kg body weight significantly reduced the duration of diarrhoea, hospitalization and excretion of rotavirus in the stool. [35] This treatment is still considered experimental [30].

Prevention :

Good hygiene reduces viral transmission but the infectivity of the virus is so high and efficient that it attacks all children under 5years of age, be it developed or underdeveloped country. Therefore some times the virus has been described as a democratic

virus. Vaccine remained the mainstay in prevention of rotavirus disease. In Asia, universal rotavirus immunization would avert about 1,10,000 deaths, 1.4 million hospitalizations and 7.7 million out patients visits.[36]

Natural infection protects partially against reinfection. Reinfection boosts and broadens natural immunity. Complete protection against severe gastroenteritis is acquired after the second infection. There fore vaccination which mimics natural infection, in early age may not prevent rotavirus disease but prevents severe forms of the disease that is responsible for morbidity and mortality[37].

Despite of the superficial nature of the infection, rotaviruses induce both local and systemic immune responses. Orally administered rotavirus antibodies successfully treated chronic rotavirus infection and diarrhoea in immuno-compromised children. Single oral dose of gamma globulin reduced the duration of illness and viral shedding. [4, 5, 10, 16]

Animal studies suggested that presence of rotavirus antibody in the intestinal lumen was co-related with protection against disease[38].

These observations indicate that intestinal immunity protects against rotavirus diarrhoea and the success of rotavirus vaccine depends upon its availability to induce mucosal immune response.

The protection after primary infection is with homotypic response but repeat infection develops both homotypic as well as heterotypic response against virus of different serotypes.[39] Placentally transferred maternal antibodies are speculated to protect an infant below 3 months of age. How ever serum neutralizing antibodies often poorly correlates with the disease.

Various vaccines with different combinations or with one serotype have been introduced in the market with the hypothesis of getting heterotypic response and prevention of severe disease after two or subsequent infection / immunization as delineated in modified Marcov model.

A tetravalent rhesus-human reassortant vaccine was introduced in USA market in August 1998 and was subsequently withdrawn due to unexpected adverse event of intussusception.[40]

A human P8-G1 Rotavirus strain (RIX4414) isolated from the stool of a sick 15 months old boy from USA was purified and attenuated by passage in vero cells. The vaccine with two oral doses showed 70% to 85% protective efficacy against severe disease including those induced by non G1 serotypes.[41], [42] It has been tested in 60 countries in a large multicentric trial with infants from 6 to 14 weeks of age without increased risk of inteussusception within 30days of vaccine administration.[43]

A pentavalent human bovine reassortant vaccine by reassortment between the naturally attenuated bovine rotavirus strain (WC3) and five different human rotavirus strains with serotype G1, G2, G3, G4 and P(8) respectively have developed. Administered in 3 doses orally the vaccine did not have any increased risk of intussusception. It offered 74% protection against G1-G4 rota gastroenteritis[44].

The vaccine was shown not to interfere with immunogenesity of Hib, DPT, Hep B, conjugated pneumococcal and inactivated polio vaccine or with concomitant administration of oral polio vaccine.[45]

Trials are on in developing countries from poor settings for immunogenesity, interference with oral polio vaccine and safety in HIV positive infants. The results are promising. WHO has recommended the vaccine since available evidence indicates that efficacy data can be extrapolated to populations with similar mortality patterns regardless of geographical locations.

The vaccine conferred protection to children in the countries of their origin but failed during field trials in some developing countries. On the other hand a vaccine with high efficacy is yet to be developed.[46]

As an Indian initiative, two rotavirus vaccines are developed by using nursery strain 116E and human-bovine reassortant strain I321 which are under field trial.[47], [48]

In china, a lamb derived monovalent P(12) G1live attenuated 3 dose oral vaccine was used with 60% neutralizing antibody response.[49]

The benefits of rotavirus vaccine in USA are observed with 50% reduction in incidence of infection during 2007-2008. During first 18weeks of 2008 only 6% of samples tested positive compared to 51% in 2006 and 54% in 2007 over the same period.[50]

The current price of the oral vaccines made them unaffordable in poor countries and new rotavirus vaccine approaches got initiated with inactivated virus vaccine, DNA vaccine, VP6 subunit vaccine and vaccine with virus like particles. The route of administration varies from parenteral, intranasal, intrarectal to oral and are found to be immunogenic in mice and rabbits[51]

The vaccine adverse reaction is observed in less than 5% cases. Fussiness, irritability, cough, running nose, fever, loss of appetite and vomiting are the reactions observed.

History of uncorrected congenital malformation of the gastrointestinal tract that would expose the infant to intussusception is the lone contraindication in vaccine administration.

Precautions have to be exercised with history of allergy to the components of vaccine including the latex rubber used for administration. In acute gastroenteritis the vaccine administration has to be delayed. Safety and efficacy has not been evaluated in chronic gastro intestinal disorders as well as primary or secondary immunodeficiency.

Points To Remember :

- Rota Virus gastroenteritis is common in infants and children.
- The episodes are more severe than the gastroenteritis of other etiology.
- Clinical diagnosis correlates well with lab diagnosis in severe cases.
- Antibiotics are unwarranted in Rota infection.
- Effective vaccine is available and trails are on for availability of cheap vaccine

References

1. Bishop RF, Davidson GP, Holmes IH, Ruck BJ. Virus particles in the epithelial cell of duodenal mucosa from children with acute non bacterial gastroenteritis. Lancet 1973; 1: 128-33.
2. Bass ES, Pappano DA, Humiston SG. Rotavirus. Pediatr Review 2007; 28:183-191.
3. Schwartzcomil I, Benureau Y, Greenburg H, Hendrickson BA, CohenJ. Heterologous protection induced by the inner capsid Proteins of rotavirus requires transcytors of mucosal immunoglobulins. J. virol 2002; 76 : 8110-17.
4. Santos N, Hoshino Y. Global sistribution of rotavirus sorotypes / Genotypes and its inplication for the development and implimantation of an effective Rotavirus vaccine Rev. Med. Virol 2005; 15 : 29-56.
5. Stoele AD, Ivanoff B. Rotavirus strains circulating in Africa during 1996-1999: Emergence of G9 strain and P(6) strains. Vaccine 2003, 21 : 361-67.
6. Parashar UD, Hummelman EG, Bresee JS, Miller MA, Glass RI. Global illness and deaths caused by rotavirus disease in children.Emerg Infect Dis.2003;9:565 – 72.
7. Molback K, Fischer TK, Mikkelsen CS. The estimation of mortality due to Rota virus infection in sub Saharan Africa. Vaccine 2000; 19: 393-395.
8. Gleize S, Desselberger U, Tatochenko V, Rodrigo C, Salman N, Meznor Z, et al. Nosocomial rotavirus infection in European countries: a review of the epidemiology, severety and economic burden of hospital acquired rotavirus disease. Padiatr Infect. Dis J 2006: 25 : S 12-21.
9. Cicirello HG, Das BK, Gupta A, Bhan MK, Gentsch JR, Kumar R et al. High prevalence of Rota Virus infection among neonates born at hospitals in Delhi, India: Predisposition of new borns for infection with unusual rotavirus. Ped Infect Dis J 1994; 13: 720 - 24.
10. Sarvanan P, Ananthan S, Anan Subramanian M, Rotavirus infection among infants and young children in Chennai, south India. Ind J of med microbiol. 2004; 22(4) : 212-221.
11. Gentsch JR, Woods PA, Ramachandran M, Das BK, Leite JP, Alfieri A, et al. Review of G and P typing results from a global collection of rotavirus strains: Implications for Vaccine development. J Infect Dis 1996; 174: S 30-6.
12. Ramchandra M, Das BK, Vij A, Kumar R, Bhambal SS, Kesari M. et al. Unusual diversity of human rotavirus G and P Genotypes in India. J Clin Microbiol 1996; 34: 436-9.
13. Bishop RF, Barnens Gl, Cipriani E, Lund JS. Clinical immunity after neonetal rota virus infection : A prospective longitudinal study in young children. N Eng J Med 1983; 309 : 72-76.
14. Velazquez FR, Maston DO, Calva JJ, Guerrero ML, Morron AL, Carter campbell S, Rotavirus infection in infants as protection against subsequent infections. N Eng J Med. 1996; 335: 10 22 -28.
15. Parasar UD, Bresee JS, Glass RI. The global burden of diarrhea disease in children. Bull World Health Organ. 2003, 81:236.
16. Jain V, Parashar UD, Glass RI, Bhan MK. Epidemiology of rotavirus in India. Indian J Pediatr 2001; 68(9) : 855-62.
17. Kang G, Kelkar SD, Chitamber SD, Ray P, Naik T. Epidemiological profile of rotaviral infection in India: Challenges for the 21st century. J Infect Dis. 2005; 192 suppl, 1 : 120-126.
18. Robert F. Ramig. Pathogenesis of Intestinal and systemic Rotavirus Infection Journal of virology. 2004, 78, (19):10213-10220.
19. Halaihel N, Lievin V, Alvarado F, Vasseur M. Rotavirus infection impairs intestinal brast border memberane Na (+) solute cotransport activities in young rabbits. AM J Physiol Gastrointest Liver Physiol, 2000, 279(3): 587-96

20. Lundgren O, Atimar - Peregrin, K. Persson, S. Kordasti, I. Uhnoo and L. svensson. Role of enteric rervous system in the fluid and electrolyte secretion of rota virus diarrhoea. Science, 2000, 287: 491-495.

21. Dennehy PH, Cortese MM, Begue RE, Jaeger JL, Roberts NE, Zhang R et al. A case controlled study to determine risk factors for hospitalision for rotavirus gastro enteritis in U.S. children. Pediatr Infect Dis J. 2006, 25; 1123-31.

22. Fischor TK, Bresee JS, Glass RI. Rotavirus vaccines and prenvetion of hospital acquired diarrhoea in children. Vaccine 2004; 22 suppl 1: S49-59.

23. Chapping E, Azzari C, Moriondo M, Galli L, Martino M, Viraemia is a common finding, in immunocompetent children with rotavirus infection.

J Med Virol. 2005; 76 : 265-267.

24. DA Sack, M Rhoads, A Molla, AM Molla, MA Wahed. Carbohydrate malabsorption in infants with rotavirus diarrhoea. AM J Clin Nutr. 1982 : 36; 1112-1118.

25. Gurwith M, Wenman W, Hinde D, Feltham S, Grenberg H.A prospective study of rotavirus infection in Infants and young children.

The J.Inf. Dis. 1981, 144(3). 218-224

26. Ruuska T and Vesikari T. Rotavirus disease in Finnish childran : use of numorical scores for clinical soverity of diarrhoeal episides. Scand J Inf Dis 1990; 22:259-267.

27. Altindis M, Yavru S, Simsek A, Ozkul A, Ceri A, Koc H, Rotavirus Infection in children with acute diarrhoea as detected by latex agglutition, ELISA and Polyacrylamide Gel Electrophoresis Ind. Pediatr. 2004; 41:590-594.

28. B.selb, H.G.Balimeister, G.Maass, H.W.Doerr. Detection of Human Rotavirus by necleic acid analysis in comparision to Enzyme linked immunoassay and Electron microscopy. Eur. J. Clin. Microbiol 1985. 4(1) : 41-45.

29. J. Buser, L. Risch, T. Rutz, S.manang and J. Munzinger. Comparition of Rotavirus agglutination test with two rapid immiuno chromatographic test devices for detection of rotavirus in Human feces. European Journal of clinical microbiology & Infectious Diseases. 2001, 20(4): 295-296

30. Dorsey M. Bass in Behrman E., Kliegman M., Jenson B Ed ted Nelson Text book of pediatrics, 17th Edition.

Rotavirus and other agents of viral gastroenteritis. Page 1081-83.

31. Bettger WJ, O'Dell BL. A critical physiological role of Zinc in the structure and function of biomembranes. Life Sci. 1981; 28: 1425 1438.

32. Lukacik M, Thomas RL, Aranda JV. A meta-analysis of the effects of oral zinc in the treatment of Acute and Persistant Diarrhoea. Pediatrics. 2008; 121:326-336.

33. Szajewska H, Mrukowicz JZ. Probiolics in the treatment and prevention of acute infectius diarrhoea in infants and children: a systematic review of published randomized, double blind, Placebo controlled trials. J pediatric Gastroenterol Nutr. 2001; 33: (2S) 17-25.

34. Ansari SA, Sattar SA, Spring Thorpe VS, Wells GA and Tostowaryk W. In vivo Protocol for testing efficacy of hand-washing agents against viruses and bacteria. Experiments with rotavirus and Escherichia coli. Appl Environ Microbial. 1989; 55 (12): 3113-3118.

35. Guarino A, Canni RB, Russo S, Albano F, Rubino A, Canani MB, Ruggeri FM, Donelli G. Oral Immunoglobulins for the treatment of Acute Rotavirus Gastroenteritis.

Pediatrics, 1994; 93: 12-16.

36. WHO, Initiatives for vaccine research, WHO. Proceedings of the 7th global vaccine research forum. Bangkok; 2006.

37. Parez M. Rotavirus gastroentoritis : Why to back up the development of new vaccines ? Comp Immunol Microbiol Infect Dis 2008; 31: 253-69.

38. Ward R. Mechanism of protection against rotavirus in humans and mice. J. Infect Dis 1996; 174:S 51-58.

39. Offit PA. Host factors associated with Protection against rotavirus disease : the skies are clearing J Infect Dis 1996; 174 : S 59-64.

40. CDC with drawl of rotavirus vaccine recommendation. MMWR, Mor Mortal wkly Rep 1999; 48:1007.

41. Salinas B, Perez Schael I, Linhares AC, Ruiz Palacios GM, Guerrero ML, Yarzabal JP, et al. Evaluation of safety, immunogenicity and efficacy of an attenuated rotavirus vacine, RIX 4414 : A randomized, Placebo controlled trial in Latin American infants. Pediatr Infect Dis J 2005; 24:807-16

42. Linhares AC, Velazquez FR, Perez-Schael I, Saez-Llorens X, Abate H, Espinoza F, et al. Efficacy and safety of an oral live attenuated human rotavirus vaccine against rotavirus gestroenteritis during the first 2 years of life in Latin American infants : a randomised, druble blind, placebo controlled phase III study. Lancet 2008; 371 : 1181-89.

43. Ruiz-Palacios GM, Perez-Schael I, Velazquez FR, Abate H, Breuer T, Clemens SC et al. Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. N Engl J Med 2006; 354: 11-22.

44. Vesikari T, Matson DO, Dennehy P, Van Damme P, Santosham M, Rodriguez Z, et al. Safety and efficacy of a pentavalent human - borine (WC3) reassortant rotavirus vaccine. M Eng J med 2006; 354: 23-33.

45. Rodriguez ZM, Goveia MG, Stek JE, Dallas MJ, Boslego JW, Dinubile MJ, et al. Concomitant use of an oral live pentavalent human-bovine reassortant rotavirus vaccine with licensed parenteral pediatric vaccines in the united states. Pediatr Infect Dis J 2007; 26 : 221 - 7.

46. T.N. Naik. Rapid diagnosis of rotavirus infection: key to prevent unnecessary use of antibiotics for treatment of childhood diarrhoea. Indian J med res 2004, 119, (PPV - vi)

47. Gentsch JR, Das BK, Jiany B, Bhan MK, Glass RI. Similarity of the VP4 protein of human rotavirus strain 116E to that of bovine B 223 strain. Virology 1993, 194 : 424-430.

48. Das M, Dunn Sj, Woode GN, Greenberg HB, Rao CD. Both surface proteins (VP4 and VP7) of an asymptomatic neonatal rotavirus strain (I 321) have high level of sequence identity with the homologous proteins of a serotype 10 bovine rotavirus. Virology 1993, 194: 374 - 379.

AMJ Physiol Gastrointest Liver Physiol, 2000, 279(3) : 587 - 96.

49. Parashar UD, Gibson CJ, Bresse JS, Glass RI; Rotavirus and severe childhood diarrhoea. Emerg Infect Dis. 2006; 12:304-306.

50. CDC, Delayed onset and diminished magnitude of rotavirus activity-United States November 2007- May 2008. MMWR Morb Mortal wkly Rep 2008; 57:697-700.

51. World Health Organization, Diarrhoea Diseases (Update February 2009)

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EVALUATION OF SCORE FOR NEONATAL ACUTE PHYSIOLOGY IN PREDICTING NEONATAL MORTALITY

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ABSTRACT :

Objectives : *To evaluate the validity of the Score for Neonatal Acute Physiology as a predictor of neonatal mortality, duration of ICU stay. The study was also undertaken to evolve the best cut-off SNAP scores for predicting neonatal mortality in different gestational ages and birth weights.* ***Methods:*** *264 newborns admitted to NICU during 2 yrs were evaluated for SNAP.* ***Results :*** *SNAP correlated well with mortality, the best cut-off SNAP value was 13 with 76.5% sensitivity 97.2% specificity, 86% positive predictive value and 94% negative predictive value. Best cut-off value for ELBW infants was 6, VLBW was found to be 9 with 87.5% sensitivity and 100% specificity and in LBW was observed to be 13 with 89% sensitivity and 100% specificity. In infants 32 wks cut-off value was observed to be 9 with 89% sensitivity and 100% specificity and above 33 wks a cut-off value of 11 was found to have 90% sensitivity and 100% specificity. The median duration of ICU stay among survivors increased as the SNAP increased with values ranging from 4 to 8 days median duration of ICU stay and in dead babies the median duration of ICU stay was 5 days with a SNAP of 6-10 and 4 days above that score.* ***Conclusion :*** *SNAP is a good measure of severity of illness irrespective of differences in the gestational age, birth weight and various morbid conditions. SNAP is a mandatory evaluation of function of all organ system in a sick baby as against the traditional practice on concentrating on the presenting features.*

KEYWORDS : *Illness severity scoring, Neonate Mortality, NICU performance, SNAP*

Introduction :

There is a wide variation in the neonatal mortality among the various NICU of both the government and private sector in India. Recent studies have demonstrated substantial variations in mortality and morbidity among neonatal intensive care units (NICUs). If these differences reflect variations in the effectivenes of current NICU technology, it would suggest that major improvement in neonatal mortality and

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reductions in complications might be achieved if all NICUs performed as well as those with the best outcomes. A variety of risk adjustment, scores have been derived and advocated for use in assessing neonatal mortality. Clinical risk index for babies (CRIB) score was created to predict mortality for infants born of less than 32 wks gestation at birth. [1] The new score of CRIB-II [2], an improved version of CRIB was intended to improve predictions for smaller, very premature infant and to exclude variables that could be influenced by care given to the infant, needs to be further validated. National Therapeutic Intervention Scoring System (NTISS) in based on the treatments received by an infant rather than measuring pathophysiological factors. As treatment depends on policy and practice in units, it can vary greatly and it is not possible to compare units using this type of adjustment. [3] Berlin score includes a number of subjective factors which limit its roles as an means of objective comparison between units. [4] National Institute of Child Heath & Human Development (NICHHD) score was created using factors noted at admission of newborns weighing 500 gm - 1500gm has not been used extensively since development [5]

Illness severity scores are now well accepted as essential tools when comparing healthcare providers. SNAP score estimates mortality risks in hospital even within narrow birth weight categories & highly correlates with several measures of medical resource use including therapeutic intensity nursing workload. [6] SNAP is a valid measure of illness severity which is specific for intensive care. [6]

The present study was conducted to evaluate the validity of the Score for Neonatal Acute Physiology (SNAP) as a predictor of neonatal mortality, duration of ICU stay in our neonatal intensive care unit. The study was also undertaken to evolve the best cut-off SNAP scores for predicting neonatal mortality in different gestational ages and birth weights.

Subject & Methods :

The material for this prospective cohort study consisted of all newborn infants admitted to the intensive care unit of SVP Postgraduate institute of Pediatrics, an attached Instituition of SCB Medical College, Hospital, Cuttack over a period of 2 years.

Inclusion criteria :

All newborn infants admitted to our intensive care unit were prospectively evaluated within 24 hours of admission for various SNAP parameters (Table I). Thus 694 babies were subjected to SNAP scoring.

TABLE -I SCORE FOR NEONATAL ACUTE PHYSIOLOGY

PARAMETER RANGE	1- POINT RANGE	3 - POINT RANGE	5 - POINT RANGE
Blood Pressure			
High	66 - 80	81-100	> 100
Low	30 - 55	20-29	< 20
Heart rate			
High	180 - 200	201 - 250	> 250
Low	80 - 90	40 - 79	< 40
Respiratory rate	60 - 100	> 100	-
Temperature F	95 - 96	92 - 94.9	< 92
PO2, mm Hg	50 - 65	30 - 50	< 30
PO2 / FiO2 ratio	2.5 - 3.5	0.3 - 2.49	< 0.3
PCO2, mm Hg	50 - 65	30 - 50	< 30
Oxygenation Index	0.07 - 0.2	0.21 - 0.4	> 0.4
Hematocrit %			
High	66 - 70	> 70	-
Low	30 - 35	20 - 29	< 20
WBC count x 100	2 - 5	< 2	-
Immature : Total ratio	> 0.21	-	-
ANC	500 - 999	< 500	-
Platelet count (x 1000)	30 - 100	< 30	-
BUN (mg/dl)	40 - 80	> 80	-
Creatinine (mg/dl)	1.2 - 2.4	> 2.5	-
Urine output (ml/kg/hr)	0.5 - 0.9	0.1 - 0.49	-
Indirect bilirubin (mg/dl)			
> 2 kg	15 - 20	> 20	-
< 2 kg	5 - 10	> 10	-
Direct bilirubin	> 2	-	-
Sodium (2mEg/L)			
High	150 - 160	161 - 180	> 180
Low	120 - 130	< 120	-
Potassium (mEg/L)			
High	6.6 - 7.5	7.6 - 9	> 9
Low	2 - 3.9	< 2	-
Calcium (mg/dl)			
High	> 12	-	-
Low	5 - 6.9	< 5	-
Glucose (mg/dl)			
High	150 - 250	> 250	-
Low	30 - 40	< 30	-
Serum bicabonate			
High	> 33	-	-
Low	11 - 15	< 10	-
Serum pH	7.2 - 7.3	7.1 - 7.19	< 7.1
Seizure	Single	Multiple	-
Apnea	Responsive to stimulation	Unresponsive to stimulation	Complete apnea
Stool guaiac test	Positive	-	-

Exclusion criteria :

1. Death or discharge from the neonatal intensive care unit in the first 24 hours of life.
2. Neonates admitted with multiple congenital anomalies.
3. Those who were shifted to NICU for observation only.
4. Where SNAP scoring could not be completed for one reason or the other.

By applying the above rigid exclusion criteria 430 newborns were excluded from the study and finally 264 newborn infants remained in our study group. All the neonates under study underwent careful clinical assessment and received the necessary treatment while concurrently being evaluated for SNAP, which consisted of 26 parameters. All the measurements were done using standard techniques and methods. The parameters used in SNAP along with the scores are given in. One point is assigned for each parameter, when the physiologic deviation was sufficiently abnormal to merit careful monitoring. Three points were assigned when deviation was such that most clinicians would alter therapy to correct it. Five points were given to items that was life threatening. Scores range from 0-42, higher the score higher is the risk of adverse outcome.

Statistical analysis was done using the Mann Whitney Test, wherever appropriate and the p value was computed. Sensitivity, specificity, positive and negative predictive values of SNAP score was evaluated in different groups of neonates. Receiver Operating Characteristic curves was constructed to derive the best cut-off SNAP values with emphasis on minimizing the false-positives, while maintaining an optimum level of sensitivity (>0.5).

Results :

During the study years newborns constituted 17.5% of all admissions of which 27.1% were admitted to ICU. 35.6% of the babies were admitted in the age group between 72 hours and 7 days followed by 30.4% babies admitted in 24 to 72 hrs age with equal contribution under 24 hrs of age and of more than 7 days each approximately 17%. Among them 64.9%, 34% and 1.1% of the babies constituted term. Preterm and postterm births respectively. Among the preterms 13.6% were very preterm and 1.1% were extremely premature infant. 55.7% of which 11.4% were very low birth weight infants and 3.4% were extremely low birth weight infants. 44.3% of infants had birth weight 2.5kg or more. In the present study sepsis was more prevalent (42%) followed by HIE, MAS and RDS in 40.8%, 13.6% and 3.4% respectively.

SNAP & Mortality (Table- II)

With SNAP value of 21 and above mortality reached 100%. Between the score of 11 and 20 mortality is between 55.6 to 71.4% with mean SNAP in survivors was 5.58 and mean SNAP in dead babies was 16.18 with Z-value of difference of 6.332 and p-value <0.001. The mean SNAP score among survivorsin various subgroups was ranging from 4.73 to 6.13 whereas the mean SNAP score among dead babies was ranging from 15.33 to 18. The nonparametric test (Mann Whitney U test) showed a highly significant (p-value<0.0001) association between SNAP score and mortality with a Z value of difference ranging from 3.937 to 11.009 among various sub-groups. Below the score of 11 the mortality is very low. The best score with higher specificity and sensitivity

TABLE -II SCORE FOR NEONATAL ACUTE PHYSIOLOGY SNAP AND MORTALITY (n = 264)

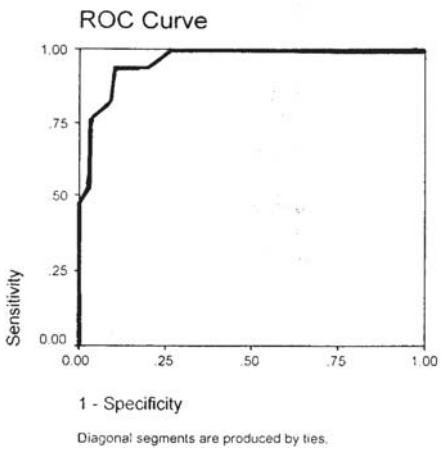
SNAP	TOTAL NO. OF CASES	SURVIVAL		DEATHS	
		NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
0-5	150	150	100	0	0
6-10	54	45	80	9	20
11-15	27	12	44.4	15	55.6
16-20	21	6	28.6	15	71.4
21-25	9	0	0	9	100
26-30	3	0	0	3	100
TOTAL	264	213	80.7	51	19.3

Mean SNAP in suvivors is 5.58, Mean SNAP in dead babies is 16.18

Z- Value of difference of 6.332, p - value < 0.001

lies at a cut-off SNAP value of 13 with 76.5% sensitivity 97.2% specificity, 86% positive predictive value and 94% negative predictive value (13 was considered as the cut-off value based on the ROC curve (Fig 1).

Fig -1
SNAP AND MORTALITY



Snap & Birth weight (Table-III)

The best estimate of sensitivity and specificity was observed at a cut-off value of 6, which showed 100% sensitivity, 100% specificity, 100% positive predictive value, and 100% negative predictive value in ELBW category. The best estimate of sensitivity and specificity was observed at a cut-off value of 9, which showed 87.5% sensitivity, 100% specificity, 100% positive predictive value, and 69% negative predictive value in VLBW category. The best estimate of sensitivity and specificity was observed at a cut-off value of 15, which showed 64.3% sensitivity, 97% specificity, 73% positive predictive value, and 95% negative predictive value in babies weighing more than 1500 gms.

TABLE -III

SNAP, BIRTH WEIGHT AND MORTALITY (n = 264)

SNAP VALUE	BIRTH WEIGHT				
	< 999g	1000 - 1499g	1500 - 1999g	2000 - 2499g	2500 - 3999g
0-5	3, 0 (0%)	9, 0 (0%)	30, 0 (0%)	30, 0 (0%)	78, 0 (0%)
6 - 10	3, 3 (100%)	9, 0 (0%)	31, 1 (33.32%)	15, 1 (6.6%)	27, 0 (0%)
11 - 15	3, 3 (100%)	–	6, 5 (83.3%)	9, 3 (33.3%)	9, 2 (22.2%)
16 - 20	–	6, 6 (100%)	3, 3 (100%)	9, 6 (66.6%)	3, 2 (66.6%)
21 - 25	–	6, 6 (100%)	–	3, 3 (100%)	–
26 - 30	–	3, 3 (100%)	–	–	–

1st number - total, 2nd number - number of deaths, In parenthesis - percentage of deaths

SNAP & Gestational age (Table-IV)

In premature babies the best estimate of sensitivity and specificity was observed at a cut-off value of 11, which showed 90% sensitivity, 100% specificity, 100% positive predictive value, and 95% negative predictive value. The best estimate of sensitivity and specificity was observed at a cut-off value of 14, which showed 83.3% sensitivity 96.2% specificity, 72% positive predictive value and 97% negative predictive value in term babies.

TABLE -IV

SNAP, GESTATIONAL AGE AND MORTALITY (n = 264)

SNAP VALUE	GESTATIONAL AGE				
	<28 wks	29 - 32 wks	33 - 36 wks	37 - 41 wks	> 42 wks
0-5	–	9, 0 (0%)	39, 0 (0%)	102, 0 (0%)	–
6 - 10	3, 3 (100%)	6, 2 (33.3%)	6, 1 (16.6%)	36, 3 (12%)	3, 0 (0%)
11 - 15	–	6, 5 (83.3%)	3, 2 (66.6%)	18, 8 (44.4%)	–
16 - 20	–	6, 6 (100%)	3, 3 (100%)	12, 6 (50%)	–
21 - 25	–	6, 6 (100%)	–	3, 3 (100%)	–
26 - 30	–	3, 3 (100%)	–	–	–

1st number - total

2nd number - number of deaths

In parenthesis - percentage of deaths

SNAP & Morbid conditions (Table-V)

With SNAP values between 6 and 10 the mortality was highest in RDS group (100%) followed by HIE III (50%) and SEPSIS group with 25%. In the score range of 11 to 15 there was no mortality in HIE I and HIE II but 2/3rd infants died in SEPSIS and MAS whereas all died in HIE III group. With SNAP values in 16 to 20 ranges 3/4th of SEPSIS cases died and all infants in HIE III and MAS died. Beyond 21 score there there was 100% mortality in SEPSIS and HIE III groups.

TABLE - V
SNAP, MORBID CONDITIONS AND MORTALITY (n = 264)

SNAP VALUE	MORBID CONDITIONS					
	RDS	SEPSIS	HIE-I	HIE-II	HIE-III	MAS
0-5	3, 0 (0%)	72, 0 (0%)	12, 0 (0%)	30, 0 (0%)	15, 0 (0%)	18, 0 (0%)
6-10	3, 3 (100%)	12, 3 (25%)	3, 0 (0%)	18.0 (0%)	6, 3 (50%)	12, 0 (0%)
11-15	3, 3 (100%)	6, 4 (66.6%)	3, 0 (0%)	6, 0 (0%)	6, 6 (100%)	3, 2 (66.6%)
16-20	–	12, 9 (75%)	–	3, 0 (0%)	3, 3 (100%)	3, 3 (100%)
21-25	–	6, 6 (100%)	–	–	3, 3 (100%)	–
26-30	–	3, 3 (100%)	–	–	–	–

1st number - total
2nd number - number of deaths
In parenthesis - percentage of deaths

SNAP & ICU stay (Table-VI)

The median length of stay in ICU of surviving infants was least (4days) with score below 5, and MLOS steadily increased as the score increased, stay being 8 days above the score of 16. The minimum duration of ICU stay for any surviving infant was 3 days and the maximum duration was 12 days. The median length of stay in ICU of dying infants was 5 days with score between 6 and 10, and MLOS remained 4 days above the score of 11. The minimum duration of ICU stay for any dying infant was 3 days and the maximum duration was 9 days in our study group.

TABLE - VI

SNAP AND LENGTH OF ICU STAY (n = 264)

	N		Minimum Duration (days)		Maximum duration (days)		Median duration (days)	
	SURVIVED	DEAD	SURVIVED	DEAD	SURVIVED	DEAD	SURVIVED	DEAD
0 to 5	150	–	3	–	12	–	4	–
6 to 10	45	9	4	5	7	6	5	5
11 to 15	12	15	4	3	8	9	6	4
16 to 20	6	15	7	3	9	5	8	4
21 to 25	–	9	–	3	–	5	–	4
26 to 30	–	3	–	3	–	5	–	4

r (Pearsons correlation coefficient) = 0.242
p - value is 0.023

SNAP & Cost :

An attempt has been made to analyze the cost of applying the SNAP score in the study group. The scores which were abnormal by 3 -points were repeated for the second time testing except for RBS which was done more frequently (4 to 6 times) whereas ABG required to be repeated 4 times in 36 babies. The total cost of 11 parameters done in the present study was found to be Rs. 206910 at an average cost of Rs. 784. the unit cost of each parameter for 11 parameters that are mandatory for every case was Rs. 485. So an additional cost of Rs. 299 was observed for SNAP evaluation in the first 24 hours.

Discussion

As the SNAP value increased the incidence of mortality also increased consistently reaching 100% mortality above the score of 21. The best cut-off score in predicting mortality with higher specificity and sensitivity lies at a cut -off SNAP value of 13 with 76.5% sensitivity 97.2% specificity, 86% positive predictive value and 94% negative predictive value. The results were comparable to the observations made by the others[6,7,8] who have reported a good predictability of neonatal outcome by using SNAP. Since SNAP reflects the physiology of the newborn as a whole, the mortality is proportional to the quantum of deranged physiology, which has reached the state that could not be reversed by treatment provided in our setup.

The best cut off SNAP value predicting mortality in birth weight <1500g in our study was lower (9) than the comparable Indian

studies (P. P. Maiya et al[7] had the best cut-off score of 10) whereas above 1500 g the best cut off score was 15 in both the studies. This difference in SNAP value was due to the absence of adequate nursing care, better facilities to manage these VLBW babies. The low birth weight by itself confers higher mortality to these sick newborns as shown by the low SNAP values with higher mortality.[9]

The best cut off SNAP value predicting mortality in preterm in our study was lower (11) than other comparable Indian studies (P.P.Maiya et al had the best cut-off score of 15) whereas in term babies the best cut off score was 15 in the author's studies and 14 in our study. This difference signifies the better available facilities, efficient care of preterm babies in those setting compared to our NICU.

The outcome in our work with respect to sepsis cases and HIE II was similar with other comparable Indian studies[7] but in other morbid condition, the mortality increases with increase in SNAP values in both the studies.

The duration of ICU stay of dead babies in different SNAP ranges. With lower SNAP values between 6-10 the MLOS was 5 days above the score of 11 with range of 3 to 9 days. There is no comparable literature for length of ICU stay of dead babies. However the shorter of ICU stay of dead babies shows that our early intervention is probably not adequate and requires more extensive analysis to arrive at a conclusion.

Benefit accrued out of SNAP were

1. Alerting the doctors and nurses for more aggressive management.
2. Higher rate of survival (213 cases) as against mortality of 51 cases in a ratio of 4.2:1.
3. A high risk of mortality of 74% was observed with a score above 13. In this high-risk group it was possible to rescue the remaining 26% of babies because of increased alertness signaled by SNAP. Similarly below a score of 13 there was 7% mortality and was due to complication during the course of illness, which could not be predicted by the initial SNAP.
4. Because of the significant predictive value observed in prognosticating mortality risk and duration of ICU stay, the cost of treatment required can be explained to the parents with a more certainty.
5. SNAP can be used effectively for research purposes and for comparison of efficiency in management in different ICU stratifying the newborn infants into various score groups, randomizing the cases and ultimately relating to the outcome.
6. The overall cost benefit analysis shows that additional expenditure of Rs. 300 is very insignificant in terms of the life saved, minimizing the parental anxiety and tension and a constant inspiration to improve the ICU management at par with better ICU's in the country.

7. SNAP is a mandatory evaluation of function of the organ system in a sick baby as against the traditional practice on the presenting features. This approach leads to better homeostasis by effective supportive management with better outcome.

Conclusion :

SNAP score is a good measure of severity of illness irrespective of differences in the gestational age, birth weight and various morbid conditions. When it is applied on admissions or during the first 24 hours it gives good information of the severity of referral cases received in ICU. When SNAP score alone is applied to measure the risk of mortality it is found to have a linear relationship i.e., with increasing score the mortality also increases. A cut-off value of 13 has 76.2% sensitivity, 97.2% speciicity and 84.9% positive predictive value beyond which the mortality increases exponentially. But within the same range of birth weight of gestational age the SNAP bears a linear relation with mortality. SNAP is a mandatory evalution of function of all the organ system in a sick baby as against the traditional practice on concentrating on the presenting features. This approach leads to better homeostasis by effective supportive management with better outcome.

References :

1. Rautonen J, Makela A, Boyd H, etal; CRIB & SNAP; assessing the risk of death for preterm neonates, Lancet, 1994; 343: 1272 - 1273
2. Parry GT, TuckerJ, Tarnow- Mordi W; CRIB-II an update of the Clinical risk index for babies score, Lancet, 2003; 361: 1789 - 1791.
3. Gray JE, Richardson DK, Mc Cormick MC, etal; Neonatal Therapeutic Intervention Scoring System, a therapy based severity of illness index; Pediatrics, 1992; 90 : 561- 567.
4. Maier RF, Casper- Karweck UE, Gravel EL etal, A comparison of two mortality risk scores for very low birth weight infants, clinical risk index for babies & Berlin Score; Intens Care Med 2002 ; 28: 1332- 1335.
5. Horbar JD, Onstad L, Wright E, etal; Predicting mortality risk for infants weighing 501 to 1500 gms at birth; a National Institute of Health Neonatal Research Network Report, Crit Care Med 1993, 21 : 12-183.
6. Richardson DK, GrayJE, Mc Cormick MC, etal, Scorefor Neonatal Physiology: a physiological severity index for neonatal intensive-care, Pediatrics 1993; 91 : 617-623.
7. P.P. Maiya etal; Role of Score for neonatal acute physiology in predicting neonatal mortality, Indian Journal of Pediatrics, Vol-68 - Sep, 2001.
8. Eleni Petridox etal; Outcome prediction in Greek Neontal Intensive Care units using a score for neonatal acute physiology (SNAP), Pediatrics, 1998 : Jun, 101(6) : 1070
9. Richardson DK, Phibbs CS, Gray JE, Mc Cormick MC, Workman Daniels K, Goldmann DA; Birthweight and illness severity, independent predictors of neonatal mortality, Pediatrics, 1993; 91 : 969 - 975.

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THE ENIGMA OF PAIN ABDOMEN IN CHILDREN

Nimain C. Mohanty

Introduction :

Very often than not, abdomen in children has been an enigma to the attending physician. The term by and large, is descriptive in nature than a diagnostic terminology. While all the presenting symptoms do not always fit into a particular organic entity as per book description, as many as 13% are of functional in nature. On the other hand, few of the kids do need life saving emergency interventions. Hence it is very important to recognize the red flag signs in time. With drastic change in our social milieu and rapid introduction of advanced diagnostic technologies, the so called functional group is shrinking further. Also important is to realize the peculiar path physiology of abdominal pain in case of children, so different from adults! Hence this review:

Seeking an immediate diagnosis for abdominal pain, particularly in children, is like exploring the so called Pandora's Box. A working diagnosis is easy if our approach is rational but often vexed otherwise in our busy office practice setting. It deserves its due, in terms of time and patience on part of the care giver as well as parents. Unlike adults and grown-up children, abdominal and pelvic pain presented differently in infants:

1. Screaming or persistent crying
2. Restlessness
3. Irritability
4. Squirming
5. Grunting respiration
6. Flexion of thighs over abdomen or,
7. Refusal to feed

Mostly we encounter children presenting abdominal pain around umbilicus or in the midline. It has got an embryogenic basis:

- Most primitive viscera develop as mid-line structures, having bilateral and symmetric innervation.
- Location of pain is perceived at a level where afferent nerves enter spinal cord segments.
- Referred pain (Hyperalgesia) is felt over cutaneous dermatomes supplied by same neural segment e.g.- Pancreatic pain over mid-back and inter-scapular (T5-9) region; hepato-biliary origin pain being referred to right sub-scapular region.

Classification of pain abdomen :

Classifying pain abdomen on the basis of its location depends on the back-ground of development, innervation and pain perception.

PrimitiveStructures	Segments	Localisation
Foregut:	Oesophagus, stomach, duodenum, liver, GB, pancreas	T5-T9 Xiphi-umbilicus (Midline)
Midgut: Periumbilical	Small intestine, appendix, ascending & proximal 2/3 of tansverse colon	T8-L1
Hindgut:	Distal 3rd of trasverse colon, Descending, recto-sigmoid col	T11-L1 Umb-Symphisis pubis (Midline)
Nephrogenic cord: (Mesoderm)	Kidneys, ureters, ovaries, tubes	T10-L1 Lateralised

Classifying pain abdomen on the basis of its origin

Visceral: Midline discomfort, poorly localised, accompay nausea, emesis, diphoresis.

Parietal: More intense, well localised, aggravated with movement.

Referred: To same dermatome represented by affected viscera.

In combinations of any of the three above.

To further understand the very basis of the above, we must realize the existence of myo-enteric nervous system (MNS) which of late has generated much interest.

Visceral pain:

- Nocieptors are present through-out walls of abdominal viscera and supporting structures.
- Once generated, pain conducted through small, un-myelinated slow conducting C-fibres; whose termination occurs 4-5 spinal segments above. Therefore, the resulting pain is less characterised and poorly localised
- GI mucosa is insensitive to pricking, cutting, crushing and therefore do not generate impulses to such stimuli. Hence, mucosal biopsy, polypectomy are painless.

Parietal pain

- Pain from superficial structures e.g. - peritoneum is conducted by both small, slow 'C' fibres and large, thinly myelinated, rapidly conducting 'A' fibres as wel.
- A and delta fibres in parietal & supporting structures also respond to tactile, thermal, chemical discriminative stimuli e.g.- location and intensity.
- Patient lies still as movement exaggerates parietal pain whereas restless in visceral pain which is vague and poorly localised.

Therefore, pain in appendicitis is initially perceived high up, may be around umbilicus initially but gets localised to right flank (Macburny's point) when local peritonitis sets in.

Acute pain abdomen in children:

Deserves prompt evaluation to rule out any surgical condition for immediate intervention. Any of the following should arouse suspicion (Red flag signs):

1. Sudden distension,
2. Bilious vomiting,
3. Exaggerated or absence of bowel sounds,
4. Guarding or rebound tenderness.

Classification basing upon etiology:

Etiology wise classification and detailed discussion are exhaustive and beyond the scope in this article. Following causes are shown to complete the list.

I. Intra-abdominal Causes

A. GIT & Mesentery

1. Infantile Colic
2. APD & H. Pylori Infection
3. Zolinger Ellison Syndrome
4. Dietary indiscretion
5. Appendicitis
6. Intussusception
7. Malrotation
8. Volvulus
9. Intra-abdominal hernia
10. Meckel's diverticulum
11. Mesenteric cyst
12. Duplication
13. Intestinal Polyp
14. Incarcenated Hernia
15. Intestinal obstruction
16. Constipation
17. Sigmoid Volvulus
18. Parasites
19. Bacterial enteritis
20. Aerophagia
21. Ulcerative colitis
22. Crohn's disease
23. Food allergy, CMPA
24. Lactose intolerance
25. Cystic fibrosis
26. Hereditary angio-oedema
27. Mesenteritis

B. Urinary Tract

1. Obstruction
2. Systemic haemorrhagic diseases, Renal calculus
3. Hyper-calciuria
4. A G N
5. PUJ obstruction

C. Liver & Gall Bladder

1. Viral hepatitis
2. Cholecystitis
3. Cholelithiasis
4. Passive congestion of liver
5. Sickle cell crisis
6. Choledochal cyst
7. Hydrops of Gall Bladder
8. Hepatic SOL
9. Budd-Chiari Syndrome

D. Spleen

1. Traumatic rupture
2. Splenomegaly
3. Congestive splenomegaly

F. Pancreas

1. Acute pancreatitis
2. Congenital fibrosis
3. Pancreatic pseudocyst

G. Ovaries & uterus

1. Torsion, cyst or tumor
2. Hematocolpus
3. Dysmenorrhea
4. Pelvic inflammatory disease
5. Endometriosis
6. Ectopic pregnancy

H. Lymph nodes

1. Mesenteric lymphadenitis
2. Iliac adenitis
3. Lymphoma
4. TB

I Bacterial peritonitis

J Mesenteric vein thrombosis

K Pelvic osteomyelitis

L Superior mesenteric artery syndrome

II. Extra-abdominal

A. Rt lower-lobe pneumonia

B. Cardiac origin

1. RHD
2. Pericarditis
3. Congenital endocardial fibroelastosis

C. CNS, spinal cord and spine

1. Abdominal epilepsy
2. SOL in brain
3. Herpes zoster
4. TB spondylitis
5. Spinal cord tumour in dorso-lumbar region
6. Discitis, collapse of vertebra

D. Blood

1. Haemolytic anemias
2. Sickle cell crisis
3. Leukemia
4. HSP
5. Hemophilia
6. Acute infectious mononucleosis

E. Metabolic

1. Lead
2. Hyperparathyroidism
3. Addison's disease
4. DKA
5. Hypoglycemia
6. Hyperlipoproteinemia
7. Acute porphyria
8. Hereditary angio-oedema
9. Familial paroxysmal polyserositis

F Miscellaneous

1. Periarteritis nodosa
2. Arachnidism
3. Epidemic myalgia
4. Rheumatoid arthritis
5. Abdominal stitch
6. Mesenteric arteritis

III. Recurrent and Chronic Pain Abdomen:

These terms are descriptive terms than diagnostic; often used interchangeably. Defined as pain occurring at least 3 episodes over last 3 months (Apley,1958), severe enough to affect daily activities. Based on his criteria, out of 1000 school children studied,

13-15% school children complained on daily to weekly basis, affecting their routine. Girls reported more frequently than boys. All such children do need evaluation although most do not have underlying disease. No organic pathology reported in 90% of such cases those days with the available investigations. The Rome III criteria of paediatric RAP includes abdominal pain of more than 8 weeks duration, as a modification over Rome II criteria (Rasquin, 2006; Hyman, 2006).

History important.

Better be obtained directly focusing on:

- Timing, frequency, location, quality, assoc symptoms e.g. diaphoresis, nausea, diziness, stool frequency, completeness of evacuation.
- Precipitating factors - food, viral g/e, stress, anxiety, medication, menses, wt loss.
- Growth failure, delayed puberty, fever, rash, joint pain.
- Family h/o IBD, APD, epilepsy, peer relations. RAP among 1st degree relatives.

Red flag symptoms / signs indicating significant pathology:

- Involuntary weight loss, reduced growth
- Pain awakening the child from sleep at night
- Significant vomiting, chronic / severe diarrhea, unexplained fever
- Clubbing, rash, arthritis, P/R findings / bleeding PR or haematemesis
- Localised pain away from umbilicus
- Family h/o IBD, organomegaly (Liver, spleen), mass, tenderness, ascites, bruits.

Investigations:

- Stool, Urine, CBC, ESR, CRP, Urea, S/E, LFT, screening for celiac, UTI

Predictive value of investigations;

(AAP Technical report, 2005)

- There is insufficient evidence in support of blood examination to look for organic pathology, even in presence of red-flag signals.
- Ultrasonography, pH probe studies and endoscopy have little additional diagnostic yield in absence of red-flag signals.
- H. pylori infestation is as common in children with RAP as those without.

Management:

- Most do not need medication.
- Reassure that there is no evidence of underlying pathology.
- Those with persistent symptoms may need multi-disciplinary approach, also involving family.
- Possible placebo effect may be borne in mind.
- Medications on selective basis.

Classification of basing upon organic or non-organic (Functional):

Organic: Discrete cause identified in 5 to 10% of cases; Yield improved to 33% applying modern tools. Recognisation of conditions e.g.- IBD, COH MAS, APD, Celiac improved the yield. Intestinal worm / parasite infestations, particularly Ascariasis or Giardiasis; constipation, GERD are common in the Indian sub-continent.

Non-organic (Functional):

That can't be explained on basis of structural or biochemical abnormalities with presently available tools, but regarded as genuine. It is not synonymous with psychogenic or 'Imaginary' pain. 'Functional' must be labeled only by exclusion. It is challenging and must be appreciated as an abnormality in 'Brain-gut' interaction and not merely as a manifestation of symptoms in some psychogenic illness. The Abnormality could be any where at levels of gut, spinal afferents, central autonomic relay system, brain

Functional GI Disorders (FGID, ROME II classification)

G2. Abdominal pain

G.2.a.1. Ulcer like dyspepsia

G.2.a.2. Dysmotility like dyspepsia

G.2.a.3. Unspecified dyspepsia

G.2.b. IBS

G.2.c. Functional abdominal pain syndrome

G.2.d. Abdominal migraine / epilepsy

G.2.e. Aerophagia

G.2a. Functional Dyspepsia:

Usual Presentation: Child complains epigastric discomfort immediately after food, often awaking patient at night. Also has nausea, fullness of abdomen; restricting food intake. No h/o retro-sternal pain, vomiting, regurgitation, pain on swallowing. Is afraid to eat and misses school bus for morning symptoms. No weight loss, growth maintained. No nocturnal symptoms., no vomiting, regurgitation or haematemesis.

Differential Diagnosis :

Unlike to be Acid related (Gastritis, duodenitis, oesophagitis) since there is no pain, nausea, heart burn related to eating, night time awakening. Neither could be due to H. Pylori (Also can be present without any specific symptom), Eosinophilic oesophagitis, Gastro-enteritis (Usually associated with atopy, abdominal pain, dysphagia, diarrhoea, eosinophilia), Crohn's, Coeliac (Diarrhoea, wt loss, pain, night awakening, other constitutional symptoms; presence of all these symptoms not a must also.)

Diagnosis:

- Symptoms consistent with dyspepsia >12 wks as per Rome II criteria.
- Not necessarily consecutive in preceding 12 months of pain / discomfort above umbilicus (As per ROME III: H2a criteria, at least once per week for 2 months) Common in 50% of referred children and 5-10% among school children.
- No organic disease to explain, even after UGI endoscopy.
- Not exclusively relieved by defecation or associated with altered stool consistency.

Types:

1. Ulcer like, 2. Dysmotility like, 3. Overlap symptoms.

Investigations:

- UGI endoscopy: Can be delayed in favour of a therapeutic trial of empric therapy, except in cases of wt loss, vomiting, hematemesis, odynophagia, dysphagia.

- UGI Ba series only for studying GI anatomy; not good for mucosal abnormality for which mucosal biopsy recommended.
- Nuclear scintigraphy: (If gastroparesis is suspected).
- USG (Only if biliary / pancreatic disease)
- H. Pylori Screening: Sero testing difficult to interpret in children, may be false +ve. Can't be used to monitor treatment. Stable isotope urea breath test not standardised for children, hence endoscopic biopsy is the gold standard.

Management :

Depends on predominant symptom of dyspepsia:

- Eliminate caffeine, fats, large meals, alcohol and smoking.
- If symptom response unequivocal, empiric treatment with H2 blockers, occasionally followed by proton pump inhibitors. Failure to respond or requirement of frequent drug therapy warrants endoscopy.
- Prokinetics (Metclopramide) in dysmotility variant. Erythrocin, a motilin receptor antagonist, can be tried.
- Antiemetics
- Low dose tricyclic anti-depressants (10-25 mg HS) often helpful in patients not responding to prokinetic agents.

G.2.b. Irritable Bowel Syndrome:

Usual Presentation: Pain abdomen in a gown-up child, waxing and waning, may be associated with intermittent diarrhoea. Pain occurs almost daily over lower quadrant; worse in morning some times sharp and crampy, forcing patient to close thighs over abdomen. There may be nausea but no vomiting. Pain may worsen with food intake. There is a feeling of urgency to defecate, pain decreasing after defecation, yet a sense of incomplete evacuation. Usually there is h/o pain of less intensity but less often for past few years. O/E: Normal anthropometry and development. Child may look pale with diaphoresis. No apparent structural or metabolic cause. Lab reports generally within normal limits. As per Rome-III (H.2.b), abdominal pain recurrent abdominal pain or discomfort for at least 3 days in a month over last 3 months; associated with 2 or more of following:

1. Discomfort or pain associated with 2 or more of these in 25% of time: (a) Improved after defecation, (b) Onset associated with change in stool frequency or (c) Form (Appearance)
2. No evidence of inflammatory, anatomic, metabolic or neoplastic process to explain symptoms.

Differential Diagnosis : MAS, Carbohydrate intolerance (Explossive, watery, with gases, peri-anal redness), Giardiasis (Diarrhoea, steatorrhea, pain, gas, bloating, weight loss), UTI (Pain lower abdomen, dysuria, haematuria; suggestive of urine exam), Crohn's, ulcerative colitis, eosinophilic gastro-enteritis etc.

Patho-physiology:

Patients with functional GI disorders have identifiable alterations in motility and sensitivity:

- Delayed transit of contrast seen in constipation predominant IBS and increased in diarrhoea predominant IBS.
- Exaggerated motility response stimuli such as- stress and meals seen.

- Visceral hyper-sensitivity due to alterations in neuro-physiology at gut level (Myenteric and mucosal plexuses involved in epithelial transport, secretion, sensation and GI motility), at spinal cord or at higher centres.
- Within the enteric nervous system (ENS) in gut, reflexes generated by activation of 'Intrinsic Primary Afferent Neuron' (IPANS) which increase it's excitability through repetitive stimulations, outlasting for hours which leads to an enhanced EPANS activity and there on to CNS. Stimuli include infection, trauma and inflammation.
- Inflammation of gut mucosa leads to changes in smooth muscle activity, enteric nerves and composition of neurotransmitters.
- Visceral hypersensitivity results in altered processing of sensory inputs at CNS level (HPA, locus ceruleus, amygdala, para-vertebral & dorsal motor nuclei); Vagus (Parasympathetic) being the primary communication link.
- Hypothalamus also involved in panic and post- traumatic stress disorders.
- Hence anxiety / depression can affect perception of pain signals arising out of gut.

Management

- Validate symptoms to patient, Placebo response rate is around 40%.
- Cut fats, caffeine, alcohol; add fibers in constipation predominant IBS.
- Lactose restriction only if H2 breath test +ve.
- Anticholinergic therapy for diarrhoea predominant or variable forms. Dicyclamine / hyosciamine could be tried.
- Bed time low dose Anti-depressants acts via affect neuro-transmission at muscarinic receptor, serotonin and nor-epinephrine reuptake.
- Alosetron (Antagonists of serotonin receptors e.g. 5HT3, 5HT4) lead to delay bowel movements and colonic transit time.
- Tagaserod, a partial antagonist of 5HT4 receptor, decreases small bowel and colonic transit time. It also increases phasic activation of colon; decrease pain, bloating and constipation.
- Add-on: Cognitive behavioral therapy.

Abdominal Migraine:

Usual Presentation: Long history of intermittent pain abdomen of acute onset. Usually comes early in the morning, almost every month. Child appears pale, diaphoretic, prefers dark room. Intense pain around umbilicus lasting for 6-12 hours, accompanied by nausea; often vomiting. Falls asleep at end of each episode, fine on awaking. No symptom between episodes. Strong family h/o migraine (65% of 1st or 2nd order). Normal growth. No hepato-biliary, pancreatic, metabolic, renal disease or SOL.

Diagnosis:

Abdominal migraine is present among 2% of children as per ROME-II classification:

- 3 or more paroxysmal acute episodes of intense mid-line pain lasting > 2 hours to several days, with symptom free intervals lasting weeks to months.

- No structural GI, CNS, metabolic, biochemical abnormality; and any 2 of following associated features:
  1. Headache
  2. Photophobia
  3. Family history,
  4. One sided headache
- Aura: Visual (blurred / restricted), sensory (Tingling, numbness), motor (Slurring, aphasia or paralysis)
- (As per Rome III H2c: 2 or more episodes in preceding 12 months and above plus Paroxysmal episodes Lasting for 1 hour or more; 2 episodes of vomiting, anorexia, nausea, headache, photophobia, palor; No evidence of inflammatory, anatomic, metabolic or neoplastic process to explain patient's symptoms.)

Differential Diagnosis :

Anatomic abnormalities (Malrotation, web, strictures, duplications, intussusceptions), Genito-urinary (UTI, hydronephrosis, ureteropelvic junction obstruction, nephrolithiasis where associated dysuria, hematuria, proteinuria are usually present), ovarian cyst, pregnancy, allergic eosinophilic oesophagitis / Gastro-enteritis, infections (Giardia, familial mediterranian fever, metabolic (Diabetes, lead, aminoacidosis showing growth failure, developmental delay and polydipsia etc)

Management :

Diagnostic :

- CBC, ESR, biochy (S/E, LFT, Metabolic), USG, Imaging of brain if indicated (Raised ICT), Urine RE/ME

Therapeutic: (Focus on preventing episodes)

1. Propranolol (10-20 mg BD) acts by B-blockade of cerebral arteries. 75% children had excellent response.
2. Ciproheptadine acts as anti-serotonin or as Ca channel blocker. 33% had excellent response; addl 50% had less frequent and less intense episodes.
3. Misc: Pizotifen – Serotonin receptor antagonist, Carbamazepine, Tricycline anti-depressants.

'Functional Pain Abdomen'

Usual Presentation:

Complain of pain over 3 months, diffuse, most of the day time (Never awakened at night). Initially may develop viral infection with fever, pain, diarrhoea and vomiting along with other family members. While others recover and other symptoms subside, abdominal pain continues. May have mild nausea but no vomiting, haematemesis or constipation. Loss of school days. Feels fatigued, often gets headache. Poor scholastic performance, no sense of belonging, felt teased by friends. O/E: WNL except diffuse abdominal tenderness.

Assessment:

Seems to have significant organic disease, possibly some psycho-social factors contributing. Fits to ROME-II criteria of "Generic functional Abdominal Pain" i.e.- 12 weeks of continuous abdominal pain in a school age child or adolescent; having no or only occasional relationship with psychogenic event; some loss of daily function, no feigning, insufficient criteria for other functional GI disorders to explain. Deserve detailed physical and per-abdominal examination, including growth.

Rome III: (H2d) Episodic or continous abdominal pain, insufficient criteria for other functional GI disorders, No evidence of inflammatory, anatomic, metabolic or neoplastic process to explain patient's symptoms.

Investigations:

CBC, ESR, Stool, Urine RE, ME, C/S, biochemistry profile, breath H2, USG, particularly when pancreatic or hepto-biliary disease suspected.

Differential Diagnosis : Acid related, unusual among children: Gastritis, duodenitis, oesophagitis

(Pain, nausea, heart burn, related to food, night time awakening).

Infection; Parasites e.g.- Giardiasis (Diarrhoea, pain, bloating, weight loss).

UTI (Pain), Allergic: Eosinophilic GE (Diarrhoea, pain, atopy,

Eosinophilia- related to food); Inflammatory: Crohn's, Ulcerative colitis,

Crohn's, Coeliac, TB, Pancreatitis (Constitutional symptoms e.g. fever, arthragia, diarrhoea with or without blood, pain, wt. loss, growth failure, night awaking).

Management

- Reassurance of child and parents regarding nature of functional GI disorders and their possible link with viral ailment.
- Dietary modifications, although improvement is minimal.
- Anticholinergic worth trying but data do not support efficacy
- Tricyclic anti-depressants used occasionally.
- Attention to psycho-social aspects (Increased nociceptive signals from Gut resulting from previous viral infection, in a child having mild depression or anxiety, can lead to continued GI discomfort)

Functional Abdominal pain Syndrome

Must include childhood functional abdominal pain at least 25% of the time and 1 or more of the following (Rome III H2d1):

1. Some loss of daily functioning
2. Additional somatic symptoms e.g.- headache, limb pain, or difficulty in sleeping.

Aerophagia :

Usual Presentation:

Abdominal distension, pain, flatulence, intermittent distention, marked as day progresses, does't want to eat. Normal bowel movement. Passes large amount of gas per rectum, loud belching. O/E: Abdominal distension but soft, no mass, bowel sounds-present. ROME-II described as: 24 wks history which need not be consecutive in preceding 12 months with 2 or more of the following symptoms / signs (Mostly by observation) (Rome III H1c):

1. Air swallowing, 2. Abdominal distension by intra-lumen air,

3. Repeated belching and / or 4. Increased flatus; Otherwise healthy

Differential Diagnosis :

Aerophagia, Coeliac, Intestinal pseudo-obstruction, Bacterial over load of small bowel, Hirschprung's disease, CHO and other mal-absorption disorders and Cystic fibrosis.

Diagnosis :

- Breath hydrogen test to t/o CHO MAS
- USG if difficult to palpate for mass
- Reassurance
- If associated with stressful events or anxiety, identify the factor responsible and suitable behavior modification / psychotherapy

- Avoid chewing gums, carbonated drinks

The 'Infantile Colic' has been described under functional category. It is common among 10 to 15% of infants. GER, CMPA, hyper-sensitivity to colonic distension, poor maternal bonding etc are attributed. Children are said to out-grow the problem by 5 to 6 months of age. Parents need to be reassured accordingly after excluding of all organic conditions.

Conclusion :

- Functional pain abdomen can occur as a well defined clinical entity or as part of a poorly defined clinical syndrome.
- Clinician is obliged to rule out organic conditions in all cases. Appropriate to take a bio-psycho-social approach.
- Understand close interaction of gut and brain; allowing child, family and physician to address pain at multiple levels.
- Further research needed to understand exact biochemical process in ENS and CNS; thereby expanding therapeutic horizons.

ROME III CRITERIA FOR FUNCTIONAL ABDOMINAL PAIN IN CHILDREN:

H2a. Functional dyspepsia:

Must include-

1. Persistent recurrent pain or discomfort centered in upper abdomen (Above umbilicus)
2. Not relieved by defecation or associated with onset of a change in stool frequency or stool form (As in IBS).
3. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject's symptoms.

H1c. Aerophagia*

Must include at least 2 of following-

1. Air swallowing
2. Abdominal distension due to intra-luminal air
3. Repetitive belching and /or increased flatus.

H2b. Irritable Bowel syndrome*

Must include all of following-

1. Abdominal discomfort or pain associated with 2 or more of following at least 25% of time:
   (a) Improved with defecation
   (b) Onset associated with change in stool frequency.
   (c) Onset associated with change in stool form.
2. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject's symptoms.

H2c. Abdominal migraine#;

Must include all of following-

1. Paroxysmal episodes of intense acute peri-umbilical pain lasting for an 1 hour or more.
2. Intervening periods of usual health lasing for weeks and months
3. Pain interferes with normal activities
4. Pain associated with 2 or more of following: Anorexia, nausea, vomiting, headache, photophobia, pallor.
4. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject's symptoms.

H2d. Childhood Functional Abdominal Pain*:

Must include all of following-

1. Episodic or continuous pain
2. Insufficient criteria for other functional GI disorders
3. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject's symptoms.

H2d1. Childhood Functional Abdominal Pain syndrome*:

Must include Childhood Functional Abdominal pain at least 25% of time and 1 or more of following-

1. Some loss of daily functioning
2. Additional somatic symptoms such as headache, limb pain or sleeping difficulty.

** Symptoms at least once per week, for minimum 2 months before diagnosis;*

 # On 2 or more occasions in preceding 12 months.

Points to Remember :

1. We must take adequate time in history taking.
2. let's keep in mind the peculiar patho-physiology in terms of ENS in case of children
3. The red-flag signs must always be borne in mind for early detection of any surgical condition and prompt intervention, where ever required.
4. we must minimize investigations to the basics first e.g.- CBC, Stool, urine and USG abdomen at the most, addition of advanced modalities can be made on specific indication as such additions do not increase the diagnostic yield impressively when generalized.
5. Follow-up is very important.

References

1. Apley J et al: Recurrent abdominal pain: A field survey of 1000 school children. Arch dis Child 1958; 33:165-170
2. Caplan A et al. Validation of pediatric Rome II criteria for FGID using questionnaire on pediatric GI symptoms. J Pediatric Gastroenterol and Nutrition, 2005; 100: 2079-2082.
3. Aziz Q et al. Brain-Gut axis in health and disease. Gastroenterology; 1998: 114: 559-578.
4. Donna K. et al: Recurrent abdominal pain in children: Pediatric GE and nutrition. PCNA; 2006: 49;1:53-7
5. Lori Mahajan and Robert W: Chr Abd pain of Childhood and Adolescence in Ped GE; 2005: 03-13.
6. American Academy of Pediatrics sub-committee on Chronic Pain Abdomen in children. Pediatrics, 2005; 115: 812-815
7. Huang RC et al. Prevalence and pattern of childhood abdominal pain in an Australian Gen practice. J Ped Child Health 2000;36:349-353.
8. NASPGHAN clinical report on chronic abdominal pain in children: Jl of ped gastro and nutrition; 40: 245248, march 2005.
9. Hyman PE et al. Childhood functional GI disorders. Gastroenterol, 2006; 130:1519-1526.
10. Rasquin WA et al. Childhood functional GI disorders.Gastroenterol, 2006; 130: 1527-1537.
11. Brenner AR, Sandhu BK. Recurrent pain abdomen in childhood: The functional Element: Indian Pediatrics,2009; 46:375-379.
12. Devanarayana NM et al. Recurrent Abdominal Pain in Children. Indian Pediatrics, 2009; 46:389-399.
13. Yip WC et al. Value of Abdominal sonography in the assessment of children with abdominal pain. J WC et al.Clin Ultrasound. 1998; 26:397400.
14. Huertas – Ceballos A et al. Pharmacological interventions for RAP in childhood. Cochrane Database Syst Rev 2004; 1: CD 003017.

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ARTHROPATHY AS A PRESENTING SYMPTOM OF WILSON'S DISEASE -A CASE REPORT

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Introduction

Wilson's disease is an inborn error of metabolism characterized by toxic accumulation of copper in liver, brain, cornea and other tissue. It occurs world wide with an estimated prevalence of 1 in 30-50.000 and is one of the leading causes of chronic liver disease in Indian children. [1] As it can have a varied clinical presentation a high index of suspicion is necessary for diagnosis. We had recently encountered a case where the initial manifestation was arthropathy simulating collagen vascular disease and was treated as a case of SLE in another institution.

Case Report

A 13 Year old female child presented with history of joint swelling and restriction of movement particularly involving the small joints for six month. She had gradual deterioration of scholastic performance for the same duration followed by dysarthria , dystonia and bizzare behaviour for four months. Fifteen days prior to hospitalisation she had progressive abdominal distention, swelling of whole body and breathlessness.

She was the 1st born female child of nonconsanginous marriage and enjoyed a sound health until six month prior to hospitalization. Her growth and development was at par. There was no history of jaundice, blood transfusion and urinary symptoms.

On examination she was found to have pallor, anasarca, genu valgum, double malleolus, and rachitic rosary with knock knee suggestive of rickets which was well supported by radiological findings. Abdominal examination revealed ascites, splenomegaly, Prominent veins over the abdomen (features of portal hypertension) with right sided pleural effusion.

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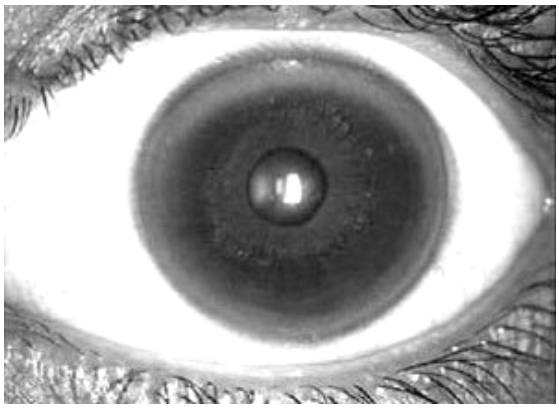
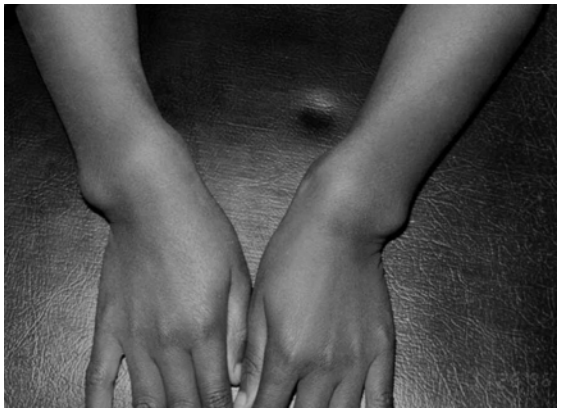
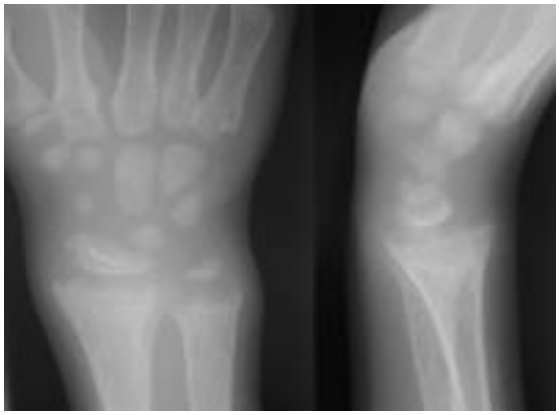


1. K F Ring



2. Widening of the wrists



3. Features of Ricket

Investigations revealed anemia (Hb=8.4gm %), deranged liver function test in the form of total billirubin 1.3mg/dl, direct billirubin 0.5 mg/dl, SGOT = 67 IU/L, SGPT = 60 IU/l, Alkaline phosphatase=497 IU/L, serum albumin = 1.7gm/dl, PT=35.3 Sec with INR = 2.79 . Serum ceruloplasmin was low (0.09gm/L) and 24 hr urinary copper measured 131.2 microgram/L. She had negative ANA, ASMA, dsDNA value and antigen study against Hepatitis B also showed negative result. Complete KF ring was found in both eyes on slit lamp examination.

Discussion:

Wilson's disease is an autosomal recessive disorder characterized by degenerative changes in brain, liver disease with Kayser Fleischer ring in the cornea. The gene responsible for this disorder is located in chromosome 13 at q14-q21 [2]. Most patients with Wilson's disease are diagnosed between 1st to 4th decades of life, [3] although the clinical disease rarely presents before the age of five. [4]

According to Sternlieb et al [5] the initial manifestations are hepatic 43%, Neurologic 34%, Psychiatric 10%, bony manifestation 12% and renal 1 %. A peculiar manifestation of Wilsons disease in India is

"Osseomuscular" type with bony deformity suggestive of resistant ricket [6] .The initial presentation with arthropathy was 8% and the mean age at diagnosis was 10.8 (±3.4yr) with survival 90% . According to Walche et al the most common radiological abnormality was a generalized increase of radiolucency i.e skeletal demineralization followed by premature osteoarthrosis. Changes in the spine were common and included osteochondritis, reduction in interverterbral joint space and osteoarthrosis. Other bony changes include fluffy irregularity of femoral trochanter, Osteochondritis dissecans of knees, Osteophytic protrusion at bony ends and Osteophytes at joint margin. [7]

There is no gold standard for diagnosis of Wilson's disease. It is based on clinical and laboratory investigations like urinary Cu>100 microgram /24hr, hepatic Cu >250 microgram/dl, serum cerruloplasmin<20 microgram/dl and presence of KF Ring. [8]

References:

1. Pandit AN, Bavdekar AR, Bhave SA, Wilson's disease. Indian J. Paediatrics 2002;69:785-91.
2. HouwenR.H et al. H714Q Mutation in Wilson's disease is associated with late neurological presentation. Journal Med Genet 1995;32:480-482
3. Schoen RE, Sterilieb I. Clinical aspects of Wilson's disease. American J. Gastroenterol 1990; 85 :1453-57
4. Sternlieb I. diagnosis pf wilson's disease. Gastroenterology 1978;74:787-789
5. Sternlieb I. Scheinberg IH : Wilson's disease. In Wright R and others, editor : liver billiary disease : Pathophysiology, diagnosis& management, LONDON, 1979, WB Saundar S, 774.
6. Bavdekar AR . Therapeutic and management challenges in Wilson's disease. Journal of Gastroenterology and hepatology, 2004 ;19: 391-395
7. J M Walshe, D N Golding et al. Arthropathy of Wilson's disease.study of clinical and radiological features in 32 patients.Ann Rheum dis.1977 April; 36(2):99-111
8. Gow PJ etal. Diagnosis of Wilson's disease:An experience over three decades.Gut 2000;46;415-419s

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