MEDICAL JOURNAL OF WESTERN INDIA

ISSN NO.
0972-9798

VOLUME - 43, NO. 1, FEBRUARY 2015

An official Publication of The Research Society
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Print ISSN: 0972-9798

Medical Journal of Western India

Official Publication of the Research Society, BJ Medical College & SGH, Pune

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The Research society of

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Printer

Rashmi Enterprises

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Medical Journal of Western India

Official Publication of the Research Society, BJ Medical College & SGH, Pune

Volume 43, No. 1, February 2015

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Dengue- Changing Scenario

Sangle S. A.

Professor of Medicine, B.J.G.M.C. & S.G.H., Pune.

Dengue is the most rapidly spreading mosquito borne viral disease in the world. There is a thirty fold rise in the last fifty years with increasing geographic expansion from urban to rural areas. It has spread to more than 100 countries in the world.

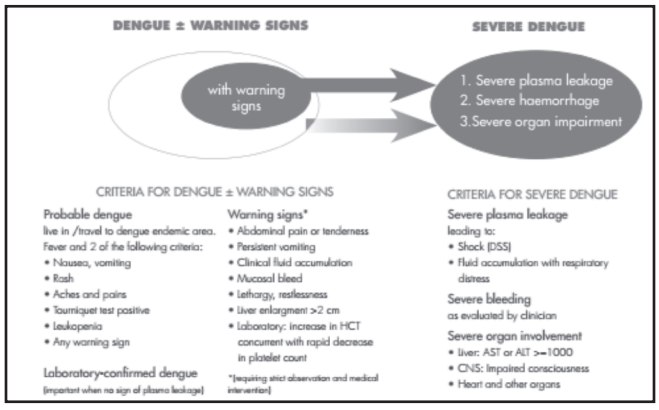
WHO estimates 50 to 100 million cases of dengue infections world wide every year with 2,50,000 to 5,00,000 cases of Dengue hemorrhagic fever and approximately 24000 deaths every year. [1]

Rising trend of Dengue infection is due to rising population, urbanization, inadequate mosquito control. Number of confirmed cases of dengue infection in 2014 in Maharashtra are 8425 with 12 deaths confirmed due to dengue(MIS data from DHS). However this is just the tip of the ice berg as many cases of viral fever still remain undiagnosed due to lack of clinical suspicion and paucity of appropriate investigations.

Classification- Old VS New[1]

According to existing WHO classification symptomatic dengue virus infections were grouped into three categories: undifferentiated fever, dengue fever (DF) and dengue haemorrhagic fever (DHF). DHF was further classified into four severity grades, with grades III and IV being defined as dengue shock syndrome (DSS). There have been many reports of difficulties in the use of this classification.

A WHO/TDR-supported prospective clinical multicentre study across dengue-endemic regions was set up to collect evidence about criteria for classifying dengue into levels of severity. The classification into levels of severity has a high potential for being of practical use in the clinicians' decision as to where and how intensively the patient should be observed and treated (i.e. Triage).



Severe Dengue[1]: Severe dengue is defined by one or more of the following: (i) plasma leakage that may lead to shock (dengue shock) and/or fluid accumulation, with or without respiratory distress, and/or (ii) severe bleeding, and/or (iii) severe organ impairment.

Severe dengue should be considered if the patient is from an area of dengue risk presenting with fever of 2–7 days plus any of the following features:

- There is evidence of plasma leakage, such as:
  - high or progressively rising haematocrit;
  - pleural effusions or ascites;
  - circulatory compromise or shock (tachycardia, cold and clammy extremities, capillary refill time greater than three seconds, weak or undetectable pulse, narrow pulse pressure or, in late shock, unrecordable blood pressure).
- There is significant bleeding.
- There is an altered level of consciousness (lethargy or restlessness, coma, convulsions).
- There is severe gastrointestinal involvement (persistent vomiting, increasing or intense abdominal pain, jaundice).
- There is severe organ impairment (acute liver failure, acute renal failure, encephalopathy or encephalitis, or other unusual manifestations, cardiomyopathy) or other unusual manifestations.

As per the above new WHO 2009 Guidelines, neurological manifestations have been included in the definition of severe dengue. Clinical presentation is changing and neurological manifestations are seen more frequently.

Neurological manifestations are classified according to pathogenesis[2,3]

- Related to neurotropic effects of virus
- Related to systemic complications of dengue infection
- Post infectious immune mediated

Neurotropic effect	Systemic complications	Immune mediated
Encephalitis Meningitis Myositis Rhabdomyolysis Myelitis	Encephalopathy Stroke Hypokalemic paralysis	ADEM Encephalomyelitis Myelits Neuromyelitis optica Optic neuritis GBS

Rare manifestations that have been reported are- Miller –Fischer syndrome, Phrenic neuropathy, Hypoglossal palsy[4], Long thoracic neuropathy, Oculomotor palsy, maculopathy, Fatigue syndrome.

Despite severe thrombocytopenia, Intracranial hemorrhage is not commonly reported.

In the months of September and October 2014, we found 1 case of GBS, 1 case of ADEM, 1 Massive MCA infarct associated with dengue infection. (Unpublished Data)

According to the new WHO Guidelines, depending on the clinical manifestations and other circumstances, patients may be sent home (Group A), be referred for in-hospital management (Group B), or require emergency treatment and urgent referral (Group C)[1].

Platelet Transfusion and Dengue

It should be noted that prophylactic platelet transfusions for severe thrombocytopenia in otherwise haemodynamically stable patients have not been shown to be effective and are not necessary. It may exacerbate fluid overload and transfusion related ARDS. Only indications for platelet transfusion are-

- Dengue patients with thrombocytopenia requiring urgent surgery
- Active bleeding inspite of blood transfusions in case of Dengue Hemorrhagic Fever, Disseminated intravascular coagulation and Intracranial Hemorrhage.

Blood transfusion is life-saving and should be given as soon as severe bleeding is suspected or recognized. However, blood transfusion must be given with care because of the risk of fluid overload. Blood transfusion should not be delayed till the hematocrit drops to low levels.

Prevention

By preventing breeding of Aedes Mosquito, eliminating breeding places, using appropriate insecticide abate, using Gambusia fish which feed on mosquito and act as larvicide, spread of Dengue can be halted.

Vaccination

No licensed vaccines/ specific treatment are available to prevent dengue infection. Various trials are underway to find out the efficacy of dengue vaccines.

Recombinant live attenuated tetravalent dengue vaccine CYD- TDV is under phase III Trial. It is found effective when given as three injections at 0, 6 and 12 months to children between 2- 14 years of age in the endemic areas in Asia with good safety profile.[5]

Acknowledgement –Dr.Niveditha Girimaji for her help in the preparation.

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REVIEW ARTICLE

Tuberculosis Diagnosis Update-MicroRNAs in Tuberculosis

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ABSTRACT

Background

Routine clinical methods for diagnosing tuberculosis (TB), involving radiography, culture of sputum and the tuberculin skin test (TST), have many shortcomings. Finding new bio- markers in tuberculosis is not only necessary for diagnosing patients with TB, but also for the staging or classification of TB, TB prognosis, and TB drug and vaccine trials.

MicroRNAs (miRNAs) are crucial regulators of human immunity e.g. against Mycobacterium tuberculosis. Against the background of still alarming high mortality of tuberculosis effective biomarkers to improve diagnosis of M. tuberculosis infection and successful treatment are of major importance.

Conclusion

Transcriptomic, proteomic and metabolomic profiling combined with broad scale immunological profiling in the form of miRNA signature scan provide clues to the key questions in TB, which will help in effective patient care. This review summarizes recent studies for identification of miRNA signatures in human tuberculosis.

Keyword

MicroRNAs, Tuberculosis, miRNA signatures.

Background

Genomic studies revealed that numerous portions of the human genome do not encode conventional protein coding genes but encode biologically active non-codingRNA species. With the rapid expansion of small RNA interference techniques over the past decade, it is now clear that many small RNA molecules could regulate gene and protein expression. One class of such small noncoding RNAs is microRNAs (miRNAs), a group of regulatory RNAs of 19-22 nucleotides involved in control of gene expression at the post-transcriptional level [1] there by acting as RNA interfering (RNAi) molecule.

Mycobacterium tuberculosis (M. tuberculosis), the causative agent of human tuberculosis, is still a major threat to humankind. About 8 million new cases and more than 1.3 million deaths annually place tuberculosis among the top three fatal infections [2]. However, the vast majority of M. tuberculosis infected individuals are capable of controlling the pathogen. These latently M. tuberculosis infected (LTBI) individuals remain infected probably for lifetime.

Protective immunity against M. tuberculosis is predominantly based on the T-helper type 1 (TH1) mediated cellular arm of the host immune response and the fine-tuned interaction of TH1 cells with M. tuberculosis infected macrophages. T-helper cell differentiation and plasticity was shown to be tightly regulated by miRNAs [3] and the same holds true for macrophages, the M. tuberculosis host cell population [4]. Therefore, the relevance of miRNAs for immune regulation in infectious diseases can be taken for granted.

Protection against progression towards active disease is strongly dependent on an effective immune surveillance. Cellular immunity, especially CD4+ T cells and macrophages, are crucial players in this highly orchestrated host-pathogen interaction.

Biogenesis and basic function of miRNAs

miRNAs, a class of small non-coding RNAs of approximately 21 nucleotides in length that are found in plants, animals, and some viruses, are more stable than mRNAs and are thus good candidates for use as bio-markers. They modulate gene function at the post-transcriptional level and act in fine tuning various processes such as development, proliferation, cell

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signaling, and apoptosis. MiRNAs were first discovered in 1993 while studying Caenorhabditiselegans. The first miRNA discovered was lin-4 that was found to play a role in the development through a negative effect on lin-14 expression [5]. After seven years (in 2000), let-7, the second miRNA was discovered, again in the C. elegans[6].

The genesis of functional miRNAs involves a complex multi-enzyme process leading from long precursor molecules into~22 nt long biologically active RNA molecules. MicroRNAs are transcribed from their own genes scattered in all chromosomes in humans, except for Y-chromosome[7].

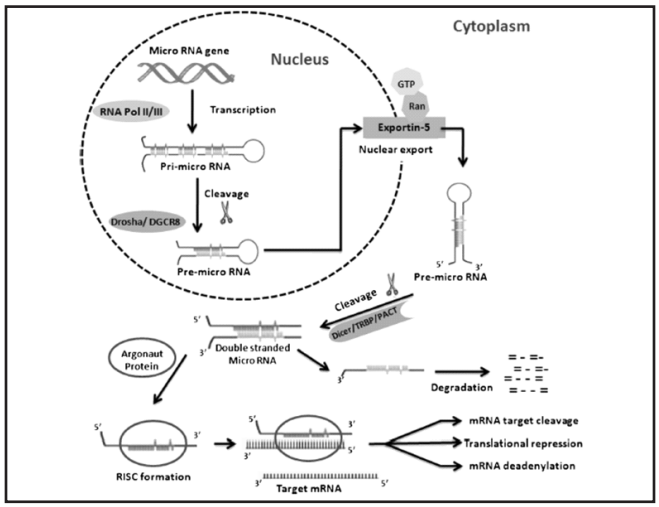

Fig 1 :- Biogenesis of miRNAs - Adapted from Pravin Kumar Singh et al (7)

Though, a few different hypothesis have been given on the action of miRNAs, in general, multi-protein RNA-induced silencing complex (miRISC) with miRNA moves toward the target mRNA, and binds miRNA in the complementary region in the 30 untranslated region(30 UTR) to either terminate the translation or to lead to degradation of the mRNA to interfere with the gene expression. Once the miRNA is bound to a completely complementary region of mRNA, like siRNA, mRNA gets degraded. However, miRNA mediated regulation does not require to have a perfect match with its target-binding region. Only, 7-base sequence between2nd and 8th nucleotide from the 50 end is called "seedregion," and a complete match of the sequence is required. It is believed that the strength of the inhibition varies depending on the sequence but, how it is done at good balance is yet to be revealed. A single miRNA may directly affect the expression of hundreds of proteins at once and several miRNAs can also target the same mRNA and result in enhanced translational inhibition[8].

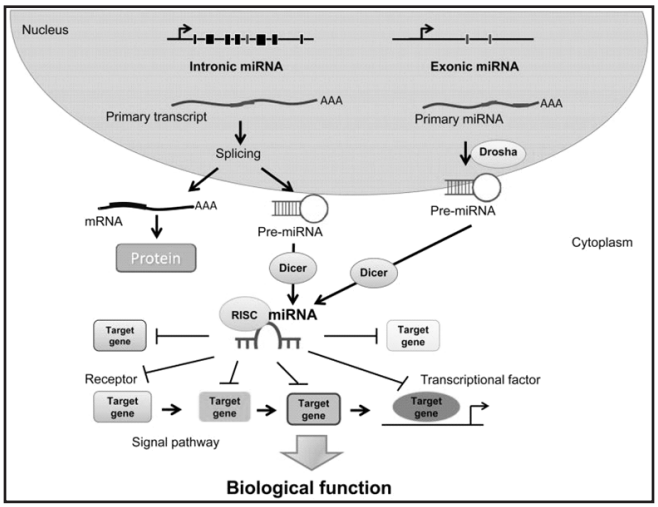

Fig2:-Functions of miRNAs -Adapted from Selbach M et al [8]

The need for biomarkers in tuberculosis

The exact underlying mechanisms of LTBI and its transition to active TB remain elusive. LTBI rely on an equilibrium in which the host is able to control the infection but does not completely eradicate the bacteria [9]. Latency may depend upon the virulence of the MTB strain [10] and upon the host immune response. Some bacteria may escape attack from the innate or acquired immune system by blunting phagosome and lysosome fusion, nitric oxide production, antigen presentation, or other bactericidal processes from the host, and therefore survive in a phenotype called dormancy.

The incidence of multidrug resistant and extensively drug resistant tuberculosis (MDR-TB and XDR-TB,respectively) is on the rise and there are even reported cases of totally drug resistant tuberculosis (TDR-TB), which leads us to the question: how are these disease-causing mycobacterial species, *M. tuberculosis* able to escape our immune defenses?

Diagnosis of tuberculosis and discrimination from LTBI in children are challenging because of the lack of clinical signs and imaging findings. Immunological tests (i.e. IFNγ release assays and tuberculin skin test) do also not discriminate active tuberculosis and LTBI. Cellular immunity, especially CD4+ T cells and macrophages, are crucial players in HIV associated tuberculosis. In

extra pulmonary tuberculosis micro-RNA analysis from body fluids may be helpful. Although there is currently a vaccine for tuberculosis, the attenuated *M. bovis* strain bacille calmette-guerin (BCG), it is considered to be largely ineffective (11).There is an urgent need for new avenues of treatment, such as host-targeted immune therapies. In childhood tuberculosis, prediction of effective treatment is particularly difficult since detection of M. tuberculosis in sputum fails due to reduced pathogen load in the majority of cases. Especially insufficient adherence to chemotherapy against tuberculosis is a major problem in high incidence countries leading to treatment failure, development of MDR, as well as spread of M. tuberculosis infections. Shortened treatment e.g. by novel drugs or combination of existing medication would largely improve this situation and biomarkers that predict successful treatment could catalyze this process significantly. The presently available diagnostic methods are not very helpful in pediatric TB and LTBI. Hence biomarkers that are specific to M. tuberculosis could help in diagnosis of TB in children and LTBI.

miRNAs in immunity against mycobacterial infections

miRNAs inhibit mRNA translation leading to mRNA target degradation and decreased protein expression. Several miRNA families regulate immune processes. miR-29 was able to block increased IFNγ levels, a typical feature of general miRNA knockout mice, and over-expression of miR-29 increased susceptibility to tuberculosis .Wu et al. demonstrated miR-21-mediated inhibition of interleukin-12 in macrophages and additionally, found increased apoptosis in dendritic cells due to miR-21 inhibition of bcl-2 [9]. They concluded that mycobacteria induce expression of miR-21 leading to impaired classical macrophage activation and dependent TH1 immunity.

The role of miR-155 in the interaction between macrophages and mycobacteria may have different aspects: interference with mycobacterial dormancy and inflammatory mediators (i.e. IL-6 and cyclooxygenase-2) [12]. Recently, Wang et al. demonstrated that miR-155 is involved in autophagy, an essential process of mycobacterial killing in host macrophages [13]. Factors that determine whether the microRNA expression profile during infection favors or targets the immune response when the host cell and *Mycobacterium* are engaged could be a key point in determining the out come of the infection. As more insight is gathered on (i) the functional consequences of microRNAs regulation during mycobacteria linfections, (ii) howthegenes and pathways they target facilitate the immune response and (iii) how they are regulated by the pathogens, an opportunity for host microRNA- directed the rapeutic intervention may become available.

miRNAAnalysis

miRNA microarray chip containing 960 probes is used to identify the differently expressed miRNAs, and real time quantitative polymerase chain reaction (qPCR) are performed for confirmation. The putative regulatory network of miRNAs that are differentially expressed in the samples from active TB and LTBI individuals are constructed based on predicted target genes and previously published genome-wide transcriptional profiles. Multiple microarrays have been performed on samples derived from tuberculosis patients, ranging from peripheral blood mononuclear cells (PBMC), pleural fluid mononuclear cells (PFMC), pooled serum and even PBMCs stimulated with mycobacteria or mycobacterial ligands *ex vivo*. While a definitive microRNA signature has yet to be determined, three microRNAs with higher expression inactive tuberculosis patients compared to healthy controls have been positively evaluated for use as a biomarker: miR-21 and miR-155 instimulated PBMCs (9, 14) and miR-29a in pooled serum (15,16). In addition to expression analysis, microRNA single nucleotide polymorphism (SNP) analysis has revealed a correlation between SNPsinmiR-146a (rs2910164) andmiR-499(rs3746444) and increased pulmonary tuberculosis susceptibility in certain populations (17).

miRNA studies in blood -

Table 1 Biomarker studies of human blood and enriched immune cell populations -

Adapted from Bianca Ueberberg et al (18)

Study	Study type	Study group sizes	Upregulated	Downregulated	Overlap of differentially expressed miRNAs
Wang et al. 2011	miRNA, array (955 miRNAs)	6 TB patients, 6 LTBIs	6 between TB and LTBI miR-21a miR-223 miR-302a miR-424 miR-451 miR-486-5p	miR-130ba	miR-424
Spinelli et al. 2013	Candidate approach (6 miRNAs)	24 TB patients, 20 TSTneg	miR-424	miR-146a	
Wang et al. 2011	miRNA, array (955 miRNAs)	6 TB patients, 3 TSTneg	4 miRNAs miR-144 miR-365 miR-133a miR-424	3 miRNAs miR-500 miR-661 miR-892b	miR-144
Liu et al. 2011	miRNA array	3 TB patients, 3controls (not further defined)	28 miRNA nv miR-144[a]	2 miRNAs nv	
Kleinsteuber et al. 2013	Candidate approach (29 miRNAs) enriched blood T cells	7 TB patients, 6 LTBIs, 3 TSTneg	No	4 miRNAs miR-21 miR	
Fu et al. 2013 [17]	miRNA array (~ 1,223 miRNAs) enriched	4 TB patients, 4 LTBIs, 4 TSTneg	6 miRNAsb miR-340-5p miR-451a miR-32-5p	6 miRNAsb miR-340-5p miR-451a miR-32-5p	miR-451 (Wang et al. 2011

Various studies identified miRNAs in human plasma associated with defined structures (i.e. exosomes and microvesicles apoptotic bodies) that are not degraded by plasma enzymes. There is arising evidence that circulating miRNAs exert biological functions e.g. as part of intercellular communication, and may be used as biomarkers for human diseases [15]. The appeal of using plasma miRNAs in clinical applications is high, as separation and preservation of plasma or serum samples is clinical routine also in M. tuberculosis endemic countries. However, variations in preanalytical processing of samples and lack of established endogenous controls limit the comparability of results [19].The majority of studies focused on comparisons between patients with active TB, LTBI, as well as non-M. tuberculosis-infected (TSTneg) controls. Wang et al. determined expression profiles of 955 miRNAs (human and human-viral) of enriched peripheral blood mononuclear cells (PBMCs) from TB patients and contacts with or without latent M. tuberculosis infection. Classification analyses did not discriminate between study groups but this may be due to small study group sizes [13]. Of 451 detectable miRNAs, a cluster of 17 miRNAs showed significant differences between active TB and M. tuberculosis-infected contacts [13].

Spinelli et al. used a candidate gene approach to determine expression of six miRNAs in PBMCs of TB patients and TSTneg individuals [20]. This study detected miR-424 to be upregulated in TB patients from both studies whereas no difference for miR-223.[20].

Detailed analyses of miR-223 have been performed by Dorhoi et al. who detected lower expression of miR-223 in PBMCs of TB patients as compared to LTBI and higher expression as compared to TSTneg [21]. Comparisons of pulmonary tissue samples revealed increased miR-223 expression in the lung of TB patients as compared to healthy controls. Contrary findings for peripheral blood may therefore indicate differential migration activity of miR-223 expressing cells to affected tissue sites at different disease stages. Therefore, although miR-223 likely plays an important role in host immunity against TB, it may not qualify as a biomarker in surrogate tissue.

miR-144* was mentioned as a candidate regulator or IFN-γ expression before Liu et al. performed global miRNA analysis of PBMCs from TB patients and healthy controls (three individuals per study group) [22]. This study identified 30 differentially regulated miRNAs but decided to focus on increased miR-144 expression in TB patients. However, contrary findings with regard tomiR-144* expression have been published. (23) Wang et al. also found increased miR-144* expression in TB patients (only in comparison to TSTneg) [13] whereas no differential miR-144 expression was found by others [22]. Since miR-144* was described as an important T-cell factor in TB, different results may be due to confounding effects of cellular heterogeneity in peripheral blood [5]. Consequently researchers performed miRNA expression analysis in enriched CD4+ T cells [16, 24] to bypass this problem.

Kleinsteuber et al. analyzed miR-144* expression in CD4+ T cells but since it was not detectable in a

subgroup of donors, miR-144* was excluded from further analyses. In addition, a global miRNA array-based approach detected decreased miR-144 expression of CD4+ T cells in TB patients as compared to LTBI but these results of pooled sample analyses were not verified by quantitative PCR. The same study focused on another promising candidate, namely miR-29, that was increased in CD4+ Tcells from TB patients (compared to LTBI and TSTneg). In contrast, Kleinsteuber et al. detected decreased miR-29a of CD4+ T cells from TB patients compared to LTBI (but not TSTneg). Taken together, as for miR-223, a role for miR-144 and miR-29 in host immunity against TB is likely but the applicability of miR-29 as a biomarker has not been proven.

So far, only one study has been performed determining miRNA expression profiles of children with TB and LTBI [24]. Kleinsteuber et al. analyzed differentially expressed candidates of CD4+ T cells from adult TB patients. This study confirmed significant down regulation of miR-26a and miR-142-3p in peripheral blood of children with TB compared to children with LTBI. In addition, a tendency of increased miR-26a and miR-142-3p expression after recovery was found [24]. Nevertheless, the study also demonstrated marked inter-individual differences of miRNA candidate expression (up to 105-fold). This finding generally questions the applicability of miRNA as robust biomarkers for discrimination. At least, one would have to apply miRNA expression pattern of several miRNA, but studies that have sufficient statistical power are not available at present.

Table 2 Biomarker studies of human blood serum and plasma

Adapted from Bianca Ueberberg et al (7)

Study	Study type	Study group sizes	Upregulated	Down regulated	Overlap of differentially expressed miRNAs
Abd-El-Fattah et al. 2013	Custom array for unspecified number of miRNAs (single samples)	29 TB, 37 healthy controls (no definition)	miR-182 miR-197		miR-197
Qi et al. 2012	Array for 667 miRNAs (pooled for study groups	30 TB, 65 healthy controls (negative chest X-ray and IGRA, free from clinical symptoms of infection	miR-361-5p miR-889 miR-576-3p		miR-25 miR-590-5p miR-885-5p
Miotto et al. 2013	Array for 671 miRNAs (pools of 10 individuals	154 pulmonary TB, 105 healthy controls (negative IGRA or TST, no risk-factors for LTBI, no clinically significant condition) over 2 cohorts	miR-148a miR-16 miR-192 miR-193a-5p miR-25 miR-365 miR-451 miR-532-5p miR-590-5p miR-660 miR-885-5p miR-223a miR-30e	let-7e miR-146	miR-365
Fu et al. 2011	Array for 1,223 miRNAs (pooled for study groups)	75 TB, 52 healthy controls (defined as 'free of active and latent TB')	miR-93a miR-29a	miR-3125	miR-483-5p miR-22
Zhang et al. 2013	Deep sequencing (20 individual samples for each group)	128 pulmonary TB, 108 healthy controls (no definition)	miR-378 miR-483-5p miR-22 miR-29c	miR-101 miR-320b	

miRNA studies in serum and plasma -

Fu et al. screened pooled serum samples of patients with pulmonary TB and matched healthy controls for differential expression of 1,223 miRNAs [7,8]. They identified 92 differentially expressed miRNAs (59 upregulated and 33 down regulated in TB patients). Three of these candidates were validated by qPCR in individual samples, but none of these three could be confirmed in later studies. Two differentially expressed candidates, i.e. miR-29a and miR-93*, were also assessed in sputum of the same patients. Notably, increased miR-29a expression was detected in sputum of TB patients. The same group investigated miRNA expression patterns of sputum in a second cohort and confirmed differential expression of miR-29a [19].

Qi et al. compared sera of TB patients to healthy controls and patients with other diseases [25]. Overall, 667 miRNAs were determined in serum pools of TB patients and healthy controls by microarray analysis. This study identified 97 differentially expressed miRNAs and selected a set of ten for verification by quantitative PCR. A set of three miRNAs, i.e. miR-361-5p, miR-889, and miR-576-3p, was identified that specifically indicated TB disease. Differential expression of these candidate miRNAs was not found by any other study. Abd-el-Fattah et al performed microarray-based analysis and validated results by qPCR to identify miRNAs for discrimination between pulmonary TB, pneumonia, lung cancer, pleural transudate, and matched controls [26]. In this study, a combination of increased miR-182 and miR-197 expression was found to be specific for TB. Correspondingly, Qi et al. also detected over-expression

of miR-197 in TB patients [26].

Miotto et al. recruited two patient cohorts: (i) children with TB, TB/HIV co-infection and controls in Tanzania and Uganda as well as (ii) adult patients with TB (pulmonary and extra-pulmonary), LTBI, or other pulmonary infections and healthy controls in Italy [23]. This study compared array-based expression patterns of 671 miRNAs using sample pools of ten patients and 18 sex-matched individuals from the different subgroups. A cluster of 15 miRNAs distinguished between pulmonary TB and healthy controls. Within this set of markers, miR-192 was the only candidate significantly differentially expressed between the adult and the pediatric study groups. Comparing these results to the study of Qi et al.(25), three miRNAs (miR-25, miR-590-5p, miR-885-5p) were found concordantly and let-7e disconcordantly regulated. Discrepancies may be due to different methods e.g. different endogenous controls used.

Zhang et al. applied deep sequencing on serum samples between groups of patients with TB, pneumonia, chronic obstructive pulmonary disease, and lung cancer and healthy controls [27]. They identified a set of 15 differentially expressed miRNAs and a subset of six; namely, miR-378, miR-483-5p, miR-22, miR-29c, miR-101, and miR-320b classified the TB patients in the study group. MiR-483-5p and miR-22 were also regulated concordantly in the study by Fu et al. whereas miR-101 was not different [6]. No differences for miR-29c were found in the study by Miotto et al. [23].

In conclusion, even though some overlap of differentially expressed miRNAs existed between the various studies; a common miRNA or miRNA pattern that classified TB patients was not found. But still miR-22, miR-25, miR-197, miR-365, miR-483-5p, miR-590-5p, and miR-885-5p are the most promising candidates since these miRNAs were validated for discrimination of TB types and can form the basis for future multicentric research related to utility of miRNA's in TB diagnosis, follow-up, treatment and treatment outcomes.

Future Implication

Recent landmark in- vitro and in-vivo studies (28, 22) in mycobacterial diseases showed that miRNA species, regulating immune modulatory genes directly or indirectly, can affect the downstream effectors of an innate immune-triggeredantimicrobial pathway and thereby contribute in development of disease. This knowledge may have implications for the development and improvement of future approaches for the prevention and therapy of tuberculosis. Micro RNA can be used as future therapeutic modalities in mycobacterial infection however, no clinical trials and progress in this field have been made so far. More work is required before microRNAs can be integrated into clinical diagnostics, therapy, prevention and care of tuberculosis patients but it is an exciting field of research.

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Emerging Viral Infections in India

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Infectious diseases continue to be a major contributor to morbidity and mortality, especially in developing countries. The turn of the century has been characterized by the emergence of novel viral diseases or the reemergence of previously known viruses as outbreaks in different parts of the country. Emerging infections are defined as: "Infections that have newly appeared in a population or have existed previously but are rapidly increasing in incidence or geographic range". [1] These have negated much of the advantages gained over infectious diseases by developments in antimicrobials and vaccines.

Majority of the emerging viral infections are zoonosis i.e. the viruses have existed in animal hosts and have recently manifested in humans. The reason for their shift into humans is predominantly due to disturbances affecting the ecological balance. These ecological disturbances could have resulted from deforestation, geographical disasters, and human encroachment on wild-life habitats. Changes in agricultural practices, wild-life trade and global warming have all added to the problem. The non-zoonotic viruses, on the other hand, have spread to new territories due to economic development and international travel and thus resulted in the emergence of disease in areas from where they had not been reported earlier.

High rates of mutation and antigenic changes in viruses along with rapid adaptation to newer ecosystems, makes them efficient at infecting new hosts including man, thus creating local or global health threats. Viruses can evolve faster than mammals. Emergence of vector-borne diseases represents a major threat in the short term and is caused by changes in the vector population. This can result in emergence and an extension of host range as a consequence. This was the case in the Chikungunya virus outbreak of 2005.

Emergence/re-emergence of several viral infections has been reported from India in the past few decades.[2] In chronological order the appearance emerging viruses in India has been as under;

1. Hanta virus 2000 (Chennai & Kochi) 2.Nipah virus (Siliguri) 2001 3. Chandipura 2003 (Andhra), 2004 (Gujarat), 2007(Maharashtra) 4.Chikungunya 2003(Andhra, Nalgonda, Rayalseema) 2005 (Hyderabad) 5. Novel H1N1 2009, 2014 (Pune, Hyderabad, Delhi) 6. CCHF Gujarat 2011. These infections have been discussed in brief in this review

Hanta Virus Infection:

Hanta viruses are enveloped, single-stranded RNA viruses belonging to the family Bunyaviridae. They are zoonotic rodent borne viruses. Hantaviruses have a tri-segmented genome, which codes for replicative enzymes, an envelope glycoprotein, and a nucleo-capsid (N) protein. The latter is abundant and highly antigenic. Man can get infected through aerosols generated from virus-contaminated rodent urine and feces, bites, scratches, and contaminated food. The incubation period ranges from1-5 weeks. Early signs and symptoms are non-specific. The virus causes a spectrum of clinical symptoms ranging from sub clinical presentations to severe hemorrhagic fever with renal syndrome (HFRS), pulmonary syndrome or cardiopulmonary syndrome (HCPS). The detection of virus specific IgM antibodies against the N antigen is the choice for early diagnosis. RT-PCR using genus specific and species specific primers can also be used for diagnosis. [2]

In 2000, human Hantavirus infection was confirmed for the first time in India from 9 cases of suspected leptospirosis, of which two cases (one from Kochi and one from Chennai) developed acute renal failure with hypoxia which proved fatal [3]. The overall positivity in

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suspected leptospirosis like infections was 12%. In 2005 hantavirus specific antibodies were detected using both an IgM ELISA and an immune-fluorescent assay in 18 (12%) of 152 patients with pyrexia [3]. In 2005 following the floods in Mumbai, five cases admitted to the intensive care unit of a city hospital with fever were confirmed to have IgM antibodies to Hantavirus, and one of these had ocular manifestations in the form of intra-retinal hemorrhages [4].

Currently, no definitive treatment for Hantavirus is available. Ribavirin has been shown to decrease the mortality due to HFRS. However it does not affect the course of HCPS markedly. An inactivated vaccine is available but the protective response is short-lived [3]

Nipah Virus Infection (NiV):

The virus is named after the Malaysian village where it was first discovered. This virus belongs to the family Paramyxoviridae and is included in a new genus, Henipa virus. Nipah virus is classified internationally as a bio-security level (BSL) 4 agent. Fruit bats of the Pteropodidae family are the natural hosts for Nipah virus. Human transmission has been attributed to the loss of natural habitats of bats. Infected bats shed virus in their excretion and secretions such as saliva, urine, semen and excreta but they are symptomless carriers. The virus is also found in fruits partially eaten by them. The period April-June is the time when viral RNA can be mainly detected in urine of bats. Pigs get infected with Nipah virus by eating fruit contaminated with bat saliva or urine, drinking contaminated water, or by eating an aborted bat fetus. Its presentation in pigs is with respiratory and neurologic syndrome as well as 'barking pig' syndrome. Pigs shed the virus in saliva, respiratory secretions and, probably, urine. Human cases and infections in domestic animals (dogs and cats) occur after close contact with pigs, through aerosols. Nipah virus has also been categorized as a food borne disease from eating dates contaminated with urine or saliva of infected bats [1].

The focal outbreak due to NiV in India in 2001 was thought to have arisen due to drinking fresh date sap contaminated by fruit bats i.e. P.giganteus. A total 66 cases of encephalitis were identified in the Nipah virus outbreak in Siliguri in 2001 with a case fatality ratio of 74%. Evidence of person to person transmission and a high case fatality rate were some of the alarming developments seen in this outbreak. The outbreak started from one hospital and went on to involve 3 others. 33 health care workers/visitors to the hospital were infected during the outbreak [5].

The incubation period in humans is 4 to 18 days. Symptoms of NiV infection in humans are similar to that of influenza such as fever and muscle pain. In some cases, inflammation of the brain leads to disorientation or coma. Encephalitis may present as acute or late onset. The latter may be difficult to diagnose since exposure may have taken place several months earlier. Respiratory symptoms (tachypnea) to acute respiratory distress may occur. Involuntary movements or convulsions are also a common presentation. Vomiting can be seen in some of the patients but no neck rigidity or cranial nerve involvement is usually observed. Diagnosis is by serology i.e. by performing an ELISA IgM. RT -PCR can be performed on urine. Virus isolation is rarely successful [2].

Treatment is mostly focused on managing fever and the neurological symptoms. Severely ill individuals need to be hospitalized and may require the use of a ventilator. Ribavirin may be useful in alleviating symptoms. Healthcare workers caring for patients with suspected or confirmed NiV should implement standard precautions [1].

Chandipura Virus Infection (CHPV)

Chandipura virus (CHPV) is a vesiculo-virus of the Rhabdoviridae family. It is an enveloped RNA virus which is transmitted to humans by sand flies, who are the main vectors and maintenance hosts. Human cases have been reported only from India

The virus was first isolated in 1965 in the Chandipura (Nagpur) region of India in two adult patients during an outbreak of febrile illness caused by Chikungunya and Dengue viruses [6]. It was subsequently detected in patients with viral encephalitis from Raipur in central India in 1980 .This virus was not considered to have an epidemic potential until an outbreak of acute encephalitis occurred in children in Andhra Pradesh due to CHP virus in 2003 with a case fatality rate of 55 per cent. Subsequently focal outbreaks were reported from Gujarat (2004), and Maharashtra (2007) [7,8]. In 2005, in an outbreak in Bhandara and Nagpur districts, 7 of the 21 cases clinically diagnosed as encephalitis were confirmed to be caused by Chandipura [9]. In a hospital-

based surveillance of acute encephalitis among children from endemic areas of North Telangana between May 2005 and April 2006, CHPV aetiology was identified in 25 of 52 cases [8]. Over the years, Chandipura encephalitis has emerged as a major public health concern in India.

The outbreaks to date have been focused in rural areas. All age groups and both sexes have been involved with a higher incidence observed in children and young adults. Neurological sequelae have been rare in recovered children. Mortality rates in most outbreaks have averaged about 50%

Clinically, the usual mild form of the illness is characterized by the sudden onset of fever with myalgia and arthralgia. Altered sensorium and vomiting may be present but no signs of meningeal involvement may be observed.Deep tendon reflexes are lost in two-thirds of the patients which may be associated with a decrease in muscle tone and power. Bilateral lung crepitations are detected in nearly half the patients. Hepatomegaly with disturbances in liver function may also occur [1].

Antibody detection by ELISA IgM as a modality for diagnosis is not recommended as most cases are fatal before the antibodies rise to detectable levels. RT- PCR for viral RNA in acute phase sera was found to be a sensitive and rapid diagnostic method. Viral culture can also be done in porcine stable (PS) and rhabdomyosarcoma (RD) cell lines or the virus grown in suckling Swiss albino mice after intra-cerebral inoculation [2].

No vaccine is available against this infection to date

Chikungunya:

The name Chikungunya is derived from word 'Makonde' meaning 'that which bends up' in reference to stooped posture developed as a result of the arthritic symptoms of the disease [10]. It is a mosquito-borne viral infection caused by Chikungunya virus which is single-stranded RNA Alpha virus, from the family Togaviridae

First reported in 1952 in Tanzania Chikungunya is believed to have originated in Africa, where it has maintained in 'sylvatic cycle' involving wild primates and forest dwelling mosquitoes such as Aedes furcifer, Ae. luteocephalus, or Ae.taylori [11]. It was subsequently introduced in Asia where it was transmitted from human to human mainly by Ae. aegypti and, to a lesser extent by Ae. Albopictus through an urban transmission cycle [12].

Outbreak of this disease occurred initially in Kolkata in 1963-64 and in Chennai in 1965, In Maharashtra; it was reported from Barsi in 1973, when a morbidity of 37.5% was reported [13]. Chikungunya virus had almost disappeared from India after 1973 and no new case was reported till 2006 when an outbreak of Chikungunya occurred in 210 districts of 13 states leading to more than 1.39 million cases of Chikungunya fever [14]. From Maharashtra, 152,086 suspected cases were reported and 6467 samples were sent to National Institute of Virology, Pune, and 804 were diagnosed serologically as Chikungunya viral fever [15] .Majority of the cases were recorded from Andhra Pradesh, Karnataka, Kerala, Tamil Nadu, Gujarat, Madhya Pradesh and Maharashtra. Currently 22 States and Union Territories of India have reported cases of Chikungunya [16].

The reason for the current reemergence was the build-up of a susceptible, non-immune population in India due to the absence of circulation of the virus for over three decades. The other reason could be that the current CHIKV strain has a unique mutation in the gene for the envelope protein E1, leading to a change in the amino acid at position 226 from alanine to valine (A226V). This has been associated with a higher epidemic potential and the possibility of transmission by Aedes albopictus in addition to Aedes aegypti, the traditional vector in India [1]

The incubation period of Chikungunya fever is 4-7 days, following which the disease has a sudden onset with fever, chills, head ache, anorexia, low back pain and conjunctivitis. 60-80% patients have morbilliform rash, occasionally with purpura, on the trunk and limbs. A prominent symptom is arthropathy manifested by pain, swelling and stiffness especially of the meta-carpophalangeal, wrist, elbow, shoulder, knee, ankle and metatarsal joints. Incapacitating arthralgia may persist for six months. Neurological syndromes in cases from Ahmedabad and Pune included encephalitis, encephalopathy and myelopathy or myeloneuropathy. Neurological complications of the disease are increasing in children and the virus has been detected in cerebrospinal fluid (CSF) samples of such patients. Non-neurological systemic syndromes included renal, hepatic, respiratory, cardiac and hematological

manifestations together with atypical manifestations which include lymphadenopathy, oral ulcers and encephalitis. The morbidity and disability caused due to Chikungunya is enormous, however no mortality has been reported. The most characteristic features of the infection in infants are acrocyanosis, symmetrical superficial vesico-bullous lesions and erythematous asymmetrical morbiliform rashes. Vertical transmission of CHIKV from mother to child has been documented [11,16].

Diagnosis is made by detecting ELISA IgM antibodies against CHIKV. However these antibodies can persist and thus a reverse transcription polymerase chain reaction (RT PCR)is preferred. A nested PCR technique can also be useful in rapidly diagnosing the disease [8]. The virus can be isolated from the blood of febrile patients by the intra-cerebral inoculation in suckling mice or on VERO cells [1].

No specific treatment is needed and the disease is usually self limiting. Treatment is primarily supportive and symptomatic. Analgesics, antipyretics along with fluid supplementation are recommended to manage infection and relieve fever, joint pains and swelling. Although there is no generally recommended specific antiviral therapy, the use of chloroquine, ribavirin and interferon-alpha might be useful [15]

Novel H1N1 Virus Infection (Swine Flu)

A novel strain of Swine-Origin Influenza A virus (S-OIV) that evolved by genetic re-assortment was first detected in April 2009 in California (USA) [18]. It was a 'triple re-assortment' influenza virus, containing genes from human, swine, and avian influenza A viruses. WHO declared H1N1 as a pandemic on 11th June 2009.The outbreak started in Mexico and travelled to other parts of North America, Europe, Australia, and Asia including India [19].

India was affected in May 2009 and the first laboratory-confirmed case was reported from Hyderabad on 16th May 2009.Soon the disease spread to other parts of the country. Subsequently, more confirmed cases were reported with the first death occurring in Pune. Subsequently Pune became the epicenter of the outbreak. In India, till, 2010, a total of 167846 persons were tested for H1N1 influenza and 23.4 per cent were found to be positive including 2113 deaths. The majority of the cases were from Delhi and Maharashtra[20].In 2014 a fresh outbreak has been reported from Hyderabad, Pune and Delhi. The strain is not as virulent as 2009 strain but mortality has been reported in this outbreak also. To date 88 cases have been reported from Telangana with 10 deaths, 25 from Pune and 31 from Delhi.[21]

The disease spreads amongst humans by inhalation of large infectious droplets and droplet nuclei as well as by direct contact with secretions or aerosols .The incubation period of the disease ranges from 1 to 7 days with an average incubation period of 4 days [22]. The clinical presentation is similar to seasonal flu and the illness remains mild and self-limiting in the majority of cases, with only 1–2% of patients requiring hospitalization. The presenting features included fever, cough, sore throat, body aches, headache, chills and fatigue and in some cases diarrhea and vomiting [23].Mortality is attributable to respiratory failure resulting from severe pneumonia and acute respiratory distress syndrome [23]. Complications are high among those who have preexisting diseases, such as asthma, heart disease, kidney disease, and among pregnant women

Diagnosis is confirmed by demonstration of viral RNA in nasopharyngeal swab or aspirate, nasal wash, or tracheal aspirates. Real-time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR)was performed on all samples at designated laboratories only to ensure reliability of diagnosis during the 2009 outbreak.

Antibody detection can also be done by heamagglutinin inhibition assay (HIA) for detection of the antibody against the HA gene of the influenza virus. Virus culture is too tedious and slow to be used for clinical diagnosis and a negative viral culture does not exclude pandemic S-OIV infection [24].

Antivirals like oseltamivir (Tamiflu) or zanamivir (Relenza) can be used for therapy.

Prevention of spread is possible by barrier nursing and immunization. An indigenous live and inactivated H1N1 vaccine was made available in the country during the outbreak. Simultaneously, Serum Institute of India (SII) also developed a H1N1 vaccine which was available as a nasal spray which was more readily accepted by health care professionals.

Crimean-Congo Haemorrhagic Fever (CCHF)

Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne disease caused by a member of the genus Nairovirus of the family Bunyaviridae. The virus is an enveloped spherical RNA virus. The lipid envelope is host derived, 5-7 nm thick, through which glycoprotein spikes protrude.[25]

It was first described as a clinical entity in 1944-1945 in Crimea during World War II. The virus was first identified in 1967 from a patient in Uzbekistan, and was found to be similar to a virus isolated in 1956 in Congo. CCHF virus circulates in an enzootic tick-vertebrate-tick cycle. There is very little evidence of clinical disease in animals but a wide range of domestic and wild animals act as reservoir for CCHFV[26]. The virus has been shown to cause disease among smaller wildlife species, e.g. hares and hedgehogs Infection is transmitted to humans by Hyalomma ticks or by direct contact with the blood or tissues of infected humans or infected animals [26].There is usually a biannual surge i.e March to May and August to October. This is related to increase in Tick reproduction and thus an increasing tick population.

The virus, though reported from several countries all over the world, has only recently been reported from India. A CCHF outbreak was reported in Rajkot in 2010 and a nosocomial outbreak in Ahmedabad ,Gujarat in 2011. This outbreak was characterized by a zoonotic origin and a person-to-person spread in hospital setting. High index of clinical suspicion, early laboratory diagnosis and institution of containment measures curtailed further spread of the disease.[27]

A serosurvey in domestic animals before and after the outbreak revealed the presence of CCHFV specific IgG antibodies and viral RNA. The virus was also isolated from Hyalomma anatolicum ticks from the Kolat village, Sanand Taluka, Ahmedabad, Gujarat [27].

The course of the disease can be divided into four phases - incubation, pre-hemorrhagic, hemorrhagic and convalescence. Infections occur after a tick bite become manifest in 3 days while after exposure to blood products it takes from 7-12days to manifest. Pre-hemorrhagic symptoms last for 7days and presents with non specific symptoms which include fever, chills, severe headache, dizziness, photophobia, myalgia and arthralagia. The haemorrhagic phase develops suddenly and lasts for 3 days. It starts with ecchymoses and may be followed by hematemesis, melena, epistaxis, hematuria, and hemoptysis. Hepatomegaly and splenomegaly may be seen in some cases [25]. Mortality rates reported vary from 10 to 80 per cent, averagely 30% and are usually associated with DIC.

Early diagnosis is important and for this a high index of suspicion must be there. Virus culture can be done on: Vero, BHK-21, LLC-MK2 and SW-13 cell lines. New born mice can be used for animal inoculation. A BSL 4 laboratory is required for working with this virus. ELISA–IgM can detect antibodies from 7th days of illness and persist for 4months after the illness. IgG antibodies persist for 5years. RT –PCR is the method of choice for diagnosis [28]

Treatment essentially includes maintaining the fluid electrolyte balance. Ribavirin has been used in humans with good results.

Minimizing human contact with infected livestock and reducing the tick burden in the animals are the most important preventive measures. Use of protective clothing, and gloves, goggles and face-masks reduces the chances of illness by indirect exposure. A formalin inactivated vaccine derived from suckling mouse brain has been used in Bulgaria and former Soviet Union [28].

Dengue virus infection which reemerged as out breaks in various parts of the country in 2014 is being discussed in another review in this issue is hence not discussed in this article.

The current review is focused only on India. The following virus infections emerged during this period causing outbreaks in different parts of the world with no human cases reported from India. They are briefly summarized here because travelers from infected countries travelled back to India and were quarantined in India. The country had to be in a state of readiness for an outbreak. They are: the Corona virus that caused severe acute respiratory syndrome (SARS), the H5N1 avian influenza virus and the Ebola virus.

SARS: On November 16, 2002, an outbreak of Severe Acute Respiratory Syndrome (SARS), began in the Guangdong province of China, which borders on Hong Kong. In February 21, a 64-year-old Chinese doctor who had treated cases in Guangdong arrived in Hong Kong and checked into the Metropole Hotel. Several guests in the hotel were infected. Health care workers attending on these sick people later got infected. It later spread to

individuals in 37 countries.

The SARS-CoV crossed into the human population of southern China in 2002 from Himalayan civets (Panguma larvata), as well as from racoon dogs (Nyctereute sprocyonoides) and Chinese ferret badgers (Melogalemoschata). Fever was the most common symptom of the outbreak. It was usually mostly associated with chills, rigors, headache, dizziness, malaise, and myalgia. There was occasionally, focal involvement of the lung which becomes widespread and death occurred due to respiratory failure. RT PCR on naso-pharyngeal aspirates was done for confirming a diagnosis. Ribavirin with or without steroids was used for therapy along with supportive measures [29]

Avian influenza, an infection caused by Influenza A (H5N1) viruses, usually infecting poultry animals and pigs. It was first reported in 1997 in Hong Kong. In 2003, changes in the strains of virus resulted in emergence of 'novel' Z strain and, infection to human beings by this virus occurred. Earlier, it was felt, that avian influenza virus cannot infect human beings due to differences in receptors. Vietnam reported first human case due to H5N1 in 2003. Cases of bird flu were reported from Navapur tehsil of Nandurbar district of Maharashtra. However, India did not report any human cases of Influenza A (H5N1)[1]as a preventive measures flocks of poultry where birds tested positive were destroyed.

Ebola Virus Infection: It is a hemorrhagic fever caused by the Ebola virus of the Filoviridae family. It is a severe, often fatal illness, with a case fatality rate of up to 90%.Ebola virus was first discovered in 1976 when an outbreak of Ebola hemorrhagic fever occurred in Zaire and another later that year in Sudan. The current outbreak of Ebola occurred in Guinea, Liberia and Sierra Leone. A case fatality of 50% has been reported so far in this outbreak. A 26-year-old Indian working in Liberia, who was treated and cured of Ebola in September, was kept in isolation at Delhi's Airport Health Organisation Quarantine Centre after his semen sample showed traces of Ebola virus.

Transmission of this virus is by direct contact with body fluids/secretions of infected persons. Indirect contact with environment and fomites soiled with contaminated bodily fluids may also transmit the infection. The incubation period varies from 2 to 21 days, with an observed average of 8 to 10 days. There is no risk of transmission during the incubation period.

Symptoms are sudden onset of fever, intense weakness, muscle pain, headache and sore throat. This is followed by vomiting, diarrhea, rash, impaired kidney and liver function, and at advanced stage, both internal and external bleeding. Laboratory findings include low white blood cells and platelet counts and elevated liver enzymes. Diagnosis can be done within a few days after symptoms begin by IgM ELISA, Polymerase chain reaction (PCR) or by Virus isolation [30].

Prevention and Control:

Outbreaks of emerging diseases vary widely in duration and frequency and case numbers. Some can be predicted as occurring annually, for example influenza, whereas many decades may elapse between episodes of others, as is the case with Ebola virus. Planning a single, integrated strategy against all eventualities is therefore almost impossible. This problem is compounded by a) emergence of escape mutants in populations vaccinated against known diseases and b) the emergence of strains resistant to antiviral therapy.

Improved epidemiological surveillance of infectious diseases is the foundation for immediate and long-term strategies for combating emerging diseases. Coordination with the veterinary community is essential for early detection and effective control of emerging disease outbreaks. Historically, there has been little integration of animal and human public health, yet the techniques and methods for diagnosing and controlling infectious disease are similar regardless of affected species. Swiftness of response to such outbreaks is critical to decrease mortality and contain the extent of the outbreak. To this end, creating increased awareness and training of physicians and clinical microbiologists for identification of new/emerging pathogens, and prompt reporting and management of outbreaks is essential to tackle the threat posed by emerging/re-emerging infections Availability of containment facilities and standard diagnostic reagents and vaccines needs to be ensured and made available at the start of an outbreak. This needs to be supplemented by adequate training of clinicians and diagnostic microbiologists in all aspects of diagnosis and control of emerging infections.

Technology can play a major role in predicting disease emergence, as for example the use of satellite imagery to

detect changing patterns of vegetation in response to rainfall. The use of satellite maps taken over East Africa accurately predicted the outbreak of Rift Valley Fever amongst livestock as a consequence of increased vector activity. The use of the internet has become an essential tool in containing disease outbreaks, allowing for rapid dissemination of serological, clinical and molecular sequencing data. Such rapid communications played a vital role in combating the SARS outbreak in 2003 and also in identifying the spread of swine-origin H1N1 influenza virus in 2010.[31]. Thus, there is a need to build resources to diagnose, prevent and treat these emerging viral infections.

Conclusions

Emergence is hard to predict, although mathematical modeling and spatial epidemiology have done much to improve this. However, much needs to be done to ensure adequate surveillance is maintained for emerging infections of humans and animals on a regular basis .Increasing general alertness among physicians, veterinarians and those responsible for formulating public health policy will assist in building resources needed to tackle emerging viral infections.

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    Microbes and Infections (2012) 1, e46; doi:10.1038/emi.2012.47

REVIEW ARTICLE

Conglomeration of Risk Factors-Metabolic Syndrome

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Introduction

Epidemiological transition has manifested in the form of increasing burden of non communicable diseases (NCDs) which is now a major concern throughout the world. India is emerging as a economic giant on the world map but not without the unstoppable rise in the risk of diseases of affluence like cardiovascular diseases (CVDs), diabetes, obesity etc. The environment today is moulded towards a favourable milieu for obesity and the NCDs associated with it. The prime factors like affluent lifestyles, rich food, sedentary habits, couch potato culture, and availability of fast foods are all associated with neo rich population.

Aggressive advertising and marketing, universal accessibility of packaged junk foods like wafers and colas add fuel to the fire. Increase in the purchasing power of youngsters marked by use of non traditional foods and snacks are making the problem complex. Attitudes and behaviour adopted by youngsters in day to day situations form the part of lifestyle and the lifestyle diseases refer to the diseases that result due to choices people make in their life. These behaviour patterns are acquired gradually, therefore it is a difficult to change, needs a lot of persuasiveness with a persistent approach.

Adverse lifestyle changes in the form of nutrition imbalance, stress, tobacco & alcohol consumption, physical inactivity, along with improved socio economic status are occurring due to urbanization, mechanization, and migration from villages to cities, from cities to metropolis. The complex demographic, epidemiological, social and economic transitions occurring in south Asia including India have led to change in the morbidity profile manifested in the form of "diseases of affluence" and now considered as "Chronic Emergency" due to its effect on individual, family and health system levels.[1]

The lifestyle associated risk factors of today are the diseases of tomorrow in the form of diabetes, hypertension, CVDs, cancer etc. The co-occurrence and conglomeration of risk factors like hypertension, low HDL cholesterol, increased triglycerides and hyperinsulinemia if observed to be existing then it was conceptualized as Syndrome X, or metabolic syndrome suggested by Reaven two decades earlier[2]. Such collection of risk factors due to their strong association with insulin resistance could be one of the fundamental reasons underlying the pathogenesis of cardiovascular disease.[2,3]

Definitions

Various criteria for diagnosis have been proposed by different organizations leading to controversies causing challenges in the management of the cases.[4]The **WHO definition**[5] includes impaired glucose tolerance, diabetes mellitus and or insulin resistance together with two or more of the following: arterial blood pressure >140/90 mm hg; dyslipidemia, defined as plasma triglyceride (TG) concentration >1.7 mmoles/l (150mg/dl) and /or high density lipoprotein cholesterol (HDL-C) <0.9 mmoles/l (35mg/dl) in men, < 1.0 mmoles /l (39 mg/dl) in women; central obesity, defined as waist-to-hip ratio >0.90 in men, >0.85 in women and /or body mass index (BMI) >30 kg/m^2; micro-albuminuria, defined as urinary albumin excretion rate >20 mg/min or albumin: creatinine ratio >30mg/g.

The **NCEP ATP III definition**[6]requires the presence of any three of the following: abdominal obesity, defined as a waist circumference of >102 cm (>40 inch) in men,>88 cm (>35 inch) in women; plasma TG > 1.69 m moles/l (150mg/dl); HDLC <1.03 m moles/l (40mg/dl) in men, <1.29 m moles/l (50mg/dl) in women; blood

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pressure > 130/85 mm Hg; fasting glucose >6.1 m moles/l (110 mg/dl). Other markers, such as chronic sub clinical inflammation, hyper uricemia and coagulation disorders, are also associated with the metabolic syndrome. Thus features of metabolic syndrome are generally accepted to include a combination of impaired glucose metabolism, hypertension, dyslipedemia and abdominal obesity. It is recognized as a precursor to the development of type 2 DM and is associated with elevated excess risk of type 2 DM and CVD risk.[7,8]

Thus these definitions are based on simple clinical and biochemical parameters which can be measured in any clinic or a simple laboratory. The **modified criteria for definition of metabolic syndrome** especially for Asians which have been accepted are: central obesity (defined as waist circumference >90 cm for males and >80 cm for females, raised TG levels : >150 mg/dl or on specific treatment for this lipid abnormality; reduced HDL : <40 mg/dl in males and < 50 mg /dl in females or on specific treatment for this lipid abnormality; raised blood pressure : systolic BP> 130mmHg or diastolic BP > 85 mm Hg or on treatment of previously diagnosed hypertension; and raised FPG > 100 mg /dl or previously diagnosed diabetes. Three out of five criteria have to be present to define the metabolic syndrome[9].

Fat Distribution in Indians - a major determinant

In India as the significant proportion of population belongs to younger age group, magnitude of problem of obesity is more due to increased purchasing power and availability of high fat foods, consumption of energy dense fast foods leading to some metabolic derangements starting in childhood responsible for increased risk of metabolic syndrome. However western population have shown a plateau in prevalence of both adult and childhood obesity during last decade[10,11]

Even with a BMI currently defined within normal limits, there is a higher magnitude of adiposity, abdominal obesity and a lower muscle in Indians leading to more risk of Insulin Resistance, Metabolic Syndrome and Type 2 DM[12]. Secondly excess truncal subcutaneous fat is a major determinant of insulin sensitivity and is associated with a high prevalence of insulin resistance in post pubertal urban Asian Indian children. Skinfold thickness as anthropometric measure shows that truncal skin folds are thicker due to increased subcutaneous fat mass in Asian Indian adolescents as compared to white Caucasians and blacks.[13]SimilarlyIndians have a higher magnitude of adiposity, abdominal obesity and a lower muscle for any proposed value of body mass index (BMI)[14].

Various studies have revealed higher prevalence of both overweight and obesity in Asian Indian children[15,16,17] Obesity is one of the most serious public health problem of twenty first century, evolving as epidemic in this decade. Human Evolution is an ongoing process, is it that increase in average body weight of human beings a part of this process? It has been observed that obesity is being noticed more commonly than was seen before, then it is likely that in future generations everyone will have a tummy, as part of central obesity ie a change in architecture of human body.[18]

Prevalence of Metabolic syndrome

Nationally representative data on metabolic syndrome prevalence are scarce. The prevalence in a south Indian study has estimated it to be 25.8 percent by IDF criteria,23.2percent by WHO criteria and 18.3percent by the NCEP ATP III criteria.[19] The prevalence in rural population in a study conducted in central India was as low as 5percent [20],whereas in urban population, about one third of people have metabolic syndrome[21]

The potential risk factors associated with development of Metabolic Syndrome in South Asian population include urbanization, lack of physical activity, high fat, carbohydrate and low fibre food, increased life expectancy, migration from villages to cities, stress, and tobacco and alcohol consumption. These risk factors lead to the individual conditions comprising the metabolic syndrome like hypertension, DM, obesity etc. These conventional risk factors are highly prevalent in Asian Indians; the abdominal obesity is 31.4percent, hypertension 55.4percent,low HDL 65.5 percent, raised fasting glucose 26.7percent.[22-23] the overall prevalence of MS among the migrant South Asian population was shown to vary between 21 percent to 46percent.[24]

The various risk factors are associated with NCDs comprising of metabolic syndrome. It is reported that the risk factors like excessive intake of saturated fats, refined sugars, trans-fatty acids are associated with obesity, hypertension, CVDs and diabetes and that 1.7 million deaths are attributed to low fruit and vegetable

consumption[25]

The global report reveals that the NCDs are the leading cause of death globally, nearly 80 percent of NCD deaths occur in low and middle income countries.[26] Worldwide currently NCDs represent 43 percent of burden of disease, expected to rise to 60 percent of burden and 73 percent deaths by 2020.[27]As per WHO statistics for 2011 in India NCDs including cardiovascular disease, diabetes etc are estimated to account for 53 percent of all deaths and 44 percent of disability-adjusted life years respectively in India[28]. Among the non communicable diseases associated with metabolic syndrome, the mortality from CHD in India was 1.6 million in the year 2000 as per the global burden of disease study report, while a staggering 3.4 million deaths are likely to occur out of the 61 million cases of CHD in the year 2015[29].

Prevention and Control

Considering the growing burden of NCDs in Asia the "Seoul Health Declaration" was announced in the fifth Asia Pacific Conference on Public Health which was organized in Seoul, Korea in April 2014 with the theme "Multidisciplinary Approaches to Emerging Challenges".Emphasis was placed on need for a "multi-sectoral, whole-of-government and whole-of-society approach to stem the "rising tide of lifestyle-related diseases" for prevention and control by reducing the common modifiable risk factors.[30.] Government of India has already taken the cognizance of the problem by initiating an Integrated National Program for prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS). The focus of program is on health promotion and prevention, strengthening of infrastructure including human resources, early diagnosis and management and integration with primary health care system through NCD cells at different levels of health system[31].

Health promotion activities should be initiated at the community level, in the form of risk reduction measures to be undertaken in schools, colleges and offices like change in diet pattern, increase in consumption of vegetables and fruits, reduction of tobacco and alcohol use, making available playgrounds, parks etc. This can be achieved by working with other sectors like environment, education, transportation, food industry to ensure healthy lifestyle. Following are some of the measures suggested for prevention and control of Metabolic Syndrome in Asians….

1. Intensive efforts should be made to make South Asians aware that they are more at risk of development of T2DM and CHD.

2. Those with family history of T2DM and premature CHD should be identified at the earliest and vigorous efforts should be taken to bring them into the orbit of special health care by lifestyle modifications.

3. The lifestyle changes should be encouraged from childhood like regular physical activity and restriction of television and internet usage.

4. Diet to be modified in the form of well planned, balanced diet with restricted carbohydrates, saturated fats, high fibre and omega-3 polyunsaturated fatty acids.

5. Body weights and anthropometric indices should be maintained within normal limits as expected for Asians ie BMI, waist circumference(BMI between 19-23 kg/m2, waist circumference<90cm in men &<80cm in women).

6. Overweight individuals and those with abdominal obesity to be actively managed to lose weight by lifestyle modifications.

7 Detection of one component of metabolic syndrome should lead to search for other components and its management.

8. Observe for change in guidelines for treatment of diabetes/insulin resistance in metabolic syndrome in future.

9. Adequate nutrition during intrauterine period should be given to pregnant women so as to prevent early-life adverse events which may promote insulin resistance in adulthood.

10. Research on insulin resistance and metabolic syndrome in South Asians in terms of its prevalence, etiological factors including genetics to be encouraged.

Thus there is a need to undertake in depth analysis of the status of this conglomeration of risk factors in the form of Metabolic Syndrome in every patient and bring about community awareness about it by the physician so that no opportunity is lost for its detection at the earliest. William Osler rightly said "The good physician treats the disease; the great physician treats the patient who has the disease" for which the physician has to ask the right

questions at the right time.

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REVIEW ARTICLE

Judicious use of blood in clinical practice

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Introduction

Blood transfusion services (B T S) is a vital part of modern health care system without which efficient medical care is impossible.

The aim of BTS should be to provide effective blood and blood products, which are as safe as possible and adequate to meet patient's need.

Optimal utilization of blood helps in reducing or eliminating the use of allogeneic blood and often prevents unnecessary exposure of a patient to the risk of blood borne endogenous infections. Appropriate and rational use of blood /blood components is required to ensure their availability to needy patients as well as to avoid the unnecessary risk of transfusion – transmitted diseases.

Rational use of blood means providing the right blood product, in the right quantity, for the right patient. It can help in bridging the gap between demand and supply of the precious blood and blood product[1].

The judicious and appropriate use of blood and blood products refers to its safe transfusion only to manage a condition which can otherwise lead to significant morbidity or mortality and cannot be managed effectively by some other means[2].

Appropriate use of blood or its components remains a formidable challenge faced by clinicians in a developing country[3,4]. It has been observed that there is a gross over and inappropriate ordering of blood and its products in many medical centers in India and abroad and transfusions are being given in response to habit or availability and not for indications. This may have medical, legal and ethical complication regarding patient care [5,6,7,8].

Developing guidelines for use of blood/ blood products [1,9,10,11]:

1. Indications and guidelines for appropriate use of blood should be developed and disseminated to various levels of health care, such as physicians and surgeons, medical college faculty, resident doctors and medical officers in blood centers.
2. Organizing clinician awareness and training session.
3. Patients should be given blood transfusion only when there is a definite indication to do so and its benefit outweighs the risk associated with it.
4. Use of whole blood should be discouraged. Instead patients can be treated with the specific components e.g., red cells, plasma or platelets. Crystalloid or colloid solutions (dextrose – saline, ringer lactate, dextran etc) may be used for mild to moderate blood loss and red cell transfusions may be limited only for patients with acute blood loss of >20% of blood volume.
5. Use of blood less than three days old should preferably be avoided as there is an increased risk of transmission of viral infections from fresh blood, which may get inactivated on storage.
6. Single unit transfusion raises the hemoglobin by 1 g/dl only, which is therapeutically insignificant. The use of a single unit of blood should therefore be strongly discouraged.
7. Each unit of alloagenic blood transfused carries an inherent risk of disease transmission and transfusion reactions. Autologous blood transfusion is unique approach of providing the patients with their own blood and it helps to avoid the use of allogenic blood. Reducing the exposure of patient to different donors will also decrease the risk of transfusion -

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transmitted diseases. This is of importance in a pediatric patient requiring 30-50 ml of blood every day or on alternate days, who may be transfused with small quantities of blood separated from a single donor blood unit. Apheresis of blood products prepared from single donors also helps in reducing number of donor exposures to a particular patient.

Role of Hospital Transfusion Committee (H T C)[9]

It is almost imperative for each hospital to constitute HTC consisting of blood users (representatives from surgical discipline, internists, hematologists and anesthesiologists), representatives from Administration and Nursing staff and blood transfusion specialist.

Following are the functions of H T C

1. Formulating the policies for use of blood and blood components.
2. Developing guidelines for use of blood/ plasma substitutes.
3. Establishing Standard Surgical Blood Ordering Schedules (SSBOS)
4. Monitoring source and supply of blood components
5. Monitoring adverse effects of blood transfusion
6. Auditing blood transfusion practices

Audits and timely feedback to the clinicians about good transfusion practices lead to improvement in blood usage. Toy pointed out that cyclic audits and education to physicians prescribing transfusions lead to identification of inappropriate transfusions, improvement of bedside blood administration practices, avoids unnecessary cross-matches and reduces outdating of precious donor blood[11].

Blood component usage[12]

Blood utilization audit helps to formulate guidelines for improving transfusion practice in a health care centre. A cross-match to transfusion ratio (C/ T) of <2.5, transfusion probability of >30 and transfusion index >0.5 is considered indicative of significant blood usage. It is calculated by the formula as follows[12.]

- C/ T ratio = Units cross-matched/ Units transfused.
- Transfusion probability = Patients transfused X 100/ Patients cross-matched
- Transfusion index = Units transfused/ patients cross-matched
- Overall blood utilization = Units transfused X 100/ Units cross-matched

WHO Guidelines regarding transfusion of blood and its products[8]

Following are the safe units of the vital investigations of the recipient patient, below which the transfusion of respective blood and blood products can be done.

Investigation	Target value
Hemoglobin (Hct)	10g/ dl (0.33)
Platelet count	>50 x 10^9/ L
Prothrombin time	<1.5 x control
Partial thromboplastin time	<1.5 x control
Fibrinogen	>0.8 g/L

Indications of blood components[13,14]

1. Whole blood/ packed red cells (PRBC) – Active bleeding, Intrauterine transfusion, exchange transfusion in neonates. Volume of 1 PRBC is 180-200 ml, which will increase the hemoglobin by 1g/ dl and hematocrit by 3%.
2. Platelets – Any group platelets may be transfused if group specific concentrates are not available. However same group donor would be needed for a single donor platelet transfusion (SDP). Platelets are not cross-matched routinely unless refractory. Indications for platelets transfusion are severe thromobocytopenia (<5000-10000/ cu mm), DIC with bleeding, hematological malignancies, supportive during chemotherapy, platelet dysfunction. One Random Donor (RD) unit is 50-70 ml and will increase the platelet count by 5000-10000 / µl. One Single Donor Apheresis platelet (SDAP) unit is of 200-400 ml, which will cause Corrected Count Increment (CCI) ⩾ 10X 10^9/ L within one hour.
3. Fresh Frozen Plasma (FFP) – ABO specific or ABO compatible FFP shall be used. Rh (D) is not significant for FFP. FFP are not cross-matched. Indications are warfarin immediate reversal, DIC coagulopathy, coagulopathy going for surgery, for

factor replacement if factor not available. Volume of one FFP is 200-250 ml, which will cause increase in coagulation factors by about 2%.

4. Cryoprecipitate – Any group Cryoprecipitate irrespective of ABOand Rh(D) can be used. No need for cross-matching. Indications are Hypofibrinogenemia, for factor replacement if factor not available. DIC, Trauma, Renal related bleeding. Volume of one unit is 10-15 ml, which will contain 80 IU of Factor VIII.

Practical aspects of transfusions[13]

Never add other medications to blood or blood components. No other infusion solutions should be added to any blood components. Use at least 20ml of Normal Saline (0.9%) to flush lines and 3-ways before or after blood components when other drugs or fluids are to be administered. Do not use 5% Dextrose via the same administration set as blood since this will cause lysis of red cells.

Time limits for Infusion[1]

1. The administration of Whole blood or red cells should be started within 30 minutes of issuing from the blood bank. If it is not required for transfusion, it should be returned immediately to the blood bank with reasons. After 30 minutes of issuing, it is not taken in the blood bank. Transfusion should be completed within 4 hours of starting the transfusion. If the room temperature is very high, shorter 'Out of refrigerator time' should be used.
2. Platelet concentrate should be administered as soon as they have been received. Infusion should be completed within 15 to 20 minutes. Platelet concentrate should be kept at room temperature 22^0 C to 24^0 C. They are not kept in the refrigerator. Platelet concentrate should be administered with transfusion set with filter. Platelets once issued are not taken back in the blood bank.
3. FFP should be infused as soon as possible after thawing to avoid loss of labile clotting factors. Thawed plasma stored at $2\text{-}4^0$ C should be used within 12 hours. In adult 1 unit of plasma should be infused within 15-20 minutes. Thawed or partially thawed plasma is not taken back in the blood bank.

Blood warming[1,13]

Routine warming of blood is not needed. Infusing 2-4 units of refrigerated blood over several hours cause no harm. Patients, who may need warmed blood include 1. Adults receiving multiple transfusions at rates >50 ml/ Kg/ Hr. 2. Children receiving multiple transfusions at rates >15 ml/ Kg/ Hr. 3. Infants receiving exchange transfusions. 4. Patients with cold agglutinins.

The rapid and massive transfusion of cold blood ($2\text{-}6^0$ C) is associated with an increased risk of ventricular fibrillation and cardiac arrest.

Blood warming is carried out using approved blood warmer devices such as Level 1 Hotline. Blood is not warmed above 37^0 C. excessive warming can cause hemolysis. Unit of blood should not be immersed in a water bath.

Conclusion

The knowledge of blood usage pattern helps to address major issues like minimization of transfusion risks, blood shortage and management of massive transfusion events[15]. Enhancement of blood component separation facility, regular auditing of transfusion services and improved communication with clinicians have been advocated as some of the steps towards judicious use of blood.

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ORIGINAL ARTICLE

"Intrapleural Urokinase for Empyema Thoracis in Children - A Randomized Controlled Trial "

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ABSTRACT

Objective : To assess the role of fibrinolytic agent - Urokinase intrapleurally in the treatment of childhood empyema thoracis.

Method : Thirty one children (median age 3.0 years) were recruited from one center and randomized to receive either intrapleural urokinase with tube drainage (study group) - 40,000 i.u. in 40 ml of normal saline 12 hourly for 3 days or Tube drainage alone (control group). Both groups received antibiotics as per the center protocol. The primary outcome measure was length of hospital stay after entry into the trial.

Results : Treatment with urokinase resulted in a significantly shorter hospital stay (12.5 vs 18 days; p = 0.047). Duration of the chest drain which ultimately decided the hospital stay was significantly shorter in the study group (7 vs 13 days; p = 0.007). Duration of antibiotics use was significantly reduced in the study group (10 vs 17 days; p= 0.001). The complications were fewer in study group patients(6 vs 12; p=0.029).

Conclusions : Intrapleural urokinase is an effective adjunct in the management of empyema thoracis in children and significantly shortens the hospital stay by reducing the duration of chest tube drainage and duration of antibiotics. Thus reducing the morbidity and also the hospital expenses.

Key words : Intrapleural Urokinase, Empyema thoracis, randomized controlled trial.

Introduction

Empyema thoracis in children usually follows an acute bacterial pneumonia and is associated with significant clinical morbidity. There is a great heterogeneity in its management reflecting the absence of good evidence on which to base the treatment.

Conservative management of empyema with antibiotics alone or antibiotics and tube drainage often fails because the infected fluid becomes loculated and cannot be drained by a ingle catheter. Operative procedures such as the so-called mini-thoracotomy" with manual attempts to break down loculations, full thoracotomy and decortication and more recently, "video assisted thoracoscopic surgery (VATS)" are all options which have been described in children.[1,2,3]

The use of fibrinolytic agents (streptokinase, urokinase) has been described in the management of empyema thoracis in adults [4,5,6,7] and children [2,3,7-11] especially in loculated empyemas. These studies have shown increased drainage of pleural fluid, clinical benefit, radiographic improvement, and reduction in hospital stay by primarily reducing the duration of chest tube drainage. There has been no published randomized controlled studies of the use of fibrinolytic agents for empyema in children in Indian literature.

In developing countries empyema management in children is associated with significant morbidity, consumption of scarce hospital resources as well as financial burden on the family due to prolonged hospitalization of the child. Optimal management is controversial, especially the duration of parenteral antibiotics and the role of surgery. Newer modalities like intrapleural fibrinolysis therapy and video assisted thoracoscopic surgery are today being offered as cost effective modalities of treatment, reducing the hospital stay and also faster recovery with less morbidity[12].

Hence the present study was planned to determine whether intrapleural Urokinase instillations adjunctive to chest tube drainage and antibiotics reduces the need for surgical intervention and improves the outcome in patients with empyema thoracis in children at the same reducing the duration of the hospital stay.

Methods

Previously healthy children aged 3 months to 12 years with no underlying cardio-respiratory disorder were

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eligible for the study if they had developed an empyema that required pleural drainage.

The following exclusion criteria was used -

1. Age less than 3 months;
2. History of recent severe trauma, haemorrhage or stroke, coagulation or bleeding disorder, low platelet counts and chronic liver disease;
3. Child on anticoagulant therapy in the previous 2 years;
4. Children with preceding drainage procedures, pneumothorax, subcutaneous emphysema.

The study was approved by institutional ethics committee.

Randomization :

This was a randomized controlled study. The randomization of the patients was done using computer generated table and the numbers were communicated to the doctor managing the patient.

Procedure :

Once the patient was confirmed to have pus in the pleural cavity by a diagnostic pleural tap, a standard chest tube (size 16 to 26 depending on the age of the child) was inserted into the pleural cavity which was attached to the underwater seal bag. A informed consent was obtained from the caretaker of the child to participate in the trial.

If the randomized patient belonged to the study group, Urokinase in the dose of 10,000 IU in 10ml of normal saline twice a day for children below one year of age and 40,000 IU in 40ml of normal saline twice a day for children over one year of age was given for three consecutive days, into the intrapleural space through the chest tube already in-situ. Prior to instillation of urokinase, the coagulation profile including prothromb in time of the child had to be normal. The children in both the groups received the same antibiotics as per the center protocol.

If the randomized patient belonged to the control group, the child received treatment with chest tube drainage and IV antibiotics similar to the study group.

Duration of hospital stay was calculated from the date of entry into the trial to the date of discharge. Once the tube stopped draining pus, it was clamped for 12 hours and if no fever or respiratory distress was noted, the tube was removed. Suggested discharge criteria were that the child should have normal respiratory rate in air, afebrile (<37.5 C over previous 24 hours), no residual pleural fluid on USG thorax. Follow -up visit was planned after one week, one month and three months. A repeat X-ray chest was taken at three months to see any residual abnormalities like pleural thickening, rib crowding or fibrosis.

Data Analysis :

The primary outcome measure was duration of hospital stay after trial entry. Comparisons between the two groups were carried out using two tailed Student t tests.

RESULTS

A total of 41 patients were assessed for eligibility. 31 patients fulfilled the inclusion criteria and were enrolled. After randomisation, at the end of the study period there were 16 patients in the Urokinase group and 15 patients in the control group. All 31 cases were confirmed cases of empyema on cytology. The two groups were comparable at trial entry. The duration of illness prior to entry into the trial was same in both the groups. The median age was 3.0 years (range 3 months to 12 years). The difference between proportions of male and female and their age in the two groups was not statistically significant. The data was analyzed according to the duration of hospital stay following entry into the trial. Children were discharged from the hospital on an average 2 days (range 2 to 8 days) after the suggested discharge criteria were met. All 31 patients followed up for 3 months as planned .

Effect of Urokinase on outcome : (Table – I)

A comparison of outcome between children treated with urokinase and those in the control group showed that the use of urokinase during the first 4 days of the hospitalization was associated with a significantly reduced hospital stay (12.5 vs 18 days; $p = 0.047$). The duration of chest tube drainage was shorter in the study group (7 vs13 days; $p = 0.007$) so also, the duration of antibiotics (10 vs 17 days; $p = 0.001$). Fewer children in the study group developed complications (6 vs 12; $p=0.029$).

Table I

Comparision between the study and control group

Parameters	Control (n=15)	Urokinase (n=16)	P value
Duration of Illness prior to admission (days)	7 (3-20)	8 (3-45)	0.82
Previous antibiotic use	8 (53%)	8 (50%)	>0.95
Duration of chest drain (days)	13 (1-36)	7 (3 – 15)	0.007
Duration of antibiotics (days)	17 (1 – 36)	10 (3-24)	0.001
Complications	12 (80%)	6 (38%)	>0.95
Death	1 (7%)	1 (6%)	>0.95
Hospital stay (days)	18 (1 -40)	12.5 (3 -25)	0.047
Follow-up Chest X-ray	(n=14)	(n=15)	
(a) Normal			
(b) Pleural thickening	6	15	
(c) Mid-zone shadowing			
	6	Nil	
	2	Nil	
Cost (Rs)	6000 – 8000	3000 - 4500	< 0.05

Urokinase Side-effect :

No child in the study group experienced any discomfort during intrapleural instillation of Urokinase or any disturbance of blood coagulation.

Other Outcomes :

One child, one year old expired in the control group within one day of admission. (Empyema complicated by tension pneumothorax) and one child in study group due to aspiration following vomiting and needed ventilation. 3 patients in the control group developed complications - Pneumothorax, Broncho-pleural fistula and Subcutaneous Emphysema respectively requiring surgical intervention but none in the study group.

Three month Follow up :

Of the 29 children who underwent chest X-ray on follow -up, 23 of them were normal. (16 in the urokinase group; 7 in the control group). In the control group 6 children had pleural thickening and 2 children developed left midzone shadowing but without clinical symptoms.

DISCUSSION

To treat empyema thoracis in children, various options are available viz, antibiotics alone or in combination with thoracocentesis; tube thoracostomy; intrapleural fibrinolysis; thoracoscopic decortication or open decortication. Ideal treatment is yet to be established. The choice is dictated by institutional raditions, personal experiences and biases.

Historically, the definitive management for empyema has been surgical debridement. In the early part of the last decade, the minimally invasive approach (VATS) became the gold standard for operative management of fibropurulent pleural space disease [13-18]. VATS has resulted in earlier and more complete resolution of empyema than chest tube drainage alone in both retrospective and prospective studies translating in shorter hospitalization with primary VATS [19-24]. A retrospective series of 89 children undergoing primary VATS found a 12% risk of a subsequent procedure to address ongoing disease or a complication [25]. However, the superiority of operative mechanical debridement as a definitive management strategy has been increasingly challenged by chemical debridement.

Chemical debridement with fibrinolytics takes advantage of the pathophysiology of empyema formation. In health there is active pleural circulation with parietal filtration and reabsorption of approximately 0.02 - 0.1 ml/kg/hr (26) During the development of empyema there is both increased production and decreased absorption of pleural fluid. When the pleural space becomes infected, the ensuing inflammatory reaction is associated with fibrin deposition and decreased fibrinolytic activity. This creates a procoagulant environment leading to the development of solid material in the form of septations or loculations[27]. A fibrinolytic agent breaks down fibrin. The common examples are urokinase, streptokinase and tissue plasminogen activator (tPA). Since fibrin is a predominant component of the extracellular matrix upon which septations and solid debris form, instillation of a fibrinolytic agent to liquefy pleural space disease has been shown to be effective in promoting resolution of empyema in multiple studies[28].

Urokinase has been used intrapleurally in adults (6) extensively and does not cause significant activation of systemic fibrinolysis. Urokinase is of human origin and allergic reactions have not been reported. Urokinase may work by decreasing fibrinous strands and reopening pleural pores blocked by fibrinous material, permitting pleural resorption.

Fibrinolysis has been shown to be superior to chest tube

drainage alone in retrospective and prospective studies, by both direct comparison and when used in patients who failed chest tube drainage only [cross ref, 33] Treatment of empyema with fibrinolytics instilled through an indwelling chest tube has been shown to be more cost-effective than treatment with a chest tube alone[29].

The timing of intervention, by fibrinolysis or VATS, is an important consideration in the treatment of empyema. Two prospective, randomized trials have been conducted independently comparing fibrinolysis to VATS upon diagnosis of empyema in children [30,31] Both studies documented significantly higher costs or hospital charges with VATS. The studies utilized an intention-to-treat analysis so the length of stay and total charges included the patients who failed fibrinolysis and were subsequently treated with VATS. The failure rate for fibrinolysis was 16.6% in both studies. When comparing fibrinolysis to VATS, the burden to the patient should be considered given that one therapy is a non-operative procedure requiring a single sedation and the other is a surgical procedure under general anesthesia.

The 2008 Cochrane review included subgroup analysis leading to the conclusion that there is an overall benefit to the use of fibrinolytics in the group with loculations (pooled risk ratio, 0.63; 95% CI, 0.46-0.85). [32]

A recent review article on management of empyema in children (33) concluded that since chemical debridement offers non-operative management with decreased resource utilization compared to VATS, chemical debridement should be first line therapy when healthcare resources allow. Definitive management with either should be initiated as soon as empyema is diagnosed. After fibrinolysis, if a patient is persistently ill after the chest tube rainage is diminished and imaging proves substantial pleural space disease, VATS should be considered.

In our study, on 31 patients with empyema thoracis, the use of Urokinase significantly reduced the duration of hospital stay (12.5vs18 days) and duration of antibiotic use (10 vs 17 days) This was mainly due to the fact that the duration of chest tube drainage was significantly reduced (7 vs 13 days) in the Urokinase group.

This is probably the first randomized controlled trial of Urokinase in childhood empyema in India. (No published data available on journal and internet search). It has shown that use of Intrapleural Urokinase reduces the hospital stay, duration of tube drainage and antibiotic use. Also no patient in the Urokinase group required subsequent surgical intervention. As a result the hospital expenses were greatly reduced. (Rs 8000 in control group vs Rs 4500 in urokinase group, $p < 0.05$)

The cost of treating patients with Urokinase is considerably cheaper than any surgical interventions. VATS is not universally available in the developing countries and requires technical skills. Open thoracotomy involves surgical and general anaesthetic risks that are not insignificant. Healing and remodeling are rapid in healthy children and we found near complete resolution of signs and radiographic appearances at 3 months in our study irrespective of initial severity or treatment.

This study was designed to meet the practical needs of the pediatricians. The decision to tap an effusion or to place a pleural drain means a procedure under either sedation or anesthesia. Patients were therefore not chosen for entry to the study on the basis of pleural fluid analysis but simply when a pleural fluid that was drained was visibly purulent. Similarly, our endpoint of length of hospital stay is simple. Given the current pressure on beds in tertiary centers, children do not linger in the hospital after they are "better".

However, simple measures such as the duration of hospital stay and the time of defervescence are too crude as outcome measures, hence today it is relevant to consider other endpoints like - parents and child's overall satisfaction with treatment at different time points. This will have several components including pain, changing attitudes to thoracotomy scar, loss of schooling and time off work for the caretakers. There is also a need to determine the effects of different treatments on subsequent lung growth and to monitor possible emergence of restrictive lung disease.

CONCLUSION

Intrapleural Urokinase is an effective adjunct to the management of parapneumonic empyema. Duration of hospital stay is shortened by reducing the duration of the chest tube drainage and thus reducing the duration of antibiotic treatment as well. It is a cost effective way of reducing the hospital expenses.

ACKNOWLEDGEMENT

We wish to thank the patients, parents, residents and the staff of the pediatric ward for their co-operation during the study period. We wish to thank all our individual donors who sponsored for the purchase of Urokinase that was used in the study.

KEY MESSAGE :

*Intrapleural Urokinase is an effective adjunct to the management of parapneumonic empyema in children as it reduces the duration of chest tube drainage significantly.

*It is a cost effective way of reducing the hospital expenses at centers where surgical options are limited.

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ORIGINAL ARTICLE

A study of endoscopic endonasal dacrocystorhinostomy with mucosal flap technique.

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ABSTRACT

A growing clinical experience has confirmed the value of the endoscopic DCR technique in the management of nasolacrimal duct obstruction. In our study, we performed endoscopic endonasal dacryocystorhinostomy (DCR) with mucosal flap technique in 50 patients referred to E.N.T OPD from Ophthalmology dept. in Sassoon General Hospital, Pune, Maharashtra. Data based on the symptomatic relief, nasal endoscopy and syringing after the management were recorded after a duration of one week, one month and six months for each patient. Our study concluded that endoscopic endonasal DCR with mucosal flap technique is an excellent technique for management of acquired nasolacrimal duct obstruction with respect to symptomatic relief and achieving an alternate drainage pathway. This procedure, which was originally described by Dr.P.J.Wormald, achieves healing by primary intention due to approximation of lacrimal flaps with adjacent nasal mucosa thus making this procedure very similar to external dacryocystorhinostomy. In addition, minimal intra-operative and post-operative complications were encountered with successful creation of a stable low resistance and a well-mucosalised alternate drainage pathway in most of the patients. The success rate of our study was 96% in terms of anatomical patency and 96% in terms of symptomatic relief.

Key words: endoscopic dacryocystorhinostomy, mucosal flaps, chronic dacryocystitis

Introduction

Tearing and recurrent or chronic conjunctival discharges are the most frequent symptoms of lacrimal pathway obstruction. Conservative treatments relieve the complaint only temporarily, thus surgery is the treatment of choice. Dacryocystorhinostomy (DCR) surgery aims to eliminate fluid and mucus retention within the lacrimal sac and to increase tear drainage for relief of epiphora. An endoscopic endonasal DCR procedure involves removal of bone adjacent to the nasolacrimal sac and incorporating the lacrimal sac with the lateral nasal mucosa in order to bypass the nasolacrimal duct obstruction. This allows tears to drain directly into the nasal cavity from the canaliculi via a new low-resistance pathway.

Endoscopic DCR has increasingly been shown to be as successful as traditional method of external DCR for the management of patient with obstruction of nasolacrimal duct system. The endoscopic DCR has distinct advantage over the external DCR as there is no facial scar and also where the patient does not give consent for the external scar and because of this reason many ophthalmic surgeons who do not perform endonasal DCR refer the cases to the ENT surgeon. Besides, the endoscopic DCR also maintains the pump action. It can be done in acute cases and both the sides can be operated simultaneously in the same sitting.

Objectives

- To evaluate the outcome of endoscopic endonasal DCR without stent by mucosal flap technique.
- To evaluate the long term effects with respect to the symptomatic relief, recurrence and complications.
- To study the advantages of endoscopic endonasal approach of DCR with mucosal flap technique.

Material and Methods

Group of 50 patients were referred by the Dept. of Ophthalmology to the Dept. of E.N.T of Sassoon General Hospital, Pune from 2013- 2014.The symptoms of epiphora due to dacryocystitis were evaluated, operated by endoscopic endonasal DCR with mucosal flap technique and followed up for a period of six months. Data based on the symptomatic relief, nasal endoscopy and syringing after the management were

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recorded after a duration of 1 week,1 month and 6 months for each of the 50 patients. Analysis of the data collected after the evaluation by nasal endoscopy and syringing and symptomatic relief in 50 patients was done to determine the achievement of aims and objectives of the study. No ophthalmic visit was done during follow up. Patients were diagnosed by detailed clinical history, lacrimal syringing, complete nasal and ophthalmologic examination, routine investigations and pre anesthetic fitness.

Inclusion criteria:

1. Patients diagnosed as Acute or Chronic Dacryocystitis due to acquired nasolacrimal duct obstruction.
2. Patients between age group of 15-60 years.

Exclusion criteria:

1. Patients having Congenital Nasolacrimal duct blockage.
2. Patients having symptoms of Nasolacrimal Duct blockage due to traumatic causes or having trauma to lacrimal apparatus, facial bones.
3. Patients having Lacrimal Canalicular Blockage.
4. Patients requiring Revision Dacryocystorhinostomy.
5. Patients aged <15 years and >60 years.

Technique of Surgery

Endoscopic Endonasal Dacryocystorhinostomy With Mucosal Flap Technique

Under general anesthesia, decongestion is achieved by patties soaked in 4% Xylocaine with Adrenaline. Lignocaine with Adrenaline (1:200000) is used for infiltration. Postal stamp incision is taken 1cm anterior and above the axilla of middle turbinate. Since approximately two thirds of the lacrimal sac is above the axilla of the middle turbinate, therefore in order to accomplish complete sac exposure during DCR surgery, a large amount of thick bone over the axilla of the middle turbinate and the lateral wall of the agger nasi has to be removed[1] with diamond bur 3.2. Lacrimal sac is opened with open book incision so as to create anterior and posterior mucosal flaps. The common canaliculus should be identified as a landmark for adequate sac exposure once the lacrimal sac is opened, because at least two thirds of the sac is below this opening. It is important to achieve primary intention healing between the edges of the sac and the nasal mucosa covering the exposed osteotomy edges.

The mucosal flap fashioned at the end of procedure allows for primary intention healing to occur. In the posterior superior region of the lacrimal sac, apposition with the nasal mucosa is difficult so the exposed agger nasi cell mucosa is routinely opened and apposed with the lacrimal mucosa in this area[2]. These flaps are further stabilized by positioning two small cut stripes of absorbable gelatin sponge along edges of the junction between the sac mucosa and nasal mucosa. This apposition of sac mucosa to nasal mucosa is similar to what is achieved in external DCR by suturing of the anterior and posterior sac flaps to the nasal mucosa. At the end of the procedure, no stents were left behind.

The powered endoscopic DCR accomplishes three principles namely, achieving full lacrimal sac exposure, marsupialization of the entire sac into the lateral nasal wall and primary intention healing between the sac and nasal mucosa[1].

The surgical technique used in this study is the same as described by Dr. P. J. Wormald with minor modifications such as non usage of stents[3,4].

Statistical Analysis

Sex Distribution Of Patients and Laterality:

Figure 1.

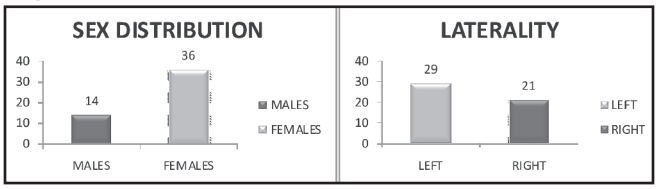
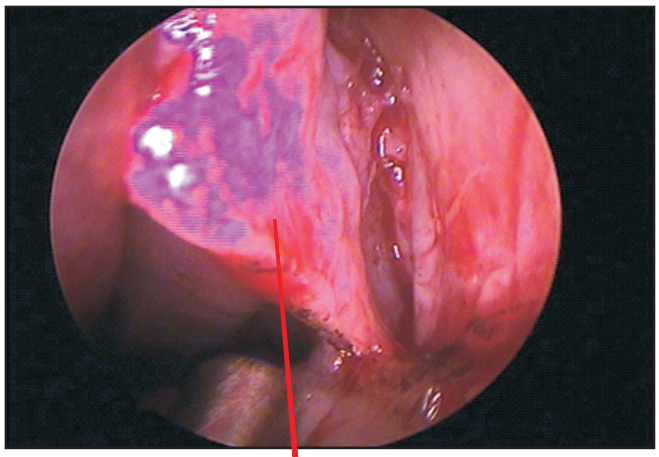


Figure 2.

FOLLOW UP	PATENCY		RHINOSTOMY SITE	
	ABSENT	PRESENT	WELL MUCOSALIZED	GRANULATIONS
1 WEEK	0	50	42	8
1 MONTH	2	48	46	4
6 MONTHS	2	48	48	2

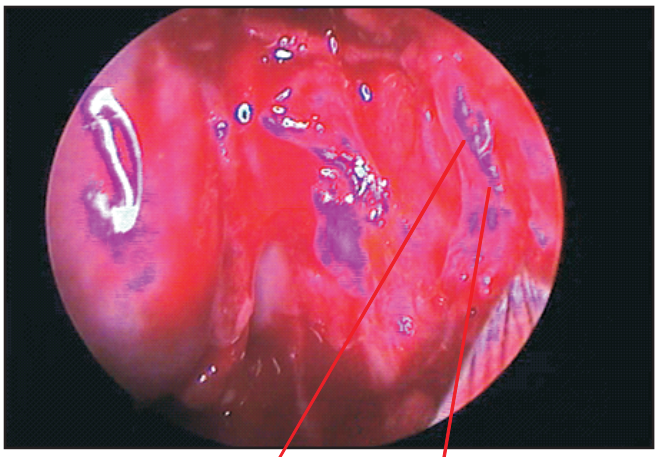
TECHNIQUE OF SURGERY

Photo 1.



mucoperiosteal flap elevation

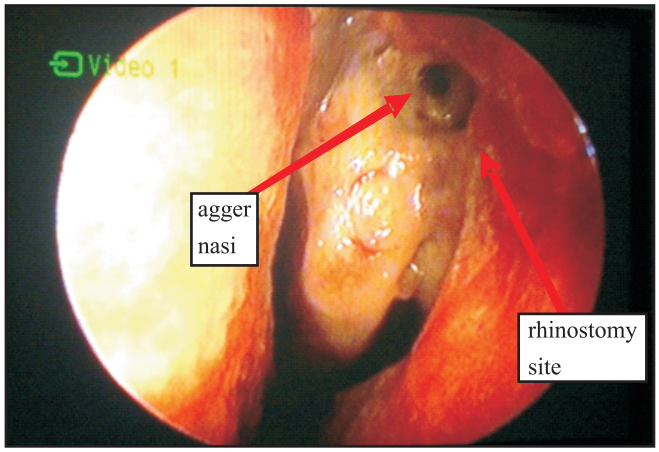
Photo 2.



posterior flap anterior lap

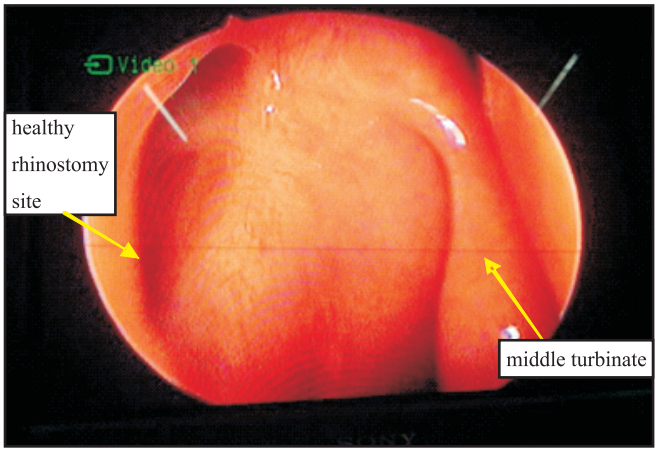
POST OP FOLLOW UP

Photo 3.



Well-mucosalised open rhinostomy site (left) at 1 month

Photo 4.



Well-mucosalised open rhinostomy site (right) at 6 months

Figure 3.

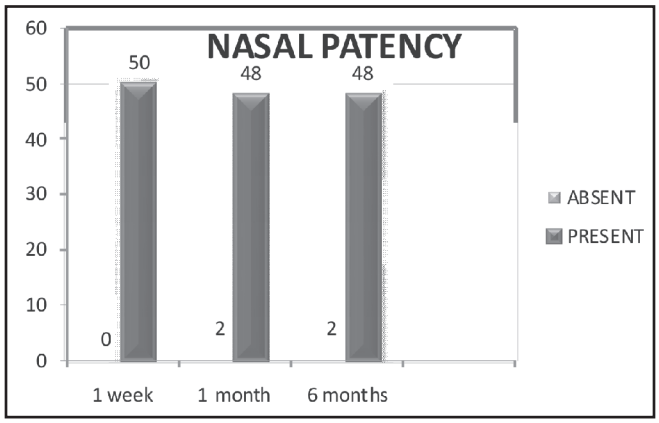


Figure 4.

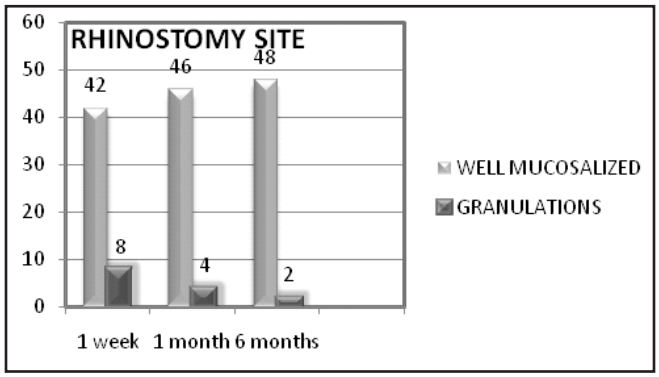
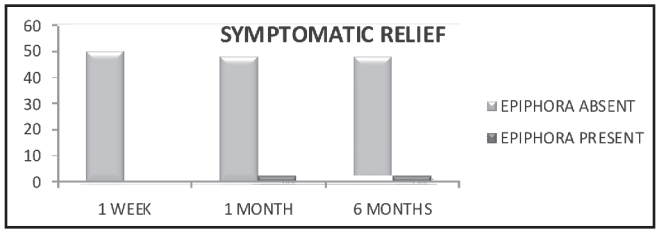


Figure 5.



Success rate at 6 months considering the anatomical patency and operative site was **96%** i.e. **48/50** patients showed desirable outcome of the procedure. Also the success rate in terms of symptomatic relief after 6 months was **96%** i.e. **48/50** patients showed complete resolution of epiphora after 6 months.

Discussion

A growing clinical experience has confirmed the value of the endoscopic DCR technique in the management of nasolacrimal duct obstruction. Refinements in technique and instrumentation coupled with an improved understanding of the endoscopic surgical anatomy are largely responsible for the excellent success rates now reported, paralleling those reported with that of conventional external techniques[5,3].Tsirbas et al. compared 31 powered endoscopic DCRs to 24 external procedures and reported the success rates to be statistically equivalent for the two techniques (93.5% versus 95.8%)[6].

Endonasal DCR offers the added advantages of being an easy procedure,is cosmetically acceptable as it avoids cutaneous incision, blood loss is minimal[7],can also be performed as a day care surgery[8] ,can be carried out in cases of acute dacryocystitis[9].Direct access to rhinostomy site limits tissue injury to the discrete fistula site without disruption of medial canthal anatomy and function[10].

It is more physiological because it preserves lacrimal pump mechanism[8]. It has less intra operative haemorrhage,less operative morbidity,short operative time and enhanced recovery.Nasal,paranasal and sinus abnormalities can be concurrently addressed in the same procedure[11,8].

The main difference between the presented technique and previous conventional endonasal technique is the creation of a large bony osteotomy by using powered instruments(microdebrider) and creation of lacrimal flaps and its apposition with the adjacent nasal mucosa, which is similar to suturing technique of both the flaps in external approach.

The procedure used in our study is based on the technique primarily described by P.J.Wormald which emphasizes the creation and preservation of mucosal flaps with primary juxtaposition of mucosal edges, the goal being healing by primary intention[3] and their technique has been shown to present a large and stable ostium with excellent functional outcomes[4].

Successful endoscopic DCR significantly depends on several important factors:

1. A thorough understanding and knowledge of the endoscopic anatomy and location of the lacrimal sac.
2. Complete removal of the frontal process of the maxilla to expose the medial wall of the lacrimal sac.
3. Precise opening of the lacrimal sac to achieve adequate exposure of the common internal punctum.

It is important to recognize that the posterior aspect of

the lacrimal sac is adjacent to the uncinate and that this structure requires to be preserved[12,13].Going posterior to this landmark leads to an increased risk of orbital fat prolapse or hematoma in addition to compromising the natural ostium of the maxillary sinus[14].

The junction of the hard frontal process of the maxilla and the thin lacrimal bone is the first landmark that is sought during the presented technique. The creation of anterior and posterior flaps in the lacrimal sac mucosa allows primary intention healing with the nasal mucosal flaps, thus marsupialising the sac into the lateral nasal wall. Poor or minimal preservation of mucosa may lead to increased granulation and fibrosis[15].

This approach preserves the general principles of creating a mucosal lined fistula so important in external DCR surgery[16]. An additional advantage was the preservation of lacrimal pump function. Previous studies have shown that successful endonasal DCR patients are more likely to have positive scintillography (A technique in which a drop of radionuclide tracer technetium 99m in saline or technetium sulfur colloid in the tear film is placed and the lacrimal area scanned with a gamma camera to follow the progress of the radioactive tracer present in the tears into canaliculi, lacrimal sac, the nasolacrimal duct and the nose and images are obtained) when compared to successful external DCR patients[17,18]. The attachments of the orbicularis to the lateral wall of the lacrimal sac are not disturbed with this approach and this may help preserve some lacrimal pump function.

In our study, the success rate was determined by anatomical patency and open well mucosalised rhinostomy site, which was ascertained by syringing and nasal endoscopy respectively. In addition, the relief of symptoms in terms of watering of eyes or epiphora at rest was considered.The success rate of our study was 96% in terms of anatomical patency and 96% in terms of symptomatic relief. External DCR, originally described by Toti in 1904 has a successful rate, when performed by properly trained ophthalmologists, of about 90%. Endoscopic DCR has a success rate of 83-94% , and has been demonstrated to offer similar outcomes when compared to external DCR, with low complication rates[24].The sucess rate of EnDCR with stents is usually lower in various studies as compared to EnDCR without stents(85% with stent and 90% without stent in one comparitive study)[25].

Comparison of our study with previous studies

AUTHOR	PROCEDURE	RESULTS
Tsirbas A, Wormald P J[19] (2003)	Mechanical EnDCR with mucosal flaps	95%
Harvinder S, Rosalind S[20] (2008)	Powered EnDCR with mucosal flaps	91.66%
Sprekelson[21] (1996)	En DCR	96%
S. Mortimore[22] (1999)	En DCR without stent	87%
Ramakrishnan V, Hink EM[23] (2007)	EnDCR without stent without mucosal flap preservation	Anatomic patency 100% Symptomatic relief 93%
Our Study (2014)	EnDCR with mucosal flap technique	Anatomic patency 96% Symptomatic relief 96%

Conclusion

The endoscopic endonasal DCR with mucosal flap technique was performed in 50 patients who were examined at the end of 1 week,1 month and 6 months. Based on the data gathered from the observations and from literature it is concluded:

- Endoscopic endonasal DCR with mucosal flap technique is an excellent technique for management of acquired nasolacrimal duct obstruction with respect to symptomatic relief and achieving an alternate drainage pathway anatomically patent even after 6 months.
- In addition, very less and minor intra-operative and post-operative complications were encountered with successful creation of a stable low resistance, well-mucosalised alternate drainage pathway in

most of the patients.

- The procedure originally described by Dr.P.J.Wormald, achieves healing by primary intention due to approximation of lacrimal flaps with adjacent nasal mucosa making this procedure very similar to external dacryocystorhinostomy.

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ORIGINAL ARTICLE

Beta Thalassemia And Splenectomy - A Case Series

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ABSTRACT

Thalassemia is a genetically determined hemolytic anemia resulting from an intracorpuscular defect and it also involves abnormalities in hemoglobin synthesis and red cell formation for which there is as yet no specific therapy.

The mainstays of diagnosis under surgical aspects are peripheral smear, hemoglobin electrophoresis and abdominal ultrasonography to rule out associated gall stones.

Spleen involvement is known to occur in thalassemia. The spleen is most commonly affected in form of splenomegaly because of excessive destruction of abnormal RBCs, extra-medullary hematopoiesis and transfusional overload. Splenomegaly further increases transfusional requirement.

The main aim of this study is to know the effect of splenectomy in these patients if it is really effective in reducing the transfusion requirement and thereby improving the well being of the patient and also to know the surgical complications in these patients.

Around 40 patients were studied in a period of 3 years and the observations were analysed.

There was a reduction in post op blood transfusion, thereby reducing the post op hospital admissions.

Surgical complications in these patients were also minimal, the most common being wound infection.

Other causes of fever post operatively were URTI and the incidence of OPSI was found to be less due to pre operative vaccination.

Introduction

Thalassemia is a genetically determined hemolytic anemia resulting from an intracorpuscular defect and it also involves abnormalities in hemoglobin synthesis and red cell formation for which there is as yet no specific therapy.[1]

Thalassemia is subdivided into alpha & beta thalassemia. Alpha thalassemia is associated with high mortality.[2]

The deficiency or absence of β-chains that characterize beta-thalassemia could potentially result from defects affecting transcription, RNA processing or RNA translation, or modifying codons into "nonsense" codons that leads to premature termination of translation.[2]

Thalassemia mutations which cause a complete absence or production of normal β-globin chains are called β°-thalassemia and those which cause reduced synthesis are known as β^{+}-thalassemia.

The mainstays of diagnosis under surgical aspects are peripheral smear, hemoglobin electrophoresis and abdominal ultrasonography to rule out associated gall stones.[4,9]

In thalassemia patients, packed cell transfusions have improved survival but transfusions also have their own complications of iron overload and so iron-chelating agents are given concurrently with transfusion.[5,6,7]

Spleen involvement is known to occur in thalassemia. The spleen is most commonly affected in form of splenomegaly because of excessive destruction of abnormal RBCs, extra- medullary hematopoiesis and transfusional overload. Splenomegaly further increases transfusional requirement. So these patients benefit from splenectomy.

Indications Of Splenectomy In Thalassemia

1. Blood transfusion requirements of more than 200-220ml/kg/year.[6,14]
2. Patients with increasing iron stores despite good chelation therapy.[5,10]
3. Hypersplenism causing leucopenia or thrombocytopenia.[9]

Complications Of Splenectomy

PERIOPERATIVE COMPLICATIONS[15,16,18]

- Bleeding

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- Atelectasis
- Subphrenic abscess
- Wound infection

POSTOPERATIVE COMPLICATIONS

- Thrombocytosis
- Overwhelming sepsis
- Portal hypertension

AIMS AND OBJECTIVES

1. To determine the efficacy of splenectomy in reducing post operative blood transfusion.
2. To identify the morbidity of splenectomy due to perioperative and post operative complications.

MATERIALS AND METHODS

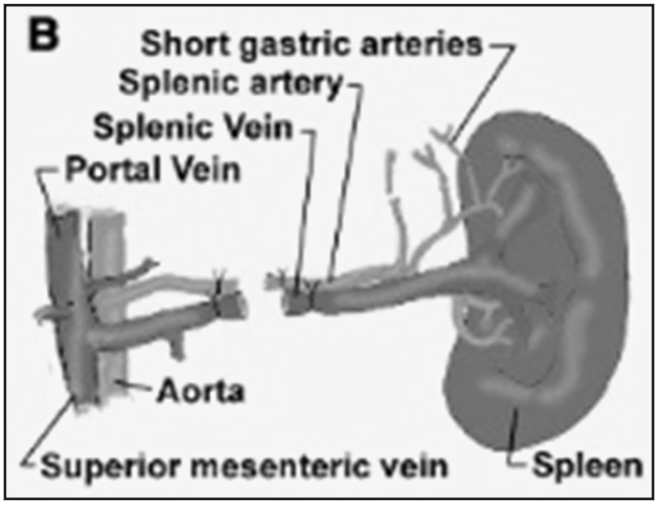
A total of 40 patients of beta thalassemia who underwent splenectomy in the past 3years in SGH were included in the study.

PRE OPERATIVE REQUIREMENTS

- USG abdomen – to look for splenic size and gallstones
- 2D echo to look for any cardiac anomalies
- Vaccination to prevent post op infections (OPSI)

With informed consent, under aseptic precautions, under GA, supine position, left subcostal incision was taken.[17] Incision deepened, abdomen opened in layers, spleen identified, dissected. Splenic artery identified & clamped, cut &ligated, reduction in size of spleen evident. Later splenic vein will be clamped, cut & ligated. Spleen taken out, haemostasis achieved. Abdominal drain kept in the splenic fossa and fixed. Abdomen closed in layers. Sterile dressing done and then patient shifted to ward.[13,17]

Post operatively patients were monitored closely, looked for any signs of active bleeding, signs of infection etc. Patientswere kept nil per oral for first two days after surgery. Liquid diet was started on day3 and on day 4 full oral diet was started. Patients were advised regular follow up.



OBSERVATION

AGE WISE DISTRIBUTION

Age in years	No. of patients	Percentage (%)
3-5	2	5.5
5-8	27	66.6
8-12	9	22.2
12-15	2	5.5

SYMPTOM WISE DISTRIBUTION

	No. of patients	Percentage (%)
Lump	40	100
Pain	30	75
Weakness	30	75
Jaundice	3	8

DISTRIBUTION ACCORDING TO PRE OP HB

Hb(g%)	No. of patients	Percentage(%)
6-8	30	75
8-10	10	25

DISTRIBUTION ACCORDING TO PRE OP BLOOD TRANSFUSION REQUIREMENT

Blood transfusion requirement(ml/kg/year)	No. of patients	Percentage (%)
220-250	15	37
250-275	20	46
275-300	5	16

DISTRIBUTION ACCORDING TO COMPLICATIONS

Complications	No. of patients	Percentage (%)
1. Peroperative		
Bleeding	0	0
Injury to surrounding organs	0	0
2. Post operative		
Pulmonary atelectasis	0	0
Bleeding	0	0
Paralytic ileus	0	0
Wound infection	3	7
Fistula	0	0

DRAINS VS NO DRAINS

	No. of patients	Wound infection
With drain	25	2
Without drain	15	1

DISTRIBUTION ACCORDING TO POST OP BLOOD TRANSFUSION REQUIREMENTS

BT requirement(ml/kg/yr)	No. of patients	Percentage (%)
75-100	4	11
100-125	23	57
125-150	13	32

RESULTS AND CONCLUSIONS

Splenectomy is beneficial in reducing the post operative blood transfusions and thereby reducing the hospital stay.

The procedure itself has less complications and is well tolerated by the patients.

There is not much difference in the outcome of the surgery depending on the presence or absence of abdominal drain.

Pre operative vaccination is very helpful in preventing post op infections(OPSI).

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ORIGINAL ARTICLE

Clinico-epidemiological Study Of Infantile And Childhood Eczemas

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Introduction

Eczema is a pattern of inflammation of the skin. Clinically, eczema is characterized by itching and soreness, and signs like dryness, erythema, excoriation, exudation, fissuring, hyperkeratosis, lichenification, scaling and vesiculation. Most of the eczemas in infants and children are atopic. In the HANES epidemiological survey[1], atopic dermatitis was the most commonly found. Major eczematous eruptions of childhood are atopic dermatitis, seborrhoeic dermatitis, diaper dermatitis, contact dermatitis, perioral dermatitis and nummular dermatitis. Others include lichen striatus, autosensitisation dermatitis, lichen simplex chronicus, papular urticaria and asteatotic dermatitis.[1] Due to paucity of data pertaining to western India, we undertook this study to document epidemiological factors and clinical profile of eczemas in infants and children.

Materials And Methods

This was a hospital based study of paediatric patients presenting with eczemas attending Dermatology Out Patient Department. Written informed consent of parents and gaurdians to take part in the study was taken. In patients of atopic dermatitis, details like present age, age at onset, area of residence, personal and family history of atopy, seasonal variation, history of breast feeding, socioeconomic status were noted. Clinical examination for presence of major and minor Hanifin and Rajka clinical criteria[3] was performed leading to diagnosis of atopic eczema. Atopic eczema was categorized as acute, sub-acute and chronic. Distribution of lesions was noted. Severity was assessed using SCORAD index.[4] For description purpose, we divided patients of atopic dermatitis into infantile (age<1year) and childhood group (age>1year). Height (in cm) and weight (in Kg) were recorded in every patient. Relevant investigations like pus culture sensitivity, KOH mount, gram stain, patch testing, stool routine microscopy for ova and cysts were done. In children with other types of eczema detailed clinical examination was carried out. The data so collected was analyzed, and Fisher's exact test was applied for statistical analysis wherever necessary.

Results

100 children with eczemas were included in the study. Maximum i.e. 36% cases were of atopic dermatitis followed by seborrhoeic dermatitis (20%), pityriasis Alba (16%), post-scabetic eczema (14%), irritant diaper dermatitis (7%), nummular eczema (4%), contact allergic dermatitis (2%) and pompholyx (1%).

Table I – Different patterns of Eczemas in children

Sr.No.	Diagnosis	Total patients		Males
		No.	%	No.
A	**Endogenous Eczema**			
1	Atopic dermatitis	36	36.00%	22
2	Seborrhoeic dermatitis	20	20.00%	12
3	Pityriasis alba	16	16.00%	9
4	Nummular eczema	4	4.00%	2
5	Pompholyx	1	1.00%	1
B	**Exogenous Eczema**			
6	Post scabetic eczema	14	14.00%	6

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7	Irritant napkin dermatitis	7	7.00%	5
8	Contact allergic dermatitis	2	2.00%	1
	Total	**100**	**100%**	**58**

In patients with atopic dermatitis, mean age of disease onset was 4.42 months and 4.02 years in infantile and childhood group respectively with males outnumbering females. Infantile group had primarily facial involvement and acute presentation whereas in childhood group a mixed picture of face, extensor and flexural lichenification was seen with majority having chronic disease. Maximum patients had moderate form of disease. Early age of disease onset and xerosis were commonly observed. Most of the patients hailed from urban background and belonged to middle socioeconomic strata. Winter exacerbation was commonly seen. Also, early weaning i.e. before 6 months of age, resulted in more severe form of disease. Height and weight observed in atopic children were below two standard deviations as compared to standard height and weight chart for Indian Children.[18]

Table II - Correlation of early weaning and disease severity in patients with atopic dermatitis

Severity	Early Weaning		Total
	Yes	No	
Mild	0	13	13
Moderate	1	16	17
Severe	3	3	6
Total	**4**	**32**	**36**

P value< 0.05

In seborrhoeic dermatitis group, all patients were infants with mean age of presentation at 7.1 weeks. Majority had scalp involvement (85%). Mean age of patients with pityriasis alba was 5.75 years with male predominance. Majority of the patients had 2-5 hypopigmented macules mainly involving face with winter exacerbation of disease. 18.7% had family history of atopy. Mean age of patients with post-scabetic eczematization was 5.28 years. Primarily hands and feet were involved. Almost all belonged to low socioeconomic strata. Mean age of patients with irritant diaper dermatitis was 9.1 months with females (n=5) outnumbering males (n=2). Few (42.85%) gave history of diarrhea. Buttocks and thighs were common sites of involvement with sparing of intertriginous areas.

There were two patients with contact allergic dermatitis. 8 year old male child had developed dermatitis over both feet due to leather shoes and 11 year old female child developed dermatitis on the neck due to metal necklace. Both had positive patch test to the suspected antigen and none gave history of atopy. Four patients of nummular eczema, two males (2year and 10year old) and two females (5year and 6year old) presented with single large hyperpigmented coin shaped plaque predominantly over the extremities. The only patient of pompholyx was a 9 year old male child who had crops of deep seated pruritic clear vesicles over sides of fingers arranged asymmetrically with history of summer exacerbation.

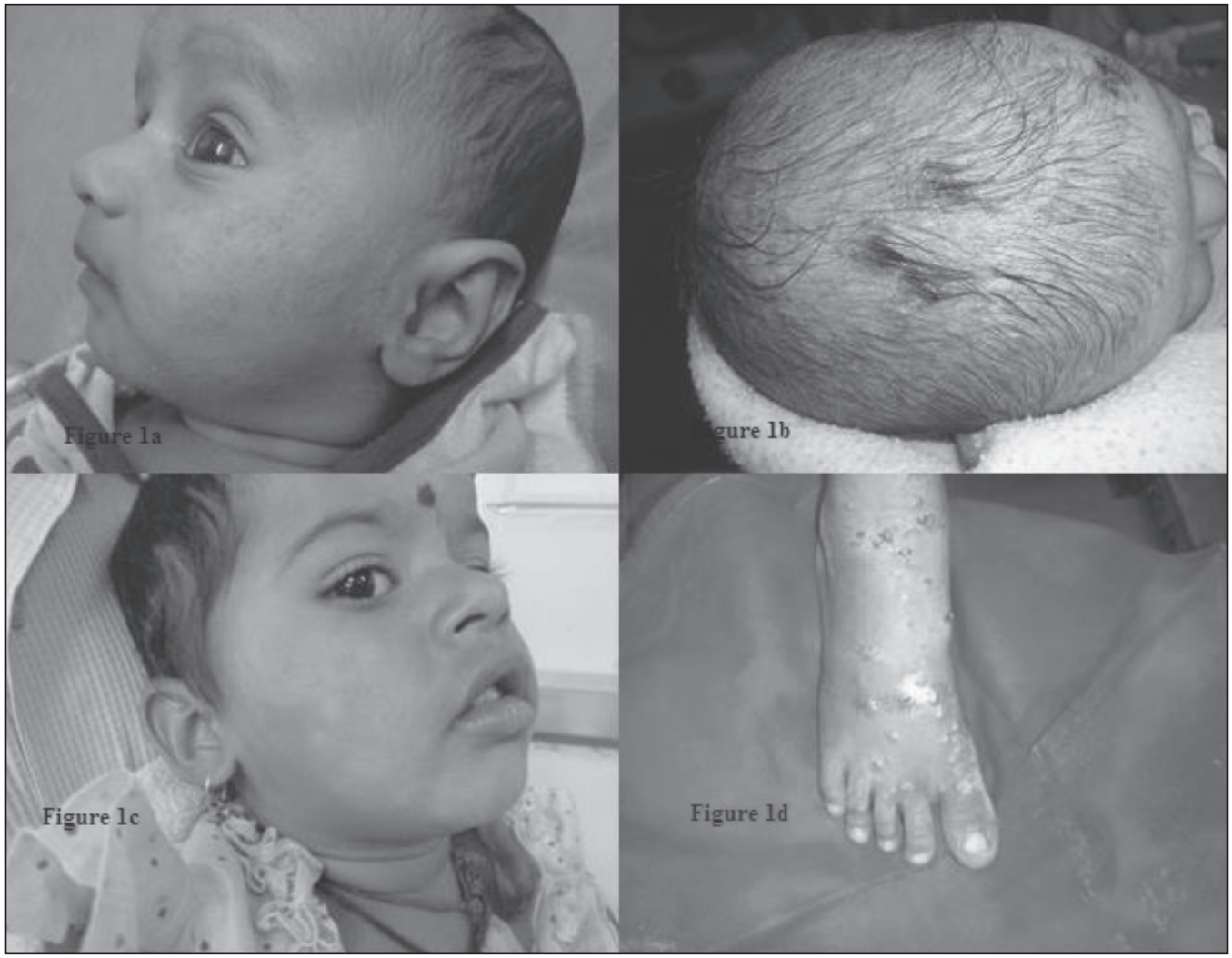
Discussion

The present study is concerned with the clinico-epidemiological profile of infantile and childhood eczemas. We came across only one Indian report which systematically described clinical aspects of eczema in infants and children by Bhattacharya et al[17] in which post-scabetic eczema was seen in majority (51.4%) of patients. Balai et al.[16] studied pattern of paediatric dermatoses, in which eczema accounted for 34.86% patients while atopic dermatitis was the commonest (55.31%) followed by seborrhoeic dermatitis (16.76%) and pityriasis alba (8.10%). Out of 100 children included in our study, the highest incidence of eczema was found in infancy with male predilection (58%). As per the classification of eczemas[2] we categorized our data in two groups, endogenous and exogenous eczemas. We found that 77% belonged to endogenous group and remaining 23% belonged to exogenous group. We studied atopic dermatitis in detail as it accounted for majority(36%) of cases.

Out of 36 patients with atopic dermatitis, 22 (61.11%) were males and 14 (38.88%) were females with M:F ratio of 1.57. Other studies too reported male preponderance[7]. Most of our patients (33%) belonged to age group 4-6 years. Dhar et al[7] reported maximum patients to be in age group of 6 months to 2 years. Family

history of atopy was present in 10 (27.77%). Dhar et al.[7] documented a higher incidence (65%) of positive family history. Only 2 (5.55%) gave positive personal history of atopy, an observation similar to Sarkar et al[6] (7%).We noted that in infantile group, all (100%) had facial involvement, 2 (28.57%) had extensor involvement and none had flexor involvement. Sarkar et al[6] too reported facial predilection. In childhood group facial, flexor and extensor involvement was seen in 22 (75.86%), 12 (41.37%) and 16 (55.17%) patients respectively. The corresponding figures by Sarkar et al[6] were, 66.7% (facial), 45.14% (flexor) and 37.4% (extensor) involvement, similar to our findings. We observed, that 13 (36.11%) had mild disease, 17 (47.22%) had moderate disease and 6 (16.66%) had severe disease. Dhar et al[9] reported mild, moderate and severe disease in 54%, 27% and 19% patients respectively. We found that 4 (11.11%) had acute, 13 (36.11%) had subacute and 19(52.77%) had chronic eczema. Dhar et al[7] found corresponding figures to be 42%(acute), 41% (subacute) and 17%(chronic) in his study. In our study, out of 6 patients with severe disease, 5 had positive family history of atopy, which was statistically significant (Fisher's Exact test: P=0.005).The common minor features seen were early onset of disease (before 5years) in 88.88% and xerosis in 86.11%. Palmar hyperlinearity, dennie-morgan fold, keratosis pilaris, ichthyosis and pityriasis alba were others. Sarkar et al[6] reported similar findings. With respect to seasonal variation, we observed that 23 (63.88%) had history of winter exacerbation. However, Dhar et al [9] observed that most of the patients (40%) had summer exacerbation. Sarkar et al [6] showed that majority (62%) had aggravation in winter, a finding close to our study. We noted that 6 (16.67%) belonged to rural background and 30 (83.33%) belonged to urban area, a finding similar to that by Dhar et al [10,] where majority of patients belonged to urban area. Majority of patients, 26 (72.22%) belonged to middle socioeconomic strata. In the study by Sarkar et al[6], 53.8% belonged to middle strata.

All patients in our study were breast fed. History of weaning before 6 months was present in 4 (11.11%). Of these 4 patients, Three had severe disease and one had moderate disease which was statistically significant (Fisher Exact test P=0.01). Interestingly, as most dermatologists do not consider breast feeding as having favourable influence on the onset or course of disease[6], larger studies need to be conducted to validate our findings. Seborrhoeic dermatitis was second most common eczema in our study. All patients were infants. There were 12 males and 8 females. The mean age of presentation was 7.1 weeks. Foley et al[15] observed that the highest prevalence of infantile seborrhoeic dermatitis was in first three months of life. 85% of our patients had scalp involvement and 55% had face involved. This was consistent with theory that seborrhoeic dermatitis occurs mostly in the lipid-rich areas of skin and, in infants, occurs predominantly on the scalp and upper face.[11] Next common eczema was pityriasis alba with male to female ratio of 1.28:1.Mean age was 5.75 years. Vinod et al[14] reported male to female ratio of 1.35:1.We found that majority (50%) had 2-5 lesions. Vinod et al[14] similarly observed that maximum (60.5%) had 2-5 lesions. All our patients had facial involvement, 5 (31.25%) had upper limb involvement, 2 (12.5%) had lower limb involved. Vinod et al[14] also found face to be maximally involved. Family history of atopy was found in 3 (18.75%) patients. None of the patients had personal history of atopy. Vinod et al[14]found 68.5% with positive family history of atopy and 17% with personal history of atopy. 62.5% patients gave history of winter exacerbation. Vinod et al[14] reported it to be 39% in their study. Post- scabetic eczema was present in 14% patients with mean age of 5.28 years. Itching was the predominant symptom with nocturnal exacerbation. Erythema, vesiculation and oozing were present along with numerous excoriations. Burrows were usually on hand, wrists, umbilicus thighs. Hands and feet were involved in eczematous reaction in most children.12 (85.71%) cases belonged to low socio-economic strata. 7% patients had Irritant diaper dermatitis with mean age of 9.1 months. 5 (71.42%) were females and 2 (28.57%) were males. Kazzi et al.[13]found no sex predilection. Female preponderance seen in our study can be attributed to smaller sample size. Lesions were erythematous, scaly, painful plaques over area of contact with diaper. Skin folds were spared in all patients as mentioned in literature.[12] 2 (2%) children had contact allergic dermatitis. One male child aged 8 year old presented with itchy erythematous papules over both feet after using leather shoes and another was an 11 year old female with appearance of erythematous itchy papules in neck area after wearing metal necklace. Findings were confirmed by patch test. The 10 year old



LEGENDS:

1. Figure1a: Infantile Atopic Dermatitis (Face involved) in a 6 month old male child.
2. Figure1b: Infantile Seborrhoeic Dermatitis with Scalp involvement in a 3 month old male child
3. Figure1c: Pityriasis alba in a 3 year old girl over face
4. Figure1d: Post-scabetic eczematization in a 8 year old male child

male child with pompholyx had deep seated pruritic clear vesicles asymmetrically arranged on the sides of fingers. The attack precipitated in summer, this is in accordance to the fact that the condition aggravates in hot weather.[2] 4 (4%) patients (2 males and females each) had nummular eczema presenting as hyperpigmented single coin shaped plaque predominantly over extremities, an observation shared by Krupa et al.[5]

Conclusion

Most common eczema in paediatric population was atopic dermatitis with majority of the patients belonging to childhood group. Prolonged breast feeding seemed to be protective in developing less severe form of disease which is a new finding we came across as compared to older studies where no such correlation was observed .Growth retardation was present in severe cases. Next common type of eczema was seborrhoeic dermatitis followed by pityriasis alba. In the exogenous group, post-scabetic eczematization was commonly observed. Overall the eczemas were commoner in males with highest incidence being in first year of life.

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ORIGINAL ARTICLE

Laparoscopic Management Of Gastric And Duodenal Perforation

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ABSTRACT

Perforation is a common surgical emergency with overall mortality of 10%. Patients present with acute abdomen followed by peritonitis and septic shock which is life threatening if left untreated. Operative treatment consists of suture repair of perforation. We have done a pilot study of thirty cases of gastric and duodenal perforation presented early which were managed laparoscopically. Suture repair of perforation was done without omentopexy and patients were studied with respect to operative time, hospital stay and cosmesis. We concluded that laparoscopic approach requires less operative time, patients have decreased hospital stay and a fewer wound complications.

Thus, laparoscopy is a safe and reliable approach for repair of gastric and duodenal perforation.

Key words: Laparoscopy, Perforation

Introduction

Approximately,10to 20% patients of peptic ulcer suffer perforation of duodenum or stomach[1] and is the second most common complication of peptic ulcer disease followed by bleeding[2]. However, perforation accounts for more than 70% of deaths associated with peptic ulcer disease[3] and it is often the first clinical presentation of peptic ulcer disease[4] . Majority of patients of perforation presents as acute abdomen resulting from chemical peritonitis that develops initially from gastric and duodenal secretions, followed by bacterial contamination. Mortality increases if perforation exists for more than 24 to 48 hours as a result of septic shock and hypovolemia. Thus, gastric and duodenal perforation is a life threatening emergency and hence early diagnosis and treatment is essential[1]. The operative management consists of suture repair of perforation which is done conventionally via open approach.

With the advent of laparoscopic surgery and increasing experience, suture closure of perforation can be performed successfully. We conducted prospective study of thirty patients of perforated peptic ulcer disease managed by laparoscopy with respect to safety, feasibility and efficacy.

Materials and methods

All patients presenting with acute abdomen to general surgical wards of Sassoon General Hospital were evaluated. After detailed clinical history and examination, those patients with signs and symptoms of perforation peritonitis were investigated. Those patients with erect abdominal Xray showing air under diaphragm were provisionally diagnosed as a case of perforation and suitable patients were taken for laparoscopy.

Patient selection:

Not all the patients are suitable for laparoscopy. Hence Boey's classification was used for inclusion of patients suitable for laparoscopic repair of perforated peptic ulcer[5,6]. The Boey score is a count of risk factors- which are: shock on admission, American Society of Anesthesiologists (ASA) grade III–V, and duration of symptoms[6]. The maximum score is 3, which indicates high surgical risk. Laparoscopic repair is reported only to be safe with Boey score 0 and 1[7,8]. Other contraindications are age>70 years, patients with previous abdominal surgery, bleeding from ulcer and other confounding medical conditions[9]. Based on these inclusion and exclusion criteria were formed. All patients with on table finding of gastric or duodenal perforation were included in the study, and were informed regarding the possibility of need of conversion to open surgery and associated risks and complications.

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Inclusion criteria:

i. Patients fit for general anaesthesia

ii. Patients willing for procedure

iii. Patients with perforation peritonitis presenting early (symptom duration <24 hours)

Exclusion criteria

i. Patients with age < 16 years

ii. Patients with age >70 years

iii. Patients in septic shock (systolic blood pressure <90 mm Hg)

iv. Patients with history of previous abdominal surgery

Symptoms :

i. Pain in abdomen

ii. Fever

iii. Vomiting

Signs:

i. Tachycardia

ii. Tenderness over abdomen

iii. Distention of abdomen

iv. Guarding

v. Rigidity of abdomen

vi. Diminished or absent bowel sounds

Method:

Patient is positioned and after general anaestesia, painting and draping is done. A pneumoperitoneum was created and four ports were inserted[10]. Upper port in subxiphoid area was used for irrigation-suction and retraction of liver. An umbilical port was used for camera and two remaining ports were placed on each side of camera port in triangular position. Surgeon stands on left of patient with assistant on each side. The gall bladder was retracted by assistant & held upwards. Inflammatory adhesions were released and suctioned. After initial exploration of peritoneal cavity, pyloroduodenal region was meticulously searched for perforation. If omentum was attached to suspected perforation site, it was gently pulled away with forceps to assess the underlying pathology. Instrumental compression of antrum of stomach & D1 facilitated identification by inducing escape of fluid and bubbles from perforation. Size of perforation was measured with reference to size of suction tube or jaws of laparoscopic grasper. Thorough peritoneal lavage was given with warm normal saline. Perforation was closed with 2 to 3 sutures using Mersilk 2-0 round bodied needle. Subhepatic drain was kept at the end of procedure. Additional pelvic drain kept if required. Abdomen is examined for bowel injury and haemorrhage. Trocars were removed under vision. Port closure done. Sterile dressing done. Size of perforation more than 10mm was arbitrarily taken as cutoff for conversion to open[10]. Biopsy was not taken for gastric perforation as there was no single suspicious case suggestive of malignant perforation based on intraoperative gross features of perforation.

Postoperative Management:

Patients were mobilized from postoperative day 2. On the postoperative day 3, the wound dressing was opened. All the port sites were carefully checked for presence of discharge and surrounding skin inflammation. Feeding resumed as soon as ileus subsided which is indicated by return of bowel sounds. Intraabdominal drain was removed once the drain output was less than 100ml/day, usually on postoperative day 5. Monitorring of vital parameters of patient including pulse , temperature and abdominal girth was done in postoperative period for assessment of the presence of intraabdominal infection or leak. Patients were assessed & discharged based on tolerability to normal diet, full ambulation and requirement of only oral analgesics. Follow up was done at 4 weeks, 3 months and 6 months after surgery.

Patients were assessed with respect to following parameters

1. Intraoperative time
2. Postoperative hospital stay
3. Wound complications and cosmesis

Results

1.Mean age group	47.7 years
2. Male: Female	6.5:1
3. Duodenal: Gastric perforation	73:26.
4. Mean size of perforation	6.6 mm

5.Mean operative time	75.11 min
6. Mean hospital stay	6 days
7.Conversion rate	10%
8. Mortality rate	0%

We conducted our study in 30 patients in which majority of patients were in the age group of 40- 60 years, with male preponderance. Male to female ratio was 6.5:1.Intra-operatively, we found duodenal perforation in 73.26% patients and gastric perforation in26.73% patients. Mean size of perforation was 6.6mm. Perforation was closed by intracorporeal suture repair without omentopexy. We used non absorbable material 2-0 Mersilk with 30mm ½ Circle Round bodied needle.Intra abdominal drain was kept in all patients, which was removed on 5th day. Our study group included 30 patients out of them 27 undergone successful laparoscopic suture repair of gastric and duodenal perforation without morbidity, while 3 patients needed conversion to open method. These patients were converted to open method because the size of perforation was greater than 10 mm.

Mean operative time for whole study group was 75.11 minutes and mean hospital stay was 6 days. Only two patient developed port site infection which was managed by local dressings and oral antibiotics. There was no surgery related morbidity or mortality.

Discussion

Perforation peritonitis is one condition in which using laparoscopic approach, not only is the site and pathology of perforation is identified but the procedure also allows closure of the perforation and adequate peritoneal toilet without a large incision.

The first successful laparoscopic suture repair for perforated peptic ulcer was described by Nathanson et al. in 1990[11,12]. Soon after that, the laparoscopic approach became a widespread procedure.

In 2002, Lagoo et al. added the sixth decision for a surgeon to be made regarding PPU to the existing five therapeutic decisions proposed by Feliciano in 1992 [5]. The first decisions were about the need for surgical or conservative treatment, to use omentoplasty or not, the condition of the patient to undergo surgery, and which medication should be given. The sixth decision was: "Are we going to perform this procedure laparoscopically or open?" Is there really a sixth decision to be made, or are there enough proven benefits of laparoscopic correction that this should not be a question anymore?[13]

Approximately, 57% of patients in our study were in age group of 40-60years and mean age of our study group was 47.7 years which correlates with literature. The youngest of the patient was 26 yearmale and the eldest was 68 year female. Another similar study performed by PN Sreeramulu et al in 2010 (n=30 for lap group), 57% of population was in the age group of 40-60 years and mean age of study group was 52 years. Previous similar study conducted by Siu et al in 2002 (n=63 for lap group)had mean age of patients as 53.8 years[10].

Our study has male predominance with ratioof male to female being 6.5:1 which correlates with analysis of previous studies. Similar study conducted by Siu et al in 2002 had 84% of male patients and 16% of female, thus ratio being 5.267.

Siu et al, 2002[10] and Katkhouda et al, 1999[8] used method of suture repair with omentopexy during laparoscopy. Seeling et al 2003[14] and Ates et al 2007[17] used suture repair without omentopexy for perforation closure. We also used method of suture repair of perforation closure.

We noted intraoperative findings such as site of perforation, size of perforation and operative time. In our study 73% of patients presented with duodenal perforation while rest of patients have gastric and mean size of perforation was 6.6mm. Similar study conducted by Siu et al in 2002 had 71.4% patients with duodenal perforation with mean size of perforation being 5.2mm[10].

Mean operative time in our study was 75.11 minutes which was comparable with other studies. In study by Seeling et al average duration of operation was 65 min[13] while in study conducted by Ates et al, it was 42.10 min[17]

In our study three patients were converted to open method out of which two had perforations each measuring 12 mm and one had perforation measuring 13mm and we had arbitrarily chosen cut off of 10 mm for conversion to open method. There was no need to convert any patient to open method due to adhesions or excessive peritoneal contamination. Thus average rate of conversion in our study was 10%.In study by Siu et

al.[10] average rate of conversion was 14% while in study by Ates et al it was 17.6%[17].

Mean hospital stay in our study group was 6 days. Mean duration hospital stay in study by Siu et al was also 6 days[10] while in study by Seelig et al, it was 9 days[14] and in study by Ates et al it was 5 days[17]. The minimal invasiveness of this procedure allows the patient to mobilize early. Also early return of bowel sounds, leading to early oral feeds and early return to routine activities.

In postoperative period patients were followed up for complications like seroma formation, port infection and leak. In our study two patients had port infection as complication. There were no complications like leak or intraabdominal collection. In study by Siu et al, 1 patient had leak, 2 had intraabdominal collection and 4 had port site infections. Mortality rate in this study group was 2%.[10]

Thus, laparoscopic management of gastric and duodenal perforation is safe and effective approach for patients presenting early. It incorporates intracorporeal suturing of perforation along with peritoneal lavage via minimal access surgery.

With the shorter duration of hospital stay and minimal pain, it has excellent cosmetic results and reduced postoperative wound infections. Reduction in burst abdomen and incisional hernias due to shorter scars has been noted. Avoiding upper laparotomy might lower incidence of chest infections and postop ileus.

We compared our study with previous similar studies and findings of which are as described below.

Name of study	Method	No. of cases	Mean operative time(min)	Postop hospital stay(days)	Conversion	Mortality
1.Siu et al[10] 2002,Hongkong	Suture with omentopexy	63	42	6	9%	2%
2.Katkhouda et al[8] 1999,USA	Suture with omentopexy	30	106	10	5%	3%
3.Seelig et al[14] 2003 Germany	Suture repair	24	65	9	13%	0%
4.Naesgaard et al[15] 1999 Norway	Suture with omentopexy	24	100	8	20%	20%
5.Mehendale et al[16] 2002 India	Suture with or without omentopexy	34	50	4	18%	0%
6.Ates et al[17] 2007 Turkey	Suture repair	35	42.10	5	17%	
Our study	Suture repair	30	75.11	6	10%	0%

Conclusion

Laparoscopic repair of gastric and duodenal perforation has certain added benefits over conventional open repair.

First of all, Laparoscopic approach reduces access trauma of midline laparotomy and can confirm or refute the diagnosis. Suture repair of perforation and peritoneal lavage can be performed laparoscopically with shorter operative time. It is associated with decreased postoperative wound pain, so patient can be mobilized and discharged early with earlier return to normal daily activities. This results in shorter hospital stay and hence reduced use of hospital resources. However, there is need for conversion to open repair in certain conditions like larger perforation or difficulty in localization.

Complication rate for laparoscopic repair is also low with better cosmesis. It is associated with potentially less wound infections compared with open repair. It is associated with overall less morbidity and mortality.

Thus, laparoscopic repair is safe, feasible and efficient method for management of early diagnosed patients of gastric and duodenal perforation. Inclusion and exclusion criteria play a key role in outcome of surgery.

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ORIGINAL ARTICLE

Role Of HPV DNA Testing In Detection Of Precancerous Lesions Of Cervix

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ABSTRACT

Cervical cancer remains the most common cancer of women in India. Regular check-ups and screening tests are required to effectively tackle this challenge. H.P.V. (Human Papilloma Virus) is associated with cervical squamous cell carcinoma and the magnitude of association is higher than that between lung carcinoma and smoking [1]. Non-randomized studies and reviews indicate that HPV testing is more sensitive than pap smear for identifying cervical cancer and its precursors in population screening [2]. Hybrid capture 2 assays detects high oncogenic risks viruses and can be used as primary screening tool for women older than 30 years. It can be a tool for follow-up post-treatment for cervical intraepithelial neoplasia and in triage of women with equivocal cytology reports. In this study, sixty women were screened for HPV-DNA. Seven women were found to be positive for HPV-DNA. They were further subjected to colposcopy directed large loop electrosurgical procedure. The positive patients were found to have either low-grade or high grade cervical intraepithelial neoplasia. The use of HPV-DNA test may make it a viable alternative to cytological screening especially as a less frequent screening. A shift from cellular to viral tests, coupled with education and vaccination will contribute to a more efficient control of cervical cancer.

Keywords - CIN, Human papilloma virus, HPV DNA

Introduction

The link between genital HPV infection and cervical cancer was first demonstrated in the early 1980s by Harold Zur Hausen. HPV has been implicated in 99.7% of cervical cancers [3]. 30 subtypes of HPV have been identified. Of these type 16 account for half the cases, while type 18, 31, and 45 account for 30% of cases [4]. Transmission of HPV occurs by sexual activity. The age is an important determinant of risk of HPV infection [5]. Most cervical cancers occur at squamo-columnar junction of the cervix. The greatest risk of HPV infection coincides with the greatest metaplastic activity occurring at the squamo-columnar junction. Greatest metaplastic activity occurs at puberty and first pregnancy and declines after menopause. The infection is very common in sexually active young women with a sharp decrease after 30 years of age. However cervical cancer is more common in women after 35 years suggesting infection at a young age and slow progression to cancer. Persistence of infection is more common with high risk HPV types and is an important determinant in development of cervical cancer. The HPV infection leads to a gradual progression to more severe disease. **CIN I** indicates a self limiting sexually transmitted lesion. Whereas HPV infection, **CIN II** and **CIN III** (high grade lesions) are the due cervical cancer precursors. [6] Early detection of these lesions can lead to several preventative strategies.

HPV-DNA testing by hybrid capture assay **(HC2)** detects 13 high risk types of HPV using signal amplification. It is developed by Digene corporation and was granted USFDA approval in 1995.

Methodology

This prospective study was carried out in Sassoon General Hospitals, Pune for women attending the OPD of department of Obstetrics and Gynaecology. The Inclusion criteria applied were:

(a) Women with complaints of white p/v discharge, post-coital bleeding, blood stained discharge, irregular menses, menometrorhagia, offensive discharge.

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b) Apparently healthy sexually active women.

Following were excluded from the study

(a) Diagnosed cases of cancer cervix.

(b) HIV positive infection

(c) Patient who have taken HPV-vaccines.

A detailed history followed by a thorough clinical and gynecological examination was carried out. HPV-DNA (HCT) samples were collected using a cytobrush. Suspicious lesions of the cervix were further subjected to colposcopy directed loop electrosurgical excision procedure (LEEP) and sent for histopathological examination in formalin. The results of HPV-DNA (HCT) and histopatholgical report were then correlated.

Results

The total number of women undergoing this test was 60. The average age of the patients was 39 years (Table 1).

Table 1. Age

AGE-GROUP (Years)	NO. OF PATIENS
30-35	06
36-41	22
42-47	16
48-53	06

The average age of the patients was 39 years.

The mean age of sexual debut for these women was also calculated to be 18 years (Table 2).

Table 2. Age at sexual debut

AGE AT SEXUAL DEBUT (Years)	NO. OF PATIENS
16	3
17	5
18	24
19	9
20	13
> 21	6

The frequency of complaints in the patients was found as follows (Table 3).

Table 3. Complaints

Complaints of the women	No. of women
White discharge p/v	13
Post-coital bleeding	9
Blood-stained discharge	7
Offensive discharge	7
Irregular menses	2
Menometrorrhagia	6
Total	44

HPV DNA reported positive in 7 women.

Table 4. HPV DNA Positivity

Women tested n=60	HPV Positive (%)
Having some symptoms n=44	6 (13.6)
No symptoms n=16	1 (6.3)
Total	7 (11.7)

Symptomatic 6 patients who tested HPV positive underwent LEEP biopsy. They had following findings.

(a) One patient was found to have microinvasive squamous cell carcinoma.

(b) Three women had high grade lesions which include both CIN-3 and CIN-2. These were distinct dysplasia with increased mitotic figures and nuclear abnormality.

(c) Two patients had low grade lesions showing koilocytic changes, with good maturation and dysplasia confined to lower third of the cervical epithelium.

Sixteen patients had no apparent complaints but were still tested for HPV-DNA of these patients. Of these 1 patient was found to be HPV-DNA positive and is in follow-up regularly.

Discussion

Epidemiological studies have identified a number of risk factors that contribute to the development of cervical cancer precursors and cervical cancer. These include persistent infection with high oncogenic HPV-DNA,

sexual intercourse at an early age, infection co-existing with HPV like Chlamydia Trachomatis [7].

HPV-DNA tasting as a primary screening tool has an important role to play. Good sensitivity (i.e. ability to detect the condition of interest in all women who have it) has to be balanced against its specificity.

Particularly in cervical cancer screening because the screening involves large number of otherwise healthy women. A woman with positive result needs further evaluation with its economic, social and emotional consequences.

The sensitivity of HPV-DNA testing is 27% higher than cytology and specificity is 8.4% lower [8]. However the performance of HPV-DNA testing in women older than 30 years is significantly better. The negative predictive value of HPV-DNA is also very high at 91.7% [9]. The high NPV has important implications for screening programmes. Thus, screening intervals can be increased in women older than 30 years [10].

Women who test negative for high risk HPV-DNA (HCT) are almost at negligible risk for developing CIN3.

In present study HPV DNA test gave a good yield of 10% women having either microinvasive cancer or CIN. This made possible to treat the patient with microinvasive cancer immediately and get read of the disease totally who otherwise would have been detected late with gloomy survival. Other women having CIN received treatment with excision halting their progression to cancer. This can be considered a good achievement.

Prevalence of HPV in normal women in Thailand is 9-20%, but HPV testing has not been used on any systematic basis to date [10]. In India, in a large study of screening 142,701 women aged 30-59 years in Osmanabad District, test positivity rates were found to be 10.3% for HPV. The detection rate of high-grade lesions was 0.9% for HPV testing [11]. In our study HPV positivity is similar i.e. 11.7 (Table 4) and high risk lesion (CIN 2+) detection rate is 6.7 %. This high detection rate in our study is due to HPV DNA testing of symptomatic women coming to hospital. This implies that symptom-wise HPV screening would be more yielding and will prove economical for low resource settings.

HPV testing in low resource settings have an important role to play. In countries with limited funds for disease prevention cancer screening programmes compete with other health needs. All cervical cancer screening programmes face common challenges to successful implementation. Barriers such at logistic and infrastructure support, cost concerns, poor follow-up and socio-cultural constraints need to be considered. Effective HPV testing programmes must develop clinical protocols based on natural history of HPV. HPV infection in older women is associated with CIN II on CIN III persistent infection along with other co-injections and early age of sexual debut are other incriminating factors. Molecular diagnostic techniques for detecting HPV may provide feasible alternative to large scale cytological screening if it is shown to be cost effective, feasible to implement and broadly acceptable.

In conclusion, HPV DNA testing of symptomatic women coming to hospital has high detection rate for precancerous lesions and will prove economical for low resource settings.

Acknowledgement

This study was carried out under the sponsorship of **STAR PROJECT** under the aegis of Medical Research Council of Maharashtra of Government of Maharashtra.

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SHORT COMMUNICATION

Predictors of Violence in Children & Adolescents

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ABSTRACT

Young adolescent including in violence is a major public health problem. Maturity reduces frequency of aggressive acts. Peer influences have now found to be correlated with harmful behaviour. The quality of parent child relationship seems to be most strongly associated with aggressive behaviour in adolescents. Day by day prevalence of child violence is increasing. The major risk factors for violence are child centred, family centred and contextual factors. Contextual factors like substance abuse, peer group influence, media and opportunity for criminal activity. Team work of psychiatrist, clinical psychologist, social workers, counsellors in conjunction with family is required to manage these behaviours. As a paediatrician concern we should pick up violent behaviours in disease like ADHD and autism and treat the same.

KEY WORDS- Violence, autism, ADHD, peers.

Young Adolescents Including in Violence is a major public health issue. Juvenile Delinquency refers to antisocial behavior.

Loeber & Hay described 3 groups of young people(3).

1) Those who desist from aggression.
2) Those whose aggression is stable and continues at the same level.
3) Those who escalate in the severity of the aggression and make the transition to violence.

Development of violent and antisocial behavior the feature of antisocial behavior diversity with increasing age. Maturity reduces the frequency of aggressive act. Peer influence has now found to be correlated with a harmful behavior. The quality of parent child relationship seemed to be most strongly associated with aggression behavior in adolescents. Parental monitory has a protective effect on many adolescent risk behaviors in middle class populations and poor urban environment Authoritative parenting generally leads to be best outcomes for teens.

Prevalence

The Prevalence ranges from 1.6 – 9.5% across different countries. The US homicide rate in the age group of 15 – 24 years is 18 times higher than for UK & 73 times higher for Austria(5).

Etiology

Numerous Theories have been put forward for violent behavior in young people. They are three major risk areas.

a) Child Centered
b) Family Centered
c) Contextual

Risk Factors

Child Factors

- Learning Disability
- Genetic Factors
- Psychiatric Disorder like ADHD(3)

Poor impulse control and educational difficulties are implicated in this risk. Depression in adolescence can manifest itself as anger, which in turn is correlated with aggression. Anxiety and post traumatic stress disorders show raised rates in violent young offenders Autistic spectrum disorders are being increasingly recognized as important etiological factors. The reason proposed for offending and aggressions in autistic person are

1) Their social naivety may allow them to be led into criminal acts by others.
2) Aggression arises because of disruption of normal routine.
3) Antisocial behavior may stem from a lack of understanding or sudden impulse.

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4) Child usually reflect some obsessions

Family Centered factors

Include poor parenting ability, Family History of Criminality and exposures to domestic violence. Primitive, harsh and inconsistent parenting styles are associated with conduct disorders in children.

Contextual factors

Include substance abuse, peer group influence, media and opportunity for criminal activity. Violence depicted on media makes the person more aggressive. Constant influence on the young mind leads to aggressive impulsive behavior. That is why television viewing by young children should have some restrictions and monitoring and supervision is important. As far as the prognosis is concerned earlier the age of onset of behavioral disturbances are more it is likely that the antisocial behavior will persist into adulthood. If juvenile delinquent are rehabilitated with employment and helped in establishing a stable work record and dear previous criminal behavior can be erased(4).

Interventions:

Most of the therapeutic modalities for management of violence in young adolescents require disciplinary heath settings where there are skilled professionals like psychiatrist, clinical psychologist, social workers, counselors working in conjunction with the family and young adolescent(5).

Young adolescent

Parent management training, family therapies, social skills training and anger management training are some of the techniques and modalities which are used by therapists.

The primary issue for pediatricians is to treat any diagnosable behavior disorder like ADHD and identifying early signs of emergence of behavior disorders(2). Moral science and Human values have to be taught with an important along with other subjects not only in school but also in colleges and they should form part of curriculum with weightage on scores deciding the result.

There is a need to design structured streamlined programmers for prevention of antisocial behaviors with a strong political and administrative will so that it can be delivered through community workers at grass root level. As good parenting enhances a Childs potential parents also require some training and teaching in identifying a high-risk behaviors and difficult adolescent(7).

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SHORT COMMUNICATION

Community Outreach Programme Squint Surgical Camp

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Misalignment of the two eyes is squint or Strabismus

Prevalence : 5 children in every 100

Indian scenario – 0.8/1000 blind children in India that means 300,000 blind children < 16 yrs

Visual morbidity due to squint 5 % of general pediatric population.

Most squints develop at some time in the first three years of life. Some develop in older children and adults. Squints that develop in children usually have different causes to those that develop in adults.

CAUSES OF STRABISMUS IN CHILDREN

Congenital strabismus of unknown cause,. Refractive errors, Paralytic strabismus, Sensory strabismus, associated with certain syndromes – CP, Downs etc.

CONSEQUENCES OF SQUINT

Amblyopia, Loss of binocularity, Cosmetic blemish

WHY COMMUNITY OUTREACH PROGRAMMES ?

If amblyopia is not treated before the age of about 7 years, the visual impairment usually remains permanent.

To understand how amblyopia occurs, it is helpful to understand how vision develops. Newborn babies can see. However, as they grow, the visual pathways continue to develop from the eye to the brain and within the brain. The brain learns how to interpret the signals that come from an eye. This visual development continues until about age 7-8 years. After this time, the visual pathways and the 'seeing' parts of the brain are fully formed and cannot change.

if, for any reason, a young child cannot use one or both eyes normally, then vision is not learnt properly. This results in impaired vision (poor visual acuity) called amblyopia. The amblyopia develops in addition to whatever else is affecting the eye. In effect, amblyopia is a developmental problem of the brain rather than a problem within the eye itself. Even if the other eye problem is treated, the visual impairment from amblyopia usually remains permanent unless it is treated before the age of about 7 years.

A squint is the most common cause of amblyopia

With normal eyes, both eyes look and focus on the same spot. This is called binocular vision . The brain combines the signals from the two eyes to form a three-dimensional image. If you have a squint, the two eyes focus on different spots.

In children the brain quickly learns to ignore the signals and images coming from the squinting eye. The child then *effectively* only sees with one eye. This means the child does not have a good sense of depth when looking at objects. As a result, he or she cannot see properly in three dimensions.

A squint can be a cosmetic problem. Many older children and adults who did not have their squint treated as a child have a reduced self-esteem because of the way their squint looks to other people.

Strabismus cases are tremendously under reported due to lack of awareness of the parents, and moreover undertreated due to unavailability and inaccessibility, unaffordability of availing the specialty care in rural India .

SARVA SHIKSHA ABHIYAN

Is government of INDIA's flagship programme for achieving universalization of elementary education in

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the country.

National Rural Health Mission launched with aim to make accessible affordable quality health care available to rural population especially the vulnerable group - children and women. school health is major part of this programme.

An lot of contribution from our side towards reducing this mammoth of cases was an enriching experience in the form of participation in a diagnostic and surgical squint camp organized by CIVIL HOSPITAL NASHIK from August 22 nd 2014 to August 23 rd 2014 at Civil Hospital Nashik.

There was an overwhelming response with a turnout of around 2500 patients in age groups between 2 years to 18 years being screened in the field by Sarvashikshan Abhiyaan and NRHM (National Rural Health Mission) health workers under expert guidance of Nashik Civil Hospital Ophthalmologists and Ophthalmic Officers.

760 patients of these were shortlisted for further evaluation at the Civil Hospital by the team from Sassoon Hospital Pune.

Team From Sassoon general hospital

DR. S.V Ambekar	Professor and HOD Dept. Ophthalmology
DR. Ranjana Pande	Associate Professor Dept. Ophthalmology
DR. Sujata Chahande	Associate Professor Dept. Ophthalmology
DR. Smita Harne	Lecturer Dept. Ophthalmology
DR. Padmaja Phade	Senior Resident Dept. Ophthalmology
DR. Vaibhav Kanse	JR II Dept. Ophthalmology

Screened patients 760

Diagnosed squint 438

Adviced conservative management - 325

Adviced squint surgery - 113

PRE OPERATIVE EVALUATION

1) Detail history
2) Visual acuity
3) Systemic examination
4) Squint evaluation
   - Unilateral vs bilateral
   - Constant vs intermittent
   - Manifest or latent
   - Comitant or incomitant
   - Head posture and tilt
   - Extraocular movements
   - Hirshbergs corneal reflex test
   - Prism bar cover test to determine the diopteric value of deviation and planning surgery accordingly
5) Cycloplegic retinoscopy
6) Detail anterior segment and fundus evaluation

CONSERVATIVE MANAGEMENT - 325 children

1. Full cycloplegic correction given for refractive squint and glasses prescribed, with detailed follow up schedule
2. Amblyopia therapy - age wise patching schedule given with close follow ups
3. Orthoptic exercises
4. Near work encouraging tasks

SURGICAL MANAGEMENT - 113 children

Out of the 113 children operated 15 were operated at CIVIL HOSPITAL NASHIK on 23 august 2014

98 were referred to SGH in batches of 15 to 20 over a period of 5 months and operated here.

An operation is advised to make the eyes as straight as possible. The main aim of surgery is to improve the appearance of the eyes. In some cases, surgery may also improve or restore binocular vision (this means that the two eyes are working together).

The exact surgery that is done depends on the type and severity of the squint. It may involve reinserting a muscle at different site (RECESSION) to weaken it or shortening. (RESECTION) of a muscle to strengthen it. Sometimes a combination of these techniques is used. Amount of recession or resection is calculated according to the preoperative prism diopter value of the deviation.

OUTCOME

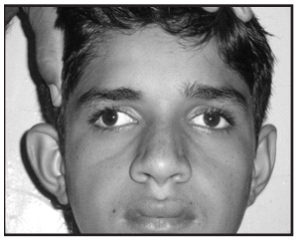
With amblyopia treatment and full correction spectacle use 1 to 2 lines of improvement in the visual acuity was noted in most of the patients 130 out of 200 who followed up - 65 %

Further improvement and decrease in angle of squint is expected.

In surgically treated group

At CIVIL HOSP NASHIK - 13 of 15 showed orthophoria, With 2 showing residual deviation. At SGH - 89 of 98 showed orthophoria. postoperative With 09 exhibiting some residual deviation Patients are still under follow up

Other than surgical rehabilitation of these children what was achieved was inculcating awareness about pediatric ocular morbidity and seeking quick specialized opinion for the same. Parents were educated and are expected to pass on the awareness in the society about the same. Stressed upon was the evil of amblyopia and feasibility of amblyopia reversal with early intervention.



Preoperative photo

Postoperative Photo

With India having 20% (7.8 million) of world's blind population (39 million) Our main objective is utilization of manpower and available resources for reducing burden of blindness in the community, with childhood blindness being identified as one of the key areas of intervention.

We are highly indebted to DR. S.V Ambekar for her constant encouragement and guidance throughout this project.

We also sincerely thank Mrs. Deepali Pujare for the technical support extended to us.

CASE REPORT

Laparoscopic Excision Of A Large Hepatic Hydatid Cyst - A Case Report

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ABSTRACT

Hydatid disease is a worldwide zoonosis produced by the larval stage of the Echinococcus tapeworm. Incidence of Cystic Echinococcus in endemic areas like India is upto 220 cases per 1,00,000 population[1]. Although Hydatid disease can involve any part of the body, the commonest sites of involvement are the liver (75% cases) and the lungs (10% cases) and both these organs may be involved in 5-13% cases.

Most patients with Hydatid cysts remain asymptomatic, even into advanced age. Some cysts may produce dysfunction of involved organs, including biliary obstruction, cirrhosis, bronchial obstruction, renal outflow obstruction, increased intracranial pressure, and hydrocephalus. The Hydatid cyst of the liver can induce obstructive jaundice and abdominal pain. Involvement of the lungs produces chronic cough, dyspnea, pleuritic chest pain, and hemoptysis. Cyst in the brain may cause headache, dizziness, and neurological deficits. Free rupture of the echinococcalcyst may cause anaphylaxis, and release of smaller cysts that can circulate to other organs.

While conventional open surgery is considered widely as principle basis of therapy, Laparoscopic surgery, although technically challenging is a novel method fast catching up as an accepted method of treatment.

We hereby present a case of 48 year old women with minimal symptoms, diagnosed with a Large hepatic hydatid cyst and treated with minimally invasive laparoscopic surgery at our

Case Report

A 48 year old female, not a known case of any illness, presented with complaints of epigastric pain, nausea, vomiting and abdominal distension since 1 month. Patient had no history of fever, jaundice, hematemesis, malena or complications pertaining to liver cell failure. She ate a mixed diet and did not have any addictions.

On examination, patient was hemodynamically stable with no icterus or signs of liver cell failure. On examination of the abdomen, abdominal distension was noted with mild right hypochondrium tenderness, moderate hepatomegaly was noted (span-18cm).

Her liver function tests were suggestive of mild liver damage.

Serum Bilirubin	SGOT	SGPT	ALP	Prothrombin time
1.6 mg/dl	83 IU/L	78 IU/L	168 U/L	18s (INR- 1.4)

Ultrasound of the abdomen was suggestive of a large multiloculated cystic lesion in the left lobe of liver measuring 11 × 11× 8 cm with thick internal septae. No IHBR dilatation. Doppler mode showed no vascular communication with the cyst and normal hepatic parenchyma with changes due to mass effect seen at the periphery of the lesion.

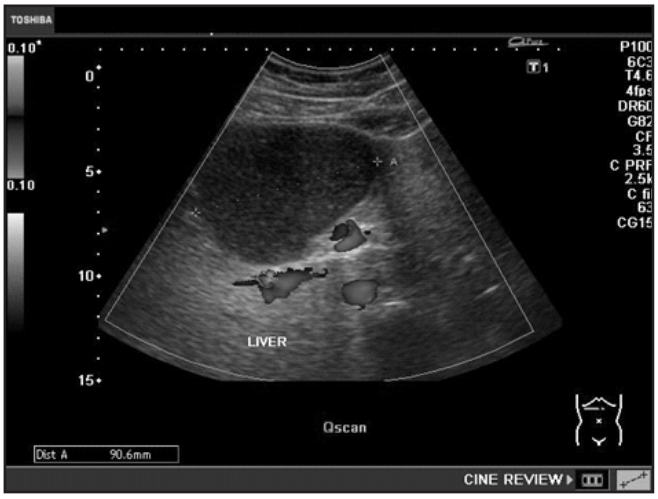

Figure 1: Pre-operative USG abdomen showing a large cystic lesion in liver.

CT Abdomen confirmed the USG findings with presence of a hypoechoic cystic lesion in segment II,III,IV of the liver with multiple hyperechoic densities suggestive of daughter cysts.

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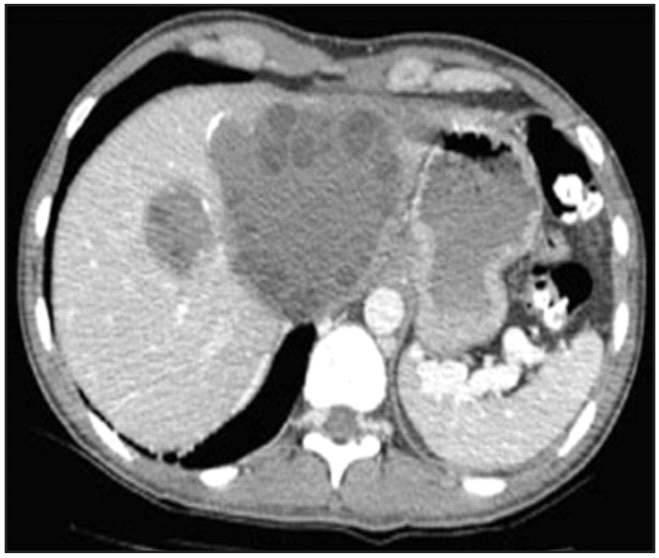

Figure 2: CT Abdomen (P+C) showing large cystic lesion in the liver

Anti-echinococcal IgM antibody was positive.

Patient was counseled about importance of surgical excision but patient was unwilling for open surgery. As the patients general condition was good, she was given a brief course of albendazole therapy. Subsequently she was taken up for Laparoscopic cyst excision and Omentoplasty. Careful dissection of the cyst was done and cyst was removed completely in one piece to avoid spillage and anaphylaxis.

Post-operatively there was minimal fluid collection on post-op day 7 and patient was discharged with advice to continue albendazole for 30 days. On follow up CT scan there was absence of any lesion in the liver parenchyma on day 30. Patient continues to be asymptomatic till today.

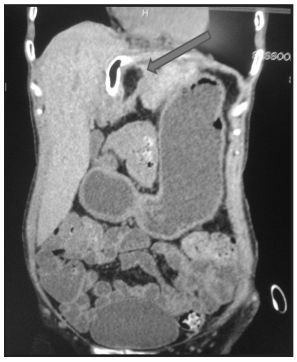

Figure 3: post-operative day 7 showing Some fluid collection and drain in left Hepatic lobe

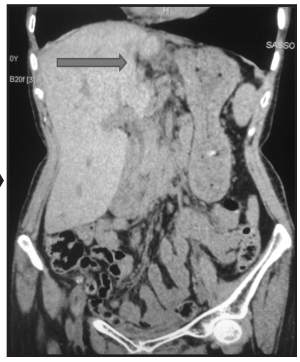

Figure 4: post-operative day 30 showing absence of collection.

Discussion

Hydatid cyst is a disease caused in the intermediate host of Echinococcus species.

Classical Cystic Echinococcosis is caused by *E. Granulosus* complex, while *E. Multilocularis* and E. *Vogeli* are responsible for alveolar echinococcosis and Polycystic echinococcosis, respectively. The definitive host of this disease are dogs, foxes and other wild canids. The infection may be acquired by contact with infected definitive hosts, egg-containing feces, or egg-contaminated plants or soil followed by direct hand-to-mouth transfer[2] . Dog ownership has not been found to be a risk factor in seropositive individuals, indicating an indirect contact with dog feces in the environment. Eggs can also be ingested with vegetables, salads, uncooked fruits, drinking water that can become contaminated.

The life cycle of Echinococcus has three developmental stages: (1) The adult tapeworms in the definitive host, (2) Eggs in the environment, and (3) the Metacestodes in the intermediate host. After ingestion by the definitive host, the Metacestodes mature into the tapeworm in the definitive host and then release eggs into the environment. The egg ingested by the intermediatehost hatches in the intestine, penetrates the gut wall, and travels through the lymphatic or blood vessels to the liver, lungs, and other organs. The Metacestodes hatched in the intermediate host may grow and occupy the residential organs, where a variety of symptoms can be produced.

The majority of the Hydatid cysts in man are seen in the liver (approximately 75%) because it is the first filtering system for all the ingested ova, which enter the portal system.[3] A few of these ova that have an average size of 35 μm, escape the sinusoidal system of the liver to enter the systemic circulation and pass through the lungs, which acts as a second filter for the ova, making it the second most common site for the disease (approximately 15%).[3] Hydatid disease of the lung occurs from the larvae, which get trapped in the arterial capillaries of the lung.

Occasionally, lung may be the site of secondary metastatic hydatidosis by rupture of a liver cyst. The fully developed cyst has 3 layers- Pericyst, middle laminated layer and inner germinal layerThe Germinal

layer is where the scolices or daughter cysts are attached. A cluster of scolices together constitute a brood capsule.

The diagnosis of hydatid liver cyst is established by imaging studies like Ultrasonography and CT abdomen.

The Ultrasonographic classification given by the WHO is helpful in taking clinical decisions regarding management of hydatid liver cyst. Not all cyst found on

Gharbi classification	Ultrasound features	WHO classification	Ultrasound features
Type I	Pure fluid collection	CL	Unilocular, no wall
Type II	Fluid collection with split wall	CE1	Cyst wall, hydatid sand
Type III	Fluid collection with septa	CE2	Multi-vesicular
		CE3	Detached laminated membrane
Type IV	Heterogeneous contents, partially solid	CE4	Heterogeneous contents, no daughter cysts
Type V	Thick calcified wall	CE5	Thick calcified wall

USG warrant surgical intervention.

Pre-operative diagnosis of Hydatid cysts can be confirmed by a CT scan. The CT scan has an accuracy of 98% to demonstrate the daughter cysts, and it is the best test to differentiate hydatid cysts from amebic and pyogenic cysts in the liver [4]. A thin rim of calcification delineating a cyst is suggestive of an Echinococcal cyst.

Several serological tests can be used for diagnosis, screening, and post-operative follow-up for recurrence. These include the Hydatid Immunoelectrophoresis, Enzyme-linked Immunosorbent assay (ELISA), latex agglutination and indirect haemagglutination (IHA) test.

Occasionally Hydatid cysts are known to regress spontaneously, but in the overwhelming majority, therapeutic intervention is necessary.[5] Conservative management in the form of medical therapy or percutaneous aspiration of cyst have been described. Pre- and Post-operative one-month courses of albendazole and two weeks of praziquantel should be considered in order to sterilize the cyst, decrease the chance of anaphylaxis, decrease the tension in the cyst wall, and reduce the recurrence rate post-operatively.

The mainstay of treatment remains surgical. A variety of surgical procedures have been described using conventional open techniques, including Pericystectomy, de-roofing the cyst with omentoplasty, Marsupialisation and liver resection.

The techniques of minimally invasive surgery have also been adopted to treat this disease but one of the chief concerns during surgical treatment of hydatid cyst remains the possibility of cyst rupture and spillage and its containment. This poses a two-fold danger-an immediate one of anaphylactic reaction as the hydatid fluid is highly allergenic and a delayed risk of dissemination of the disease in the peritoneal cavity. The difficulty in containing spillage, should it occur, during laparoscopic management is much greater than in open conventional surgery. This factor has always been a deterrent to surgeons from widely adopting laparoscopic surgery as the mode to treat this disease.[6,7]

This is a rare case in which laparoscopic techniques were used with success in order to treat a hepatic hydatid cyst.

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CASE REPORT

Unusual case of Sertoli-Leydig cell tumor

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ABSTRACT

Sertoli-Leydig cell tumors belong to the group of sex cord stromal tumors of the ovary. They account for less than 0.5% of all the ovarian neoplasm.

The majority of these are seen in women younger than 40 yrs of age. and are benign and almost all are localized . Herewith, we describe ovarian sertoli-Leydig tumor in forty two year old female presented with acute abdominal distension .

Patient was posted for surgery after investigation. Exploratory laparotomy done.

Patient was given postoperative chemotherapy. Six week and three month follow up did not reveal any recurrence.

Key words: Sex cord cell ovarian tumors, androblastoma, sertoli-leydig cell tumor

Introduction

Of all the gynecologic cancers, ovarian malignancies represent the greatest clinical challenges. Ovarian malignancy accounts for 8% of all malignancies.[1] Ovarian cancer represents a major surgical challenge, requires intensive and often complex therapies. As the management is directly related with the fertility, it also involves the psychological aspect of the patient.

Sex cord-stromal tumors of the ovary account for about 5-8% of all ovarian malignancies.[2] The tumour usually composed of various combinations of element, including the female cells that is grannulosa cell tumour and male cells that is sertoli and leydig cell tumour

75% cases of Sertoli-Leydig cell ovarian tumours are seen in women younger than 40 years.[1] These lesions are extremely rare and account for less than 0.2% of ovarian cancers.[2] Sertoli-Leydig tumours are most frequently low-grade malignancies, although occasionally a poorly differentiated variety may behave more aggressively.

Because these low grade lesions are only rarely bilateral (<1%), the usual treatment is unilateral salpingo-oophorectomy and evaluation of contralateral ovary for patients who are in their reproductive age.[1] For older patients, hysterectomy and bilateral salpingo-oophorectomy are appropriate.

The 5-year survival rate is 70-90%, and recurrences thereafter are uncommon.[2] Most fatalities occur in the presence of poorly differentiated lesions

Case Report

42 yr old married since 28 yrs P3L2D1 postmenopausal since 2 years resident of Ahmednagar came with chief complaints of abdominal distention sudden onset since 15 days and breathlessness on exertion since 15 days. She had no complaints of pain in abdomen/vomiting, chest pain /palpitations, No bowel/ bladder complaints, nor weight loss and loss of appetite.

Patient was postmenopausal since 2 years. She had three full term normal deliveries, out of which two are alive and well.

She had no significant medical/surgical illnesses or any personal history. Patient's Family history did not reveal any history of Cancer ovary, breast, endometrium in family.

On examination patient's vital were stable. There was no pallor, icterus, edema, lymphadenopathy. On Cardiovascular system examination- S1S2 heard normal, no murmur. Respiratory System examination - within normal limit.

Per abdominal examination, on inspection there was uniform distention of abdomen, midline mass arising from pelvis above the umbilicus, no scars, sinuses, dilated veins. On Palpation- 30 weeks midline mass arising from the pelvis could be palpated. Mass had smooth surface, was firm to cystic in consistency, with

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regular margins, not fixed to overlying skin, side to side mobility was present, lower margin of the mass could not be reached. Ascitis - clinically not evident.

On local examination-labia majora, labia minora were normal. There was no evidence of clitoral hypertrophy. Per speculum examination cervix was hypertrophied. On per vaginal examination mass of 28 - 30 wks was palpable which was mobile. Uterus could not be palpated separately from mass. Movement of the mass was not transmitted to the cervix. There was no nodularity felt in Pouch Of Douglas, Nor forniceal fullness. On Per Rectal Examination, No nodularity felt. Rectal mucosa - free. Mass was felt high up.

Patient was investigated including Chest X ray. CA 125 which was 618 U/ml(normal <35).

USG Abdomen and Pelvis revealed large solid cystic lobulated lesion 18×16×13 cm size arising from the pelvis extending into the abdomen mostly from ovaries could be s/o neoplastic origin. Both ovaries not seen separately. There was minimal vascularity on Doppler. No Metastasis, No lymph node enlargement. Minimal Ascites present.

CT SCAN Abdomen and pelvis revealed large solid cystic lesion of 15×16×15 cm arising from left adnexa extending into the abdomen. Left ovary not seen separately. Right ovary normal. Uterus normal in size . Rest organ normal.

Patient was posted for Exploratory Laparotomy High risk consent was taken in view of need of surgical intervention, malignancy, metastasis, if required bowel bladder surgical intervention, need of blood transfusion.

Surgical standby was kept ready if required.

On exploration there was evidence of 20×25×25 cm left ovarian mass, regular margins solid to firm in consistency with few areas of capsule rupture was noted .Uterus deviated to right side. Right ovary was 4×3×3 cm cystic in consistency with smooth surface. Bowel & omentum checked for malignant deposits. There was no evidence of deposits. Minimal ascitis was present – fluid sent for cytology. Liver surface was smooth. Pre & Para aortic nodes were not palpable. Decision of Total abdominal hysterectomy with bilateral salpingo-oophorectomy was taken procedure performed. Omental biopsy taken, specimen was sent for histopathological examination. Procedure was uneventful. Haemostasis confirmed, drain kept, Instrument & mop count checked abdomen closed in layers. Patients vitals stable postoperatively. Postoperative period was uneventful.

Histopath report - Sertoli Leydig cell tumour Intermediate type II. Omental biopsy unremarkable. Ascitic fluild cytology - no e/o malignant cells. After histopathology report serum Testosterone levels were done 19.05ng/dl which was within normal limit.

Oncology reference was done. Patient was given postoperative chemotherapy. Till now patient has completed three chemocycle and tolerated them well and is following up regularly with us.

Figure 1: Ovarian mass during exploratory laparotomy

Discussion

Sertoli-Leydig cell ovarian tumors, formerly called androblastoma/arrhenblastoma are one of the rarest of all ovarian tumors accounting for <0.1%.[3] morphologically resembles cells of testis at various stages of development, but ultrastructurally resembles ovarian grannulosa cell tumours and contain female sex chromatin.

Though it presents with virilisation in 30-50%[2] with oligomenorrhoea, amenorrhoea, loss of secondary sex characteristics, breast atrophy, deepening of voice, temporal baldness, clitoral hypertrophy, in our case these features were absent. Feminine characteristics usually returns after surgery.

50% have no endocrine abnormalities[2], usually there is increase in serum testosterone levels. Only 2% are bilateral.[3] Majority (97%) are detected in first stage and only2% tumors spread beyond ovary. 5% of all

tumors recur and metastasize[2]. Post operative management and prognosis mainly depends on surgical staging and on histopathological picture which can be

1)Well differentiated (Meyer's type I)

Common in older age usually not associated with masculinisation and clinically benign. On microscopically 11% nodular, tubular pattern and easily identifiable sertoli and leydig cell in tubular pattern is seen.[4]

2)Intermediate differentiated(Meyer's type II)

Associated with virilisation, 11% are clinically malignant.[4] On microscopically 54% outlines of immature sertoli and large leydig cells are seen. It may have mucus filled epithelial cells, cartilage and skeletal muscle cells.

3)Poorly differentiated(Meyer's type III)

59% are clinically malignant, on microscopy 13% resemble indifferent gonad, may have sarcomatous appearance.[4]

In our case it was intermediate that is Meyer's Type II with surgical staging Ic hence decision of postoperative chemotherapy after oncologist opinion was taken. Treatment of this pathological conditions has to be individualized according to patients age, stage of tumor and degree of differentiation.

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CASE REPORT

Gonadal Torsion - Rare Presentation Of Testicular Feminization Syndrome

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ABSTRACT

A 13-year-old phenotypic female, presented in the emergency department because of pain and swelling in the left inguinal region. A high index of suspicion lead to thorough evaluation of the case and subsequent diagnosis of testicular feminization syndrome. Contrary to the usual presentation with primary amenorrhoea in such cases, torsion of the undescended left gonad had brought the girl to medical attention. This kind of presentation of testicular feminization syndrome is extremely rare. Hence, the case report.

Keywords : Testicular Feminization Syndrome, Gonadal Torsion, Primary Amenorrhoea, Baldwin's Vaginoplasty, Hormone Replacement Therapy (HRT)

Introduction

Testicular feminization syndrome, also known as androgen insensitivity syndrome (AIS), was first described by Morris at Yale [1]. The phenotype is a female, despite normal male karyotyping i.e. 46, XY without any mosaicism. The gonads are testes; however they are unilaterally or bilaterally undescended. The individual with complete form of this syndrome (CAIS) have normal-looking female external genitalia; while those with partial form (PAIS) have a variable ambiguity of genitalia and often need extensive reconstructive surgery [2].

Case Report

13- years-old school going girl presented in emergency department with history of Pain in left inguinal region of 3-4 days' duration. Swelling was noticed in both groins since childhood and there was recent increase in size of the left groin swelling. There was no history of vomiting, constipation or any urinary complaints. On detailed enquiry history of primary amenorrhoea was revealed.

On examination, she was tall, thin built. Her height was 160cm and weight was 55 kg. Pubic and axillary hair were absent. There was no development of breasts (Fig 1). Systemic and abdominal examination were normal. She had swelling in the left inguinal region with induration and inflammation of the overlying skin. The gonads were bilaterally undescended and palpable. She had well developed labia; the right labial fold being more prominent (Fig 2). External urethral meatus was patulous. Enlarged clitoris was seen. A blind pouch of about 1.5 cms length indicating rudimentary vagina was seen behind the urethral opening (Fig 3). Ultrasonography of abdomen and pelvis showed absent uterus and ovaries. Both kidneys, ureters and the bladder were normal. In view of history of primary amenorrhoea and clinical findings of bilaterally palpable gonads, diagnosis of testicular feminization syndrome was suspected. The parents and the child were counseled in detail. They were explained about the need of bilateral gonadectomy and consent for same was obtained.

Diagnostic laparoscopy confirmed absence of uterus and ovaries. In the same sitting, both inguinal regions were explored. There was torsion of the left gonad (Fig 4), the right one looking overtly normal. Bilateral gonadectomy was done. The histopathology of the right gonad was suggestive of testicular tissue (normal Leydig and Sertoli cells; small hyalinised seminiferous tubules), without any premalignant changes, whereas on the left side there were gangrenous changes. The child was completely worked up for evaluation of the anomaly. The sex chromatin was negative. Karyotyping was 46 XY. FSH was 81 mIU/ml and LH was 19 miu/ml respectively. Serum testosterone was 400 nmol/L i.e. in the normal male range.

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A panel of developmental pediatrician, gynecologist, endocrinologist, psychiatrist and pediatric surgeon, together counseled the parents and the child. All their queries were addressed to. In view of the child's age and her psychosexual development as a female, it was unanimously decided to rear her as a female. They were also explained about the absence of cyclical bleeding (menstruation) and conception of foetus in future; though after vaginoplasty the girl could marry and have active sexual life. Three months later, Baldwin's vaginoplasty (vaginoplasty using ileal conduit) was done. The child was put on oral estrogen supplements for breast development. Following estrogen supplements, she has grown axillary and pubic hair. Presently at a follow up of 2 years, there is satisfactory breast development to give a look of phenotypic female. The vaginal orifice is patent. The girl and her parents are satisfied with the results of the treatment in terms of feminine appearance.

Discussion

Testicular feminization syndrome or androgen insensitivity syndrome is a rare disorder with an incidence of 1:20,000-64,000 male births. It may present as a complete form (complete androgen insensitivity syndrome or CAIS) or an incomplete form (partial androgen insensitivity syndrome or PAIS)[3]. In the complete form, there is no androgen response, therefore normal female external genitalia develop and these infants are reared as females. These patients most often present in late adolescence with primary amenorrhoea. They have short and blind ending vagina, absent mullerian structures (absence of uterus and ovaries), and abdominal, inguinal or intralabial testes giving rise to labial or inguinal swellings[4]. Solari A et al have reported 83% of patients with CAIS having childhood inguinal hernias [4]. Similar is the experience of Deeb A et al who found more than half of the patients with CAIS presenting with inguinal hernia, of which half were bilateral and a third contained the gonads[5]. Though, reconstructive surgery to external genitalia is often not needed, gonads need to be removed before the age of puberty due to risk of malignancy[2]. Hormone replacement therapy (HRT) has a role to induce puberty and/or maintain secondary sexual characteristics, to optimize bone mass accrual, and to promote physical and social well-being of these children[6].

Our case, a 13- years-old phenotypic female presented in an emergency setting with pain and recent increase in size of the pre-existing left inguinal swelling. On direct questioning history of primary amenorrhoea was revealed. She was tall, asthetically built and had very scant pubic hair. There was absence of axillary hair and development of the breasts. History of primary amenorrhoea and examination findings of bilaterally palpable gonads led to suspicion and eventual diagnosis of testicular feminization syndrome. Diagnostic laparoscopy confirmed absence of uterus and ovaries. Hence, bilateral gonadectomy was done at the same sitting. Three months following this surgery, Baldwin's vaginoplasty (vaginoplasty using ileal conduit) was done, to give functional vaginal length. Satisfactory breast development resulted following oral estrogen supplements, improving her overall body image.

This case highlights the importance of high degree of suspicion and thorough clinical and laboratory evaluation of any phenotypic female, presenting at puberty with primary amenorrohea, absent vagina and undeveloped secondary sexual characters to rule out testicular feminization syndrome. Awareness of this entity among clinicians is important as with early diagnosis, such disorder can be managed appropriately and accurate information can be given to parents regarding long term issues of fertility and HRT. Close liaison between developmental pediatrician, gynecologist, genetist, endocrinologist, psychiatrist and pediatric surgeon is required, to address various complex issues involved in management of this rare disorder.

Legends for Figures :

Figure 1 - Lack of breast development

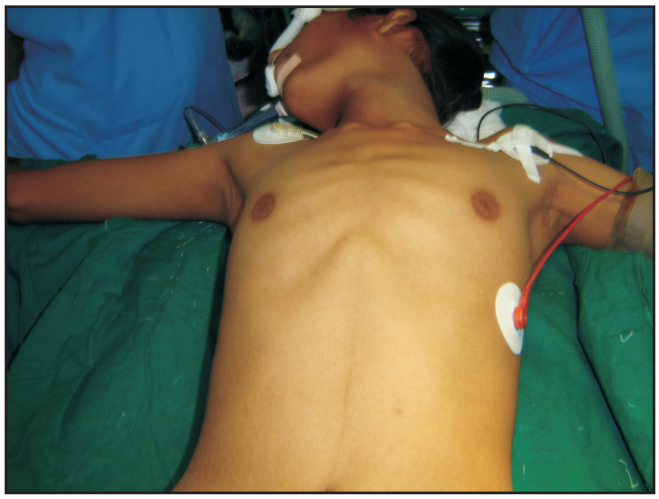


Figure 2 - Bilaterally palpable gonads, well developed labia and prominent right labial fold

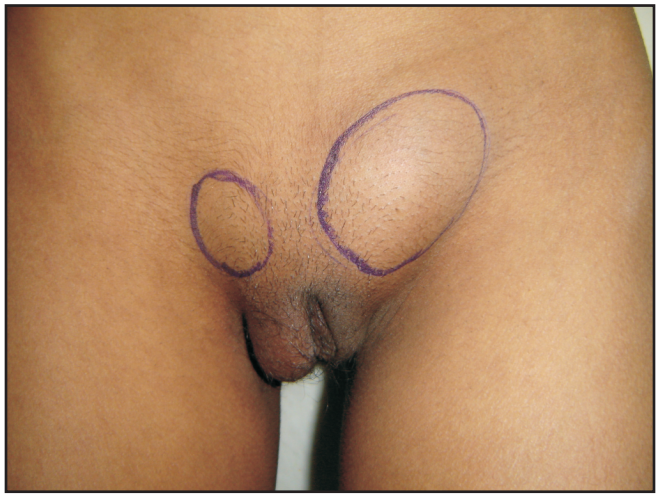


Figure 3 - Blind pouch (rudimentary vagina) behind the urethra

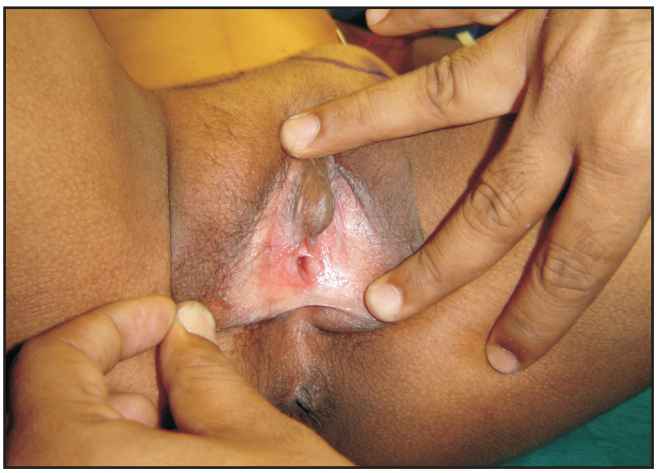
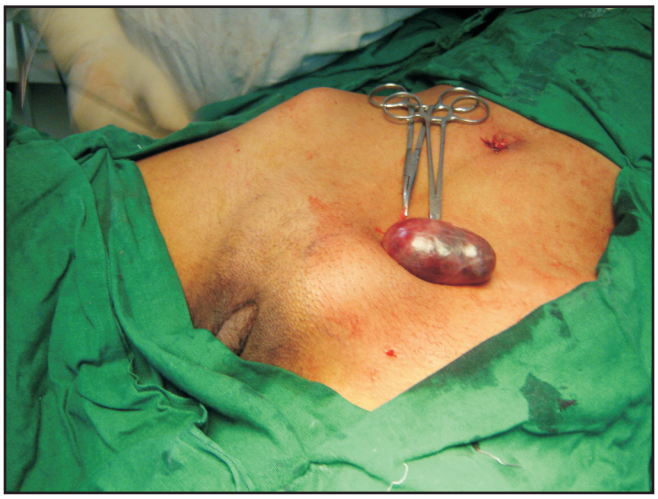


Figure 4 - Intra-operative photograph of gangrenous left gonad



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CASE REPORT

A case of Adult Bartter's syndrome

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ABSTRACT

A middle aged male was admitted with Recurrent Quadriparesis, LMN type without sensory & autonomic involvement or neck muscle weakness. Laboratory investigatons were suggestive of Bartter's syndrome. Most of the cases have been noted in the pediatric age group and adult-onset cases are very rare.

Introduction

Bartter's Syndrome is characterized by renal potassium wasting with hypokalemia, metabolic alkalosis, increased renin-angiotensin-aldosterone system, normal blood pressure, resistance to the pressor effects of angiotensin II and juxtaglomerular cell hyperplasia.

Case Report

50 years old male was admitted with complaints of Weakness in all 4 limbs since 3 days and neck pain since 2 days. Patient was apparently alright 3 days back, noticed weakness in all 4 limbs which was gradual and progressive, first noticed in lower limbs followed by upper limbs but could walk with support. Patient complained of neck pain since 2 days, which was not associated with movement or without any precipitating or relieving factor.

Negative History

There was no history of fever, nausea, loose motions, vomiting, trauma, convulsions, breathlessness or, bowel and bladder involvement,. There were no Sensory or cerebellar symptoms. There was no double or decreased vision, deviation of angle of mouth, slurring of speech, hearing lossor decreased hearing. There was also no history of any diuretic medications.

Past History

Two months back patient had loose motions, vomiting, fever and weakness in all limbs for 1 day. He didn't take any hospital care but improved completely. He did not have any residual weakness. There was no history of DM, HTN, IHD or TB in the past. **PERSONAL HISTORY** He had mixed diet, was a Tobacco chewer and chronic alcoholic. **FAMILY HISORY** No h/o similar episode in the family.

On General Examination : Patient was afebrile, Pulse was68/min, BP was 100/60 mmHg and RR was 16/min. There was no pallor, icterus, cyanosis, clubbing or Lyphadenopathy. Fundus examination was Normal. On neurological examination the patient was conscious, well oriented to time, place and person. His higher mental functions and cranial nerves were normal. There was no wasting and the tone was decreased in all limbs. Power was grade III in all limbs. Reflexes in upper limbs were++ and Lower Limbs were 1 +. Planters were bilaterally flexors. Pupils were bilaterally equal and reacting to light. Neck muscle weakness was present. There were no sensory symptoms, no cerebellar signs, no involuntary movements and no signs of meningeal irritation. Examination of other systems was normal. His laboratory investigations showed - urine exam - normal–Blood gas analysis - PH-7.54.PCO2-42,PO2-86, HCO3-34, Sat 96%, Na 118 meq/lit, K2.1meq/lit, suggestive of metabolic alkalosis, hypokalemia and hyponatremia, HB was 10.1 gms%, TLC 6400/cmm, Platelet count 2.48lacs CXR -WNL, cervical spine AP/LAT-WNL, USG abdomen and Pelvis s/was suggestive of fatty liver & bilateral raised cortical echogenicity, kidney sizes were Rt 9.8x5.5, Lt 10.9x5.4cm. Other lab was as follows- Creatinine 1.5mg/dl. Se calcium w 8.5 mg/dl, phosphorus 3mg/dl, se Magnesium was 1.9 meq/liter, Se chloride was 89 meq/lit, se osmolality 263 mos/kg (normal 285 to 295 momol/kg), urine Na 37mmol/day, urinary potassium 16.3 mmol/day, Urine chloride 54 mmol/lit, urine calcium to creatinine ratio 0.25, urine osmolality, 75

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mosm/kg(500to800 momol/kg), TTKG was 11.8. So in view of Hypokalemia, alkalosis, Hyponatremia excess urinary chloride loss urinary ca/ cr ratio=0.25 and low serum osmolality, normal sr mg hence a diagnosis of **BARTTER'S SYNDROME, ADULT VARIANT** was made.

TREATMENT- The patient was treated with intravenous kesol infusion and later oral kesol. Tab. Spiranolctone was also started. He improved and was discharged.

Discussion

Bartter syndrome is a group of closely related hereditary tubulopathies characterized by renal salt wasting, hypokalemia, metabolic alkalosis and hyperreninemia andhyper-aldosteronism with normal blood pressure [1,3,4]. The renal salt loss in Bartter syndrome is caused by impaired transepithelial transport in thick ascending loop of henle. The resultant defect in sodium transport leads to reduction in trans tubular potential difference resulting in decrease in paracellular calcium reabsorption in thick ascending Loop of henle[1,8] Reduction in intravascular volume also induces aldosterone mediated metabolic alkalosis Some patients have an autosomal recessive mode of inheritance in classic Bartter syndrome, although many cases are sporadic. In classic Bartter syndrome, the defect in sodium reabsorption appears to result from mutations in the chloride-channel gene[2]. The consequent inability of chloride to exit the cell inhibits the sodium chloride/ potassium chloride cotransporter. Increased delivery of sodium chloride to the distal sites of the nephron leads to salt wasting[8], polyuria, volume contraction, and stimulation of the renin-angiotensin-aldosterone axis. These effects, combined with biologic adaptations of downstream tubular segments, specifically the distal convoluted tubule (DCT) and the collecting duct, result in hypokalemic metabolic alkalosis The clinical features are Fatigue, Polyuria (rate as high as 12-50 mL/kg/h). Polydipsia, Nocturia, Generalized weakness, Salt Cravings Dehydration, Mental confusion, Vomiting, Muscle weakness, Muscle spasms, Tetany, Failure to thrive and Short stature If untreated. Lab findings in these patients are Low serum potassium, sodium, chloride, Low-normal magnesium levels, Increased renin, and aldosterone Metabolic Alkalosis, Increased Prostaglandin E2 excretion, Increased angiotensin II levels, Normal - Low Blood Pressure, Increased urinary potassium excretion Increased urinary chloride excretion Urinary Ca/cr ratio >0.20 and Renal stones.

We reviewed the literature for adult onset Bartter's syndrome. Only three cases have been reported to our knowledge. Sekhar et al.[7] reported a A case of bartter syndrome-adult variant where they reported 42year old male who presented with quadriparesis and weakness of neck. Jong Woo etal [5] reported a case of 40 year female who presented with generalized weakness and was diagnosed as Bartter's syndrome. Sami Ullah et al [6] reported a case of 29 year male who came with lower limb weakness and was eventually on laboratory investigations was diagnosed to have Bartter's syndrome.

Conclusion

Athough Bartter's syndrome is a disease of childhood but rarely we may come across an adult case, This diagnosis should be considered in any patient with hypokalemia and metabolic alkalosis and who presents with weakness of limbs.

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CASE REPORT

Case Report Of Multiple Rectosigmoid Adenomatous Polyps & Its Management i.e TEM

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ABSTRACT

Adenomatous polyps of colorectal region are common, occurring in up to 25% of the population older than 50 years of age in the United States. Tubular adenomas are associated with malignancy in only 5% of cases, whereas villous adenomas may harbor cancer in up to 40%. Tubulovillous adenomas are at intermediate risk 22%. We are presenting this case of multiple adenomatous polyp of rectal region in 28 years old male presenting with per rectal bleed. The most distal polyp was only 3 cm from anal verge. The biopsy was adenomatous polyps. We present this case on account of its rarity, and successful removal using newer technique of Transanal Endoscopic Microsurgery (TEM) with help of Covidien Small Incision Laproscopic System(SILS) Port. **TEM is not recorded in our country uptill now. This is the first time it is performed in our country.**

Key words - Adenomatous polyp, TEM

Introduction

The term 'polyp' is a clinical description of any protrusion of the mucosa [1]. Polyps can occur singly, synchronously in small numbers or as a part of a polyposis syndrome [1]. According to their attachment to bowel wall polyps are subdivided into sessile and pedunculated. Based on histology intestinal polyps are classified into inflammatory polyps as in ulcerative colitis, hyperplastic polyps, hamartomatous polyp like juvenile polyp and neoplastic i.e adenomatous polyps. Adenomatous polyps are the most common and may be present in any part of colon though 70% are left sided [1]. They are mostly asymptomatic [2]. Polyps more than 1 cm are more likely to produce symptoms, and polyps less than 0.5 cm rarely produce symptoms [3,4]. The most common symptoms attributable to polyps are rectal bleeding, abdominal pain and change in bowel habits [5]. A rectal polyp can rarely cause rectal prolapse or can form leading edge of colonic intussusception [6]. However definitive management of intestinal polyps is important because of their significant malignant potential [1]. This is one case of rectal adenomatous polyps presented with per rectal bleed managed by newer technique of TEM

Case Report

A 28 years old male came to OPD of Sassoon Hospital with chief complaints of per rectal bleed since 4-5 years. There was no History of (H/O) loss of weight and appetite.

There was no H/O of similar complaints in any of his family members. On examination, patient has average build and nutrition with no pallor and lymphadenopathy His vitals were stable and per abdominal examination was normal. His other systemic examination was normal. Hemogram and routine blood investigations: were normal. On Digital Rectal Examination (DRE) there were no external piles/ fistula in ano / fissure in ano, however a single sessile polyp was palpable 2-3 cm from anal verge. There was no evidence of active bleed. On proctoscopic examination findings of DRE were confirmed i.e. visualization of sessile polyp approximately of size 4-5 mm at 3 '0'clock position; 2-3 cm from anal verge. On ultrasonography of abdomen and pelvis there was no evidence of any abnormality. CT Abdomen & pelvis suggestive of bowel loops unremarkable with no evidence of any significant lymphadenopathy. On barium enema study there were multiple barium coated sessile polypoidal protrusions of varying sizes mostly arising from right lateral wall seen, projecting into the rectum which appear smooth in outline.

On colonoscopic examination there were 5-6 polyps in rectosigmoid region. The most distal polyp was 2 -3 cm

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from anal verge. Average size of polyp was 2 cm.

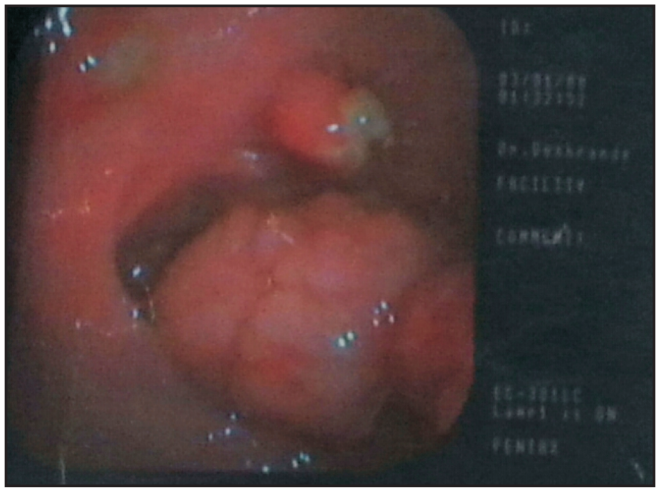

Fig:1 Colonoscopic View Of Adenomatous Polyp

On colonoscopic biopsy: Adenomatous polyp & there was no muscularis involvement.

Management :

With provisional diagnosis of adenomatous polyp of rectal region and considering his age, patient was taken for transanal endoscopic microsurgery (TEM). The patient was placed in lithotomy position under general anesthesia, TEM combination system with Covidien Small Incision Laproscopic System(SILS) Port system. Covidien SILS Port was inserted through anal canal. It is flexible port that sits snugly in anus maintaining a seal and contains three lumens. Three short removable ports may be inserted through the lumens allowing an interchangeable combination of up to three 5 mm ports or two 5 mm ports and one 12 mm port. A separate insufflation line controlled by two way valve.

Fig. 2 COVIDIEN SILS PORT

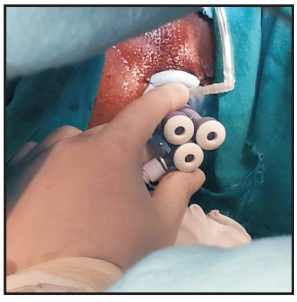

Fig. 3 INSERTION OF PORT

The TEM System was used in combination with standard laproscopic unit. The CO_2 insufflation was done with pressure of 10 mm of Hg. After insertion of laproscope. 5-6 sessile polyps identified in rectosigmoid region. The excision of polyps were performed with harmonic ultrasonic shear. The polyp and the surrounding mucosa was removed up to muscularis propria. The specimen was retrieved transanally. A warm Normal saline irrigation was done. Haemostasis was confirmed. Intra-operatively there was no evidence of colon breach. At the end colorectal region was carefully verified for any missed polyp and bleed. Patient tolerated the procedure well.

Histopathology examinations : Gross specimen consists of received 5-6 mucinous soft tissue bits, grayish tan in color collectively measuring about 8-10 cm.

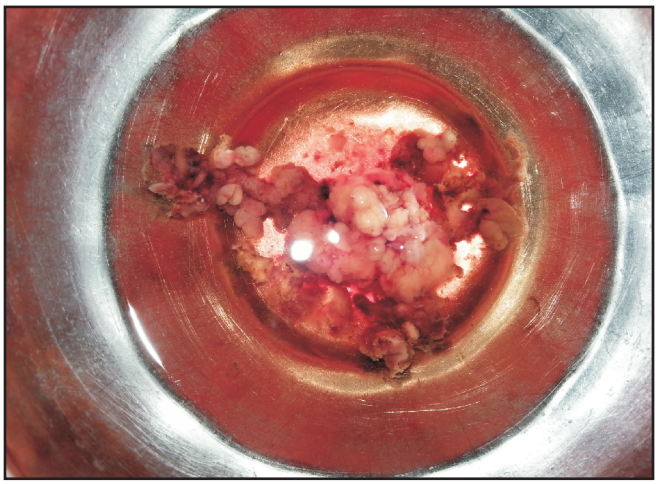

Fig. 4 SURGICAL SPECIMEN

Microscopy show tubulovillous adenoma. There is no evidence of mucularis involvement. No dysplasia or malignancy seen.

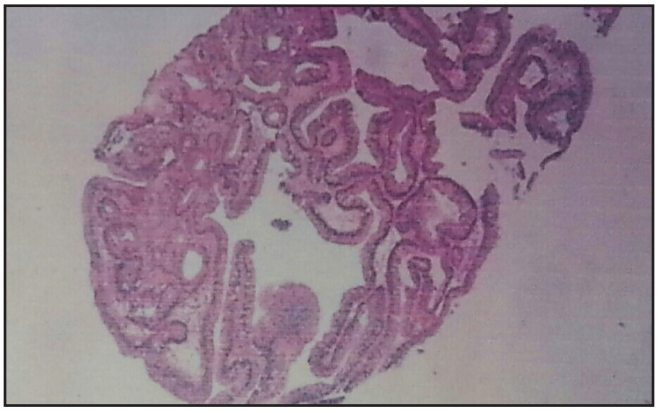

Fig.5 Microscopic examination

Discussion

Various treatment options [7] :

1. Hot biopsy for polyp < 0.8cm
2. Colonoscopic snare polypectomy for polyp> 0.8 cm. Most pedunculated polyps are amenable to colonoscopic snare excision.
3. Endomucosectomy : (combined technique of submucosal injection of normal saline at polypectomy site to permit lift and deep resection of submucosa followed by snare polypectomy) for large sessile villous adenoma and T0 or T1 lesion
4. Piecemeal snare excision - Done for larger polyps >3cm.
5. Endoscopic mucosal resection (EMR) [8] : Typically used for removal of lesions < 2cm 0r piecemeal removal of larger lesions. Most commonly used techniques can be subdivided as injection-, cap-, and ligation -assisted EMR.
6. Endoscopic submucosal dissection (ESD) [8] : Technique has been developed for en bloc removal of large (usally > 2 cm), flat GI tract lesions. Procedure involves several steps first, the margins of lesions are marked by electrocautery, and submucosal injection is used to lift the lesions. Then, a circumferentional incision into the submucosa is performed around the lesion with specialized endoscopic electrocautery knifes. Finally, the lesion is dissected from underlying deep layers with the electrocautery knife and removal en-bloc.
7. Transanal Endoscopic Microsurgery (TEM) [9]: For rectal sessile polyps, transanal operative excision is preferred because it produces an intact, single pathology specimen that can be used to determine the need for further therapy.

Conventional EMR cannot provide an en-bloc resection in case of large lesions and incomplete or piecemeal resection may occur in up to 50% of cases [10]. After piecemeal resection, pathological assessment of complete resection is challenging and the risk of local recurrence is high [11]. In addition, EMR does not provide a submucosal dissection, therefore precluding an accurate staging in case of malignancy. In the last few years, the ESD technique was introduced to overcome these difficulties and to allow en bloc resection of specimens, especially in case of lesions larger than 20mm [12]. Low complication rates and low local recurrence rates have been reported after ESD[13,14] However, compared with conventional EMR, ESD is technically more challenging and time consuming, requiring a steep learning curve [13,15]. As a result, ESD has not gained wide acceptance and transanal surgery is still the approach of choice for the excision of large rectal adenomas. Therefore, based on the data reported in the literature, TEM represents the current standard of treatment for large rectal adenomas and conventional Trans Endoscopic (EMR/ESD) should be abandoned. Residual adenomatous tissue is detected in the surgical margins in 0-37% of TEM procedures and positive surgical margins are independent risk factors for local recurrence [8,16]. Despite such high positive-residual-margin rates, reported recurrence rates are significantly lower, ranging from 3-16% [17].This could be explained by the fact that diathermic damage to the remaining adenomatous tissue during the dissection may cause the sterilization of the margins. Another risk factor for local recurrence is the size of the adenoma. In our case, the colo-rectal wall is always excised at a distance of approximately 5mm around the polyp. Since a local recurrence is relatively common after excision of adenomas larger than 5 cm, a strict clinical and endoscopic follow-up is highly recommended in these cases. However, TEM has been shown to be an important therapeutic option even in the treatment of recurrent adenoma, when the endoscopic resection is not feasible. Several series have reported on the safety and effectiveness of TEM in the treatment of recurrent adenoma and no increased perioperative morbidity and no further cases of local recurrence have been described [8,18-23]. TEM technique has shown to be highly efficacious in several retrospective and prospective case series with reported recurrence rate of 0-19% and complication rate of 2-21 % [24].

Conclusion

TEM is the safest and most effective treatment modality available for colorectal adenomas, with significantly higher complete resection and lower local recurrence rates than conventional transanal excision. Further studies are needed to evaluated the safety and efficacy of TEM compared with EMR/ESD. Adenomatous polyps confined to the superficial submucosa (i.e. pT1 sm1),

well or moderately differentiated, without lymphovascular invasion, are the only malignant lesions currently suitable for TEM. In skilled hands TEM is a conservative, safe, and feasible option for selected colorectal mucosal lesions with low risk for perioperative morbidity and mortality. It seems an effective substitute to traditional approaches for such tumors. Additional clinical studies are needed to further demonstrate its acceptability on a large scale.

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Obituary

Prof. Bheemsen Sannacharya Raichur
(20/05/1928 - 20/01/2015)

Dr Raichur hailed from an educated, middle class family of Dharwad, where he completed his high school and pre-medical college education. In 1948, he secured admission in the Veterinary Medical of Mumbai and completed the course in 1952. On the basis of creditable performance in the said course he sought and was granted admission to the Grant Medical College, Mumbai. For a second time, he was a medical graduate in 1957. As an undergraduate student he was always on the forefront of social and cultural activities of the college.

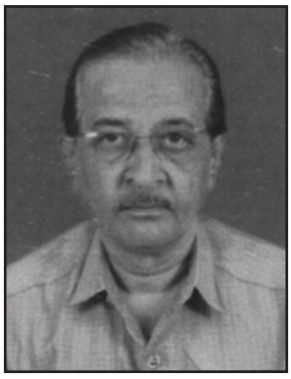
He joined the Pathology School for pursuit of post graduate studies in Pathology and Microbiology and obtained M. D. in 1961. Having been trained in an institute like the J. J. Group of Hospitals, where the number of autopsies is largest (2000 Clinical and about 15000 Medico Legal, per year), Anatomic Pathology, gross as well as Microscopic, was his forte. Through hard and sincere work he climbed the ladders of promotion and became the Professor and Head of Pathology. In that capacity he served at the Medical Colleges in Nagpur and then Pune, from where he retired in (31/05/1986). Thereafter he served Medical College of Pravara Rural Medical Sciences till 1993 in the capacity of founder Professor and Head of Pathology.

He remained a dedicated teacher throughout his academic career. Well wisher of his students, he was always a most fair and friendly examiner, whichever university and examination he went to. He encouraged post graduate students of his departments to undertake research projects, publish their findings and to present them in regional and national conferences, a legacy from his teacher, Dr. R. K. Gadgil.

Peacefully and without much suffering, he left for his heavenly abode on the early morning of 20th January 2015, at Solapur. He is survived by his wife, a son, a daughter and grand children. With the family, we condole his death. May his soul rest in peace.

(Dr. Ulhas Wagholikar)

Obituary



Dr. Vijayrajan Ganesh Aundhakar
(Birth 11th January 1954, Death 1st February 2014)

Dr. Vijayrajan Ganesh Aundhakar passed his M.B.B.S. from G.M.C. Miraj and M.D.Physiology from B.J.Medical College, Pune. He joined as a lecturer in Pathology for a year & then in Physiology from 9th September 1980. He was an excellent medical artist and used to prepare slides for slide projector presentation of many authors for research society conferences with various letterings, fonts, diagrams, pictures till the computer came into existence.

He has prepared original teaching models in Physiology which were presented & won prizes in conferences. He was invited to present all models in 32nd All India APPI conference at Hydrabad.

Dr.Vijay has shown his artistic skills in Medical Expo 1984, organized by State Government of Maharashtra, Indian Science Congress organized by University of Pune in 1988, 34th APPI conference organized by Physiology Department B.J.M.C. in December 1988. He had prepared a video film on Frog's heart experiment displayed in APPI conference in Pune which was appreciated by delegates all over India.

Dr.Aundhakar Sir was a multifaceted personality. Very few people know that he used to write scripts of all Indian languages. Delegates were always welcome by blackboards written by him & All India delegates of APPI conferences were welcome by "Aapka Hardik Swagat Hai" written in all Indian languages by him.

Dr.Aundhakar Sir worked in B.J.Medical College, Pune, Dr.V.M.M.C. Solapur, G.M.C.Bombay. He became Professor & Head at G.M.C. Latur & G.M.C. Miraj and worked only for the students. He was appreciated as "Best Teacher" all over Medical Colleges in Maharashtra. He worked for Dr. Ambedkar Medico's association, National Service Scheme (N.S.S.) of University and Chairman of B.J.Co-operative store.

Dr. Aundhakar Sir used to do oil painting and those who have seen his painting like 'The Last Supper' portraits of Asha Bhosale &Indira Gandhi, Jawaharlal Nehru. Could not believe that an excellent Medical teacher like him can paint such beautiful portraits.

Dr. Aundhakar Sir has been the only person who organized the 17th Annual conference of the research society when he was lecturer in Physiology in 1990. He motivated all staff members to become life members. Unfortunaely due to this enthusiasm to teach Physiology to students all over Maharashtra, he had accepted transfers at many Medical Colleges in Maharashtra and that resulted into his untimely premature death. We are all sure that his excellent teaching, his artistic skill, his music skill, and above all his friendship with all students for the benefit of all his students he has created a special place in the heart of all of us. We all will miss and remember him forever.

'May his soul rest in peace.'

---- From Teachers & Students of Physiology

Obituary

Dr Abhijit Dasgupta
DOB: 29 April 1983
DOD: 16 July 2014

Dr Abhijit Dasgupta was the only child of his parents, his father retired from defence establishment and mother being housewife.

He completed his schooling from Loyola High School Pune and completed MBBS and MD (Medicine) from BJ Medical College. He was one of the most sincere student and stood first in both examinations. After that, he did his DM in Neurology at GB Pant hospital, New Delhi and was Assitant Profressor In Neurology at Bharati Vidyapeeth Medical College, Pune.

Abhijit was a core physician at heart and loved Clinical Neurology and liked to teach. In a short span of career he had many publications to his credit.

Apart from his academic achievements 'Dasu' as his friends called him will always be fondly remembered as a kind, humble and warm hearted person always ready to help others. He also had a uncanny sense of humour with his sarcastic punch lines fondly known as 'Dasu jokes' amongst his friends.

His untimely demise was shoking for everyone. May his soul rest in peace and his parents have strength to bear with this enormous loss.

Contributed by :

Dr Nilesh R Palasdeokar

Assist Prof Neurology

BJGMC and SGH, Pune

The Research Society

B. J. Medical College And Sassoon General Hospitals, Pune - 411 001

ANNUAL REPORT

(April 2013 To March 2014)

Dear Life Members,

I. GOVERNING COUNCIL:

The office-bearers of the current Governing Council (2013-2014) were :

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Vice-President	Dr. Maya Jamkar
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Dr. S.P Rao community Medicine

Dr. Sunita Menon Biochemistry

Dr. Medha Khandekar Pathology

II. MEMBERSHIP:

Following members have been enrolled as life members.

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Dr. Nagnath Redewar	Dr. Kala Baviskar
Dr. Vaijayanti Gaikwad	Dr. Pravin Shimpi
Dr. Uma Ramaswamy	

III. NEW RESEARCH SCHEMES AND OTHER ACTIVITIES : No new research projects were received.

International workshop was held on - curriculum development with Dr. Shivyogi Bhusnutmath, Dean Academic affairs St Georges University school of Medicine, St Georges, Grenada West Indies. In this workshop problems in medical education were discussed with possible solutions. This was attended by M.E.T cell members of our college, Representatives of M.E.T cells of AFMC and Bharati Vidyapeeth Medical college, Pune and faculty members of Pre, Para and clinical branches of our college.

Two Research methodology wokshops for resident doctors were held.

IV. MEDICAL JOURNAL OF WESTERN INDIA: Volume 41, issue no.1 was released on the occasion of inauguration of annual conference of Research society of B. J. Medical college and Sassoon general hospitals Pune. It had an editorial on millennium development goals : Maharashtra, by Editor Dr S.P Rao. had 6 original articles, 4 reviews, one article on Obstacles and recommendations for adaptation of art and science of Kangaroo mother care practices at resource limited center in Maharashtra by Dr. Sandhya Khadse Professor of Pediatrics. There were 6 case reports and one current view article on Health hazards of e-waste.

Volume 41 issue no. 2 was released in July 2013. it had

an Editorial by Dr. J. V. Dixit on "How many doctors do we need?",10 original articles and 3 case reports.

V. ANNUAL CONFERENCE :

A. The 40th conference was held between 5th to 7th March 2014 by the Department of community Medicine under the able guidance of the organizing secretary Dr. P. S. Adhav There were 1219 delegates. The conference was inaugurated by Padmashree. Dr. S. M. Hardikar in the presence of Dr. Satyanarayana from Department of health, Govt of India.

B. Total Number of Poster Presentations were 63, Total number of Case Reports were 43 and Total number of Oral Presentations were 83.

C. Dr. B. B. Dixit oration was delievered by Padmashree Dr. S. M. Hardikar. The topic was "Research in Medicine"

D. There was a full day pre-conference workshop on Clinical Trial, study Designs and Data Analysis. The number of participants was 628. The Maharashtra Medial Council granted 2 credit points to the workshop and four credit points to the Conference. The Workshop was inaugurated by Dr. S. M. Sapatnekar, WHO consultant.

E. The following Symposia and panel discussions were held during scientific programme1. Panel discussion on "Malnutrition: Battle for healthy India. the following speakers took part- Dr. Raji Nair, Dr. Bharti Kulkarni, Miss vandana Krishna. Dr. Geeta Dharmatti and Dr. Kanade

2. Symposium on "Resurgence of Malaria and other vector borne disease: role of Medical College".Thepaticipants were Dr. H. B. Prasad, Dr. Rina Tilak, Dr. Paresh Shah, and Dr. Awate

3. Symposium was held on "Cosmetic Surgery: Present and Future trend". the speakers were Dr. Parag Sahastrabuddhe, Dr. Anand Joshi, Dr. Satish Arolkar and Dr. UddhavPatil

4. Another Symposium on "Preventive Cardiology: Mitigation Strategies" was conducted and the speakers were Dr. Jagdish Hiremath, Dr. Rajiv Adkar, Dr. Nityanand Thakur

5. Panel Discussion on: The Craft of Scientific Paper Writing" was held. the speakers were Dr. Satyanarayana, Dr. Payal Bansal, Dr. Ravi Wankhedkar, Dr. Amtav Banerjee

6. Symposiumon "Tele-Medicine: Health Care Delivery with Technology was held. the following topics were discussed" the speakers were Dr. Telang, Dr. B. S. Ratta, Dr. S. Wagh, and NIC

7. Symposiumon "Trends in Replacement Surgery". the speakers were Dr. Parag Sancheti and Dr. Vijay deshmukh

PRIZES- Apart from annual prizes the recipients of regular prizes of the society are as follows

1. Dr. K. B. Niphadkar Award Rs. 1000 Sushma Kulkarni Dept. of Pathology, DY Patil Med. College
2. Dr. K. B. Niphadkar Award Rs. 1000 Deb A Dept. Of Microbiology, BJGMC
3. Suchintan Trophy [Rolling] Rs. 1000 Rajni Shivkar Dept. of Biochemistry, BJGMC
4. Harshwardhan Prize Rs. 500 Rajni Shivkar Dept. of Biochemistry, BJGMC
5. Dr. A. R. Bhadkamkar Award Rs. 100 Sheetal Joshi Dept. of Anatomy, BJGMC
6. Dr. Mrs. V. A. Bhadkamkar Award Rs. 100 Sandeep Patil Dept. of Pharmacology, BJGMC
7. Dr. M. B. Gharpuray Award Rs. 1500 Swati Mittal Dept. of Skin, BJGMC
8. Dr. S. J. Kinikar Award Rs. 1000 Akhil Patil Dept. of Medicine, BJGMC
9. Dr. S. J. Kinikar Award Rs. 1000 Vikrant Deshmukh Dept. of Medicine, BJGMC
10. Roentgen Teachers Trophy Rs. 2000 Sandeep Bendale Dept. of Radiology, BJGMC
11. Dr. E.P. Patil Award Rs. 2500 Sandeep Sharma Dept. of Orthopaedics, DY Patil Med. College
12. Dr. Ajit Gokhale Prize Rs. 1000 Mathew J Dept. of Pharmacology, DY Patil Med. College
13. Dr. Jejurikar Award Rs. 400 Shital Dikle Dept. of CVTS, BJGMC
14. Dr. D. J. Patil Award Rs. 1000 Sachin Sanagar Dept.

of CVTS, BJGMC

15. Best paper in the category of Junior Faculty (teachers with less than 5 years experience) Rs. 500 K Madhuri Dept. of Microbiology, BJGMC
16. Best paper in the category of Senior faculty (teachers with more than 5 years experience) Rs. 500 Anita Basavaraj Dept. of Medicine, BJGMC
17. Best paper in the UG category Rs. 500 Tanvi Shah BJGMC
18. 2nd Best paper in the session on Poster presentations Rs. 500 Agarwal PB Dept. of Physiology, BJGMC
19. 3rd prize in the session on Poster presentation Rs. 150 Mihir Joshi, BJGMC
20. 3rd prize in the session on Poster presentation Rs. 150 Radhika Puntambekar BJGMC
21. 2nd Best paper in the session on Interesting case presentation Rs. 500 Sampat Chougule Dept. of Medicine, BJGMC
22. 3rd prize in the session on Interesting case presentation Rs. 300 Abhijeet Karad Dept. of Medicine, BJGMC

Total **Rs. 17200/-**

VII. AUDITORS

Deekey and Company Pune was continued as Auditor for this period

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Research Society
B.J.M.C. & S.G.Hs, Pune 411 001.

ACKNOWLEDGEMENTS

The honorary secretary is thankful to the members of the governing council, past office bearers, Editor -in- chief, and the members of the organizing committee of the annual conference for their valuable help in fullfiling the objectives of the trust.

Medical Journal of Western India

Instructions To The Contributors

Medical Journal of Western India is a peer reviewed journal. It is published biannually. It accepts original articles, review articles related to the different disciplines, case reports and short communications in the field of clinical practice and medical education. Case reports of only unique and rare character will be accepted. Papers are published in English. Submitted papers are accepted after peer review. To achieve wider dissemination of knowledge and information, the published articles can be accessed online at www.bjmcpune.org/medicine.htm.

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1. Undertaking : The manuscript must be submitted with a statement, signed by all the authors, regarding the originality and authorship.

2. Covering Letter : It should include name, designation, address, contact details including e-mails and mobile number of the corresponding author.

3. Title page : It should include the title and the names of authors. Surname of authors are to be followed by initials and affiliations. Title should be informative, specific and short.

4. Abstract and key words : Abstract should not exceed 250 words for Original Articles and 150 words for case report.

For original article, the abstract must be in a structured form (Objectives, Methods, Results and Conclusion) and explain briefly what was intended, done, observed and concluded. Case report should have sections as: *abstract, introduction, case presentation and discussion.*

Key words: should not exceed 5- 6 words.

5. Manuscripts should be typewritten, with wide margin on an A-4 size paper. It should be of 3000-4000 words for review article, 1500 to 2000 for original article and 750 to 1000 for case report.

Tables/Figures / Graphs.

i) The tables should appear in the text itself and should be numbered in Roman numbers (Table. I, II etc.)

ii) Should be limited to the essential (preferably not exceeding four).

iii) For figures: should be referred to as figures and numbered in Arabic numerals (E.g. Figure 1, 2)

Photographs:

i) The photographs should be of high definition type with legends. Maximum 4 photographs for original article,2 for case report.

ii) The size of the photograph should not exceed 8 X 12 cm.

iii) Coloured photographs will be charged extra as per the applicable rates.

6. Acknowledgment : Acknowledge only those who have contributed to the scientific content or provided technical support. Sources of financial support if any, should be reported.

References:

i) The list of references should be in the Vancouver style.

ii) References should be cited in the text in Arabic numbers. E.g Our observations are similar to those of Dowling et al.1.

iii) Maximum number of references: for reviews articles-40, original articles-20, case reports-06, short communications- 10

Note: 1.Accuracy of the references cited is the sole responsibility of the author/authors.

2. Views expressed by the authors do not necessarily reflect those of the Research society.

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(ISOTRETINOIN CAPSULES USP 10 mg)

Tretin-Iso® 20

(ISOTRETINOIN CAPSULES USP 20 mg)

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