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Indexed with

Index Copernicus-International and Indian Science Abstract

Index

CONTENTS **Page No.**

Editorial

Are Generic Drugs as Good as Brand Named Drugs ?
Shilin N. Shukla 03

Innovative Diagnostic Tools for Tuberculosis: Shifting Core Approach Globally. .
Viral Dave, Urvesh V Shah..... 05

Original Articles

Analysis of Outcome Of Ultrathin Epidermal Skin Grafting In Stable Vitiligo
Anshul Jain, Nayan Patel, Yogesh shah 10

A Study on Screening of Various Premalignant and Malignant Conditions of Uterine Cervix by PAP Smear
Rupal shah, Jalpa Bhatt, Anupama Dayal, Sadhna Kothari, S M Patel 14

Knowledge and Perception Regarding Medical Certification of Cause of Death Among Resident Doctors of One of The Teaching Hospitals of Ahmedabad, Gujarat
Venu Shah, D V Bala 20

Target Controlled Infusion Vs Manual Controlled Infusion of Propofol For General Anaesthesia In Adults
Heena R. Parikh 24

Study of Treadmill Exercise Stress Test In Tobacco Smokers In Relation With Coronary Artery Disease
Urja Dholakia, Jaydeep Kagathara, Anand Mistry, Suresh Goyal, Lopa Vaidya, Chirag Shah 29

Bacteriological Profile and Antibiotic Susceptibility of Common Isolates From Burns Patients At Tertiary Care Level Hospital
Sanjay Rathod, Payal Dholaria, Parimal Patel, Jayshree Pethani, Bimal Chauhan, P.D.Shah..... 33

FNAC: An Easy and Accessible Diagnostic Aid For Cervical Lymphadenopathy A Study of 150 Cases
Sadhna Kothari, Arpit Gohel, Anupama Dayal, Rupal Shah, S M Patel 37

Study of Laparoscopic Intraperitoneal Meshplasty In Abdominal Surgeries Using Prolene Mesh
Shah A.G., Bhatt Hardik, Raswan Uday Singh, Patil Salil, Mangal Akshay kumar, Nalawade Nikhil . 41

Study and Comparison of Lipid Profile of Normal, Premature and Small For Gestational Age Neonates
Hetal Jeeyani, Sheela Bharani, Anjana Shah 45

Study of Pulmonary Function Tests In First Year M.B.B.S. Students of GCS Medical College In Ahmedabad, Gujarat
Anand Mistry, Jaydeep Kagathara, Vilas J. Patel, Suresh Goyal, Lopa Vaidya, Urja Dholakiya, ... 52

Case Reports

Acrodermatitis Enteropathica: A Rare Case Report with Follow up
Pinakin Trivedi, Anjana Shah, Hetal jeeyani, Nayan Patel.....57

An Unusual Case of Parotid Tuberculosis
Vidhyasagar M. Sharma, Sushil D. Akruwala, Shashank Desai, R. I. Dave.....59

Identification of An Emerging Pathogen Pythium Insidiosum From A Case of Onychomycosis
Neha N. Patel, Manisha N. Dhamecha, Urvesh Shah, Nayan Patel 61

Essential Thrombocythemia in A Patient With Portal and Superior Mesenteric Vein Thrombosis
Amar R Shah, Sanjay Chaudhari , Monica Gupta, Menka Shah 64

A Case Report on Classic Ehler-Danlos Syndrome
Nayan Patel, Anshul Jain, Yogesh Shah 66

Unusual Presentation of Tuberculosis With Candida In Maxillary Sinus
Parimal Patel, Sanjay Rathod, Afroz Bloch, P.D.Shah 69

A Case Report: Absence of The Quadratus Femoris Muscle
Kiran Arora, Sudarshan Gupta 71

Guidelines for Preparation of Manuscript 74

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Are Generic Drugs as Good as Brand Named Drugs?

Dr. Shilin N. Shukla, MD

Brand named drugs in the West are often the original molecules. They are often referred to as innovators or pioneers. However, when they are out of patent protection, other companies also manufacture and market their copies. They are called the generic drugs. The generic drugs are expected to be the copies of brand-name drugs and have exactly the same dosage, indications, effects, side effects, route of administration, risks, safety and strength as the original drug. In other words, their pharmacological effects are expected to be exactly the same as those of their brand-name counterparts [1]. In USA, 80% prescriptions are for generic drugs. The use of generic drugs is expected to grow over the next few years as a number of popular drugs come off patent through 2015 [2]. In India, their use is ever increasing.

The generic drugs are often substantially cheaper than the brand-name drugs. Therefore, often people may feel that their quality and effectiveness may have been compromised in an effort make them less expensive products. The Indian Drug Controller as well as the US-FDA (Food and Drug Administration) try to ensure that safety and effectiveness of the generic drugs are at par with the brand-name drugs. When a drug, generic or brand name, is mass-produced, very small variations in purity, size, strength, and other parameters are allowed [2]. A study evaluated the results of 38 published clinical trials that compared cardiovascular generic drugs to their brand name counterparts. There was no evidence that brand name heart drugs worked any better than generic heart drugs [2]. FDA recently evaluated 2,070 human studies conducted between 1996 and 2007 that compared the absorption of brand name and generic drugs. The mean difference in absorption into the body between the generic and the brand name was 3.5 % [3].

To be cheap is not to be low in quality and less in safety. The side effects are being monitored by FDA and investigated. The adverse effects are often due to the inert ingredients. The generic drugs are cheaper only because the manufacturers had not spent anything in their development and initial marketing. Because the companies developing a new drug have to spend substantially on research, development, marketing and promotion of the new drug, a patent is generally granted for an exclusive right to sell the drug for a specified period when the patent expires, other manufacturers may apply for permission to manufacture and market generic versions of the drug. They can afford sell it cheaply. That generates competition and further bring down price [1]. In 2010 alone, the use of FDA-approved generics saved $158 billion, an average of $3 billion every week [4].

Sometimes, because of competition, litigations and legal strategies come into play. Brand-name drug companies try to extend the period of market exclusivity on their drugs and prevent generic competition. With the change in the patent law that protects both the process and the molecule, innovators have an upper hand in such litigations in India. There is often aggressive litigation to preserve or extend patent protection on brand-named medicines. This process is referred to by critics as *ever greening* . Beyond the initial patent time, 5 year extension of patent may be granted by FDA in certain situations.

Whereas original brands are needed for development of science and knowledge, the generics help make these inventions affordable and available to a larger population. Controlling agencies have to ensure quality and efficacy. The Drug Controllers require that generic drugs work as fast and as effectively as the original brand-name products. They apply the same standards for all drug manufacturing facilities [1]. Drug Controllers require all drug manufacturers to perform bio-availability and bio-equivalence / pharmacokinetic tests on their products to ensure efficacy.

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Some companies manufacture both brand-name and generic drugs. In USA the 50% of generic drug production is by companies manufacturing the original brands. Trademark laws in the United States do not allow the generic drugs to use name of the original brand [1]. Though they have same efficacy, they should not look alike and hence the generics may have different colours, flavours or combinations of inactive ingredients as compared to the original medications. It is possible, rarely, that one of these inert ingredients may cause an allergic reaction or react with other medication prescribed to the patient. For this reason, a doctor may choose to prescribe the brand name drug instead of the less expensive generic drug.

In summary, there is no substantial difference between generic and brand name medications, other than price and appearance. Unless the doctor specifically prescribes the brand name medication, one may save a lot of money by purchasing its generic version without compromising quality or effectiveness.

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Innovative Diagnostic Tools for Tuberculosis: Shifting Core Approach Globally...

Viral Dave, Urvesh Shah***

Background :

Tuberculosis is an age old disease known to mankind taking toll of life if not treated appropriately with lots of suffering and parting behind several numbers of secondary cases among contacts of patient. Geographically, the burden of TB is highest in Asia and Africa. India and China together account for almost 40% of the world's TB cases. [1] About 60% of cases are in the South-East Asia and Western Pacific regions. Tuberculosis (TB) remains a major global health problem. It causes ill-health among millions of people each year and ranks as the second leading cause of death from an infectious disease worldwide, after the human immuno- deficiency virus (HIV). The latest estimates revealed that there were almost 9 million new cases in 2011 and 1.4 million TB deaths (990 000 among HIV- negative people and 430 000 HIV-associated TB deaths). This is despite availability of treatment that will cure most cases of TB.[1]

In 2009, out of the estimated global annual incidence of 9.4 million TB cases, 2 million were estimated to have occurred in India, thus contributing to a fifth of the global burden of TB. The nationwide annual risk of tuberculosis infection (ARTI) study conducted in 2000-2003 suggest the incidence of new smear positive TB cases in the country is estimated as 75 new smear positive cases per 100,000 population. The prevalence of TB has been estimated at 3.8 million bacillary cases for the year 2000, by an expert group of Govt. of India. World Health Organization (WHO) estimated TB mortality in India was 23/100,000 population in 2009.[2] The clinicians, who treat tuberculosis, are always in search of the best diagnostic test form a wide variety of choices. Here, common diagnostic tests are described shortly with comparison of their advantages and disadvantages. Special consideration is given to Xper/RIF, as WHO has specially advised large scale roll-out for the same to incorporate such advance diagnostic technology in national Tuberculosis control programme to all countries.

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Definitions of TB cases : [1]

Definite case of TB is a patient with Mycobacterium tuberculosis complex identified from a clinical specimen, either by culture ***or by detection of MTB specific gene with various nucleic acid techniques***. In countries that lack laboratory capacity to routinely identify M. tuberculosis, a pulmonary case with one or more initial sputum specimens positive for acid-fast bacilli (AFB) is also considered to be a definite case, provided that there is functional external quality assurance with blind rechecking.

Microscopy, Culture, Nucleic acid amplification techniques (NAAT) and Antigen detection provide direct evidence of Tuberculosis infection while tests for indirect evidence are: Immunological tests, Cytology and histopathology, ESR and ADA.

Need for newer diagnostic method :

The tubercle bacillus was invented by Robert Koch in 1882 and thereafter methods of staining these microorganisms were developed to assist the diagnosis of the disease. Early diagnosis of tuberculosis in patients is a challenging task especially in the pauci-bacillary and extra-pulmonary forms. The conventional methods that are still the mainstay of the diagnosis of TB are like Tuberculin test/ Mantoux test, sputum smear microscopy and radiological examination as well other imaging methods have their own limitations.

Sputum smear microscopy requires 10,000 to 1, 00,000 organisms/ ml and acid fast bacilli could be any pathogenic or saprophytic mycobacteria.[3] Sputum-smear microscopy the most commonly used diagnostic test for TB is more than 100 years old. Acid Fast Bacilli (AFB) staining of clinical material followed by smear microscopy remains the most cost effective and frequently used test for detection of TB, BUT the major drawback of sputum smear microscopy

is its poor sensitivity, especially to be ~70% in a recent review.[4] The advantages of AFB microscopy are well known: it is inexpensive to perform, is very specific in high prevalence settings and detects the most infectious subset of patients. For these reasons, microscopy rightly retains its primary role in case detection in developing countries like India.

In many ***developed countries***, the value of sputum smear examination for acid-fast bacilli has been diminished by increasingly common phenomenon of Non tuberculous *Mycobacteria* being found in sputum of patients. This has resulted in a marked decrease in the specificity and positive predictive value of the sputum smear, in some cases to as low as 50%. [5][6] In clinical practice, the value of a test with a sensitivity of 50% and a specificity of 95% is vastly greater than a test with the same sensitivity but a specificity of only 50%.

Various novel diagnostic modalities for Tuberculosis :

Optimized smear microscopy :

Considerable research has been done to identify methods that can optimize the yield and accuracy of smear microscopy. These include light-emitting diode (LED)-based fluorescence microscopy (FM), use of sputum processing methods and optimization of specimen collection for same-day diagnosis (i.e., front-loaded microscopy).[7] FM is on average 10% more sensitive than conventional microscopy. Specificity of FM and conventional microscopy is similar. FM is associated with improved time efficiency. Centrifugation and overnight sedimentation preceded by any of several chemical methods (including bleach) for concentration of bacilli are more sensitive than direct microscopy; specificity is unaffected by sputum-processing methods.

Improved and newer *broth-based culture systems :*

Research has shown that liquid systems are more sensitive for detection of mycobacteria and may increase the case yield by 10% compared with solid media (LJ media). The results can be available within days rather than weeks.[7] Automated liquid culture systems such as BacT/ ALERT (bioMerieux Inc, Durham, NC, USA) and BD BACTEC MGIT (Becton Dickinson, Sparks, MD, USA) are currently considered the gold-standard approach for isolating mycobacteria. However, liquid cultures are prone to contamination, require stringent quality assurance systems and training standards and are more expensive. Cultures for mycobacteria are not widely available in many parts of the world mainly due to the expense involved and diagnosis rests mainly on clinical findings, radiographs, and sputum smear examination.

Interferon- γ release assays (IGRAs) :

Tuberculin skin test (TST) is being used for diagnosis of latent tuberculosis infection since long. A major advance in recent times for diagnosis of latent tuberculosis has been the development of T-cell-based interferon- γ release assays (IGRAs). IGRAs are in vitro tests based on interferon- γ (IFN- γ) release after stimulation of pre-sensitized T cells by antigens such as early secreted antigenic target 6 (ESAT6) and culture filtrate protein 10 (CFP10) which are more specific to *M tuberculosis* than the purified protein derivative (PPD). Two IGRAs are commercially available: the (QuantiferonH TB-Gold In Tube test (QFT-IT) and the T-SPOT:TB assay.

The drawback is that sensitivity of TST and IGRAs are not consistent across tests and populations, they do not directly detect *M tuberculosis*; they merely indicate a cellular immune response to recent or remote sensitization with M tuberculosis. Because IGRAs cannot distinguish between latent and active TB, a positive IGRA result may not necessarily indicate active TB. A negative IGRA result would not conclusively rule out active disease in an individual suspected to have TB (similar to the results of a TST).[7] Certain investigators [8] suggest that IGRAs had a sensitivity of 90% and a specificity of 98% when compared with tuberculin skin test results while a recent American trial[9] for the same among cohort of HIV positive and HIV negative individuals yield not very promising results.

The sensitivity of QFT in detecting active TB disease in children does not seem to be significantly better than that of TST. Machingaidze et al [10] in their study meta-analysis of QFT sensitivity specifically in children showed a significantly reduced sensitivity of QFT in detecting active

TB disease within high-burden TB settings when compared with low-burden TB settings.

For serological Tests, it is strongly recommended by WHO[11] that commercially available serological tests for pulmonary and extra-pulmonary TB are not to be used for diagnostic purpose. They provide inconsistent and imprecise findings. There is no evidence that existing commercial serological assays improve patient outcomes, and high proportions of false-positive and false-negative results may have an adverse impact on the health of patients.

Measurement of ADA (Adenosine Deaminase) levels in pleural, pericardial and ascitic fluid has high sensitivity and specificity for extrapulmonary TB. It is also being used for diagnosis of Pulmonary tuberculosis from the clinical material (Broncho-Alveolar Lavage) revealed by Bronchoscopy also.

Nucleic Acid Amplification Assays (NAA) :

After identification of three *Mycobacterium tuberculosis* specific protein antigens (ESAT 6, CFP10, and TB 7.7), several new diagnostic tests have emerged [12][13] including two technologies co-developed with FIND (Foundation for Innovative New Diagnostics) which are loop mediated isothermal amplification (Eiken Chemical Co Ltd, Tokyo, Japan), a simplified manual NAAT designed for peripheral laboratory facilities and Xpert MTB/RIF assay (Cepheid, Sunnyvale, CA, USA), a fully automated NAAT platform that can detect TB and Rifampin resistance. Both of these tests are formatted for use outside reference centers, to replace or supplement microscopy at health centers and district hospitals. FIND is currently evaluating these tests in high-burden countries.[7]

For smear, sensitivity was an expected 50 - 70% and for culture it was nearly 100%. For the NAA assays, sensitivity was in the 80 84% range. Thus, the overall accuracy of the NAAs- are much higher than that of smear and not very much lower than that of culture.[6] At present, the cost of NAA tests is around $50 $100 per assay in most laboratories: quiet costly for individual laboratory. But, in certain settings such as centralized laboratories to which a large number of specimens can be quickly and easily referred, these tests may in fact be economically feasible and clinically useful.[14]

In some developed countries, it is now recommended that AFB smear and NAA be performed on the first sputum smear collected. If smear and NAA are both positive, tuberculosis is diagnosed with near total certainty. If the smear is positive and the NAA negative, then test the sputum for inhibitors by spiking the sputum sample with an aliquot of lysed M. tuberculosis and repeating the assay. If inhibitors are not detected, the patient can be presumed to have non-tuberculous mycobacteria (NTM). If sputum is smear-negative but NAA positive, send an additional sputum sample. If positive, the patient can be presumed to have tuberculosis. If both smear and NAA are negative, an additional specimen should be tested by NAA. If negative, the patient can be presumed not to have infectious tuberculosis.[6] The ultimate definitive diagnosis rests on response to therapy and culture results.

These recommendations are expensive and technically quiet difficult to be implemented in developing countries like India. Sputum smear microscopy is commonly used to measure both infectiousness of a patient and response to therapy. No data are available regarding the utility of NAA for these purposes. NAATs have high specificity and positive predictive value but they have lower (and highly variable) sensitivity and negative predictive value for all forms of TB, especially in smear negative and extrapulmonary disease.

Xpert MTB/RIF :

The Xpert MTB/RIF is a new rapid molecular test that can diagnose TB and rifampicin-resistant TB within hours simultaneously using the GeneXpert platform. It is a real-time PCR assay that is a design-locked, all-within-cartridge test and has demonstrated high performance and could be deployed in a range of low and middle income settings [15][16] ***It has recently been endorsed by the World Health Organization (WHO) as a promising new rapid diagnostic technology that has the potential for large-scale roll-out*** (www.who.int/tb/laboratory). The test entails fewer biosafety and human resource requirements than

conventional culture or DST. Furthermore, its sensitivity for detecting TB is signi?cantly higher than that of microscopy, particularly in patients with HIV infection.

As the cost of Xpert is considerably higher than that of smear microscopy, there is a concern among TB program managers and policy makers that Xpert may not be cost-effective in low and middle income settings. Although Xpert is a highly promising technology, it has incomplete sensitivity for smear-negative TB and rifampicin resistance and does not detect resistance to isoniazid and other drugs.[3] geneXpert is also not free from disadvantages. There are a number of disadvantages which include: a very stable electricity supply is required, the instrument needs to be recalibrated annually, and temperature ceiling is critical and obviously cost of the test (around US$9.98 for India after negotiation by FIND and help from other NGOs.) [17] Xpert is commercially produced and sold at concessional prices.

Rapid Detection of Drug Resistance :

Conventional methods used to diagnose multidrug-resistant TB (MDR-TB) rely on culturing of specimens followed by drug susceptibility testing (DST). Results take weeks to obtain and not all laboratories have facilities to perform DST for second-line drugs.

In parts of the world where MDR tuberculosis is a significant problem, rapid detection of drug resistance would be greatly beneficial to tuberculosis treatment and control efforts. In most instances, detection of rifampin resistance alone would suffice to signal the need for treatment with second line drugs. Rapid detection of rifampin resistance is technologically feasible by several approaches that examine either genotypic abnormalities (by identifying mutations in the region of the *M. tuberculosis rpoB* gene associated with rifamycin resistance) or actual phenotypic resistance (persistence of the organism in a rifamycin-containing medium). Conventional AFB culture and drug susceptibility testing (DST) requires significant laboratory infrastructure and long time.

Several molecular based methods have been developed recently including the commercially available line probe assay, the Genotype MTBDR plus assay [18] which can resolve the problem. They can diagnose resistance to RIF (in rpoB gene) and INH (in katG and inhA genes) within 8 hours. WHO has approved the use of line probe assays (LPA) for rapid MDR-TB screening.[7] In 2009, a newer assay (GenoType MTBDRs/assay)[19] became available. This assay allows the simultaneous detection of the *M tuberculosis* complex and resistance to fluoroquinolones or aminoglycosides/cyclic peptides or ethambutol from smear-positive pulmonary specimens or culture isolates. Thus, the combined use of GenoType MTBDR *plus* and GenoType MTBDRs/assays allow the rapid detection of XDR-TB. LPAs currently require complex technology and are thus limited to use in reference laboratories.

Conclusion :

The final goal of World Health Organization or any other international or national agency dealing with public health and for control of infectious diseases at large is first try to stop the transmission i.e., to eliminate the disease and ultimately eradicate the disease by vigorous measures. For developed countries, it is comparatively easier task than developing countries like India with limited resources. Various Operational researches related to geneXpert/RIF are going on globally as well as in our country to find out the possibility of implementing it or similar diagnostic modalities of tuberculosis as a core-test for Tb diagnosis. The final aim is to get results rapidly and with more accuracy, i.e., molecular based rapid diagnostic test with more sensitivity and specificity. ***WHO did also emphasize that the test (geneXpert/RIF) does not eliminate the need for conventional microscopy culture and drug sensitivity testing, as these are still required to monitor treatment progress and to detect resistance to drugs other than rifampicin.*** To implement the geneXpert/RIF as routine diagnostic procedure for Tuberculosis and to incorporate same in the national health programme for control of Tuberculosis in countries like us, we will be in need of a long time span and economic support certainly. The peripheral and rural centers, where the burden of tuberculosis is maximum are still running scarcity of

electricity, water and obviously skilled manpower to implement the necessity of these modern techniques for early and accurate diagnosis of Tuberculosis. In our opinion, though WHO and other agencies are suggesting implementation of such recent technologies for diagnosis of TB, it will be better to switch over gradually from sputum smear microscopy to other techniques, which indeed will require training of all medical and para medical staff involved in TB control activities. Initially it can be started with tertiary care hospitals of urban regions with advance technology and competent staff available and then gradually taking over rural and remote area after necessary manpower training with at least minimum infrastructural laboratory facility. Without directly relying upon other countries' researches, we can implement such projects on pilot base under various conditions in our own country and can recommend changes to policy makers as per our own requirements and ground facilities.

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Analysis of Outcome of Ultrathin Epidermal Skin Grafting In Stable Vitiligo

Anshul Jain, Nayan Patel**, Yogesh shah****

Abstract

Background: Ultrathin epidermal grafting is a new surgical modality for management of stable vitiligo. **Objective:** To assess the outcome of ultrathin epidermal grafting. **Method:** 35 Indian patients with stable vitiligo were treated with ultrathin epidermal grafting and followed for 24 weeks. **Results:** Almost 63% patients got excellent results with ultrathin epidermal grafting at the end of 24 weeks follow up, 37% patients got good colour match with minimal complication at donor as well as recipient site. **Conclusion:** Results suggest that ultrathin epidermal grafting is a good alternative to medical treatment in stable vitiligo.

Introduction :

Vitiligo is a common acquired pigmentary disorder, usually progressive, melanocytopenic of obscure aetiology, clinically manifested by circumscribed achromic macules often associated with leucotrichia.

The disease affects subjects of either sex with a heritable constitutional predilection. Vitiligo and other depigmented diseases, although not life threatening are considered as a cause of psychological disturbance and social stigma, because of severe cosmetic disfigurement produced by irregularly distributed depigmented patches interspersed among the normal skin colour giving an unsightly appearance.

The various medical therapeutic modalities used for treatment of leucoderma have certain limitations and several patients are left with some areas which do not regain pigment. Surgical modalities are therefore useful especially in stable or non- progressive type of depigmentation. Several surgical techniques such as punch grafting[1,2,3], suction blister grafting[4], ultra thin skin grafting[5], cultured and non-cultured melanocyte grafting[6,7] etc. have been used with success.

Objective: To assess the outcome of ultrathin epidermal grafting as an alternative to medical treatment in stable vitiligo.

Method :

A study of 35 patients of age group 10-55 years of which 15 were males and 20 were females was carried out from Jan 2011 to Jun 2012 with stable and non progressive (for at least two years) preferably localized lesions of vitiligo. All patients were of skin prototypes IV and V. All patients were followed for 24 weeks after procedure. None of the patients had any keloidal or bleeding tendencies, past history of koebnerisation or coexistent herpes simplex infections. The study was carried out at the Dermatology department of a teaching hospital in Ahmedabad city of Gujarat, India.

For selecting a patient for the surgical modality, following points were taken into consideration[8]

a) The location of the anatomical areas to be treated,

b) Extent of the vitiligenous areas,

c) Whether there were several small lesions or one large lesion,

d) Type of vitiligo or leucoderma,

e) Texture of the skin on the recipient and donor areas,

f) Absence of history of Koebner phenomenon, and

g) Absence of history of hypertrophic scars and keloids.

All patients were counselled prior to the procedure regarding the risks, benefits and anticipated outcome. A written informed consent was taken. Detailed history was taken so as to know the age of onset, duration of lesions, site of lesions, state of progression, medical treatment taken and response in the form of re-pigmentation and to confirm no change in the lesion or new lesion in the previous 2 years.

Ultra thin epidermal grafting was performed in single or multiple sessions depending upon the area of skin to be treated. The donor site chosen for harvesting the grafts was the anterior aspect of upper thigh in all patients. The whole procedure at the donor as well as the recipient sites was done under the influence of local anaesthesia using 1%

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lignocaine in all the patients. To take ultrathin epidermal grafts from the donor area, the skin on the thigh was stretched both proximally as well as distally by applying a tangential force and epidermal grafts of uniform thickness were obtained using Silver's knife. The grafts taken differed from the traditional split-thickness grafts as there was no or minimal dermal tissue on their under surface. The quality of the grafts was gauged by means of their translucent nature; grafts showing any dermal component in the form of a whitish under surface were discarded; only translucent grafts were used for the procedure.

The recipient area was first cleaned with povidone iodine lotion and then dermabraded using the manual dermabraders. Dermabrasion was performed 0.5 mm beyond the margin of the recipient area to prevent any perigraft halo of depigmentation. The ultrathin epidermal grafts suspended in isotonic saline were then spreaded onto the dermabraded recipient sites with the help of glass slides and graft spreaders. The recipient area was then covered with double layer of antibiotic (chlorhexidine) coated gauze dressings. Oral antibiotics were also administered for 1 week after the procedure. Saline-soaked gauze dressing was then applied over the same, and lastly, a pressure dressing was applied to secure the grafts. The donor site was also covered with double layer of antibiotic-coated gauze dressing followed by pressure dressing. The dressing at the recipient area was kept for duration of 7 to 9 days and then the dressing was removed carefully to keep the grafts in place.

Results:

Majority (51%) of the patients were young, mostly unmarried females in the age group 21-30 years. No difference in degree and rapidity of repigmentation was seen in the two sexes though the number of female patients outnumbered the male subjects in the study group (20 out of 35). 24 out of 35 patients had disease duration of up to 5 years. Only 9 patients out of 35 had duration of 5-10 years and 2 patients had duration >10 years.

When the degree of repigmentation was compared with the mean duration of the disease prior to transplantation in each group, a clear association was seen, indicating that patients with long disease duration repigment less well than patients with a shorter disease duration. The 'age of onset' variable was not significant nor could any conclusions be drawn about the age of onset in relation to the outcome of the treatment.

Among the study subjects, 21 out of 35 patients had only single macule. Distributions of lesions were as shown in Table no 1.

Table 1: Sites of Disease in the Patients

Location	No. of cases	Percentage
Face	03	8.5
Neck	01	2.8
Lip	09	25.7
Trunk	01	2.8
Arms	02	5.7
Elbow	-	-
Hand	04	11.4
Legs	05	14.2
Knee	01	2.8
Feet	09	25.7
Total	**35**	**100**

Among the 35 patients treated, 4 patients of vitiligo had leucotrichia at the recipient site and the color of their hair did not show any pigmentation even after 24 weeks of follow up. None of the patients had any other associated autoimmune or endocrine disorders. No dropouts, till 24 weeks were noticed in the study during follow up.

Of the total 35 patients of UTSG (Ultra Thin Skin Grafting), only 1 patient had rejection of graft from the recipient site at the end of fifth postoperative day because of infection at the site as proper post-operative care was not taken by the patient since the graft involved whole of the lower lip and was dressed, making it important to maintain the hygiene while eating.

Out of the 35 patients treated, 25 patients were treated with post-op PUVAsol (Psoralen plus solar radiation) therapy, 5 patients with basic fibroblast growth factor and sun-exposure and the rest of the 5 patients with topical corticosteroid cream (mometasone furoate 0.1%) application. Maximum response with early repigmentation was found in the group treated with PUVAsol therapy. So it appears that the patients having more UV light exposure proved to have a higher degree of repigmentation of the transplanted lesions at follow-up, compared with the less UV light group. More than 60% of the patients observed a repigmentation of more than 50% at the end of 4 weeks while it took approximately 8-12 weeks to show complete results in most of the cases.

No koebnarization or scarring was seen at the donor site in any of the 35 patients treated with UTSG. Hyperpigmentation was noticed in 8(22.8%) patients while hypertrophy at the donor site was seen in 2(5.71%) patients. Out of the 35 patients 1(2.85%) came with secondary bacterial infection of the donor site after 2 weeks of surgery. No patient reported with hypopigmentation of donor site. In our study group, none of the patients developed hypertrophic scar or keloids at the recipient site. The most common complication at the recipient site was hyperpigmentation and hypopigmented perilesional halo, experienced in 4(11.33%) and 4(11.33%) patients respectively. Few patients who had developed hyperpigmentation after complete healing got a perfect color match by 24 weeks with the application of the steroid cream. 1(2.85%) patient did not have any repigmentation due to rejection of the graft because of infection in the 1st week of follow up i.e. on removal of the dressing. None of the patients reported reactivation of vitiligo lesions.

The extent of pigmentation was measured using the serial photographs taken on the follow up visits at 1, 2, 4, 8, 10 and 24 weeks with the pre-operative documented photographs. Physician's response was graded as excellent (4), good (3), fair (2) or poor (1) depending upon the extent of pigmentation of the recipient area, the color match with the surrounding skin, the uniformity of pigmentation with minimal complications on the donor as well as recipient areas with subsequent follow up visits. Out of the 35 patients, excellent color match was present in 22 (62.85%) patients, while 13 (37.14%) patients had good and 1 (2.83%) patient each experienced fair to poor response at the end of 24 weeks.

In our study group 29 (82.8%) patients had a diffuse uniform pigmentation. There was only a single patient with lesions over lower lip that had a poor outcome of the procedure. Five (14.27%) patients had incomplete patchy pigmentation which was attributed to excessive mobility of the joint in the vicinity of the procedure site, which resulted in dislocation of the epidermal graft and consequently led to inadequate results. Except in few cases, all patients showed drying and peeling of the necrosed grafted skin by the end of 2 weeks. 29(82.83%) patients showed slight pigmentation and erythema at the end of two weeks while 6 (18.71%) patients showed pigmentation from border at the end of 2 weeks. A patient with lesion over the lower lip , who had a poor outcome of the procedure experienced swelling, purulent discharge from the grafted site and finally ended up with depigmentation at the site.

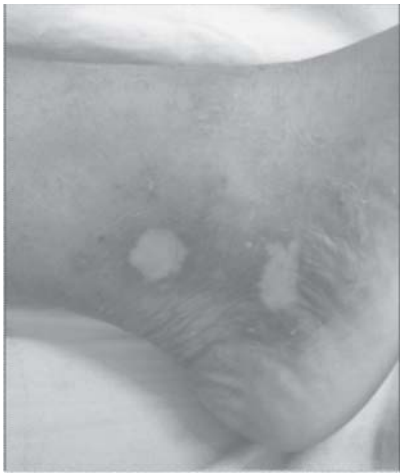

Figure 1 : Pre procedure vitiligo

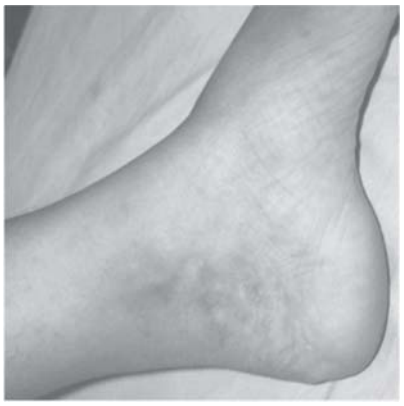

Figure 2 : Post procedure after 24week

Discussion :

Vitiligo which is stable and does not respond to medical lines of treatment can be managed by certain surgical procedures in the form of tissue or cellular grafting techniques like ultra thin skin grafting[9], suction blister grafting, mini punch grafting, thin-thiesch's split thickness graft or autologous melanocyte culture[10] . Any form of resistant vitiligo like focal or segmental vitiligo or even any residual lesions of patchy or generalized vitiligo can thus be treated satisfactorily in affected patients. Ultra thin epidermal grafting, wherein a thin sheet of epidermis is taken from an appropriate donor area and then transplanted on the dermabraded vitiligo lesion [11], offers certain advantages over other tissue grafting procedures like mini-punch grafting and suction blister grafting. The

cosmetic outcome achieved after ultra thin skin grafting at the recipient as well as the donor site depend the most on the quality of the grafts taken. With ultrathin grafts having no accompanying dermal tissue, the quality of pigmentation achieved at the recipient site is usually excellent.

By definition, an ultra thin skin graft is one that contains the full thickness of epidermis along with some portion of the papillary dermis. The grafts used in the present study were all translucent grafts without any whitish tissue at the base. With the use of ultrathin grafts, there are minimal chances of scarring at the donor site owing to the loss of epidermis alone from the area. It was observed that if one is able to achieve an ultrathin graft at the donor site, the same site can even be repeatedly used for taking similar grafts in the future. In fact, it was found that it becomes easier to obtain a graft at the next session as the epidermis gets easily separated once it has regrown over the already-used donor area.

Grafting procedures are supplemented with PUVAsol [11] [12] [13] ,or topical corticosteroid, or Fibroblast growth factor to increase the chances of repigmentation as well as to achieve quicker results. PUVAsol therapy scores over topical steroids and Fibroblast growth factors as a treatment option in vitiligo. Thus one can use PUVAsol to achieve a rapid repigmentation when it is used as a supplementary therapy along with any grafting procedure. PUVAsol has been used in combination with mini-punch grafting and autologous epidermal cell culture procedure with good results.

Complications described in case of Thin thiesch's split-thickness skin grafting at the recipient site are hyperpigmentation, curling of the graft, milia formation, and lastly graft contracture leading to achromic fissures between the individual grafts or perigraft depigmentation at the margins. Similarly, there are chances of scarring and hyper- or hypo-pigmentation at the donor site. We did observe some perigraft depigmentation in our patients, but the other adverse effects were not seen in our study. This can possibly be ascribed to the use of ultrathin grafts in this study population.

Split-thickness skin grafting is claimed to be the most successful tissue-grafting procedure in vitiligo and this has been our observation as well. With the use of ultrathin skin grafts, the outcome at both the donor as well as the recipient sites can be improved further. The procedure, when performed in carefully selected patients with a proper technique, can certainly provide excellent cosmetic results in resistant stable vitiligo. Concurrent use of PUVAsol therapy gives faster and better cosmetic results.

Limitation of Study

Considering natural history of vitiligo and unstable nature of disease, long term follow up of recipient and donor site is required for loss of pigmentation which could not possible in this study. Many other surgical modalities are available for stable vitiligo. For further evaluation of ultrathin grafting technique, comparison of these modalities in terms of efficacy and complication is required.

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A Study on Screening of Various Premalignant and Malignant Conditions of Uterine Cervix by PAP Smear

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Abstract

Background: Cancer of cervix remains an important health problem for women worldwide. PAP smear is an effective means of screening for premalignant and malignant conditions of cervix **Aim:** To identify patterns of various epithelial abnormalities in premalignant and malignant conditions of cervix by PAP smear. To find out prevalence of various risk factors of cervical carcinoma among study subjects. **Methodology:** The study is based on 500 PAP smears reported at Pathology Department at one of the tertiary care hospital of Ahmedabad city of Gujarat, India, during the period of February 2011 to September 2012. Cervical smears were prepared from symptomatic women, stained by RAPID PAP STAIN and reported according to TBS. **Results:** Epithelial abnormalities were found in 4.8% of smears, ASCUS in 0.4%, AGCUS in 0.2%, LSIL in 3%, HSIL in 1% and SCC in 0.2%. Maximum number of cases 162(32.4%) were in the age group of 31-40 years. Chronic vaginal discharge was the most common clinical complaint of women with abnormal cervical cytology detected in 62.5% cases. A statistically significant association of abnormal cervical cytology was observed with poor socioeconomic status, early age at first coitus, poor vaginal hygiene and low literacy levels. **Conclusion:** PAP smear is a simple, safe and effective screening tool to detect various premalignant and malignant conditions of cervix at an early stage.

Key words: Papanicolaou Smear, Squamous Cell Intraepithelial Lesion, Cervical Cancer

Introduction :

Death incidence figure show uterine cervical cancers as a top leading cause of cancer in all developing countries [1]. Nearly 4 lacs new cases of cervical cancer are diagnosed annually worldwide and 80% of them are from the developing countries. Currently, 1.7 million cases of cervical carcinoma cases are registered in the developing countries and as many as 5 to 13 million women have precancerous lesions [2]. As per the National Cancer Registry, uterine cervical cancer follows breast cancer by showing the second highest incidence in all cancers of women [3]. Invasive cervical cancer incidence can be brought to a low level through early detection by using several screening techniques. PAP smear is a sensitive test for screening of cervical lesion and classified as per The Bethesda System (2001) [4]. Getting a PAP smear done is not a difficult task. An ordinary lady health worker or nurse can be trained to get it. General practitioners and family physicians should not miss the opportunity to take PAP smear from patients with complaint of chronic vaginal discharge.

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Aims :

To identify various epithelial abnormalities in premalignant and malignant conditions of cervix by PAP smear. To find out prevalence of various risk factors of cervical carcinoma among study subjects.

Methodology :

The present study is based on 500 PAP smears reported at Pathology Department at one of the tertiary care hospital in Ahmedabad city of Gujarat, India, during the period of February 2011 to September 2012.

PAP smears were prepared from patients with various gynecological complaints like chronic vaginal discharge, post coital bleeding, inter menstrual bleeding, lower abdominal pain, something coming out per vaginum, postmenopausal bleeding etc. Patient's history included caste, age, socioeconomic status, literacy, age at marriage, age at first coitus, parity, menstrual history, any surgeries under gone, clinical complaints, contraception used, obstetric history etc.

Per speculum examination of cervix was carried out before the PAP smear and findings were reported on Proforma. PAP smear was taken with a disposable wooden spatula. Scrapings from squamocolumnar junction of cervix were spreaded on a glass slide and dipped in methanol- spirit container. The sample was sent to Pathology Department for cytological examination. PAP smears were stained by

Rapid PAP Stain (Bio Lab Diagnostics ltd, certified ISO 9001:2000) and mounted in DPX. Each smear was carefully examined by two cytopathologists and reported according to The Bethesda System, developed in 1988 & modified in 2001, which assesses the following factors: Adequacy of specimen, general categorization and descriptive diagnosis.

1. Negative for intraepithelial lesion or malignancy

a. Organisms
   - T. vaginalis
   - Fungal organisms morphologically consistent with candida spp.
   - Shift in flora suggestive of bacterial vaginosis
   - Bacteria morphologically consistent with actinomyces spp.
   - Cellular changes consistent with Herpes Simplex virus

b. Other non neoplastic findings
   - Reactive cellular changes
   - Atrophy

2. Epithelial cell abnormalities

a. Squamous cells
   - ASCUS :Atypical Squamous Cells of Undetermined Significance
   - ASC-H :Atypical Squamous Cells cannot exclude HSIL
   - LSIL: Low Grade Squamous Cell Intraepithelial Lesion encompassing mild dysplasia or CIN 1
   - HSIL : High Grade Squamous Cell Intraepithelial Lesion encompassing moderate to severe dysplasia, CIN 2 or 3 with features suspicious for invasion
   - Squamous cell carcinoma

b. Glandular cells
   - AGCUS : Atypical Glandular Cells of Undetermined Significance
   - Endocervical Adenocarcinoma

3. Other malignancies

Results:

Sociodemographic data analysis:

Table 1 shows frequency of normal and abnormal PAP smears in relation to age groups: It can be observed from analysis of 500 cases that maximum number of cases 162(32.4%) were in 31-40 years age group, followed by 161(32.2%) in 41-50 years age group. Table 1 also suggests that out of 162 cases in 4thdecade, 157(96.9%) were normal and 05(3.08%) were abnormal, followed by 153(95%) normal and 08(5%) abnormal out of 161 cases in 5thdecade and so on. The same suggest that chances of getting abnormal cervical cytological finding were on increasing trend as the age of females' increase which is also statistically significant.

Table 1: Frequency of normal and abnormal PAP smears in relation to age groups

Age Group (years)	No. of Pap smears	Normal cytology	Abnormal cytology
21-30	88 (17.6%)	87 (98.9%)	01(1.1%)
31-40	162(32.4%)	157(96.9%)	5(3.08%)
41-50	161(32.2%)	153(95%)	8(5.0%)
51-60	62(12.4%)	56(90.3%)	6(9.7%)
61-70	21(4.2%)	18(85.7%)	3(14.2%)
>70	6(1.2%)	5(83.3%)	1(16.7%)
Total	**500**	**476(95.2%)**	**24(4.8%)**

Chi square value: 12.84, P=0.024

With reference to caste and literacy level (Table 2), 454(90.8%) cases were Hindu and 46(9.2%) cases were Muslim. Abnormal cytology was detected in 22 (4.9%) cases of Hindu and 02(4.4%) cases of Muslim (P >0.05). This indicates that caste has no significant effect on cervical carcinoma incidence. Out of 500 cases, 353 (70.6%) cases were illiterate and among this group, 6.23% had abnormal cytological changes on PAP smear examination (p=<0.05). This indicates that illiteracy has a significant effect on cervical epithelial abnormalities.

Table 2 : Relation of literacy level and caste of women with cervical epithelial changes.

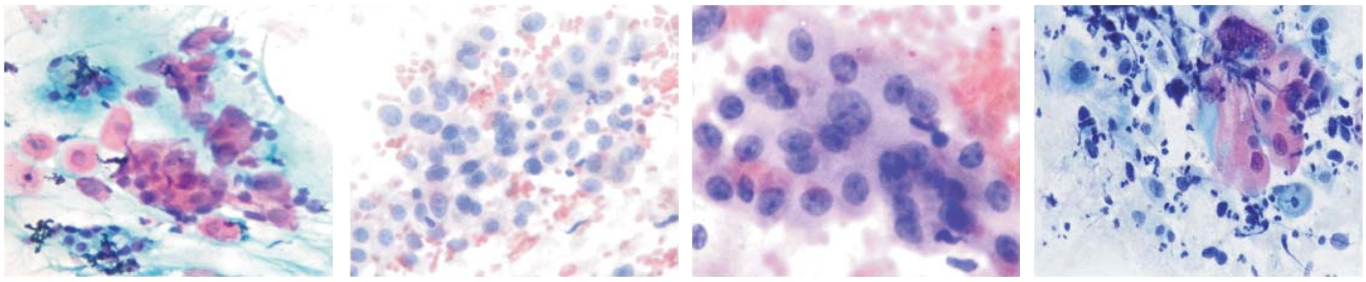
	Literate	Illiterate	P value	Hindu	Muslim	P value
Normal Cytology	145 (98.6%)	331 (93.7%)	<0.05	432 (95.1%)	44 (95.6%)	>0.05
Abnormal Cytology	2 (1.3%)	22 (6.23%)		22 (4.9%)	2 (4.4%)	
Total	147 (29.4%)	353 (70.6%)		454 (90.8%)	46 (9.2%)	

Analysis of premalignant and malignant conditions of cervix (Table 3) shows that out of 500 cases, 24(4.8%) were abnormal, 257(51.4%) were inflammatory, 170(34%) were normal (NILM) and 36(7.2%) were atrophic. Out of 24 abnormal cases, LSIL was detected in 15 (3%), HSIL in 05(1%), ASCUS in 02 (0.4%), AGCUS in 01(0.2%) and SCC in 01(0.2%). Adenocarcinoma was not found in any of the studied cases.

Table 3 : Detailed elaboration of relationship between age of women and cellular changes in cervical epithelium.

Age group (Years)	NILM (34%)	Atrophic (7.2%)	Inadequate (2.6%)	Inflammatory (51.4%)	Neoplastic lesions (n=24, 4.8%)					TOTAL
					ASCUS	AGCUS	LSIL	HSIL	SCC	
21-30	30	00	02	55	00	00	00	01	00	1(4.1%)
31-40	65	01	04	87	01	00	04	00	00	5(20.8%)
41-50	53	11	05	84	01	00	05	02	00	8(33.3%)
51-60	16	13	01	26	00	01	05	00	00	6(25%)
61-70	06	07	01	04	00	00	01	01	01	3(12.5%)
>70	0	04	00	01	00	00	00	01	00	1(4.1%)
Total	170	36	13	257	02 (0.4%)	01 (0.2%)	15 (3%)	05 (1%)	01 (0.2%)	24

The malignant features of LSIL, HSIL and SCC are shown in figure 1(A-D).



A B C D

Figure 1 : (A) LSIL (Pap, X400) ; (B) HSIL (Pap,X400) ; (C) HSIL (Pap,X400) ; (D) SCC (Pap,X400)

Among 24 positive cases (Table 4), 23 (96%) were above the age of 30 years and 20(83.3%) were of low socioeconomic class. Regarding contraception, 07(29.1%) were using oral contraceptive pills, 04(16.67%) were using IUCD and 03(12.5%) were using barrier method. The age at first coitus was below 20 years in 17 (70.8%) while 05(20.8%) cases were having history of abortion. Most common clinical complaint was of vaginal discharge which was detected in 15(62.5%) cases.

Table 4: Various epidemiological variables in patients with abnormal smears.

Epidemiological Variables		Frequency and Percentage (n=24)
Age	Below 30 year	1 (4.1%)
	Above 30 year	23(96%)
Economic group *	Lower class	20(83.3%)
	Upper class	04(16.6%)
Method of Contraception	IUCD	04(16.67%)
	Barrier contraceptive	03(12.5%)
	OC Pills	07(29.1%)
	No contraception	10(41.6%)
Age at 1st coitus	<20 years	17(70.8%)
	20-30years	07(29.1%)
Vaginal discharge	Abnormal vaginal discharge	15(62.5%)
	No abnormal vaginal discharge	09(37.5%)
Abortion	Once	02(8.3%)
	More than one	03(12.5%)
	No abortion	19(80%)

* Economic group as per Modified Prasad Classification.

Discussion :

Cancer of the cervix is considered to be an ideal gynaecological malignancy for screening as it meets both test and disease criteria for screening. It has a long latent phase during which it can be detected as identifiable and treatable premalignant lesions which precede the invasive disease. Cost of screening for premalignant lesions is very less compared to cost of treatment after invasive lesions have developed [1]. Most cervical cancers start from an area of dysplastic epithelium (Transformation Zone) which can be detected well by taking a good PAP smear[5] - the best screening programme worldwide recommended for sexually active women[6,7] .

The PAP smear was originally developed by George Papanicolaou in 1930s. It has been the method of choice for cervical cancer screening since the 1950s, proving valuable for mass screening and enabling detection of lesions at an early stage enough for effective treatment.

Age is significantly associated with development of premalignant and malignant conditions of cervix. A higher percentage (96%) is found in the above 30 years age group in most studies. In the present study, 32.4% women were in 4th decade which is comparable to results of Chankapa YD et al[8] and M S Bal et al[9] with 33.7% & 33.3% respectively. Majority of women enrolled in this study were illiterate housewives (70%) belonging to low socioeconomic class(83.3%) and low economic class by itself is a risk factor for development of cervical neoplasia[10]. These results are comparable with 88% women with low socioeconomic class in study of Khattack[11]. Our study shows that patients were having scarce knowledge and information about cervical cancer and its risk factors.

Several authors emphasize that early initiation of sexual activity seems to be positively related with this disease and that sexual intercourse at an early age is an important risk factor [12]. In present study 70.8% cases with positive cytology have first coitus below 20 years of age. Our results are comparable to Khattack et al[11] with 62% women having first coitus below 20 years of age.

Overall frequency of normal, inadequate, atrophic and inflammatory smears was 34%, 2.6%, 7.2% and 51.4% respectively. 4.8% cases were having abnormal cervical cytology. These results are comparable to Chankapa YD et al[8] with 4.85%, Khattack[11] with 2.6%, Nausheen[13] with 4.16% and M S Bal et al[9] with 5% abnormal cervical smears. In present study, 3.0% cases of LSIL, 1.0% case of HSIL, 0.4% case of ASCUS and 0.2% case of SCC were found. These results are also comparable to MS Bal et al [9]

having LSIL -2.7%, HSIL -0.7%, ASCUS-0.3% and SCC-1.0%. Other studies of Patel et al [14] and Anuradha & Sinha[15] have detected similar results.

In the present study, most common clinical complaint was chronic vaginal discharge(62.5%) and this can be attributed to poor vaginal hygiene, age at marriage below 20 years and perhaps presence of sexually transmitted diseases. This result is comparable to M S Bal et al[9] with 71.4% and Khattack[11] with 75% cases with complaint of chronic vaginal discharge.

Out of the 24 smears with abnormal cytology, the number of women using barrier contraception was the lowest (12.5%) which indicates that barrier contraception has a protective effect on cervical inflammations. Khattack[11] et al detected similar results, with women using barrier contraception having the lowest incidence (10.6%) of abnormal cervical cytology.

80% of women with abnormal cervical cytology are not having history of abortion in current study. This indicates that h/o abortion has no significant effect on cervix. Similar results are detected by Chankapa YD's[8] with 74.4% women without history of abortion having abnormal cervical cytology. Among risk factors associated with morbidity among these women, age at marriage below 20 years and illiteracy leading to poor vaginal hygiene are observed to be the most important. Some other studies have also reported a significant association of cancer cervix with these risk factors[16].

Summary and Conclusion :

Significant associations of premalignant and malignant condition of cervix were observed with poor vaginal hygiene, early age at first coitus, low socioeconomic class and low literacy levels. Muslim women were more prone: probably as a result of early marriage, multiparity, long sexual life and illiteracy. ASCUS and AGCUS epithelial abnormalities were detected in fair number of cases (0.6%) and they are warning signals for clinicians for close follow up of these patients. Cases of LSIL are common in 4th, 5th and 6th decade which indicate that PAP smear must be applied as a routine screening method for sexually active women of these age groups.

Thus by early diagnosis and treatment of premalignant conditions, we can prevent development of invasive malignant diseases. This study shows barrier contraception has protective effect and number of abortions has no significant effect on cervical cancer.

Recommendations :

The burden of cancer in developing countries is very high which calls for better awareness programme and regular screening. Premalignant and malignant lesions of cervix are fairly common in our country. Cervical cytology by PAP smear is simple, safe and effective tool to detect premalignant and malignant lesions of cervix at an early stage and is recommended as a routine test for all sexually active, young females with or without complaint of chronic vaginal discharge. Chronic vaginal discharge is the leading complaint detected in abnormal cervical cytology and this calls for clinicians to at least perform a per speculum examination as a primary screening tool in areas with limited resources for screening cervical cancer[17].

The American Cancer Society recommends that all women should have cervical cancer screening after 3 years of beginning of coitus. It is also recommended every 1-2 years for women who have crossed the age of 30 years. Those who had 3 consecutive negative PAP results may be screened after 2-3 years.

Abbreviations used :

ASCUS : Atypical Squamous Cells of Undetermined Significance.

AGCUS : Atypical Glandular Cells of Undetermined Significance.

LSIL : Low Grade Squamous Cell Intraepithelial Lesion.

HSIL : High Grade Squamous Cell Intraepithelial Lesion.

SCC : Squamous Cell Carcinoma.

TBS : The Bethesda System.

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Knowledge and Perception Regarding Medical Certification of Cause of Death Among Resident Doctors of One of The Teaching Hospitals of Ahmedabad, Gujarat

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Abstract :

Background: Medical Certification of Cause of Death (MCCD) scheme is basically a part of International Statistical Classification of Diseases and Related Health Problems (ICD) formulated by World Health Organization. MCCD scheme is implemented in almost all the teaching hospitals of Gujarat. All resident doctors are given training regarding accurate filling up of MCCD forms. The knowledge of resident doctors needs to be evaluated in order to find out whether they are having any difficulties in filling up of MCCD forms. Present study was conducted among the resident doctors working in one of the teaching hospitals of Ahmedabad. **Objectives :** 1) To examine the knowledge regarding MCCD among the resident doctors involved in the process of filling Medical Certificate of Cause of Death. 2) To know about their perception in filling up of MCCD forms. **Materials and Method :** A cross sectional study was conducted among the 60 resident doctors of one of the teaching hospitals of Ahmedabad using pretested questionnaire. **Results:** Three- fourths of doctors had received training for issuing MCCD forms. Most of them (63.3%) opined that there is need of refresher training. All the three definitions (immediate, antecedent and underlying cause of death) were correctly answered by 16.6% of respondents. Among those(8.3%)who faced difficulties in filling forms, most of the doctors (60.0%) reported concluding exact cause of death was difficult. One-fourths of the doctors were not satisfied with the accuracy and completeness of MCCD forms filled by them. **Conclusion:** Correct knowledge regarding various aspects of MCCD was lacking. There is a need of refresher training for all the doctors who had received training.

Key words : Knowledge and perception, Resident doctors, MCCD forms.

Introduction :

Death certification is a public health surveillance tool and is very important because case specific morbidity and mortality statistics often come from death-certification data.[1] Mortality statistics is essential for welfare of the community, health planning and management of programmes, deciding priorities for policy makers and for prevention and control of an epidemic[2]. The Medical Certification of Cause of Death(MCCD) Scheme is basically a part of International Statistical Classification of Diseases and Related Health Problems (ICD) formulated by World Health Organization(WHO). As such, the causes of deaths are classified according to ICD in three character category which is mandatory level of coding for international reporting to the WHO mortality databases and for general international comparisons.[3]

Accurately filled up MCCD forms can supply very crucial information. It can provide a feedback about the pattern of mortality and morbidity prevailing in particular area. On the contrary, if the MCCD recordings are poor, then the whole exercise will remain a futile effort as the reliability of information will be questionable. Key to avoid such problem is to give training to the doctors regarding accurate filling of MCCD forms. Several studies have showed that a simple educational intervention can improve the accuracy of death certificate completion and reduce major and minor error rates in the section of cause of death.[4,5] Evaluation of such kind of educational intervention is also required. In the teaching hospitals, resident doctors are usually involved in process of filling the MCCD forms. Accurate knowledge regarding each and every aspects of MCCD is desirable among them. As such the training programmes for accurate filling of MCCD forms are conducted on regular basis in co-operation with government health officials. Present study was conducted in order to evaluate the knowledge of resident doctors regarding Medical Certificate of Cause of death.

Materials and Methods :

A cross sectional study was carried out at one of the teaching hospitals of Ahmedabad city. Resident doctors who fill up MCCD forms in routine practice were interviewed. Open-ended questionnaire was used for data collection. Proforma consisted general information of resident doctors. They were asked to define the immediate,

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antecedent and underlying cause of death. Questions regarding difficulties felt while filling up the forms were also included. Informed verbal consent from all the participants was taken. The study was conducted during the period of May- July 2009. Those doctors who were not filling up MCCD forms routinely were excluded from the interview. Also resident doctors who have recently joined the post graduate course were excluded from the study as they were not accustomed in filling of MCCD Forms. Total 60 doctors were interviewed. Data was entered and analysed using appropriate statistical package.

Results :

Resident doctors from 8 major clinical departments (Medicine, Surgery, Pediatrics, Gynecology, ENT, Ophthalmology, Orthopedic and Psychiatry) were interviewed to evaluate their knowledge and practice of filling up of MCCD forms. Total 60 resident doctors have participated in the study.

The purpose behind selecting only resident doctors was that they fill up MCCD forms in routine practice. Those who were not filling up MCCD forms routinely were excluded from the interview. Out of 60 resident doctors, 23(38.3%) were second year residents while 27(45%) were third year residents. (Table 1)

Table 1 : Distribution of Resident doctors according to their designation

Designation	Training received n(%)	Total n(%)
Resident- 1st Year	0(0)	7(11.7)
Resident- 2nd Year	21(46.6)	23(38.3)
Resident- 3rd Year	22(48.8)	27(45)
Senior Resident- 4th Year	2(4.6)	3(5)
Total	**45(100)**	**60(100)**

Each doctor was asked whether he / she had taken any training on MCCD in the past. On the basis of their reply they were categorized into two-categories viz. training received and training not received. It was found that 45(75%) doctors had received training on MCCD after joining their post graduate course. Most of the respondents were from Pediatrics, Surgery and Medicine department. (Table 2)

Table 2 : Department wise distribution of respondents according to their status of training regarding MCCD (n=60)

Departments	Training		Total
	Received n (%)	Not received n (%)	
Pediatrics	12 (85.7)	2 (14.3)	14(23.3)
Surgery	12 (80)	3 (20)	15 (25)
Medicine	8 (66.6)	4 (33.4)	12 (20)
Obstetrics-Gynaecology	7 (55.5)	4 (44.5)	11(18.3)
Orthopedic	2 (50)	2 (50)	4 (6.66)
Ophthalmology	2 (100)	0 (0)	2(3.33)
Psychiatry	1 (100)	0 (0)	1(1.6)
ENT	1 (100)	0 (0)	1(1.6)
Total	**45 (75)**	**15 (25)**	**60 (100)**

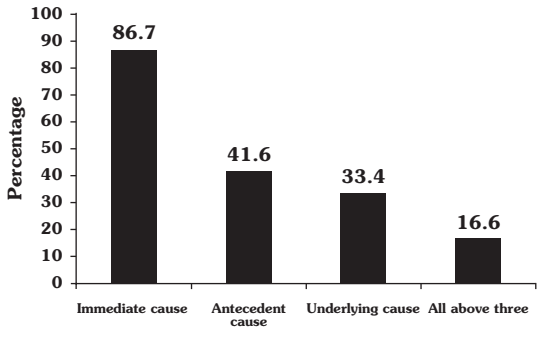
Among those who were trained, 38 (63.3%) were of the opinion that there is a need for refresher training. (Table 3)

Table 3 : Distribution of respondent according to their opinion about requirement of training for filling of MCCD forms

Refresher Training	No.	Percentage (%)
Necessary	38	63.3
Not Necessary	20	33.4
No Reply	2	3.3
Total	**60**	**100.0**

Respondents were asked about the correct definition of immediate, antecedent and underlying cause of death. It was observed that 52(86.7%), knew correct definition of immediate cause. Antecedent cause was known to 25 (41.6%) residents while underlying cause was known to 20 (33.4%) resident doctors (figure1).

Figure 1 : Frequency of respondents having accurate knowledge regarding Immediate, Antecedent and Underlying cause of death



Further analysis of data revealed that only 10(16.6%) of the respondent knew correct definition of all the three causes of death. It was found that trained study subjects (n=45) were having comparatively more knowledge about immediate (95.6%), Antecedent (51.1%) and underlying cause (64.4%). Results were significant statistically for Immediate and underlying cause. (P<0.05) (Table 4)

Table 4: Status of correct knowledge among those who had received training (n=45)

Cause of death	Knowledge		Chi-square Value	P value
	Correct (%)	Incorrect (%)		
Immediate	43(95.6)	2(4.4)	12.3	<0.05
Antecedent	23(51.1)	22(48.9)	3.8	>0.05
Underlying	29(64.4)	16(35.6)	2.8	<0.05

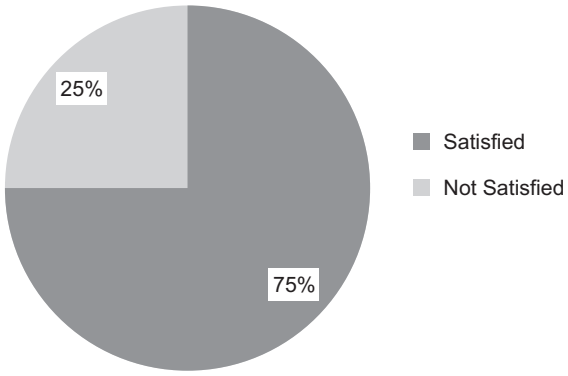
On asking about difficulties felt in filling up of forms, most of the respondents (93.3%) replied that they did not face any difficulty while filling up MCCD forms. Among those doctors who faced difficulties, 3(60%) doctors informed that it was difficult to conclude the exact cause of death. (Table 5)

Table 5 : List of difficulties felt while filling MCCD forms (n=60)

List of difficulty faced while filling up of MCCD forms	Frequency	
	No.	Percentage (%)
In mentioning exact cause of death	3	5.0
Difficulty in mentioning cause of death in some medico legal cases	2	3.3
Do not feel difficulty	55	91.7

Perception of respondents about accuracy of MCCD forms filled by them was noted. It was found that, 45(75%) doctors were satisfied with the accuracy and completeness of the death certificates. Around 25% of the doctors were not satisfied with it.(Figure 2)

Figure 2 : Self-Perception of respondents about the accuracy and completeness of MCCD form



Discussion :

To obtain the correct mortality statistics, it is necessary to raise the awareness among the doctors regarding correct filling up of MCCD forms. At the same time, it would make such efforts more successful if we evaluate their impact. The institute where the present study was conducted is involved in regular training regarding MCCD. In order to find the impact of the training, the study was conducted among the resident doctors involved in filling of MCCD forms. Their knowledge regarding correct filling up of MCCD forms were evaluated. Out of 60 resident doctors, 52(86.7%), knew correct definition of immediate cause. Antecedent cause was known to 25 (41.6%) and underlying cause to 20 (33.4%) resident doctors and only 10(16.6%) respondent knew correct definition of all the three causes of death.In the study of Solanki et al(2005)[6]it was observed that,66.7%, 54.4% and 54.4% doctors gave correct answer for immediate, antecedent and underlying cause of death respectively. Results of present study revealed that correct knowledge regarding all three aspects of cause of death (immediate, antecedent and underlying cause) were more among those who have received training.

In present study most of the respondents (93.3%) did not face any difficulty while filling up MCCD forms. Among those doctors who faced difficulties, 3(60%) doctors informed that it was difficult to conclude the exact cause of death. Similar findings were seen in the study carried out by Dhanunjaya et al (2004).[7] They found that 61% of respondents were not comfortable with filling the MCCD forms. A total 73% of respondents were unaware of the

death certificate completion guidelines in their study. In study of Solanki et al (2005),[6]19.3% of doctors faced difficulty in filling up of MCCD forms.

In our study we found that three-fourths of the doctors were satisfied with the accuracy and completeness of the death certificates filled up by them. However, 25% of the doctors were not satisfied with it. Similar finding was there in the study of Solanki et al (2005).[6]

In present study though it was observed that 75% doctors had received training but on inquiry 38 (63.3%) of them were of the opinion that there is a need for refresher training. Solanki et al (2005)[6]in their study reported that more than 50% of doctors had received training, but 89.5% have asked for a refresher training.Christian et al (2007)[8] has concluded that increased education and better documentation leads to improvements in accuracy and legitimacy of MCCD forms.Dhanunjaya et al (2004)[7] reported that out of 590 resident physicians selected randomly from Graduate Medical Education Residency Directory, 81% requested further training. Myers and Farquhar (1999)[9] also interpreted in their study that the accuracy of death certification could be improved withthe re-implementation of a simple educational intervention. These findings suggest that there is a need for refresher training along with the original training soon after joining residency.

Conclusion and Recommendations :

Correct knowledge regarding various aspects of MCCD was lacking. All post graduate medical students should be given refresher training regarding MCCD, once they enter the post graduate course in order to clarify their doubts regarding filling up of forms. Internship is the compulsory training which every medical students is suppose to under go. It is our recommendation that all intern doctors should be trained in filling up of MCCD forms. So that they can fill up the MCCD forms in future correctly wherever they are posted. Filling MCCD is necessary not only at the teaching medical institutes where post-graduate doctors are working but each and every hospital is in need of doctors, who have expertise in filling MCCD. That is why internship is considered better duration for giving basic training regarding filling MCCD to fresh doctors and a refresher training as mentioned above. It would be beneficial if regular internal audits of filled MCCDs are carried out with regular feedback to the doctors of the hospital who are filling up them.

Limitation of the study : Present study was carried out in single post graduate institute and knowledge of doctors working there was checked. More information can be gathered if similar study is carried out in both teaching and non-teaching hospitals where doctors are involved in filling of MCCD forms.

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Target Controlled Infusion Vs Manual Controlled Infusion of Propofol For General Anaesthesia In Adults

Heena R. Parikh*

Abstract :

Background : Total intravenous anaesthesia, based on administration of propofol combined with an opioid, has become a popular anaesthetic technique. Usually continuous infusion devices either by manual or target controlled are used for induction and maintenance of anaesthesia. This review explains the fundamentals and applications of intravenous drug delivery by TCI (Target Controlled Infusion) as well as MCI (Manually Controlled Infusion). **Objectives :** To assess effectiveness of TCI Vs. MCI with respect to quality of anaesthesia, ease of use, pattern of propofol administration and time to recovery from anaesthesia. **Methodology :** Hundred patients in the ASA I/II (American society of anaesthesiologist) risk groups, were randomly divided in two groups: The TCI (group 1, n=50) and the MCI (group 2, n=50). In both groups, patients were anaesthetized with propofol by infusion, using either TCI (Group one) or MCI (Group two) system. In addition to propofol, patients received Midazolam (0.1 mg/kg), a single dose of fentanyl (2 µg/kg) and 60% nitrous oxide in oxygen. Induction time, Intubation time and recovery time were noted in both groups. Pulse, Blood pressure, SpO_2 and $EtCO_2$ were also noted in both groups. **Results :** Use of TCI resulted in more rapid induction of anaesthesia and allowed earlier insertion of endotracheal intubation ($P<0.05$). Recovery time was far earlier in TCI as compared to MCI. There was no significant difference in haemodynamic variables in two groups ($P>0.05$). Incidence of apnoea was less in TCI group ($P<0.05$). **Conclusion :** The overall preference is there for TCI system as it led to smooth induction, reliable, rapid emergence and titrable maintenance. At the same time improved understanding of drug kinetic, dynamics and interactions has facilitated optimal drug selection and method of administration, which can be easily tailored to clinical requirements.

Keywords: Intravenous anaesthesia, propofol, infusion systems, computer TCI

Introduction :

Total intravenous anaesthesia (TIVA) can be defined as technique of general anaesthesia using a combination of agents given solely by the intravenous route. The provision of anaesthesia by intravenous route using chloral hydrate was documented as early as 1870. Propofol was introduced in clinical practice in 1986 and become widely used as a component of TIVA. It has become popular, practical and possible only in relatively recent times due to suitability of modern anaesthetic drugs for continuous intravenous infusion and development of sophisticated delivery systems of anaesthetic drugs. This new system allows rapid, precise and independent control of amnesia, hypnosis and analgesia.[1]

'Diprifusor ' was the first commercially available TCI system launched for propofol in 1996.[2] Target-controlled infusion (TCI) device offers a means for automatic adjustments of infusion rate of drugs to maintain a desired target concentration. Since drug effect is more closely related to blood concentration than to infusion rate, drug delivery via TCI is capable of creating stable and controllable blood concentration of intravenous anesthetics and analgesics.[3] TCI of propofol allows anaesthetists to target constant blood concentrations and respond promptly to signs of inappropriate anaesthetic depth and accurately predict the time course of drug effect.[4] [5] Accuracy of administration is essential for effective anesthesia with minimal adverse drug effects. Excessive administration may compromise cardiorespiratory system. The basic principle is that anaesthetist sets and adjusts the target blood concentration and depth of anaesthesia as required on clinical grounds.[6]

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Objectives :

The aim of the study was to explicate use of modern TCI systems, the underlying scientific concepts, the relevance for clinical practice and comparison of TCI against MCI with respect to quality of anaesthesia, pattern of propofol administration and time to recovery from anaesthesia.

Materials and Methods :

Total 100 adult patients of American society of anaesthesiologists grade I/II, aged 18-80 years; weighing

40-90 kg, scheduled for planned surgical procedures like spine surgery, modified radical mastectomy, tympanoplasty, radical neck dissection etc. were selected. Permission from institutional ethical committee was obtained before initiating the study. Written informed consent was taken. It was a prospective randomized double blind study. Patients with unstable cardiac conditions, severe liver disease, pregnancy or known allergy to propofol or its emulsion, patients on regular sedatives or narcotic medications were excluded from the study.

Before induction of anaesthesia, the patients', weight, age, sex, height and target of effect site concentration of propofol were entered in to the TCI system. Schnider pharmacokinetic model for propofol was used. [7] Here the anaesthetist has choice of selecting higher or lower target blood propofol concentration and therefore titrated according to clinical signs.[8]

Patients were randomized to one of the following two groups: Group one is TCI (n=50) and Group two is MCI (n=50).On arrival to recovery room, the weight of the patient were measured by electronic weighing machine and height of the patient were measured by height scale. A 20 gauge IV cannula was cited in a forearm vein in all patients and an infusion of ringer lactate 10 cc per body weight commenced prior to the induction of anaesthesia. Minimum standard monitoring like ECG leads, pulse oximetry and non-invasive blood pressure monitoring were used throughout the procedure. All patients received Midazolam (0.1 mg/kg) IV and fentanyl (2 µg/kg) IV prior to induction of anaesthesia. 2 min later propofol infusion was started. Patients were asked to count out aloud during induction and the time to achieve induction was defined as loss of verbal command, were recorded. Patient in TCI group received a propofol infusion driven by a Fresenius Kabi syringe pump (Injectomat TIVA Agilia INT Fresenius). Initial effect site target concentration of propofol was 5-7 µg/ml which for a 50 kg patient and this was titrated upward until loss of verbal command maintained by 2 3.5 µg/ml. Similarly in manual group, propofol was infused at a rate of 600 ml/hr with use of a Fresenius kabi simple infusion pump until loss of verbal command, thereafter the propofol was administered at a rate of 6-8 mg/kg/hr.

After induction with propofol, scoline (2mg/kg) IV was administered slowly to achieve muscle relexation for endotracheal intubation. Ventilation was assisted with maintenance dose of atracurium (0.1mg/kg). Anaesthesia was maintained with oxygen (40%) and nitrous oxide (60%) from a close circuit. Additional analgesia supplemented as per the requirement or patient movement. Propofol administration was adjusted throughout by alteration to either the target concentration or manual infusion system as appropriate. Heart Rate, Systolic and diastolic BP, mean BP, EtCO2 were recorded during pre-incision, early (2 min after incision) middle (10-30 min after incision), late (> 30 min after incision).

Following parameters were recorded in the predesigned study proforma.

1) Induction time (Start of propofol to loss of verbal command)
2) Intubation time
3) Recovery time
4) Orientation
5) Total Propofol consumption

Wake up concentration of propofol 1.5 µg/ml in last 5 min of surgery in TCI group were noted. On completion of surgery, administration of nitrous oxide and propofol were discontinued, reversal was given and the time to recovery (eye opening spontaneously or to verbal command) and orientation (recall of date of birth) were recorded. Inhalational agents neither for induction nor for maintenance of anaesthesia were used.

Results :

All the data are expressed as mean and standard deviation. Student's t-test was used as a test of significance. All statistical analysis were conducted using SPSS 15.0 version and the value of $P<0.05$ was considered significant and $P<0.0001$ was considered highly significant. The two groups were compared in patient characteristics with respect to age, gender, ASA physical status and mean weight ($P>0.05$) [Table 1].

Duration of propofol administration were 78.4± 33.87 min in group TCI and 81.51± 35.60 min in MCI group, the values being comparable ($P>0.05$). [Table1]

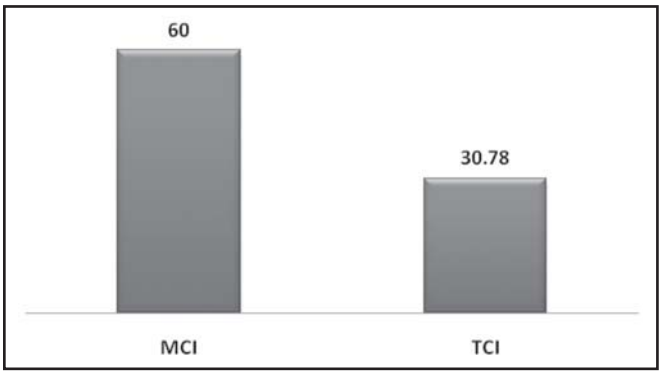
Table 1: Demographic details of patients of two study groups (Values in Mean ±SD)

Variables	MCI	TCI
Age (years)	43 ± 18	37 ± 16
Gender(M:F)	32M:18F	28M:22F
Weight (kg)	56.33±10.56	50.84±10.23
Duration of propofol administration (min)	81.51±35.60	78.43±33.87
American society of anaesthesiologists grade I/II	28/22	30/20

TCI resulted in more rapid induction of anaesthesia. (30 sec in TCI Vs 60 sec in MCI, P<0.05) [Figure 1] and allowed earlier insertion of an endotracheal intubation. (60.39 sec in TCI Vs 70 sec in MCI, P<0.05).

Figure 1: Comparison of Induction Time between MCI & TCI

(Values in Mean ±SD in seconds, p<0.05)



There were no statistical significant differences between Two procedures in SAP, MAP, DAP measured on Pre-incision, post-incision 5, 10, more than 30 minutes. (P>0.05) [Table 2]. Frequency of apnoea were less in group TCI (56% TCI Vs 64% MCI, P=0.4161). On comparing end tidal concentration of CO_2 ($EtCO_2$)values it was found that in early and late part of surgery, both group revealed no significant differences (P> 0.05) but in middle part of surgery (10-30 minute) TCI group (31.19 mm of hg) revealed significantly increased $EtCO_2$ values than MCI group (27.12 mm of hg) (P< 0.0001).

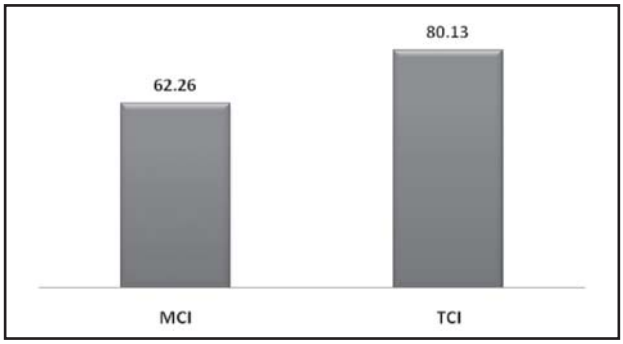
Table 2 : Hemodynamic Changes between MCI and TCI (Values in Mean ±SD, P>0.05)

Hemodynamic Variables	MCI	TCI
Preincision :		
SBP (mm Hg)	127.27 ± 15.58	127.09 ±19.00
DBP (mm Hg)	83.39 ± 13.54	83.70 ± 13.10
HR (beat/min)	92.80 ± 13.86	88.12 ± 15.46
MAP (mm Hg)	102.86 ± 17.74	99.78 ± 15.61
Early (2 min after surgery)		
SBP (mm Hg)	120.04 ± 18.72	120.08 ± 17.42
DBP (mm Hg)	78.47 ± 11.73	83.29 ± 15.04
HR (beat/ min)	89.49 ± 13.30	88.12 ± 15.46
MAP (mm Hg)	94.45 ± 16.28	97.47 ± 15.16
Middle (10-30min after surgery)		
SBP (mm Hg)	123.96 ± 20.32	126.59 ± 18.23
DBP (mm Hg)	81.00 ± 15.04	85.94 ± 15.43
HR (beat/min)	85.06 ± 12.95	84.76 ± 12.40
MAP (mm Hg)	96.59 ± 18.31	101.18 ± 17.12
Late (>30 min after surgery)		
SBP (mm Hg)	124.57 ± 19.84	124.35 ± 18.50
DBP (mm Hg)	80.06 ± 15.37	84.75 ± 15.76
HR (beat/min)	80.43 ± 11.50	78.02 ± 11.60
MAP (mm Hg)	97.55 ± 20.60	98.82 ± 17.75

Another interesting finding was that overall total consumption of propofol was higher in TCI group 80.13 mg as compared to MCI group 62.26 mg .(P<0.05). [Figure 2]

Figure 2 : Comparison of Total propofol consumption between MCI & TCI

(Values in Mean ±SD in mg, p<0.05)

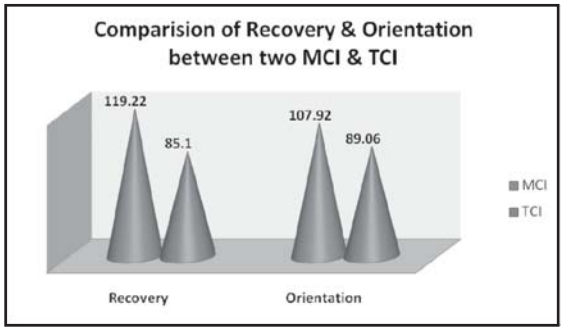


Patients exhibited some remarkable statistical differences during recovery in TCI group as compared to MCI group (85.1 min in TCI Vs 119.22 min in MCI) (P<0.05). [Figure 3] Similarly for orientation period, there was a significant statistical differences in TCI group as compared to MCI group (89.06 min Vs 107.92 minute).(P<0.05). [Figure 3]

Figure 3 : Comparison of Recovery & Orientation time between MCI & TCI

(Values in Mean ±SD in minutes

P=0.001(recovery) P=0.030(orientation time)



Discussion :

This study was conducted to demonstrate the efficiency of TCI in controlling anaesthesia depth during induction and maintainance phase. Target-controlled infusion (TCI) devices allow relatively stable, controllable plasma concentrations of drugs administered intravenously. Drug administration by iv boluses produce rapid fluctuations in plasma drug concentrations, whereas a constant rate infusion produces plasma concentrations that slowly rise to reach a stable concentration only after 5 7 drug elimination half-lives.[9] Only a few studies have compared the clinical profile of TCI with that of MCI and fewer have demonstrated a clinical advantage for TCI.

TCI resulted in more rapid induction of anaesthesia (30.78 sec-TCI Vs 60 sec-MCI) and allowed earlier insertion of endotracheal intubation (60.39 sec- TCI Vs 70 sec-MCI). Chaudhry [10] et al in their study found, with TCI, induction of anaesthesia is achieved more rapidly with higher initial target concentrations leading to faster attainment of an adequate effect site concentration. Furthermore, the target controlled system is designed to maintain a steady blood propofol concentration until a higher or lower target concentration is selected, and this may not have been achieved with the manual system.

Previous studies shown that significantly more propofol was administered during both induction and maintenance of anaesthesia with TCI.[11][12] This was confirmed in current study in which more propofol consumption with TCI.

It was found that $EtCO_2$ was significantly increased during middle part of maintenance in TCI as compare to MCI. Explanation for that was probably caused by increased blood propofol concentration.In MCI, there is a constant infusion rate, therefore drug concentration increases with time while in TCI, there is a constant blood concentration therefore infusion rate decreases with time. So there are more chances of apnoea in MCI as compare to TCI group.[13]

We hypothesized that in TCI group, tight control over propofol effect site concentration might decrease the incidence of apneas (56% vs 64%) and improve control over respiratory depression and haemodynamic responses. Sylvie passot et al [14] studied that during induction in MCI group, the infusion rate of propofol led to a large initial blood concentration, which was maintained until loss of verbal contact. This created a large blood/effect site concentration gradient and resulted in an overshoot of effect site concentration, thus causing an increased incidence of adverse effects such as initial apneas.

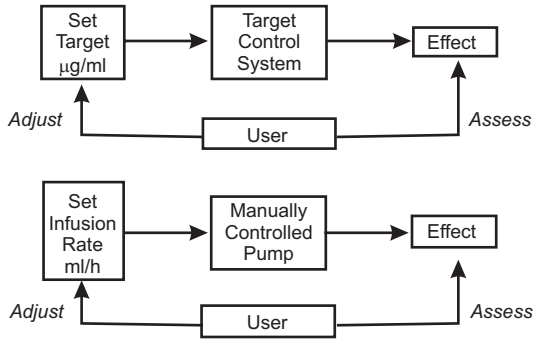
When targeting effect site concentration in TCI group, the initial calibrated bolus provided a large but brief initial plasma concentration to drive the drug into effect site, allowing quicker equilibration of compartments, and was calculated to achieve the targeted effect site concentration and not more. [15] To achieve and maintain a set drug concentration in the blood, a TCI system will calculate and delivering with a short rapid infusion of amount of drug required reaching the target rapidly. Thereafter the TCI system will automatically reduce infusion rate overtime, delivering sufficient drug to compensate for loss from the circulation by redistribution and elimination. Thus the blood concentration is constant and infusion rate decreases over time. If an increase in drug concentration is required, a further small bolus is administered by TCI system and maintenance rate is adjusted to maintain this new target.

If a decrease in target concentration is required, TCI system will stop infusion until the model within pump calculates that blood concentration will have fallen to the new target. Infusion then recommences automatically at a lower rate to maintain this lower target. Thus with TCI, when a given target setting is changed the response in the blood concentration occurs more rapidly and more reproducibly than with MCI [16] [Figure 4]

Figure 4: Target controlled infusion Vs Manual (Rate) controlled infusion

(source : http://www.biosun.com.hk/UploadFile/20070316102134677.jpg)

Target Controlled Infusion (TCI) versus Rate Controlled Infusion (RCI)



Unfortunately in present study, we did not find significant difference of MAP in either TCI or MCI group. Few authors also did not find major haemodynamic side effects in either group.[17][18] In our study we have shown that in TCI group in spite of increased propofol administration during induction

and maintenance did not result in cardiovascular depression. In TCI group early recovery and rapid orientation were better compare to MCI in our study. It has been reported that rapid recovery profile is more acceptable in TCI than in MCI. [19] [20] we found significant differences among two groups although increased propofol rate during maintenance in TCI group.

We achieved a deeper level of anaesthesia more easily due to flexibility of TCI as compare to MCI. However, some authors did not find clinical advantage of TCI over MCI. [21-25] The ultimate goal is to obtain the desired clinical effect when administering a particular dose of a drug, taking into account inter-individual pharmacokinetic and pharmacodynamic variability. Rapid and precise titration of anaesthetic drugs to provide smooth onset and short, predictable drug offset is now feasible. This may be advantageous in the context of a cost conscious health service moving towards ever shorter inpatient stay and more patients treated as day cases. The increasing popularity of TIVA is testament to its use and perceived benefits and for the modern anaesthetist it represents a new branch of the speciality with major advantages.

Conclusion :

It was concluded that TCI technique is safe, effective and better acceptability as compare to manual system. Moreover, TCI will prove as a valuable tool towards our professional development.

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Study of Treadmill Exercise Stress Test In Tobacco Smokers In Relation With Coronary Artery Disease

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Abstract :

Introduction : Cardiovascular diseases (CVDs), as a group, are the leading cause of death in the world. Tobacco use is a major known risk factor for CVD and it leads to a high burden of early death and disability. There is sufficient evidence to assume a causal relationship between smoking and vascular diseases. **Method :** The study was conducted at one of the cardiology hospitals of Ahmadabad. 50 male smokers in the age group of 18-60 years with no cardiopulmonary or medical aliments were approached. The detailed history was taken along with physical, general and systemic examination. They were subjected to Tread Mill Stress Test (TMT). Their blood sample was collected for assessment of blood sugar and lipid profile. **Results :** The high Systolic Blood Pressure (SBP) and TMT positive found in smokers. The smokers with elevated Post-Prandial Blood Sugar (PPBS) level were detected with TMT positive finding. The alteration in lipid profile, like increase in LDL-C level, with TMT results were observed in smokers. **Conclusion :** TMT positivity and thus the risk of Coronary Artery Diseases are more in smokers with SBP >140 mm of Hg, smokers with post prandial blood sugar (PPBS) level >180mg/100ml, smokers with higher serum LDL-C level.

Key words : Coronary Vascular Disease, Smokers, Tread Mill Stress Test, Post Prandial Blood Sugar

Introduction :

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels. According to the WHO report, Cardiovascular diseases accounted for 17.3 million or 30 % of the total global deaths in 2008 [1]. The contribution of developing countries to the global burden of CVD, in terms of disability-adjusted life-years (DALYs) lost, was 2.8 times greater than that in developed countries [1].

India contributed to 17% of the worldwide CVD mortality in 1990. CVD-related deaths in India are expected to rise from about 2 million in 2000 to 4.8 million in 2020. Tobacco use is a major known risk factor for CVD and leads to a high burden of early death and disability. Smoking is estimated to cause nearly 10% of CVD [2]. CVD is also the largest contributor to tobacco-related deaths, in terms of absolute numbers. The recent WHO data suggest that prevalence of current daily tobacco smoking in India are 28 38 % and 3- 7 % among male and female respectively [3]. The WHO in 2004 projected 58.8 million deaths occurred globally out of which 5.4 million were tobacco-attributed and 70% of the deaths were in developing countries.

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The chemicals released from tobacco and its metabolites have deleterious effect on blood vessels such as increase inflammation of blood vessel, activated clotting mechanism, etc. There is observed increase in blood pressure and heart rate with electrical instability of cardiac tissue. There is also altered endocrine profile like insulin resistance with raised blood glucose level and persistence high level of catecholamines. [1] High blood pressure is a major risk factor for CAD. CAD risk is concerned with high systolic blood pressure (SBP) which is more important. The smoking has toxic effect on lipid profile, which facilitates growth of atherosclerosis in tobacco consumer [5].

The exercise has two major implications on cardiovascular disease.

1. Regular exercise helps to prevent Atherosclerosis and eventually coronary heart disease.
2. Supervised graded exercise testing plays an important role in assessing coronary artery disease. For the standard risk assessment of CAD, the exercise-ECG test should be performed on subjects who are able to do exercise, have normal ECG and not consuming digoxin. In patients who are unable to do exercise, pharmacological stress testing with imaging should be used.

Objectives :

To study the occurrence of latent coronary artery disease in tobacco smokers on the basis of TMT stress test.

Methodology :

In this study, 50 tobacco smokers were studied for existence of the coronary artery disease, by subjecting them to treadmill stress test.

Inclusion criteria for case selection

1. A male in the age group of 18-60 years.
2. A tobacco smoker: one who smoked any tobacco product daily for 3 months or more at the time of the study.
3. Individual must not be a proved case of coronary artery disease.

Exclusion criteria for case selection

1. Past history or present history of any cardiopulmonary conditions, other severe general medical condition or orthopedic conditions which interfere with the patient's ability to exercise.
2. Ex- smoker who already quit smoking for last one year.
3. One who started smoking within last 3 months.

Our study was O.P.D. based. Patients were selected from one of the Cardiology Institutes in Ahmedabad from August 2009 to January 2010 duration. The individuals were subjected to detailed clinical history, physical examination, and investigation like lipid profile, Post Prandial Blood Sugar (PPBS), X-ray chest, resting ECG and Tread Mill Stress Test (TMT).

- All the individuals having study criteria were asked for TMT stress test.
- Stress testing is the process by which the performance of the cardio vascular system can be tested to ascertain its capacity for effort, diagnose ischemia and myocardial functional status.

BLOOD GLUCOSE (PPBS)

2 ml of blood collected in fluoride bulb. This sample centrifuged at 2000 rpm for 5 min and platelet free plasma collected in aliquots. Plasma Glucose concentration was determined by Hexokinase method [6] with using Architect c system (Roche, Indianapolis, IN) automated analyzer and reagents from Abbott Diagnostic (Abbott Laboratories, IL, USA).

SERUM LIPID PROFILE

Serum concentration of Triglyceride, Cholesterol, LDL, VLDL and HDL were measured by Architect c system (Roche, Indianapolis, IN) automated analyzer using reagents from Abbott Diagnostic (Abbott Laboratories, IL, USA).

Substrate	Normal value (mg/dl)	Test Principle
Cholesterol	<200	Enzymatic CHOD-PAP [7]
Triglyceride	≤160	Glycerol Phosphate Oxidases [8]
HDL-C	>55	Accelerator Selective Detergent [9]
LDL-C	≤150	Measured Liquid Selective Detergents (Direct LDL) [10]
VLDL-C	≤30 mg/dl	Friedewald Equation [11]

TMT

Test was done by following Bruce Protocol [12].

Machine standard treadmill machine.

Maximum target heart rate (THR) can be calculated by 220-Age of the person.

Procedure :

Subject underwent a standardized sub-maximal treadmill exercise test adopted with Bruce protocol. The TMT consists of 7 stages each of three minutes duration followed by 8 minutes period of post exercise observation. In sub maximal TMT, THR reached as 90% of the predicted maximal heart rate. A 12-lead ECG should be done prior to test to exclude acute changes. The patient should be tested for at least 2 hours before the test. The heart rate, blood pressure and 12-lead ECG were monitored throughout the procedure automatically and displayed on the screen of the machine. Heart was assaulted at every three minutes interval for the development of S3, S4 gallop sound and systolic murmurs. At frequent intervals individuals were asked about the symptoms.

All the necessary equipments and emergency drugs were kept ready to manage unexpected complications like. Fall in BP, Myocardial Infarction (MI), Cardiac arrest, Ventricular tachycardia, Ventricular fibrillation.

Indications of Stopping TMT were Failure of monitor system, Progressive angina, Dyspnea and fatigue, Leg fatigue claudicating, joint pain, S.T. Segment changes, Sustained supra ventricular teaching cardiac, Significant drop in SBP or heart rate, Light headedness, confusion, cyanosis and pallor, Excessive BP response (> 240/120) or hypotension SBP (< 80 mm of hg), Acute MI.

Statistics

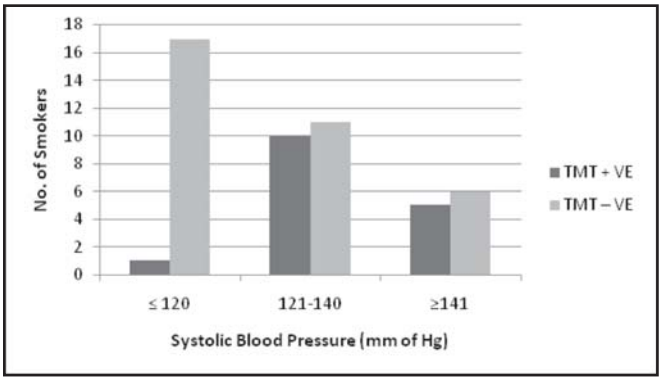
The data were collected in Microsoft Office® Excel and analyzed by Graph Pad Instat software. The methods for analysis were Chi-square test, Fisher's Exact Test and ANOVA, with significant level set at 0.05.

Results :

In present study the relationship between Tobacco smoking and Coronary artery disease was carried out on 50 individuals who fulfilled all criteria.

SYSTOLIC BLOOD PRESSURE

Figure 1 : Relationship between TMT and Systolic blood pressure among smokers



Graph shows relationship between systolic BP and TMT stress test results. It is seen that the percentage of positive TMT test increased with higher SBP (p=0.2).(Figure 1)

BLOOD SUGAR :

Diabetes mellitus was screened by post prandial Blood sugar.

Table 1: Levels of Post Prandial Blood Sugar (PPBS) among TMT positive and negative group

Post prandial blood Sugar (mg/100ml)	No. of Smokers	TMT+VE Group	TMT VE Group
≤120 = normal	27	7(26%)	20(74%)
120-180=Impaired Glucose Tolerance	16	4(25%)	12(75%)
>180=Diabetes mellitus	7	5(71%)	2(29%)
TOTAL	50	16	34

ANOVA Test p = 0.05

The data in table pointed relation between PPBS level and TMT result. Results clearly states that, there is linear correlation between high PPBS level and positive TMT. (Table 1)

LIPID PROFILE

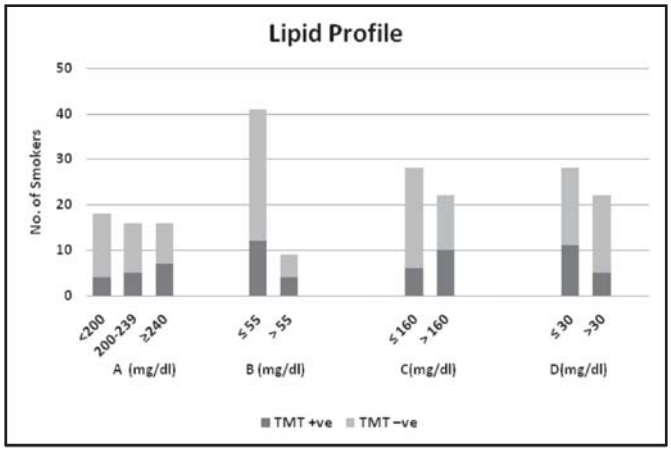


Figure 2 shows numbers of TMT positive/negative patients in relation between **(A)** serum Total Cholesterol, **(B)** Serum HDL-C, **(C)** Serum Triglyceride and **(D)** Serum VLDL-C and P values are 0.4, 0.4, 0.1 and 0.2 respectively. The results suggest that there is no significant relation between changes in lipid profile and positive TMT result in smoker. The less HDL level was consistent in smoker. The relation between S. HDL-C level and TMT was not statistically significant. (Figure 2)

Table 2: Level of LDL-C among TMT positive and negative group

LDL-C Level mg/100ml	No. of Smokers	TMT +VE	TMT VE
≤ 150	17(34%)	9(18%)	8(18%)
> 150	33(66%)	7(14%)	26(52%)
TOTAL	50(100%)	16(32%)	34(68%)

Fisher's Exact Testp = 0.02

Upper limit of LDL-C Level in normal healthy adult is 150 mg/100ml of serum. Table 2 explains, 66% of sample population has high Serum LDL-C level. The relation between LDL-C serum level and TMT showed that TMT positive results were more in high serum LDL-C level smokers. It was statistically highly significant. (Table 2)

Discussion :

The high blood pressure and coronary artery disease have positive correlation.[13] The Framingham study of 1984 suggested that an increase in total to high-density lipoprotein cholesterol ratio, hypertension, cigarette smoking, excess weight, elevated blood sugar levels, lack of exercise, stress, electrocardiographic abnormalities, and other factors are associated with the development of CAD.[14][15] Gupta B K et al (Jan 2007), said that there is a greater

prevalence of high SBP in tobacco users as compared to non users. [16] In present study we found that, hypertensive smokers with high SBP level and healthy smokers were not having statistically significant differences with their TMT positive results. The study by Julie C Willa et al (2000) said that a dose-response relationship seems likely between smoking and incidence of diabetes. [17] The similar Meta analysis by Willi C et al (2007), reported that smoking increases the risk of type 2 diabetes this article is also in favor of our study. [18] The alteration in lipid profile had significant role in development of CAD. [5] [19] Gupta B K et al (2007) said that there was a greater prevalence of high total and LDL cholesterol in tobacco users as compared to non users. [20] Khurana M et al (2000) said that smoking had adverse effect on lipid profile and therefore rising cardiovascular risk. [4] In present study high LDL-C level in smoker found with Positive TMT test, which support the findings of previous studies. [4], [5], [19], [20] Garrison RJ et al (1978) found that there was negative correlation between HDL-C level and smoking in CAD patients. [21] Our findings are very similar with the previous study.

Conclusion :

Following conclusions are derived from our study.

- TMT positivity and thus the risk of CAD is not significantly greater in smokers with SBP >140mm of Hg.
- TMT positivity and thus the risk of CAD is higher in smokers with post prandial blood sugar level >180mg/100ml.
- TMT positivity and thus the risk of CAD are greater in the smokers with higher serum LDL-C level.
- No definite relationship could be established between Total Cholesterol, HDL-C, TGs and VLDL-C levels of smokers and TMT status.

Recommendation :

The statutory notice Smoking is injurious to the health had no other alternative. Our study suggests that periodic screening of smoker for hypertension, diabetes and lipid profile shall be mandatory. The patient with positive findings should be treated promptly to control the progress of disease. This way we can reduce the risk of coronary artery disease in smokers.

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Bacteriological Profile and Antibiotic Susceptibility of Common Isolates From Burns Patients At Tertiary Care Level Hospital

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Abstract :

Background : Burns are one of the most common and devastating form of trauma. Patients with serious thermal injury require immediate specialized care in order to minimize morbidity and mortality. Significant thermal injuries induce a state of immunosuppression that predisposes burn patients to infectious complications. The major challenge for clinicians is nosocomial infection in patients of burns, which is known to cause over 50% of burn deaths. This study was undertaken to determine bacterial cause of infections and its antibiotic susceptibility in burn patients in our institute. **Materials and Methods :** During the period of six month (January 2011 to June 2011), 705 specimens were collected from burn patients after admission to our hospital. Isolation and identification of microorganisms was done using the routine standard conventional methods. Kirby-Bauer disk diffusion test was performed for all the isolates for antimicrobial susceptibility. **Results :** Of the 705 specimens, 401(56.87%) were culture positive and 271(38.1%) showed polymicrobial infection. The microorganisms causing infections were *Pseudomonas aeruginosa* 169(25.22%), followed by *Klebsiell sp.* 164(24.47%), *Escherichia coli* 108(16.11%), *S.aureus* 53(11.77%), *Proteus sp.* 38(5.67%), *Enterococcus species* 36(5.37%), *Enterobacter sp.* 28(4.17%), *A.baumanii* 22(3.13%),*CONS* 17(2.53%) and few other Gram negative bacilli. Among these isolates, 56.2% of *P. aeruginosa* were found to be resistant to piperacillin-tazobactam and 99.2 % to cefotaxime. 37.7% of *S. aureus* and 29.4% of coagulase negative *Staphylococcus* were methicillin resistant. **Conclusion :** High prevalence of nosocomial infections and the presence of multidrug resistant bacteria, and Methicillin Resistant *S. aureus*(MRSA) suggest continuous surveillance of burn infections and develop strategies for antimicrobial resistance control and treatment of infectious complications.

Key words: Burn, nosocomial infection, antimicrobial resistance

Introduction :

The skin has an important role in the fluid and temperature regulation. If enough skin area is injured, the ability to maintain that control can be lost. Most of the burn victims, who survive including the initial 24 hours after burns, succumb to infection of the burnt area and its complications. Factors are disruption of the skin barrier, the possibility of the normal bacterial flora becoming opportunistic pathogens, severe depression of the immune system that contribute towards the sepsis in a burn victim.[1]

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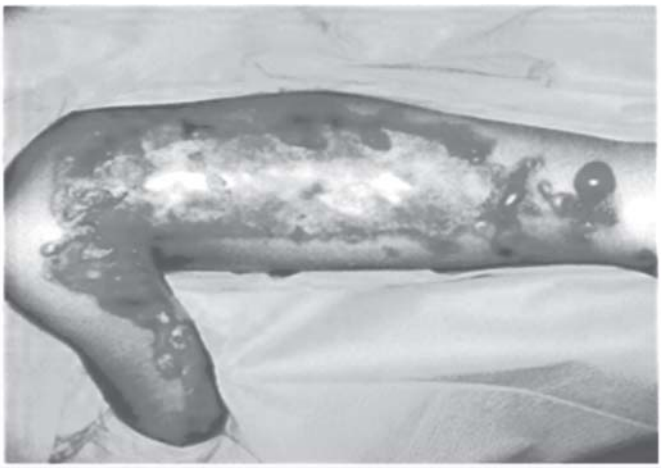

Figure 1: A burn case

Approximately 73 per cent of all death within the first five days post-burn have been shown to be directly or indirectly caused by septic processes.[1] The common pathogens isolated include *Pseudomonas aeruginosa,*

Staphylococcus aureus, Klebsillea spp, and various coliform bacilli. Multidrug resistant bacteria have frequently been reported as the cause of nosocomial outbreaks of infection. Gram-negative bacteraemias have been associated with a 50% increase in predicted mortality for patients with bacteremia compared to those without bacteremia.[2] If antibacterial treatment is necessary; awareness should be heightened for the possibility of super infection with resistant organisms, yeasts, or fungi. Based on National Nosocomial Infection Surveillance System (NNIS) criteria, all the burn patients are required to follow the distribution of bacterial species among burn isolates, and the antimicrobial susceptibility of the pathogens in order to adapt empirical antibiotic strategies.[2] This study was carried out to determine bacteriological profile & its antibiotic susceptibility of common isolates from burns patients at our institute.

Materials and Methods :

This retrospective study was conducted for a period from January 2011 to June 2011 in our institute on patients admitted in the burn unit. Burn patients who fulfilled the standard criteria for admission were admitted in burn unit. A total of 705 specimens were taken into study. The burn wound swabs, urine, catheter tip, blood cultures etc. were collected following a thorough inspection and examination of an infected area of each patient. The specimens were processed by standard laboratory techniques. Battery of biochemical tests had been carried out for species identification by routine standard conventional methods. Antibiotic susceptibility testing was done by Kirby-Bauer disc diffusion method (Shown in Fig.2) and it was interpreted by CLSI (2010) guidelines.

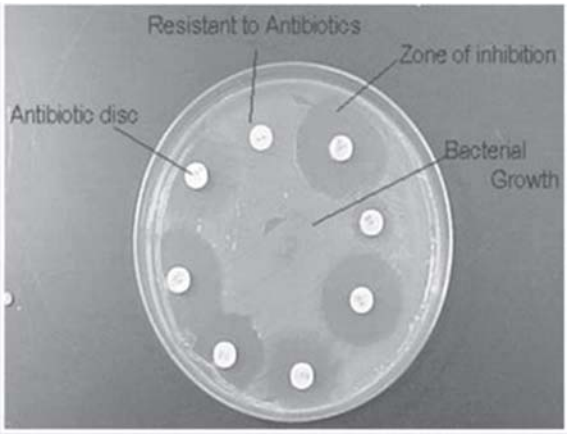

Figure 2 : Antibiotic susceptibility testing by disc diffusion method

Results :

Of a 705 specimens 401(56.87%) showed bacterial growth and 271(38.1%) of specimens showed polymicrobial infection. The most predominant bacterial isolate was *Pseudomonas aeruginosa* 169(25.22%), followed *by Klebsiella sp.*164(24.47%), *Escherichia coli* 108 (16.11%), *Staphylococcus aureus* 53(7.9%), *Proteus sp.*38(5.67%), *Enterococcus sp.* 36(5.37%), *Enterobacter sp.* 28(4.17%) *Acinetobacter baumanii* 22(3.28%), *Coagulase negative staphylococci* 17(2.53%) and other organisms including other *Pseudomonas sp., Citrobacter sp., Morganella morgagni, Providencia sp. , Candida* and other gram negative rods accounting for 5.07% of total isolates. Incidence of isolates in burns patients shown in figure 3.

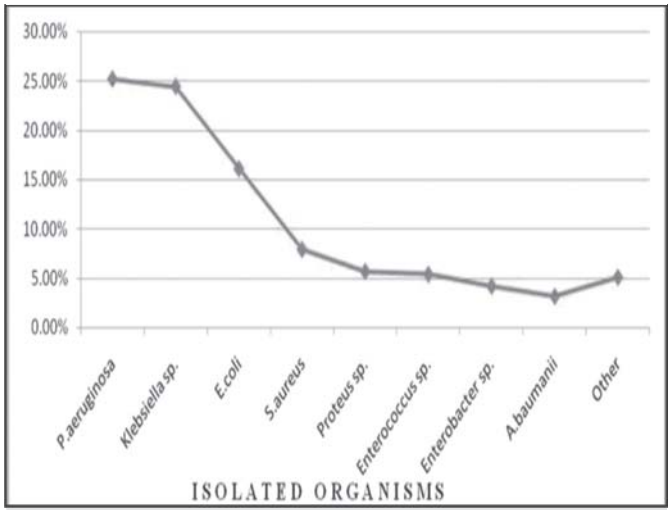

Figure 3 :
Organisms isolated from burn patients

Different antibiotics were tested against the Gram negative bacilli and Gram positive cocci. Most of the Gram-negative isolates obtained were found to be multidrug resistant. 37.7% S.aureus isolates were resistant to oxacillin and all staphylococcus were resistant to erythromycin. whereas all strains were susceptible to Vancomycin. 29.4% isolates of Staphylococci from samples were MRS (Methicillin resistant Staphylococcus). List of antibiotics tested and the relative resistant patterns is presented in Table 1.

Table1. Antibiotic resistance pattern of common isolated organisms from burns patients

Antibiotic	*P. aeruginosa*	*Klebsiella sp.*	*E.coli*	*A.baumanii*	*S.aureus*
Pip.-Tazobact.	56.2	-	-	-	-
Amikacin	70.4	74.4	85.2	54.5	56.2
Imipenem	2.7	0.7	00	05	
Doxycyclin	-	83.5	85.2	68.2	58.5
Ceftazidim	98.8	98.2	99.1	100	-
Cefotaxime	99.2	98.2	99.1	100	-
Penicillin	-	-	-	-	100
Vancomycin	-	-	-	-	00
Erythromycin	-	-	-	-	100
Cotrimoxazole	-	61	74.7	86.7	80

*Pip-Tazobact.= Piperacillin-Tazobactam
*Antibiotic resistance shown in table is in percentage
*- = Antibiotic is not tested

Isolated *P.aeruginosa* were highly resistant to tested cephalosporins and amikacin and 56.2% for piperacilin-tazobactam while only 2.7% of strains were resistant to imipenem. *Klebsiella sp.*, *E.coli* and other Gram negative bacilli were also highly resistant to tested antibiotics except imipenem and polymixin B. *S.aureus* showed 100% resistant to erythromycin, penicillin and 80% to cotrimoxazole. Isolated all Gram positive cocci were sensitive to vancomycin.

Discussion :

The burn wound is considered one of the major health problems in the world, and the infection is frequent and severe complication in patients who have sustained burns. Despite significant improvement in the survival of burn patients, infectious complications continue to be the major cause of morbidity and mortality. Though control of invasive bacterial burn wound infection, strict isolation techniques and infection control policies have significantly minimized the occurrence of burn wound infection.[3] In our study, multiple isolates were noted in 38.1% cases, *P. aeruginosa* was the most common isolate coincides with many of aerobic bacteria. Our study shows *P. aeruginosa* as a common cause of infection. Other studies also showed that infection caused by *P. aeruginosa* was the major danger in burn patients in India.[2] [4] [5] Prevalence of *Pseudomonas spp.* in the burn wards may be due to the fact that organism thrives in a moist environment.[4] The present study has shown that most common isolates in burn injuries was *P. aeuginosa* followed by *Klebsiella sp., E.coli* and Staphylococcus aureus which is similar to other study but rate of isolation and isolation of *Klebsiella sp.* are different.[5] But in contrast to some other studies especially from developed countries which report *S. aureus* as predominant organism.[6] The study result of various worker reveal that the bacteriology of burn infection has been changing from time to time and also the antimicrobial sensitivity pattern.[5] Antibiotic sensitivity patterns served as a useful guideline for choosing the appropriate antibiotic. When we analyzed the resistant pattern of our isolates we found that *Pseudomonas aeruginosa,* the commonest isolate, was resistant to Piperacilline-tazobactum combination in 56.2% cases. Resisitance for cefotaxime and ceftriaxone were in 99.2% and 98.8 % of isolated *Pseudomonas aeruginosa.* This is in contrast, however, some other study which report *Pseudomonas* was highly sensitive to Ceftazidime.[7] Imipenem 97.3% and Polymyxin-B was found to be sensitive 100% against *P. aeruginosa* in our study. Over all Gram-negative Organisms were highly resistant to Cefotaxime (98.7%), Ceftriaxone (98.8%) followed by Amikacin. Vancomycin aginst *S.aureus* was 100% sensitive in our study similar to

other. *S.aureus* was highly resistant to Erythromycin & Penicillin, this was almost similar to report by other.[2] [4] While in contrast with other.[7] Resistance patterns among nosocomial bacterial pathogens may vary from country to country and also within the same country, over time.[8]The subsequent development and use of broad-spectrum antibiotics led to the emergence of resistance among Gram negative organisms, particularly *P. aeruginosa*, as the predominant organism causing invasive burn wound infections in burn patients.[4]The high percentage of multidrug resistance is probably due to empirical use of broad-spectrum antibiotics and non-adherence to hospital antibiotic policy. The early detection of isolates is also very important to prevent treatment failure as the time involved in isolation, identification and performing antibiotic sensitivity can take as long as 48 hours from the receipt of the specimen. This time period may be enough to allow a sub clinical infection to become life threatening illness. Secondly, in burn wound, because of the mixed infection, the potential virulence of one organism may affect another organism growing alongside.

Another factor adding to the complication is multidrug resistance (MDR) of the organism. Once MDR strains become established in the hospital environment these can persist for months. Therefore, careful microbiological surveillance and in vitro testing before the start of antibiotic therapy and restrictive antibiotic policy may be of great help in prevention and treatment of MDR isolates in burn units.

To conclude, patients suffering from burn injury were most commonly infected with multidrug resistant strain of *P.aeruginosa.* Our study will be helpful in providing useful guidelines for choosing effective empirical therapy which will have a great impact on morbidity and mortality of burns patients due to bacteremia or septicemia and study strongly suggest that prevalent organisms, their sensitivity and resistance pattern should be studied in every burn unit in order to prevent the emergence of multi drug resistant strain. A nosocomial infection surveillance system may be introduced to reduce the rate of nosocomial infections among burn patients, and for better therapeutic options.

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FNAC : An Easy and Accessible Diagnostic Aid For Cervical Lymphadenopathy A Study of 150 Cases

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Abstract :

Introduction : Lymphadenopathy is an abnormal increase in size and/or consistency of lymph nodes & tubercular lymphadenitis is its most common cause. It is a clinical manifestation of local or systemic tuberculosis and serves as an excellent clue to the underlying disease. **Methodology :** This prospective study was conducted to find the prevalence of tuberculosis in patients with cervical lymphadenopathy in the Department of Pathology of a teaching institute and tertiary care hospital of Ahmedabad city of Gujarat, India. Total 150 patients of all ages & both genders with enlarged cervical lymphnodes were studied attending the out patients department. All patients were evaluated through detailed history, general physical and systemic examination & laboratory investigations. Fine needle aspiration cytology (FNAC) of lymphnode was done using 22 G needle. Lymph node excision biopsy was also performed whenever necessary. **Result :** Tuberculosis was found to be the most common cause of cervical lymphadenopathy (58%) followed by chronic non specific lymphadenitis (14.7%), reactive lymphadenitis (10%), metastatic lymphadenopathy (13.3%) and lymphoma (4%). Constitutional symptoms and family history were not present in most of the patients with tuberculosis. **Conclusion :** FNAC was established to be a reliable, safe and accurate test as a first line of evaluation of cervical lymphadenopathy, playing a vital role in the management, as it could differentiate infective processes from neoplastic ones and avoided unnecessary surgeries.

Key Words : FNAC, Tuberculous cervical lymphadenopathy, Reactive hyperplasia, Tuberculosis.

Introduction :

There are approximately 800 lymphnodes in the body and no fewer than 300 of them lie in the neck [1]. Lymphadenopathy is an abnormal increase in size and/or consistency of lymphnodes and tubercular lymphadenitis is its most common cause. It is a clinical manifestation of local or systemic tuberculosis and serves as an excellent clue to the underlying disease. [2] The frequency of various etiological processes for lymphnode enlargement varies with geographical conditions and socioeconomical setup. [2] Cervical lymphadenopathy remains a diagnostic and therapeutic challenge because it mimics other pathological processes and often has inconsistent physical and laboratory findings, making diagnosis difficult, often requiring biopsy. A complete history and physical examination, FNAC with staining for AFB, and polymerase chain reaction (PCR) are helpful in obtaining early diagnosis. The commonest presentation is neck swelling (92%), followed by fever, cold abscess, nonhealing ulcer, discharging sinus, anorexia and weight loss. [3] FNAC of cervical lymph nodes has a high diagnostic accuracy & provides important clues in guiding subsequent clinical management. However for detailed sub typing of certain disease entities such as lymphoma, surgical biopsy for histological and immunohistochemical studies are required. [4] Hodgkin's lymphoma, squamous cell carcinoma and metastasis from papillary thyroid cancer (PTC) can co-exist with tubercular infection in cervical lymph nodes. [5] FNAC is an easy, quick, inexpensive technique for diagnosis of enlarged lymphnodes, with a high degree of accuracy [6]. It causes minimal trauma to the patient, carries virtually no risk of complications and the technique is painless and inexpensive. The sensitivity of FNAC for diagnosis of lymphadenopathy averages 90% with a specificity of 95%. Objective of this study was to find out the prevalence of tuberculosis in cervical lymphadenopathy and to find out other variables like age and gender distribution, role of clinical assessment and investigations for the diagnosis. In the present study we established the frequency of tuberculosis in patients with cervical lymphadenopathy in view of the high prevalence & atypical presentation of tuberculosis in our country. Microscopic examination for AFB was confirmatory especially in purulent aspirates which did not show granuloma, necrosis or epithelioid cells & which in absence of Z-N staining could be missed as acute lymphadenitis. [7]

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Methodology :

This prospective study was conducted at Department of Pathology of *a teaching institute and tertiary care hospital of Ahmedabad city of Gujarat, India, from April 2011 to October 2012*. Variables studied were age, gender distribution and prevalence of tuberculosis in cervical lymphadenopathy. FNAC of the enlarged cervical lymphnodes was performed with informed consent of the patient following thorough clinical examination. All patients were asked about history related to neck swelling and questions relevant to the etiology like present, past and family history of tuberculosis, history of sexual exposure for syphilis and AIDS etc. The palpable cervical node was fixed with one hand, the skin cleansed and a 22 gauge 1.5 cm long needle with 10 ml syringe was inserted into the lymph node and a full suction pressure was applied. The tip of the needle was moved around. The pressure was neutralized and the needle was withdrawn. The aspirated material was placed on glass slides, smears made, fixed with alcohol and stained with H & E. The cases were divided into five groups: Tuberculous lymphadenitis, chronic non-specific lymphadenitis, reactive lymphadenitis, metastatic carcinoma and lymphoma. Subjects with acute febrile illness, acute lymphadenitis, a localized inflammatory process (abscess) and suspected vascular swellings were excluded. Hypocellular slides & cases with haematological malignancy were also excluded. Related investigations were carried out in all cases including complete blood picture, ESR and chest x-ray. FNAC was done for tissue diagnosis. Specific investigations like pus for AFB / culture and excision biopsy were employed where FNAC was inconclusive.

Results :

Total 150 patients of all ages & both genders with enlarged cervical lymphnodes were studied attending the out patients department, of which 73 were male and 77 were female. Most of the patients were between 10 40 years. Majority of the patients were otherwise healthy adults and constitutional symptoms were present in 10% only. Posterior triangle of the neck was most commonly involved in Tuberculous lymphadenopathy. In five patients submandibular lymph nodes were also affected. The diagnostic outcome is summarised in Table1. 58% were tuberculous & 42 % were non-tuberculous lesions. Out of 58% (87) of tuberculous lymphadenopathy patients 48.3% (42) males and 51.7% (45) females were found to have tuberculosis in our study. The gender distribution of various lesions is summarized in Table 2. Of the non Tuberculous lesions, approximately 17% were malignant & 83% were benign. Among the malignant lesions 23% were lymphomas & 77% were metastases. Overall prevalence of various lesions was: tuberculosis 87 (58%), chronic non specific inflammation 22 (14.7%), reactive 15 (10%), lymphoma 6 (4%) and metastases 20 (13.3 %).

Table 1 : Prevalence of various lesions responsible for cervical lymphadenopathy

Sr. No	Cytological Diagnosis	No. of patients	Frequency (%)
1	Tuberculosis	87	58.0
2	Chronic non-specific	22	14.7
3	Reactive hyperplasia	15	10.0
4	Metastasis	20	13.3
5	Lymphoma	06	4.0
	Total	**150**	**100**

Table 2 : Gender distribution of various lesions.

Sr. No	Cytological Diagnosis	Total	MALE	FEMALE
1	Tuberculosis	87	42(48.3%)	45(51.7%)
2	Chronic non-specific	22	08(36.4%)	14(63.6%)
3	Reactive hyperplasia	15	06(40.0%)	09(60.0%)
4	Metastasis	20	16(80.0%)	04(20.0%)
5	Lymphoma	06	01(16.7%)	05(83.3%)
	Total	**150**	**73**	**77**

Discussion :

Cytology of lymph nodes has become a window for diagnosis of many diseases. Optimal material and an experienced eye, when combined, give cytological diagnosis of significance equal to histopathology [8]. Early diagnosis is particularly important in tubercular lymphadenopathy, where the cure rate is high in contrast to lymphomas and metastases. Metastases were most commonly from squamous cell carcinoma in the head & neck regions. In developing countries where facilities for biopsy are not readily available, FNAC is a completely safe, quick and inexpensive method for quick diagnosis of lymphadenopathy and reduces the need for surgical biopsy. We have presented our experience with 150 cases of lymphadenopathy over a period of one and half years. The pattern of lesions (non-neoplastic lesions consisting of

tuberculosis, reactive hyperplasia, & chronic non-specific lymphadenitis and neoplastic lesions including metastatic carcinoma and malignant lymphoma) seen in our study is more or less the same as reported in other studies from India and other developing countries. [9] Tuberculous lymphadenitis proved to be the most common diagnosis in our study (58%) which is comparable to other studies In India. [9] [10] In a study conducted in Kathmandu, causes of cervical lymphadenopathy were tuberculous lymphadenitis (54%), reactive hyperplasia (33%) and metastatic lesion in lymph nodes (11.1%). [11] Their data are in accordance with the data of our present study. Our study was also in accordance with findings of Abdul Haque Khan *et al*[12] Farzana Shahid *et al*[13] Saira Fatima *et al*[14] Mazhar Iqbal *et al*[15] Ruchi Khajuria *et al*[16] FNAC was found to be highly effective (94%) in diagnosis and lymph nodes in the posterior triangle of neck were mostly involved. In current study also tuberculosis was the main cause of cervical lymphadenopathy which is relatively high as compared to the study cited above. Tuberculous cervical lymphadenopathy usually presents with multiple lymph node enlargement without constitutional signs. The diagnosis is based on high index of suspicion with pathological and laboratory investigations. Disease can be diagnosed with FNAC and PCR. An incorrect diagnosis can be made on FNAC. Thus if patient does not improve on drug therapy an excision biopsy is warranted. This was experienced in our study. ESR and chest x-ray were not reliable in most of the patients. FNAC and surgical biopsy of lymph nodes should not be delayed in cases of doubt. The diagnostic outcomes of study, comparable to seven similar studies, is shown in Table 3.

Table 3 : Showing results of various studies across the world.

Cytological Diagnosis	Present Study	Abdul Haque Khan *et al*[12]	Farzana Shahid *et al*[13]	Saira Fatima *et al*[14]	Mazhar iqbal *et al*[15]	Ruchi Khajuria *et al*[16]	Kataria *et al*[17]	Shakya G *et al*[18]
Tuberculosis	58.0	52.0	66.9	52.7	70.45	52.3	24.25	32.4
Reactive 10.0	28.0	15.2	16.1	13.63	37.2	30.3	50.4	
Chronic Non specific	14.7	-	-	04.2	02.27	-	-	-
Lymphoma	04.0	02.0	06.7	05.5	04.54	02.0	-	02.0
Metastatic	13.3	06.0	04.5	08.7	11.36	03.8	09.05	02.8
Abscess / Acute Inflammation	-	10.0	06.7	-	-	01.15	30.3	12.4

Conclusions :

Prevalence of tuberculosis in cervical lymphadenopathy was high. Constitutional symptoms were absent in most of the patients. Clinical examination, ESR and x-ray chest had a limited role in diagnosis of tuberculous cervical lymphadenopathy. FNAC was the investigation of choice though excision biopsy was required occasionally. FNAC was the most effective diagnostic tool (90%), ESR was raised in 17 patients out of 87 (19.5%) with tuberculous cervical lymphadenopathy & X-ray chest with positive lesions was found in only 3 patients (3.45%). Family history was uncommon.

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Study of Laparoscopic Intraperitoneal Meshplasty In Abdominal Surgeries Using Prolene Mesh

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Abstract :

Introduction : Laparoscopic repair of ventral hernia has gained popularity over the past decade. The intraperitoneal placement of polypropylene mesh in repair of ventral hernias was theoretically said to cause bowel adhesions and post operative complications. Our study demonstrates the safety of intraperitoneal polypropylene mesh placement with comparable postoperative course and at significantly reduced cost. **Aims and Objectives :** To study laparoscopic intraperitoneal placement of polypropylene mesh during ventral hernia repair with respect to operating time, patient comfort and post operative complications and cost effectiveness. **Materials and Methods :** A non randomised prospective study of 30 patients undergoing laparoscopic intraperitoneal repair of ventral hernia with polypropylene mesh from July 2010 to January 2012 in surgery department of teaching hospital in Ahmedabad, Gujarat, India. **Results :** Mean operating time was 124 minutes, with average post operative stay of 3 days, post operative complication rate 12.32%, including pain (12.32%), seroma formation (6.66%) and bowel injury (0.33%). 3 patients were converted to open procedure due to dense adhesions at hernia site and bowel injury. Post operative infection and recurrence rate was nil. **Discussion :** The intraperitoneal placement of polypropylene mesh is a cost effective method of ventral hernia repair with comparable post operative complications as compared to use of other materials. Long term follow up is necessary to establish safety with respect to post operative bowel adhesion formation

Introduction :

Ventral hernias (VH) occur as a result of weakness in the musculofascial layer of the anterior abdominal wall [(1)]. The most popular classification of the same is: congenital, acquired, incisional and traumatic [(2)]. A successful series of laparoscopic repair for VH was done by LeBlanc in 1993. Operative costs may be optimized with selection of mesh and optimal use of trans-abdominal suture and fixation devices. Common indications and Contraindications for laparoscopic intraperitoneal meshplasty are as mentioned below.

Indications :

Laparoscopic ventral hernia repair can be accomplished in almost all patients with excellent results. Defects less than 3 cm are better done by conventional approach and laparoscopy is reserved for patients with larger defects. In obesity and recurrent incisional hernias laparoscopy is indicated even in smaller sized defects. The Swiss cheese type of hernias (multiple smaller defects) is ideally managed by laparoscopy as the defects are more clearly delineated when compared to open repair. [(2)]

Contraindications :

(A) Absolute: 1.Infection, 2.Strangulation, 3.Koch's abdomen or other infective pathology, 4.Peritonitis (B) Relative: 1.Morbid obesity, 2.Extensive adhesions due to previous abdominal surgery, 3.Very large ventral hernia

Contraindications to laparoscopy : 1. Severe cardiomyopathy, 2. Pulmonary disease, 3. Pulmonary hypertension

The common complications[(2)] after laparoscopic intraperitoneal meshplasty are as mentioned follow: Bowel injury, Seroma formation, Mesh infection, Persistent pain, Recurrence, Wound infection etc. This study deals with intraperitoneal placement of a polypropylene mesh in the repair of ventral hernias.

Aims and Objectives :

To study the laparoscopic method of ventral hernia repair with intraperitoneal placement of a polypropylene mesh in view of operative time, complications, post-operative pain, recurrence, morbidity and mortality, duration of hospital stay, return to activities of daily routine and patient compliance.

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Materials and Methods :

This study which is non-randomized and prospective, involved 30 patients with ventral hernia that presented during the period of July 2010 to January 2012 in Surgery department of Civil Hospital, Ahmedabad and were subjected to laparoscopic intraperitoneal meshplasty.

Operative procedures :

Anaesthesia : General anaesthesia was given with endotracheal intubation **Patient and operative team position :** In lower abdominal hernias, the surgeon stands near the right shoulder of the patient, the assistant surgeon near the left shoulder with the monitor at the foot end. The patient is in supine position with 10-15 degree Trendelenburg tilt to allow the bowel loops to fall away from the pelvis. In upper abdominal defects, the patient is placed in modified lithotomy position with 10-15 degrees head up tilt. The surgeon stands between the legs of the patients with the monitor near the head end, while the camera assistant stands on the right side of the patient. Operations on lateral defects of the abdominal wall, such as those in sub costal or flank areas will need semi or full decubitus position. **Instrumentation :** 3 CCD digital cameras with Xenon light source, 30 degree scopes were most frequently used. The camera port was usually 10 mm and the working ports 5 mm. The camera port is also utilised for introduction of the mesh and suture materials. Routine laparoscopy instruments were utilised. A specially designed suture passer for fixing the mesh to the fascial layers was used. Monopolar & bipolar cautery with harmonic scalpel was used as and when required.

Table 1: Port placement and operative technique for laparoscopic intraperitoneal meshplasty

Port No.	Instruments	Place
1.	Camera	Epigastrium 10mm
2.	Right hand working port	Right hypochondrium 5 mm
3.	Left hand working port	Left hypochondrium 5mm

Marking of the defect and possible site for transfascial sutures was done beforehand. Careful adhesiolysis was performed and the content of the hernia sac which was either omentum or bowel were reduced. The extent of the defect was assessed thoroughly. The measurement of the defect was drawn on the external surface of the anterior abdominal wall and a mesh of adequate size that covers the whole defect overlapping up to 3 to 5cm from the edge was selected. All the necessary precautions were to be taken to avoid contamination of the mesh with skin pathogens. Then the mesh was rolled and inserted in a port of adequate caliber to the abdominal cavity, the mesh was unrolled and fixed by stitches to the abdominal wall without dissecting peritoneum. The corners of the mesh were fixed to abdominal wall by transfascial sutures with Cobbler's needle. We fixed the edges of mesh to the abdominal wall by intracoporeal suturing using vicryl. We found the use of conventional sutures for this purpose is more cost effective when compared to devices such as staples, anchors and tackers. The sutures were placed 2-3 cm apart in all the four sides of the mesh. Once the suturing was completed, the pneumoperitoneum was deflated and the ports were closed. As per Pascal's Law: wide mesh overlap of defect distributes pressure equally over larger area.

Figure 1: Diagrammatic representation of position of intraperitoneal mesh.

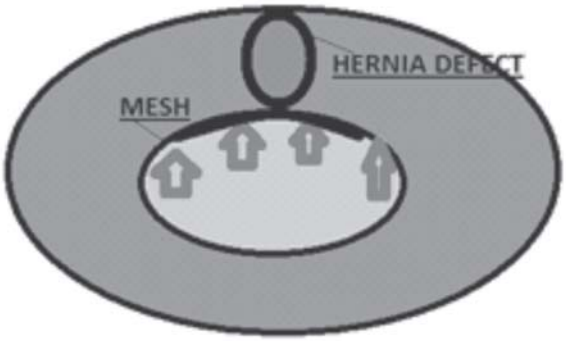


Figure 2 : Polypropylene mesh with intracorporeal sutures.

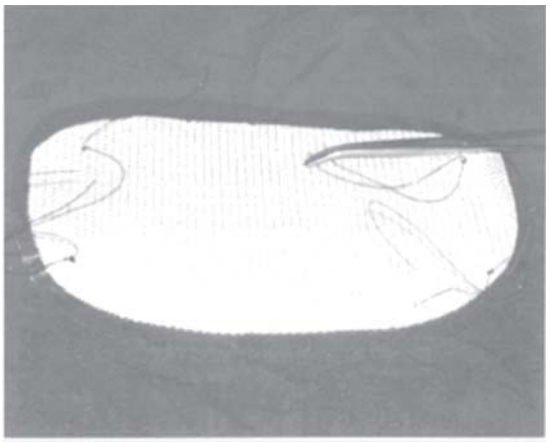


Figure 3: Intra operative photograph of completed transfascial repair

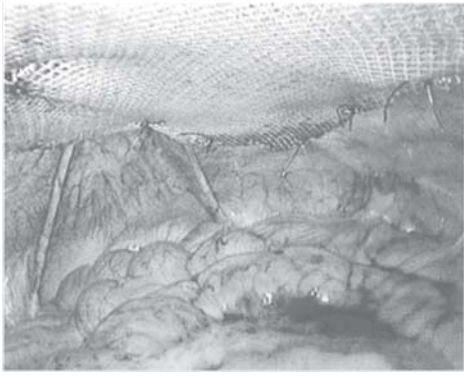
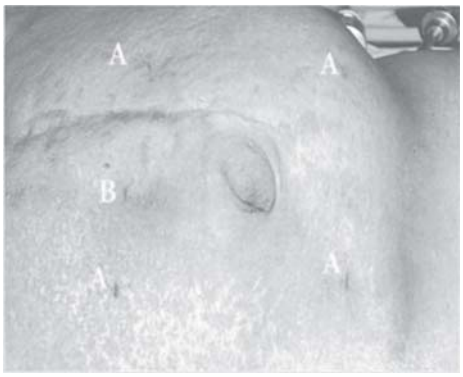


Figure 4 : External view after completion of suturing



Results :

The laparoscopic approach results in lower post operative pain & wound complication rates including haematoma, infections and wound dehiscence were quiet less as compared to the open technique. All the patients were followed up at 1st, 3rd, 6th, 12th & 18th month.

Table 2 : Post operative pain (by Visual analogue scale) after laparoscopic intraperitoneal meshplasty

PAIN SCALE	DAY 3	DAY 7
P1	3(10.71%)	4(13.33%)
P2	6(21.42%)	4(13.33%)
P3	1(3.5%)	0

Table 2 shows assessment of post-operative pain complaint by patients, which was assessed by visual analogue scale, divided in 3 grades. On 7th post-operative day, 4 patients had complaint of mild pain (P1) and 4 had moderate pain (P2) while none of the study subjects had severe pain (P3).

Table 3 : Duration of hospital stay after laparoscopic intraperitoneal meshplasty

Duration of hospital stay (Days)	No. of patients
3-6	28 (93.33%)
> 6	2 (6.67%)
Total	**30**

Table 3 suggests duration of hospital stay for study subjects operated for laparoscopic intraperitoneal meshplasty. Almost 94% of patients were discharged before 6 days while 2 (6.67%) had stayed in hospital for more than 6 days.

The mean operating time was124 minutes for laparoscopic intraperitoneal meshplasty.

Conversion rate

In 3 patients (10%), the laparoscopic procedure was converted to an open procedure due to dense adhesions at the hernia site. Bowel injury occurred in 1 patient (0.33%) which was closed primarily with intraperitoneal drain for 5 days and subsequent uneventful recovery.

Cost effectiveness

In our study 15x15cm prolene mesh was used (Rs. 3500). The cost to the hospital per patient was around Rs.6500-Rs.7000 inclusive of hospital stay, drugs and consultant charges, surgical equipment and materials etc. As the study was done in CIVIL HOSPITAL, there was no expenditure on part of the patient.

Return to routine work

All patients were able to return to activities of daily life within 7 days after surgery. After 3 months, patients were relatively pain free and no post operative complications were noted.

Discussion

As described in Table 4, present study demonstrated comparable operating time, post operative hospital stay and seroma formation rates, with reduced incidence of post operative complications, especially infection and recurrence compared to other case series. In present study, patients had least Post-operative complications (12.32%) as compared to similar studies conducted by Holzman et al[6], Park et al [3], Carbajo et al [7] , Ramshaw at al[8] and de Mario[9] .

Table 4 : Comparison between present study and other studies

Observation	Our Study	Holzman et al [6]		Park et al [3]		Carbajo et al [7]		Ramshaw et al [8]		deMaria et al [9]	
		Lap	Open	Lap	Open	Lap	Open	Lap	Open	Lap	Open
Operating time (min)	124	128	98	95	78	87	112	58	82	-	-
Length of hospital stay (days)	3	1.6	5	3.4	6.5	2.2	9.1	1.7	2.8	1	4
Post operative complications (%)	12.32	23	31	18	37	20	50	15	26	19	50
Infection rate (%)	0	5	6	0	2	0	18	0	3	4.7	0
Seroma rate (%)	6.66	5	0	4	2	13	67	0	0	-	-
Recurrence (%)	0	10	13	11	35	00	07	03	21	1	0
Patients	30	20	16	56	49	30	30	79	174	21	18

The lower cost of polypropylene mesh also greatly reduced total operative expenditure per patient.

Conclusion and summary

Return to activities of daily routine is earlier in patients with laparoscopic repair mainly due to decreased pain, fewer complications, early mobility and faster return of bowel movements.[3] [4] [5] Laparoscopic repair is more expensive and operative time is greater as compared to open method. In all 30 patients, prolene mesh was used for hernia repair. Theoretically adhesion formation is higher with a prolene mesh, but longer follow-up period is required before further conclusions can be drawn. Early complications like pain, seroma, abdominal distension are less in laparoscopic surgeries due to less tissue dissection and lipolysis. If meticulous and good aseptic precautions taken chances of complications of surgery like wound infection and abdominal distension are minimised. Recurrence rate was nil, however larger study and a longer follow up period is required to substantiate this difference

The longer operating time in our study is a reflection of the learning curve, with procedures performed at later stages having a shorter operating time.

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Study and Comparison of Lipid Profile of Normal, Premature and Small For Gestational Age Neonates

Hetal Jeeyani*, Sheela Bharani**, Anjana Shah***

Abstract :

Aims and Objectives : To study lipid profile of newborns at birth and establish whether there is any significant effect of maturity, intrauterine growth restriction (IUGR) and maternal malnutrition on its levels. **Methodology :** A prospective study was undertaken which included 70 neonates. These neonates were divided into four groups - fullterm appropriate for gestational age (FT AGA), fullterm small for gestational age (FT SGA), preterm - appropriate for gestational age (PT AGA) and preterm small for gestational age (PT SGA). Mothers of neonates were examined for malnutrition. Cord blood was collected and following biochemical estimations were done total serum cholesterol (TC), serum triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterol. **Results :** The study showed that in both, AGA and SGA, premature newborns had significantly higher TG and VLDL levels ($p<0.001$) as compared to term newborns. In both, term and preterm, SGA newborns had significantly higher TC ($p<0.05$), LDL and atherogenic ratios ($p<0.001$) as compared to AGA newborns. There was high rate of birth of premature (42.9% vs. 19%) and IUGR (53.5% vs. 23.9%) newborns in malnourished mothers as compared to normal mothers. **Conclusion :** Newborns that were small in size at birth have adverse lipid profile which suggests that these newborns are more likely to suffer from diseases resulting from atherosclerosis, particularly coronary artery disease at an earlier age as compared to full term healthy newborns. Hence, this study suggests various newer strategies for prevention of atherosclerosis which includes prevention of maternal malnutrition and early introduction of dietary and lifestyle modifications in children who were small at birth.

Introduction :

Incidence of coronary artery disease is increasing and so is the death due to coronary artery disease. Coronary artery disease is responsible for 25-30% of deaths throughout world. It is a modern epidemic and so research is going on from genetic base to environmental and lifestyle factors. It has been well established that male gender, obesity, excessive fat intake, cigarette smoking, hypertension, diabetes, hyperlipidemia, sedentary habits, stress etc. are various risk factors responsible coronary artery disease [(1)]. The earlier belief that the chronic diseases like atherosclerotic disease, hypertension, and diabetes mellitus are diseases of adulthood and are due to result of adult lifestyles were added with the concept that the process of atherogenesis begins not only from childhood but from fetal period [(2)]. Fatty streaks were demonstrated in aorta and extracranial arteries of human fetuses [(3)].

David Barker, a well-known research scientist 20 years ago showed for the first time that people who had low birth weight are at greatest risk of developing coronary artery disease. He subsequently showed that they are also at greater risk of stroke, high blood pressure and type 2 diabetes mellitus. He and his co workers did large scale epidemiological and experimental studies in Europe, USA and Asia and proved that fetal growth restriction due to nutritional deprivation in early life is an important cause of some most common disorders of adulthood [(4)].

Barker's fetal origin hypothesis states that fetal undernutrition in middle to late gestation, which leads to disproportionate fetal growth programmes persisting changes in metabolic, structural and physiological parameters leading to an increased propensity to adverse health outcomes which includes abnormal blood lipid values, diabetes, hypertension and ischemic heart disease [(2)].

It is well established in adults that low level of high density lipoprotein fraction of cholesterol and high level of low density lipoprotein fraction of cholesterol as well as serum triglycerides are associated with higher incidence of Coronary artery disease [(1)]. Barker and his colleagues showed that abnormalities in choleseterol concentrations were linked to disproportionate size at birth i.e. short body in relation to size of head (sparing of brain growth at cost of other vital organs like liver). Impaired liver growth results in reprogramming of liver metabolism which leads to raised atherogenic lipids [(2)]. Studies of serum lipid at birth acts as a

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baseline data and reference point to trace till adult levels. Also, whether IUGR (intrauterine growth restricted) newborns have adverse lipid profiles can be known. Risk of development of atherosclerosis can be predicted at an earlier age and dietary and lifestyle modifications can be advised. Difference between serum lipid profile levels in newborns of different race and ethnic origin can suggest racial and ethnic influence on atherosclerotic disease. Maternal malnutrition can lead to low birth weight babies and preterm birth and hence effect of maternal malnutrition on serum lipid levels of newborns can be studied and appropriate actions can be taken to decrease maternal malnutrition.

Aims and objectives :

1. To establish reference range of serum lipid levels in newborns of western region of India.
2. To establish whether there is any difference in lipid levels between term and preterm newborns and appropriate for gestational age and small for gestational age newborns.
3. To study effect of maternal malnutrition on lipid levels of newborns.

Methodology :

A prospective study was undertaken from April 2005 to May 2006 in Sir Sayajirao General Hospital, Vadodara. The subjects were neonates delivered at SSG hospital. A total of 70 neonates were enrolled in the study.

Following newborns were excluded from study: Twins, Presence of congenital anomalies, Moderate or severe birth asphyxia, early onset septicemia, Respiratory distress syndrome, History of diabetes mellitus, thyroid disease or hypercholesterolemia in mother.

All the neonates were weighed on electronic weighing scale within one hour of birth after routine stabilization. Maturity scoring was done using Meharban Singh scoring methods. Measurements were taken using standard methods. The newborns were divided into four groups: full term appropriate for gestational age (FT AGA), full term small for gestational age (FT SGA), preterm - appropriate for gestational age (PT AGA) and preterm small for gestational age (PT SGA). Maternal history was obtained using a structured questionnaire. History of diabetes mellitus and thyroid disorders was inquired into and maternal serum cholesterol was measured to look for hypercholesterolemia. Neonates of these mothers were not included in the study. Any morbidity during pregnancy particularly anemia and pre-eclampsia were noted. Hemoglobin less than 10gm% was considered as an evidence of anemia. Proteinuria, edema and hypertension were considered as evidence of pre eclampsia. Weight, height and midarm circumference of mother was recorded by standard methods. Weight less than 40 kg and height less than 145 cm were considered evidence of maternal malnutrition.[5]

Present study included 30 FT AGA, 20 FT SGA, 15 PT AGA and 5 PT SGA neonates. Blood samples were collected from umbilical cord using all aseptic and antiseptic precautions in sterile plain bulb. The following biochemical estimations were done total serum cholesterol, serum triglyceride, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol and very low density lipoprotein (VLDL) cholesterol. Statistical analysis was done using EPI 6 software program using a Pentium 3 computer and statistical tests were considered significant at $p<0.05$ and highly significant at $p<0.001$.

Observations :

A total of 70 neonates were included in the study out of which 20 (28%) were premature, 43 (61%) were low birth weight and 25 (35%) were IUGR (intrauterine growth restricted). (Table 1) The rate of malnutrition, anemia and pre eclampsia in the mothers of the neonates who were included in the study were 40%, 37% and 15.7% respectively. (Table 1)

Table 1: Clinical parameters of neonates and mothers

Sr.no.	Variable	N=70
1.	**Sex of baby**	
	Male	35
	Female	35
2.	**Maturity**	
	Preterm	20
	Full term	50
3.	**Birth weight**	
	Wt < 2.5 kg	43
	Wt >= 2.5 kg	27
4.	**Intrauterine growth restriction**	
	Present	25
	Absent	45
5.	**Maternal morbidity**	
	Malnutrition	28
	Anemia	26
	Pre-eclampsia	11

It was observed in the present study that 23.9 % of the normal mothers gave birth to small for gestational age (i.e., IUGR) newborns whereas this rate was as high as 53.5% in malnourished mother. Similarly preterm birth was found in 19% of normal mothers whereas in malnourished mothers it was 42.9%. (Table 2 and Figure 1)

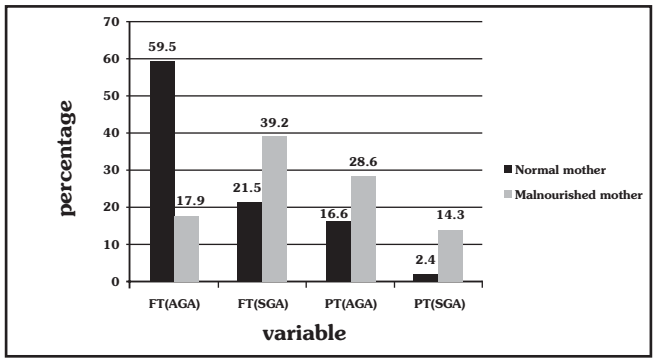

Figure 1 : Effect of Maternal nutritional status on birth of small for gestational age and premature newborns

Odd's ratio was calculated for IUGR newborns in normal and malnourished mothers which was 3.6. This shows that risk of IUGR baby is 3.6 times higher in malnourished mother as compared to normal mother. (Table 2) Odd's ratio for preterm newborn in normal and malnourished mother was 3.18. This shows that the risk of preterm baby is 3.18 times higher in malnourished mother as compared to normal mother. (Table 2)

Table 2 : Relationship between maternal malnutrition and birth of small for gestational age and premature newborn

Variable	Full term (n = 50)		Preterm (n = 20)	
	AGA(n=30)	SGA(n=20)	AGA(n=15)	SGA(n=5)
Normal mother (n=42)	25 (59.5%)	9(21.5%)	7(16.6%)	1(2.4%)
Malnourished mother (n=28)	5(17.9%)	11(39.2%)	8(28.6%)	4(14.3%)

On comparing cord blood lipid profile with foreign studies (Casaneuva et al[6], Kaplan et al[7]), it was found that newborns of western region of India had higher total cholesterol, LDL fraction of cholesterol and serum triglycerides and low HDL fraction of cholesterol. (Table 3) On comparing cord blood lipid profile with Indian studies (Kalra et al[8] , Kumar et al [9]) it was found that total serum cholesterol levels were comparatively similar but serum triglycerides were comparatively high and HDL fraction comparatively low in newborns of western region of India as compared to North Indian newborns. (Table 3)

Table 3: Comparison of lipid profile of full term healthy neonates with different studies

Name of the study	Total cholesterol (mg/dl)	HDL - C (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)	Serum triglycerides (mg/dl)
Present study	75.66±4.27	12.83±1.31	53.86±3.96	9.1±0.8	45.53±4.24
Casaneuva et al [6]	64	24.9	28.3	-	37.5
Kaplan et al [7]	68	35	29	-	34
Kalra et al [8]	76.6	22.5	-	-	20.7
Kumar et al [9]	85.83	-	-	-	35.27

In both, appropriate for gestational age and small for gestational age, premature newborns had significantly higher (p value<0.001) serum triglyceride and VLDL levels as compared to term newborns. (Table IV and V)

Table 4 : Lipid profile in relation to term at delivery in appropriate for gestational age newborns

Sr. no.	Variable	Fullterm (AGA) (n=30)	Preterm (AGA) (n=15)	p value
1	Total cholesterol TC (mg/dl)	75.66+4.27	72.25 + 3.02	0.28
2	HDL C(mg/dl)	12.83 +1.31	12.5 +1.41	0.49
3	LDL-C (mg/dl)	53.86+3.96	50.31+ 3.09	0.12
4	VLDL-C (mg/dl)	9.1 +0.84	10.93+ 0.85	<0.001
5	Serum triglycerides(mg/dl)	45.53+4.24	54.5+ 4.60	<0.001
6	L/H	4.24+ 0.56	4.05+ 0.39	0.67
7	TC/H	5.94+ 0.63	5.84+ 0.61	0.39
8	TC/L	1.40+ 0.05	1.43+ 0.07	0.09

Table 5 : Lipid profile in relation to term at delivery in small for gestational age newborns

Sr. no.	Variable	Full term(SGA) (n=20)	Preterm(SGA)(n=5)	p value
1	Total cholesterol TC (mg/dl)	83.70+3.86	72.25 + 3.02	0.06
2	HDL C(mg/dl)	11.5 +1.10	13.25 +0.95	0.08
3	LDL-C (mg/dl)	63.65+3.37	50.5+ 6.45	0.11
4	VLDL-C (mg/dl)	9.1 +0.85	11+ 0.81	<0.001
5	Serum triglycerides(mg/dl)	45.25+4.3	55.25+ 1.75	<0.001
6	L/H	5.58+ 0.65	3.82+ 0.52	0.24
7	TC/H	7.34+ 0.81	5.48+ 0.57	0.34
8	TC/L	1.31+ 0.06	1.44+ 0.13	0.05

In both, term and preterm, small for gestational age (IUGR) newborns had significantly higher serum cholesterol levels (p value <0.05) as compared to appropriate for gestational age newborns. LDL fraction of cholesterol and atherogenic ratios were significantly increased in small for gestational age newborns (p value <0.001). (Table 6 and 7)

Table 6 : Comparison of lipid profile in between full term appropriate for gestational age and small for gestational age newborns

Sr. no.	Variable	Full term(AGA) (n=30)	Full term(SGA) (n=20)	p value
1	Total cholesterol TC (mg/dl)	75.06+4.27	83.70 + 3.86	0.03
2	HDL C(mg/dl)	12.83 +1.81	11.50 +1.10	0.05
3	LDL-C (mg/dl)	53.86+3.96	63.65+ 3.37	<0.001
4	VLDL-C (mg/dl)	9.1 +0.8	9.10+ 0.85	0.96
5	Serum triglycerides(mg/dl)	45.53+4.24	45.25+ 4.3	0.87
6	L/H	4.24+ 0.56	5.58+ 0.65	<0.001
7	TC/H	5.94+ 0.63	7.34+ 0.81	<0.001
8	TC/L	1.4+ 0.05	1.31+ 0.06	0.07

Table 7 : Comparison of lipid profile between preterm appropriate for gestational age and small for gestational age newborns

Sr. no.	Variable	Preterm(AGA) (n=15)	Preterm(SGA) (n=5)	P value
1	Total cholesterol TC (mg/dl)	72.25+3.02	75.25 + 3.5	0.04
2	HDL C(mg/dl)	12.50 +1.41	11.25 +0.95	0.08
3	LDL-C (mg/dl)	50.31+3.09	54.5+ 6.45	<0.001
4	VLDL-C (mg/dl)	10.93 +0.85	11.0+ 0.81	0.08
5	Serum triglycerides(mg/dl)	54.5+4.60	55.25+ 1.75	0.06
6	L/H	4.05+ 0.39	4.9+ 0.52	<0.001
7	TC/H	5.84+ 0.61	6.81+ 0.57	<0.001
8	TC/L	1.43+ 0.07	1.38+ 0.13	0.06

Discussion :

Cardiovascular disease accounts for approximately 12 million deaths annually and is the commonest cause of death globally. Previously considered a disease of affluent, the past three decades have seen considerable decline in the incidence and prevalence of atherosclerotic disease in industrialized western world whereas at the same time this disease is assuming epidemic proportions in the developing world. Asian Indians, whether living in their own country or elsewhere have much higher incidence as compared to all ethnic groups. The classical risk factors that have been identified for coronary artery disease are hyperlipidemia, hypertension, diabetes mellitus, cigarette smoking and strong family history. Newer risk factors include elevated homocysteine, C reactive protein, lipoprotein (a), t plasminogen activator, factor VII, infection and inflammation[10].

One of the new risk factor which has been identified is fetal undernutrition. The association between fetal undernutrition and coronary artery disease was laid down by Barker and his co-workers by large scales studies. It was based on simple strategy of examining men and women in middle and late life whose body measurements at birth were recorded. These studies showed that death rates from coronary artery disease fell progressively with increase in birth weight[11]. Also it was found that men who were small at birth because they failed to grow, rather than those who were small because they were born prematurely were at increased risk of disease [12]. He subsequently showed that they were also at greater risk of stroke, high blood pressure and type 2 diabetes mellitus. This led to the idea that these disorders originated through malnutrition in the womb of mother.

Various studies have shown that fetal undernutrition as measured by low Ponderal Index is associated with insulin resistance syndrome occurrence of impaired glucose tolerance, raised blood pressure and disturbed lipid metabolism in adult life[3][13]. Study done by Yagnik et al [14] on four year old Indian children concluded that those children who were low birth weight babies have evidence of insulin resistance at four years of age. The proposed mechanism was that during fetal undernutrition, brain grows at the cost of liver and skeletal muscles. To achieve this, skeletal muscles need to become resistant to insulin as insulin is a potent stimulator of cell division. This peripheral insulin resistance may persist into adult life resulting in diabetes mellitus.

Raised blood pressure is associated with interference in fetal growth at any stage of gestation since it is found in individuals who were both proportionately and disproportionately small. Law et al did a longitudinal study of children and adults whose birth weights were recorded and found that at all ages beyond infancy, people who had low birth weight had higher blood pressure[15]. The possible mechanism includes loss of elasticity of vascular wall and excess of glucocorticoids resulting from fetoplacental stress due to maternal malnutrition, pre eclampsia or pregnancy induced hypertension.

Barker et al showed that reduced abdominal circumference and body length was associated with raised serum low density lipoprotein fraction of cholesterol in adult life. The proposed mechanism is that fetal undernutrition in late gestation leads to diversion of oxygenated blood away from the trunk in order to sustain brain which reduces linear growth as well as growth of abdominal viscera. This impaired growth might lead to reprogramming of liver

metabolism which may persist into adult life resulting in derangement in cholesterol levels and its various constituents[16].

This study observed that lipid profile of normal healthy newborns in western region of India (Gujarat) showed higher total cholesterol, LDL fraction of cholesterol and serum triglycerides and low HDL fraction of cholesterol as compared to foreign studies. It is known that higher levels of LDL fraction of cholesterol, serum triglycerides and low level of HDL fraction of cholesterol are associated with increased risk of coronary artery disease. Hence it can be said that newborns of this region are more likely to develop coronary artery disease in adulthood at an earlier age as compared to newborn of other countries.

When cord blood lipid profile was compared with Indian studies (Kalra *et al*[8] ,Kumar *et al*[9]) it was found that total serum cholesterol levels were comparatively similar but serum triglycerides were comparatively high and HDL fraction comparatively low in newborns of western region of India as compared to north Indian newborns. When such comparison was made in the adult levels between various parts of India it was found that adults of western India also have lower HDL levels as compared to north India[17]. Hence this concludes that HDL cholesterol which is protective cholesterol is lower in newborns of western region of India which would make these newborns more vulnerable to coronary artery disease.

On comparing the lipid profile of full term and preterm newborns in both appropriate and small for gestational age group, no significant difference was found in total cholesterol, LDL and HDL cholesterol. However, preterm newborns showed significantly higher triglyceride and VLDL cholesterol levels. This is in conformation with study done by Kalra *et al*[8], Kumar *et al*[9] and Haridas *et al*[18]. The proposed mechanism is that preterm birth is not a normal physiological phenomenon and hence it imposes a large amount of stress on the baby. Since stress in any form raises triglyceride levels, the results of the present study and various other studies show variations in rise of triglyceride levels depending on the level of stress to the premature newborn. Pardo *et al* demonstrated significantly raised atherogenic indices in Brazilian premature newborns which were not found in our study[19]. Possible reasons could be racial, genetic and dietary factors. Thus, we can say that preterm newborns are born with adverse lipid profiles. Barker's studies say that large number of individuals with coronary artery disease, raised blood pressure and diabetes mellitus were small at birth. Small at birth is a generalized term which refers to both prematurity and intrauterine growth retardation. Still more studies are required which can correlate only prematurity with these chronic diseases of adulthood.

The present study showed significantly higher total cholesterol, LDL cholesterol and atherogenic indices in small for gestational age newborns as compared to appropriate for gestational age. The levels of HDL, VLDL cholesterol and serum triglycerides did not show any statistically significant difference between both the groups. This is in conformation with Haridas *et al*[18] who reported higher cholesterol levels in small for gestational age newborns. From the present study it can be said that IUGR newborns are born with adverse lipid profile which can predispose them to early coronary atherosclerosis.

This study showed that there is high incidence of prematurity and intrauterine growth restriction in malnourished mothers. Since adverse lipid profile has been documented in preterm and IUGR newborns, maternal malnutrition although indirectly is responsible for adverse lipid profiles.

Conclusion :

This study concludes that newborns of the western region of India have higher total cholesterol, LDL cholesterol and serum triglycerides and lower HDL cholesterol levels as compared to newborns of other countries which suggest that newborns of this region have more adverse lipid profile and have more likelihood of developing early atherosclerosis. Preterm newborns had higher triglyceride and VLDL cholesterol levels as compared to term newborns. Small for gestational age newborns had higher total cholesterol and LDL levels and adverse atherogenic ratios as compared to appropriate for gestational age newborns. Malnourished mothers showed significantly higher birth rate of premature and IUGR newborns. Newborns that were small in size at birth had adverse lipid profile which suggests that these newborns have chances of developing atherosclerotic plaques in arteries earlier that normal full term healthy newborns.

Hence, this study suggests various newer strategies for prevention of atherosclerosis which includes prevention of malnutrition in mother, early counseling regarding lifestyle modification in children who were small at birth such as reducing intake of excessive saturated fats, avoidance of sedentary lifestyle, stress, smoking, tobacco chewing etc and monitoring them for hypertension, diabetes mellitus and hyperlipidemia since early childhood.

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Study of Pulmonary Function Tests In First Year M.B.B.S. Students of GCS Medical College In Ahmedabad, Gujarat

*Anand Mistry**, JaydeepKagathara*, Vilas J. Patel***, Suresh Goyal**, LopaVaidya**, UrjaDholakiya**

Abstract :

Introduction : Pulmonary function tests (PFT) have been evolved as a powerful clinical tool in diagnosis, management & follow up of patients with respiratory diseases and also as outcome tool in research studies. **Objective :** The present study was aimed to evaluate pulmonary functions among young male & female students of first M.B.B.S. to evaluate their respiratory efficiency & compare the data with other population studies from different parts of the country. **Methodology :** A cross sectional study was carried out using spirometry data of 150 students aged 17-18 yrs. Spiroexcel computerized spirometer was used in the study. The data were compared for gender differences and with previous Indian studies. The PFT data were correlated with body surface area of subjects. **Results :** PFT parameters FVC, FEV_1, PEFR, $FEF_{25-75\%}$ and MVV were higher in male group ($p < 0.05$) and showing strong positive correlation with body surface area (BSA) ($p < 0.0001$). The FEV_1/FVC ratio showed no significant difference in gender group ($p > 0.05$) and there was no positive correlation with BSA. **Conclusion :** The present study brings out substantial variation in most of the parameters of PFTs between young male and female group confirming PFT values are less in females due to less body mass and body surface area compared to males. Results were different compared to previous Indian studies may be due to diversity of population in country. We established univariate regression norms between different parameters of PFT and body surface area.

Key words : Pulmonary function test, body surface area, first M.B.B.S. students

Introduction :

Pulmonary function tests (PFT) have been evolved as a powerful clinical tool in diagnosis, management & follow up of patients with respiratory diseases and also as outcome tool in research studies. PFT for lung can be comparable to ECG for heart. There are several PFT parameters value published from different part of the world such as in European population,[1][2] North American population,[3] Chinese,[4] non-Caucasian populations [5][6] and population from different part of Indian Subcontinent[7][8][9][10] The medical parameters values are universally accepted but pulmonary function shows wide variation in normal. The sources of variation in pulmonary function have been summarized by the American Thoracic Society.[11] The differences in pulmonary studies in western countries, Asian subcontinents and even in states of India were because of diversity of ethnic groups, anthropometric parameters[12][13] and environmental factors. The results of one group could not apply to all society. While analysis of PFT studies were based on comparison of patient results with healthy matched subject data. Since habitat is one of the diverse factor which influence lung function tests.[14]

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The present study was aimed to determine the pulmonary parameters in normal young healthy non-smoking students of first M.B.B.S. studying at GCS Medical College, Gujarat, India.

Aims and objectives :

The present study was aimed to evaluate pulmonary functions among young male & female students of first M.B.B.S., to evaluate their respiratory efficiency & compare the data with other population study from different parts of the country.

Methodology :

The cross sectional study was done in first MBBS students of GCS Medical College, Ahmedabad, Gujarat, India. The Inclusion Criteria were: Apparently healthy Medical students and Non Smoker. While Exclusion Criteria were: Suffering from obstructive restrictive lung disease, Any Cardio - Respiratory pathological condition, and any other medical/surgical Illness.

The study was approved by Institutional ethical committee. The GCS Medical College has intake capacity of 150 students per academic year. During the academic year of 2012-13 total 150 students were enrolled in first counselling and after two month in second counselling 8 students were reshuffled. Thus we had data of total 158 students. Consent from each participant was taken and

they filled up a questionnaire form to record their personal data and current health status. The students with acute upper respiratory tract infection were allowed to recover & then tests were performed. We collected information of all 158 students and among them 8 students were excluded according to exclusion criteria. Body height was measured with the subject standing barefoot on a stadiometer with an accuracy of ± 0.50 cm whereas the body weight was measured to an accuracy of ± 0.1 kg by using a standard spring balance (Seca, Germany) with the subject wearing minimum clothing. Body surface area (BSA) was calculated automatically by Spiro excel software. All tests were done between 3 P.M. to 5 P.M. to avoid possible diurnal variation. The details of the test were explained and demonstrated to each of them. All the measurements were recorded with subjects in sitting position & wearing nose clips.

Pulmonary function test was done by a computerized spirometer (Spiro Excel, Medicad, INDIA) with all necessary precaution. For each volunteer three satisfactory efforts were recorded with at least 3-5 min rest between consecutive trials as per standard norms and the highest reading accepted. In one subjects all the records i.e. anthropometric measurement & pulmonary function test recording were done in single sitting on the same day.

The various pulmonary function tests included in the assessment of subjects were:

Volumes	Flow rate
FVC	PEFR
FEV_1	$FEF_{25-75\%}$
MVV	FEV_1/FVC ratio

1) Forced vital capacity (FVC) The subject was asked to take a deep inspiration from outside and then to expire in the spirometer with maximum effort followed by deep inspiration from spirometer. The graph was recorded.

2) Forced expiratory volume in 1st second (FEV_1) while taking FVC spirometer software calculated the value of FEV_1.

3) FEV1/FVC ratio - The software also calculated the ratio in percentage (%).

4) Peak expiratory flow rate (PEFR) the subject was asked to take deep breath and exhale as forcefully as possible in to the mouthpiece in single blow. The spirometer software also calculated PEFR while doing FVC. It was expressed in litre/second.

5) Mid expiratory flow rate ($FEF_{25-75\%}$) This is the average rate of air flow between 25% to 75% of total airflow in liter/second. The spirometer software calculated $FEF_{25-75\%}$ while doing FVC.

6) Maximum voluntary ventilation (MVV) It is the maximum volume of air expired in one minute with forceful effort. Subject was asked to take rapid and deep breathing in to spirometer for 15 seconds. Subject also instructed to stop doing test if he/she feels any giddiness. Simultaneous pulse rate also measured by an expert. This was also expressed in litres/minute.

Statistical analysis: All data were compiled in MS Office® Excel. The data were analysed by Graph Pad software. The mean of data were compared by Student t-test. The Correlation coefficient and Regression coefficient were calculated using SPSS statistical software. The level of significance was set at 5 %.

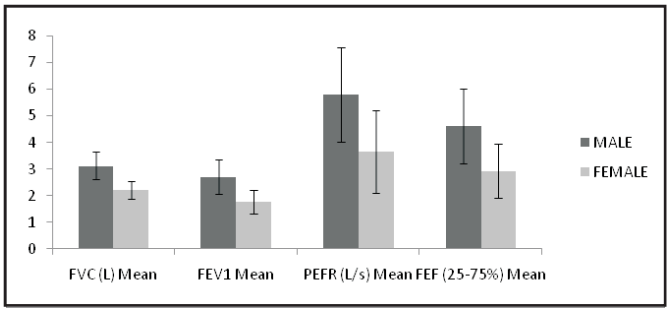
Results :

Table 1 showed participants' anthropometric parameters. Total 150 students were selected, out of which 75 subjects were males & 75 were females. The study population belongs to the age group of 17 to 18 years. All the subjects were healthy and coming from similar socio-economic background. The gender distribution was equal in population. The mean height, weight and body surface area of male and female have shown in Table 1.

Table 1 : Anthropometric data of subjects

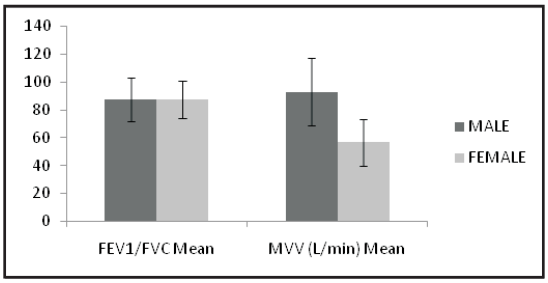
PARAMETER	MALE	FEMALE
Total No	75	75
Ht (cm) Mean	172.32	155.89
Wt (kg) Mean	68.9	51.3
BSA (m2) Mean	1.80	1.48

The **graph** 1 describes comparison of various PFT parameters in gender. Mean values of parameters were calculated. The student t-test was applied to compare mean of male and female. The p value of FVC, FEV_1, PEFR and $FEF_{25-75\%}$were <0.05.



Graph 1: Gender wise distribution of PFT Parameters

The **graph 2** showed comparison of FEV_1/FVC ratio in gender. There was no significant (p> 0.5) difference found in gender. The gender difference in MVV was significant (p <0.05).



The Correlation between Pulmonary function test measurements and Body surface area among young medical students was analysed. No significant gender difference was noted in FEV1/ FVC ratio. All other PFT parameters show statistically significant positive correlation with body surface area. (Table 2)

Graph 2 : Gender-wise distribution of FEV1/FVC

Table 2: Correlation between various PFT parameters with Body surface area

PFT Parameter	Correlation coefficient	P-value	95% Confidence interval
FVC (L)	0.7160	<0.0001	0.6278 to 0.7861
FEV1 (L)	0.5390	<0.0001	0.4146 to 0.6437
PEFR (L/S)	0.4697	<0.0001	0.3346 to 0.5859
FEF 25to75%	0.4860	<0.0001	0.3532 to 0.5996
FEV1/FVC ratio (%)	-0.1066	0.1942	-0.2624 to 0.0546
MVV (L/min)	0.5302	<0.0001	0.4039 to 0.6367

Simple regression norms for the prediction of pulmonary function measurements with known body surface area was analysed among male and female young medical students. The results are shown in Table 3.

Table 3 : Univariate Regression analysis between various Pulmonary Function Test parameters(Y) with Body surface area(X)

Pulmonary Function Test Parameter (Y)	Regression equation	F ratio	P-value
FVC (L)	Y = -1.2817 + 2.3372 X	155.6902	< 0.001
FEV1 (L)	Y = -0.7086 + 1.7942 X	60.6056	< 0.001
PEFR (L/S)	Y = -2.2731 + 4.2580 X	41.8931	< 0.001
FEF 25to75% (L/S)	Y = -1.6394 + 3.2925 X	45.7629	< 0.001
MVV (L/min)	Y = -35.4077 + 66.8738 X	57.4914	< 0.001

Discussion :

The purpose of present study was to observe the PFT parameters of young healthy students from medical college and derive predictive equations for pulmonary function in them. Reference value described the level of an index for a group of healthy persons that was the reference population in terms of defining variable, known as reference variable. The spirometer we used in study was operated by software which showed predicted values of all PFTs on the basis of inbuilt Kamat formula, in male with 17 to 18 years age having height 172.32 cms (mean height in male group) and weight 68.9 kg (mean weight in male group) predicted FVC 5.1 litres, PEFR 9.94 litres/sec, $FEF_{25-75\%}$ 5.26 litres/sec and MVV 152.04 litres/minute. In current study male group had mean FVC 3.12 litres, PEFR 5.8 litres/second, $FEF_{25-75\%}$ 4.62 litres/ second and MVV

92.82 litres/minute showing all PFT values are significantly less compare to reference standard value in this age group. Software reference values of PFT in females with 17 to 18 years age having height 155.89 cms, weight 51.3 kg are of FVC 3.55 litres, PEFR 6.93, $FEF_{25-75\%}$ 4.26 litres/ second and MVV 114.15 litres/minute. In our study female group had mean FVC 2 litres, PEFR 3.66 litres/second, $FEF_{25-75\%}$ 2.91 litres/ second and MVV 56.53 ± 16.56 litres/minute also exhibit all PFT values in female group are less compare to reference standard value. Currently there are no reliable prediction equations for pulmonary function applicable to Guajarati Population of INDIA. We tried to produce PFT norms of various parameters in 17 -18 years non-smoking apparently healthy medical students. These norms can be utilized in future studies.

Table 4 : Comparison of Current study with other Indian Data (FVC & FEV1%)

Sr. No	Year Author (Ref.)	Age (Years)	No. of subjects	FVC (litres)	FEV1 (L/S) (%)
1	Current study	17 - 18	150	2.56	2.24 (87.5)
2	1997 Fulambarker A et al [15]	16 - 80	137	2.55	2.12 (83.1)
3	1990 Vijyan [16]	15 - 40	130	3.99	3.31 (82.9)
4	1988 Chatterjee & Saha [9]	20 - 60	334	3.97	3.23 (81.3)
5	1977 Kamat et al [17]	25 34 35 44 45 - 54	205 157 72	3.594 3.313 3.140	2.90 (80.6) 2.60 (78.4) 2.44 (77.7)
6	1970 Singh et al [18]	30 39 40 49	49 30	3.454 3.090	2.86 (82.2) 2.57 (80.6)
7	1967 Kamat et al [19]	30 34 35 44 45 54	26 17 16	3.000 3.080 2.57	2.56 (85.5) 2.39 (77.7) 1.96 (76.4)
8	1958 Singh et al [20]	40 62	25	3.15	2.43 (76.8)
9	1957 Singh & Prabhakaran [21]	30 39	28	3.50	2.77 (78.1)

In present study males (75) & females (75) matched for age & socioeconomic status had completed the study. The mean height of male and female was 172.32cm and 155.89 cm respectively. Male showed more body mass than female in comparable group, which was reflected in pulmonary function tests. The mean ± SD of FVC was 3.12 ± 0.52 litres in male and 2 ± 0.33 litres in females with significant difference in values observed between two groups ($P < 0.0001$). FEV1 mean ± SD value in male was 2.725 ± 0.641 litres and in females it was 1.764 ± 0.437 litres with significant difference in values observed between two groups ($P < 0.0001$). $FEF_{25-75\%}$ in male group was 4.62 ± 1.41 litres/ second while in female it was 2.91 ± 1.04 litres/ second with significant difference. Gupta KB in 2012 found similar variations in gender. No significant difference was observed for FEV1/FVC between genders in present study. In MVV male has mean ± SD value 92.82 ± 24.28 litres/minute and female has 56.53 ± 16.56 litres/minute with significant difference. ($P < 0.0001$)

Present study showed significant positive correlation between FVC & FEV_1 with body mass index (P value for both < 0.0001). Doctor et al in 2010 found such difference in gender for FEV_1 and FVC. The FVC and FEV_1% data from various Indian studies were compared with present study. The interpretation of previous studies was higher than current study. As lung function showed wide variation in normal subjects and it was multi factorial we could not relate on specific factor. India had very diverse population it required specific target population for reference. Since PEFR which is considered as one of the most significant parameter to indicate one's pulmonary function status, PEFR also exhibited strong positive correlation with body mass index and this is also established between MVV and $FEF_{25-75\%}$ with BSA. Kamath et al in 1967 presented PEFR as very sensitive tool for rapid assessment of lung function in field. Our study had supported previous results. BSA (with height & weight) shows highest values of correlation coefficient with FVC, FEV_1 and PEFR in both genders. The

BSA was considered as the independent variable to compute the univariate regression norms for prediction of pulmonary function measurements in studied population.

In present study all pulmonary function tests except FEV1/FVC ratio were showing positive correlation with BSA. Similar findings were observed in recent study presented by Gupta KB in WISC 2012. They explained that there was correlation between PFT values and age, height, BSA & BMI of subjects. Akgün and Özgönül were also found similar findings in young children and adults.

Conclusion :

The present study brings out substantial variation in most of the parameters of PFTs between young male and female group confirming PFT values are 20-25% less in females compare to males due to body mass and body surface area difference between two group. Most of the variables of PFT also show significant positive correlation with body surface area. Applicability of Caucasian prediction equation for spirometry interpretation for Indian population is not appropriate and there is a need for reference equation in Indian subcontinent. So, in the age group of 17 to 18 years we try to established univariate regression norms between different parameters of PFT and body surface area. This will helpful in western region of India for prediction of normal spirometric parameter in young healthy subject.

Various parameters of PFT comparison with predicted values of spirometry software used in this study exhibited that there might be a possibility of regional variation or a sedentary life style in this age group need further comparison of PFT between exercising and non-exercising group.

Acknowledgment :

I am also thankful to the entire staff of Physiology Department, GCS Medical College and students for their elective participation.

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Acrodermatitis Enteropathica : A Rare Case Report with Follow Up

Pinakin Trivedi, Anjana Shah**, Hetal jeeyani*, Nayan Patel****

Abstract :

Acrodermatitis enteropathica is a rare disorder of zinc metabolism. Zinc deficiency hereditary or acquired is an important disorder of children, predominantly affecting the skin, hair, nails and the gastrointestinal system. Incidence is 1: 5, 00,000 in Danish study. Here is a case of 3 years and 3months old male child presented with multiple skin lesions all over body, predominantly on the lower limbs and buttocks since 2 months of age. Lesions were erythematous, dry, scaly & having tendency of central clearing with hypo pigmentation. He was having alopecia & angular cheilosis. Child was diagnosed as a case of Acrodermatitis enteropathica with low serum zinc & alkaline phosphatase levels. He responded dramatically to zinc therapy.

Key words : Acrodermatitis enteropathica, Zinc deficits

Presentation :

A 3years & 3months old male child came to G.C.S. Medical collage Ahmadabad with history of non healing ulcers on sheen of both tibia (Figure 1), hair loss on scalp & brows (Figure 2), low grade fever off & on, irritability, not gaining weight, and edema on both legs. He was born of non consanguineous marriage, delivered at full term with 2.750 kg. weight. He was fully breast fed up to 7 months & given primary vaccinations. He started skin lesions in the form of erythema, dry scaly plaques, vesiculobullous lesions on both limbs, buttocks & sole of foot around web areas. He was having cheilosis at angles of mouth & having poor appetite. He was treated with various antibiotics orally & local applications without any relief.

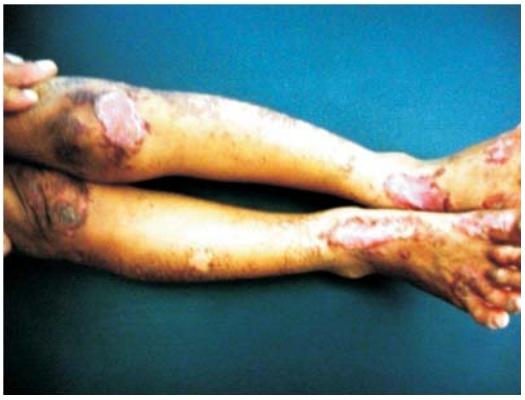

Figure 1: Non healing ulcers on sheen of both tibias (presenting feature of Acrodermatitis Enteropathica)

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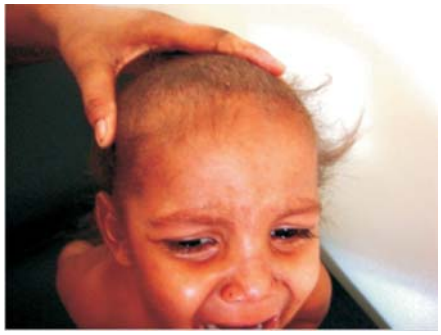

Figure 2 : Hair loss on scalp & brows (presenting feature of Acrodermatitis Enteropathica)

Examination :

Patient was weighing 10kg at 3years & 3 months with PEM grade 3. He was pale, irritable with mild pitting edema on both limbs. Alopecia was remarkable, loss of brow hairs & angular cheilosis was noted. He was running low grade fever of 100 degree F. Ulcers on both sheen of tibia was like thermal burns, Peri-anal redness & plaques & bullous lesions were noted at sole of feet.

Case evaluation & investigations :

Patient was referred from skin department & jointly investigated & managed. His Hb level was 9.5gm% with hypochromic microcytic anaemia; total WBC count was 11500 with 62% polymorphs. Total proteins were low 4.7gm/dl (6-8.3gm/dl).Clinical diagnosis was Acrodermatitis enteropathica, so serum zinc & Alkaline phosphatase levels were advised and serum zinc was 16 microgram/dl (normal range of 50 to 120microgram/dl) while Alkaline phosphatase was16.68IU/L(normal 38-94IU/L) . Which confirmed the clinical diagnosis..

Management :

Patient was given oral antibiotic Cefdinir 40mg B.D. for 10 days, supplemented with high protein diet, Iron& local application with Betadine. After confirmation of diagnosis,

orally 20 mg zinc sulphate started per day (2mg/kg). He responded fast with healing of skin lesions within 7 days of zinc therapy .His appetite improved with feeling of wellness.

Follow-up :

He started putting on weight, his scalp regained hair (Figure 3) and Hb improved to 10.9gm% within a month. His Hb improved at 11.4gm% after 5 months of treatment. Skin lesions were healed (Figure 4). His anthropometric data improved. He became playful & agile. Though he was advised lifelong treatment, He stopped zinc treatment after 1 year and 3 months. Once again skin lesions reappeared with bullous skin lesion in poplitial region& buttock. Reappearance of skin lesions on stoppage of zinc again supports the diagnosis.

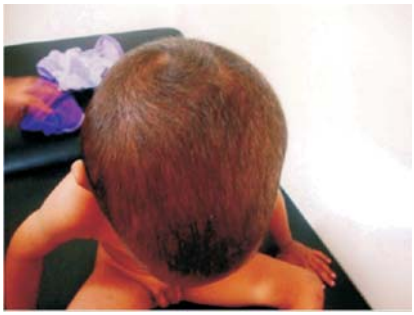

Figure 3 : Scalp regained hair after treatment of Acrodermatitis enteropahica

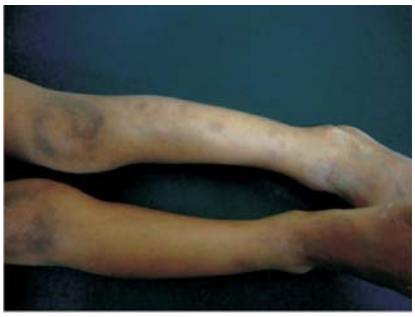

Figure 4 : healed skin lesions after treatment of Acrodermatitis enteropahica

Discussion :

Acrodermatitis enteropathica is a rare disorder of zinc metabolism. Zinc deficiency hereditary or acquired is an important disorder of children, predominantly affecting the skin, hair, nails and the gastrointestinal system.[1] Incidence is 1: 5, 00,000 in Danish study.[2] Acrodermatitis is now being used to include all acral dermatitis due to zinc deficiency i.e. hereditary or acquired. Zinc is most important trace element in humans, playing critical role in more than 200 zinc dependent metalloenzymes that regulate lipid, protein& nucleic acid synthesis & degradation. [3] Alkaline phosphatase is zinc dependent enzyme which decreased in the disease. Typical triad of alopecia, Diarrhea & dermatitis is noted in classical Acrodermatitis. Mutation at SLC39A4 gene on chromosome 8q24-3 gene erodes transmambrane protein serving as zinc uptake protein. It is autosomal recessive in character. Mainly manifest at weaning as human milk contain beneficial substance which help intake of zinc. Skin manifestation are due to zinc deficit interrupt with vitamin A metabolism-Zinc deficit impair synthesis of retinol binding protein. .Dermatitis accompanied by infection with opportunistic organisms like staphylococcus or fungal (Candida). This disease is also known as Brandt Syndrome (1936) or Danbolt- Class syndrome (1942). [4] Moyanahan in 1974 pointed out that disease is because of zinc deficit. Zinc plays vital role in immune response. In our case diarrhoea & heredity were absent. Complete triad is only found in less than 20% of cases. Such case was reported in 2002 by S. Kaur et al.[5] Naik and Beliga [6] also reported that diarrhea may not be a constant feature.

Sharma et al [7] classified hypozincemia of infancy in 3 categories. (A) Type 1: Classical AE; autosomal recessive with inheritance& manifestation after weaning. (B) Type 2: Acrodermatitis enteropathica like clinical picture seen in breastfed infant without diarrhea. There is deficiency of zinc binding legand in breast milk. This is called hypozincemia of infancy (C) Type 3: seen among Preterm infant without zinc supplement. The characteristics like distribution of dermatitis over face, limbs, hands, ano-genital area recognized as pathognomic cuteneous marker of zinc deficiency. The cuteneous lesions are psoriasiform, annular, erythematous, scaly, crusted plaques, vesiculobullous, pustular & erosive. Stomatitis, apathy, irritability, failure to thrive, hair loss & delayed wound healing may be present. Differential diagnosis may be with atopic dermatitis, Candidiasis, refractory diaper rash, epidermolysis bullosa, biotion deficit, aminoacidopathies, methymalonic acidurea, But all these do not respond to zinc. Oral zinc is available as sulfate, gluconate,citrate & acetate. 2mg/kg elemental zinc gives dramatic response. Michalss was first to use zinc as therapy.

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An Unusual Case of Parotid Tuberculosis

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Abstract :

Primary tuberculous parotiditis is a rare disease. Tuberculous abscess of right parotid gland in a 45-year-old male patient is described here. Patient underwent incision and drainage of an abscess in the right parotid swelling. The aspirate was positive for acid-fast bacilli by Z-N stain and subsequently grew Mycobacterium tuberculosis on culture. Antitubercular medications were started postoperatively. Patient was successfully managed by anti-tuberculosis chemotherapy then.

Key Words : Parotid gland, Tuberculosis, abscess.

Introduction :

Parotid gland is one of the salivary glands which are rarely infected in tuberculosis. It usually presents as a unilateral swelling or abscess involving the parenchyma of the gland either through haematogenous spread or from infection of lymph nodes within or around it. Clinical symptoms vary from an acute infectious process to an indolent chronic presentation. We represent a case of parotid gland tubercular abscess.

Case report :

A 45 year old male patient presented with a lump in right parotid region for last 1 year. The swelling was gradually increasing in size and was painless. There was no history of fever, cough, weight loss, or any other systemic symptoms. He denied any difficulty in swallowing, change in voice, or discharge into the mouth. He gave no personal or family history of tuberculosis.

General physical examination was normal. Local examination revealed a lump in the left parotid area, 5 x 4 cms in size, mobile and not attached to the underlying bone or surrounding soft tissues. It was soft-to-firm in consistency with fluctuation at the centre. There was no palpable lymphadenopathy. Facial nerve was intact and the movements of cervical spine were also normal. No discharge or calculus in the region of the salivary ducts or any tonsillar enlargement was noted. The systemic examination was also unremarkable.

The haematological and biochemical profile were absolutely normal. Chest radiograph were also normal. Ultrasonography of the lump showed a hypoechoic area in the superficial lobe of right parotid gland. Fine needle aspiration from the right parotid lump yielded purulent material, and the smears prepared show few inflammatory cells and histiocytes. No atypical or malignant cells were seen. Ziehl-Neelsen (ZN) staining for acid-fast bacilli (AFB) was negative. Culture showed no growth.

Abscess was drained surgically. Pus and scrapped material was sent for biopsy and culture which turned out positive for acid fast bacilli both on histopathology as well as on culture. Wound dressing was continued for 1 month. Simultaneously Anti-tuberculous chemotherapy (Cat-3 regimen) was started. Patient was on continuous follow-up for 6 months and he was cured then.

Discussion :

Despite tuberculosis commonly involving the lungs, extrapulmonary forms are not at all uncommon and account for approximately 20% of overall active tuberculosis, but the salivary glands appear to be rarely infected [1] [2] [3]. This may be due to the inhibitory effect of saliva on mycobacteria [3]. Tuberculous involvement of the parotid gland is extremely rare even in those areas where tuberculosis is endemic [4] [5]. The first case of parotid gland tuberculosis was reported by C De Paoli in 1893 [6]. Since then, only about one hundred cases have been reported in the literature, mostly following the parotidectomy [7].

It is thought that parotid gland tuberculosis possibly occurs by two different modes. Firstly, it may begin as infection of the teeth, tonsillar tissue or by autoinoculation with infected sputum, which reaches the parenchyma and/or lymphatics of the parotid gland by the afferent lymphatics or by ducts. Secondly, the parotid gland may be infected by metastases from the lungs by a haematogenous or lymphatic route [6] [8]. Tuberculous involvement of the parotid gland can occur in two forms. One is a diffuse, parenchymatous disease resembling common parotid inflammation and another one is involvement of intra-glandular lymphnodes. The latter usually presents with chronic, slow growing, painless, and firm parotid lump simulating a neoplasm [9]. Both the parenchymal and intra-parotid lymph nodal form may occur separately or in combination. In our case, the patient

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presented with abscess formation, suggesting the late stage of the disease process.

Figure 1: The Giant cell (a characteristic feature of TB admist plenty of lymphocytes)

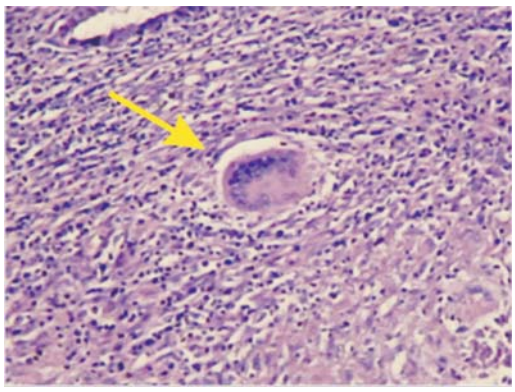
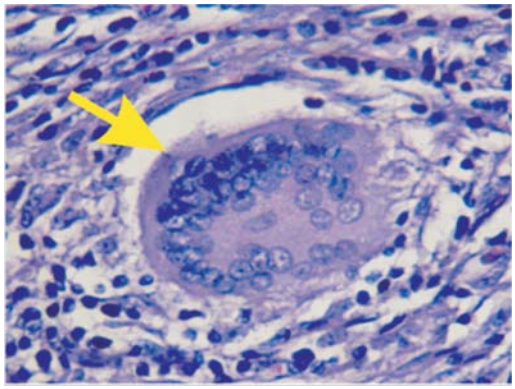


Figure 2: Magnified view (45X) of Giant cell multinucleated (Langhans type) of TB



Clinically, parotid gland tuberculosis is indistinguishable from a neoplasm, although benign neoplasms of parotid gland tend to grow slowly over years rather than over a few months, as in case of tuberculous involvement. Constitutional symptoms are usually absent, and often there is no evidence of active tuberculosis elsewhere in the body. Our patient did not have chest radiographic evidence of either active or prior pulmonary tuberculosis. In our case also, the search for primary focus of the disease was fruitless.

Imaging studies generally involve ultrasonographic examination, computerized tomography and/or magnetic resonance imaging. But there is no specific sign of tuberculosis in the parotid with any of these imaging techniques.

Although histopathological examination of the parotid gland following surgical resection remains the definitive diagnostic test, there are reports of pre-operative diagnosis of parotid gland tuberculosis by FNAC of the lesion [5] [7]. A sensitivity of 80 percent and a specificity of 93 percent have been reported for FNAC of the tuberculous lesions [10]. Thus, FNAC should be performed first in the evaluation of a parotid mass. But it is not always contributory to a diagnosis in large parotid neoplasms as these are often found necrotic. All attempts should be made for early diagnosis of parotid gland tuberculosis. The mainstay of treatment is medical in the form of anti-tubercular chemotherapy for at least six months.

Conclusion :

Tuberculosis of the parotid gland is a rare clinical entity which presents difficulties in diagnosis because of the similarity of the presentation to that of a neoplasm. Diagnosis mainly relies on the treating physician having a high index of suspicion. Although rare, tuberculosis should be kept in mind and considered in the differential diagnosis of any patient presenting with a solitary tumor in the parotid gland.

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Identification of An Emerging Pathogen Pythium Insidiosum From A Case of Onychomycosis

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Abstract :

Pythium insidiosum is a well-known fungus like plant and animal pathogen that is an emerging pathogen in humans, primarily in tropical and subtropical regions of the world. We reported a case of human pythiosis in a male patient with onychomycosis of right foot with the involvement of surrounding skin. Aseptate or sparsely septate broad hyaline hyphae were seen on primary scraping of nail. Species conformation was done by colony morphology on Sabouraud dextrose agar, production of zoosporia and motile zoospore in an induction liquid medium.

Key words : Pythium insidiosum, onychomycosis, zoospore.

Introduction :

Pythiosis is caused by genus Pythium (Gr. 'pythein'-to make rot).[1] The organism presents in two forms including right-angle branching & broad hyphae and aquatic motile biflagellate zoospore, which is a specific characteristic of the Oomycetes.[2] Pythiosis in humans is life-threatening with high rates of morbidity and mortality, especially in regions with a lack of tools for early diagnosis and effective treatment.[3] The clinical manifestations are divided into cutaneous/subcutaneous pythiosis, vascular pythiosis, ocular pythiosis and miscellaneous pythiosis or pythiosis of unusual type.[4]

Although the cases were reported from India, still the disease is not very common here and may be under diagnosed. So the purpose of this study was to increase awareness among clinicians & microbiologist about human pythiosis.

Case report :

A 35 yr old male patient, auto driver, presented at skin OPD with complaints of infection of nails of the right foot with the involvement of surrounding skin (Figure 1A) on 14th December 2011. Patient was prescribed fluconazole 150 mg, terbinafine cream, levocetrizine for 3 months. After this treatment, skin infection became restricted but nail infection still persisted, so they sent the patient to the Microbiology department for culture examination. KOH smear of nail scraping reveals broad non-septate or sparsely septate hyaline hyphae with wide-angle branching (Figure 1B).

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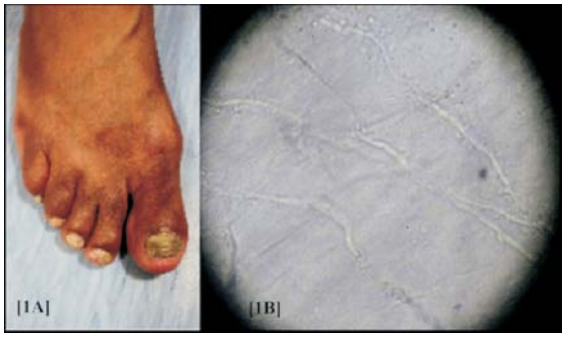
Figure 1: Photograph 1A showing patient's right foot showing onychomycosis; Photomicrograph 1B showing broad hyaline aseptate hyphae (KOH wet mount X400)



It was cultured on Sabouraud's Dextrose Agar (SDA) and incubated at both 37 C and 25 C. Growth appears after 48 hours on SDA incubated at 37 C & 25 C. Colonies were white & filamentous initially, which later on turned cream coloured (Figure 2). The LCB (Lacto phenol cotton blue) mount of culture isolate reveals broad non-septate or sparsely septate hyaline hyphae with granular cytoplasm & terminal swellings.

Figure 2 : Photograph showing colony of P.insidiosum on SDA

We had demonstrated zoosporangia & motile zoospores. A few boiled grass leaves are placed on *P. insidiosum* culture and after 24 hours of incubation at 37^{0}C, zoosporangium-containing zoospores may be observed at the edges of leaves. The parasitized grass leaves are then placed in beaker containing dilute salt solution for 2-3 hours at 37^{0}C. They are then transferred to slides and motile zoospores were observed.[1] After reporting of organism the same treatment was continued for 2 months more, when patient came for follow up, nail infection was also become restricted & under control. At that time repeat culture was negative.

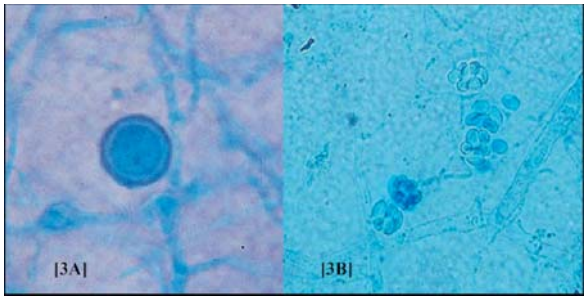
Discussion :

P. insidiosum is cosmopolitan soil & aquatic organism, which has an ecological preference for swampy environment (farming field, river, and pond). [1] [2] A common route of infection by *P. insidiosum* via zoospores through small cuts or body cavities of individuals who spend time in or drink from stagnant swampy waters or fields. [7] Once the zoospores are in contact with mammalian or plant tissue (in wet environments), they encyst on the surface of the injured tissue(s). [1] [3] Pythiosis occurs in tropical, subtropical and temperate areas, being reported in several countries including Argentina, Australia, Brazil, Colombia, Costa Rica, Egypt, USA, Greece, Haiti, India, Indonesia, Japan, Papua New Guinea and Thailand. [5]

Pythium insidiosum infections occur mostly in apparently healthy humans and animals. [3] There are some human pythiosis with unusual sites of infection including the gastrointestinal tract, brain, and rhino sinus. This indicates that P. insidiosum can infect various types of host tissues.[2] To our knowledge, this is the first case of P.insidiosum isolated from nail infection in humans from India. The source of infection in this patient remained unclear & this patient was apparently healthy. He belongs to lower socio economic class so source of infection may be muddy water or temperate river water. [1]

It is diagnosed by culture examination, serological test or molecular methods. The serodiagnostic tests, includes ID (immuno-diffusion) test, ELISA, and Western blot method, but have a limited use due to a low sensitivity (especially in ID test) or a requirement of skilled personnel and special equipments. [2] In this patient, nail scraping shows yellowish scraping material which on KOH wet mount shows aseptate or sparsely septate broad hyaline hyphae & growth was also filamentous & white initially. So it should be misdiagnosed as mucormycosis or entomophthoromycosis.[1] Since P. insidiosum was recognized as the only oomycete pathogenic for mammals for a long time, induction of zoosporogenesis was considered enough for a presumptive diagnosis of pythiosis. [3] Zoospores swim in a helical or spiral pattern interrupted by random changes of direction. [1] [3] Zoospores moved very actively for about 10 to 60 min before encystment and germination. [9] We could also demonstrate LCB mount zoospores (Figure 3B) & oospores (Figure 3A) from very old culture of *P. insidiosum* on SDA.

Figure 3 : Photomicrograph 3A showing oospore of P.insidiosum (LPCB preparation X 1000); 3B showing zoospores of P.insidiosum (LPCB preparation X 1000)



There are no recorded cases of spontaneous remission in human pythiosis. Therefore, if left untreated, infection is bound to be life- threatening in due course of time. [1] Successful treatment of pythiosis in humans has involved the use of potassium iodide, administration of an immunotherapeutic vaccine and, usually, surgical excision of the infected tissue. [6] The true fungi contain chitin and β -glucan in their wall, while *Pythium* contains cellulose and β -glucan. The plasma membrane is free from sterols (as ergosterol), a pathway where most of the antifungal drugs act. [5] Therefore, successful treatment with either amphotericin alone or the azole fungicides might not be expected. However, one patient with deeply invasive facial infection was successfully treated with a combination of terbinafine and itraconazole. [6] In this patient also fluconazole along with terbinafine seems to be very effective by resolving the lesions as seen in case reported by Jerry L. Shenep and collegues. [8] Use of β-glucan inhibitor including caspofungin, micafungin, or anidulafungin may be effective in the treatment of pythiosis. [2]

We conclude that Pythium insidiosum is a causative agent of pythiosis and is distributed worldwide. Diagnosis of pythiosis is time consuming, and requires skilled personnel. It may be under diagnosed due to unfamiliarity among clinicians and microbiologists & sometimes also

misdiagnosed as mucormycosis or entomophthoromycosis. The disease has high morbidity & mortality. So early detection and effective treatment are needed for possible cure.

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Essential Thrombocythemia in A Patient With Portal and Superior Mesenteric Vein Thrombosis

Amar R Shah [*], *Sanjay Chaudhari* [**], *Monica Gupta* [**], *Menka Shah* [***]

Abstract :

Essential thrombocythemia is associated with abdominal thrombotic complications including portal and superior mesentric vein thrombosis. Essential thrombocythemia in a latent form is difficult to identify at onset due to the absence of an overt disease phenotype. In the presented case report, patient had chief complaint of abdominal pain on admission in hospital. Portal and superior mesenteric vein thrombosis was confirmed by Computed Tomographic (CT) Scan. Persistent increased platelet count, increased mature and hyperlobated megakaryocyte in bone marrow, JAK2 mutation confirmed the diagnosis of essential thrombocythemia.

Key-words : Essential thrombocythemia, platelet Count, portal and superior mesenteric vein thrombosis, JAK2 mutation.

Introduction :

Essential thrombocythemia is a chronic myeloproliferative disorder characterised by sustained elevation of the platelet count with a tendency to thrombosis and haemorrhage.[1] The prevalence of ET is around 1.5/1,00,000 inhabitant.[2] The diagnosis of ET is more established today than in the past.[3] The reason being a wider use of automated cell counter in routine examination leading to the increased diagnosis of more non symptomatic ET patients. Patients often (upto 50%) present with asymptomatic thrombocytosis, however half the patients present with haemorrhage or thrombosis.[4] Bleeding occur most commonly from mucosal surfaces such as gastrointestinal tract or upper airway passages.[5]

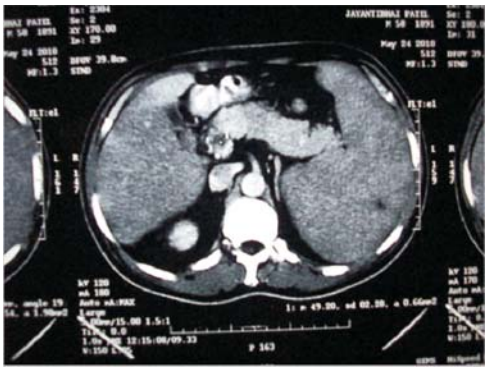
Case Report :

A 55 years old male patient presented with chief complaints of abdominal pain, easy fatigability, and generalised weakness. On examination pulse rate was 72 /min, blood pressure 150/90 mm/Hg and respiratory rate was 20/ min. There were no signs of pallor, jaundice or lymphadenopathy. Per abdominal examination revealed an enlarge spleen, 2 cm below the left costal margin and the liver was 1 cm below the right costal margin.

Complete Blood Count findings revealed Hb-135 g/L , Hct-51.1, MCV-75.7 fl, MCH-22.3 pg , MCHC-29.4% , Total count-32.4x10^9/L, RBC-6.75x10^{12} /L , platelet count 472x10^9/L. Peripheral smear findings revealed normocytic and normochromic RBCs and also confirmed the increased total count and platelet counts. Bone marrow aspiration and biopsy findings revealed a hypercellular marrow, with increased M:E ratio (6:1), increased megakaryocytic precursors with large size and hyperlobulation. The granulocytic and erythroid lineage were unremarkable.

Computed tomography scan showed thrombosis of portal and mesenteric vein. (Figure 1)

Figure 1 : Computed tomography scan showed thrombosis of portal and mesenteric vein



JAK 2 mutation[6] was positive (JAK2 mutation was confirmed by PCR analysis at Super Religare Lab. Mumbai) and Philadelphia chromosome was negative. (Philadelphia chromosome (BCR- ABL) analysis was done by Bone marrow culture metaphase karyotyping (G banding) at Gene Lab Surat)

Discussion :

Essential thrombocythemia (ET) is a chronic myeloproliferative neoplasm that involves primarily the megakaryocytic lineage. There is sustained thrombocytosis >450x10^9/L in the peripheral blood, increased numbers of large, mature megakaryocytes in the bone marrow (BM). It is characterised clinically by episodes of thrombosis and/or haemorrhage. ET is frequently

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associated with thrombotic complications in the large abdominal vessels. ET usually carries the best prognosis among the MPD, but abdominal vein thrombosis was identified as a risk factor for poor survival and appeared to be the result of excess death from leukemic or fibrotic transformation and hepatic failure. [7]

Because there is no known genetic or biological marker specific for ET, other causes for thrombocytosis must be excluded including other MPN, inflammatory and infectious disorders, haemorrhage and other types of haematopoetic and non haematopoetic neoplasms.

The morphological findings in the bone marrow biopsy are essential to distinguish ET from other myeloproliferative neoplasms, myeloid disorders and reactive conditions that present with sustained thrombocytosis. The findings of even a mild degree of combined granulocytic and erythroid proliferation should raise consideration of prodormal stage polycythemia vera and the findings of granulocytic proliferation associated with bizarre, highly atypical megakaryocytes should prompt concern for the prefibrotic stage of primary myelofibrosis. Marked proliferation of megakaryocytes with a predominance of large to giant forms displaying abundant, mature cytoplasm and deeply lobulated and hyperlobulated (stag-horn like) nuclei is the most striking diagnostic abnormality in ET.

Recently the discovery of a mutation in V617F of the *Janus Kinase* 2 gene in a significant proportion of ET patients provides a new strategy for molecular diagnosis. Although helpful in distinguishing ET from reactive conditions that may cause thrombocytosis, the mutation is not specific for ET but is found in polycythemia vera and primary myelofibosis as well.

Differential diagnosis : Reactive thrombocytosis, Other Chronic myeloproliferative disorder e.g.: Polycythemia Vera, Myelofibrosis, CML.

In present case of 55 year old male patient, the haemoglobin level was 13.5 g/dl, the bone marrow showed only megakaryocytic hyperplasia in the absence of panmyelosis. So the diagnosis of polycythemia vera was ruled out. The absence of a BCR-ABL 1 fusion gene excluded the diagnosis of Chronic myeloid leukemia. Absence of anaemia and leucoerythroblastic blood picture and absence of fibrosis in bone marrow go against the primary myelofibrosis. Presence of JAK2 V617F mutation, absence of iron deficiency, a normal MCV, negative history of malignancy, splenectomy and chronic inflammatory disease exclude reactive thrombocytosis. Therefore, diagnosis Essential thrombocthemia was rendered.

Treatment :

Harrison et al[8] reported that hydroxyurea and low- dose aspirin was superior to anagrelide, which is blocking megakaryocyte differentiation, and aspirin for patients with ET at high risk for vascular events. They defined patients with ET as high risk if they met one or more of the following criteria: an age older than 60; platelet counts more than one million; a history of ischemia, thrombosis, or embolism; hemorrhage caused by ET; hypertension requiring therapy; and diabetes mellitus requiring hypoglycemic agents. The patient was given hydroxyurea and is currently on low dose aspirin therapy. Condition of the patient is stable and is on regular follow up.

Conclusion :

In patient with episode of thromboembolic disorder and elevated platelet count, detail investigations like bone marrow examination and molecular studies like JAK-2 mutation should be done to rule out latent form of essential thrombocythemia.

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A Case Report on Classic Ehler-Danlos Syndrome

Nayan Patel, Anshul Jain**, Yogesh Shah****

Abstract :

Ehlers-Danlos syndrome also know as cutis hyper elastica is a heritable connective tissue disorder with skin involvement comprising a phenotipically diverse group of conditions characterised by defect in various collagens genes. We present a case of 12 year old female with typical cutaneous and joint involvement diagnostic of classic variety of Ehlers- Danlos syndrome.

Key words : Ehlers-Danlos syndrome, Joint Hypermobility, Absent Frenulam

Introduction :

Ehlers-Danlos syndrome is group of more than 10 heterogeneous groups of inherited connective-tissue disorders characterized by joint hypermobility, cutaneous fragility, and hyperextensibility due to genetic defect in collagen and connective-tissue synthesis and structure. Reported prevalence is 1 in 400,000 persons which have no race or sex related predilection. Out of all type described in Vascular type(type 4) patient has shortened life span due to organ perforation or major arterial rupture [(1)], rest all type are not as dangerous and affected individual can live healthy if somewhat restricted life.

Case presentation :

12 year old Muslim girl born out of consanguineous marriage was referred to skin department from Dental department for evaluation of her abnormal skin condition as she wanted to underwent excision of tooth from oral cavity.

Otherwise healthy patient had history of prolong healing time and healing with thin scar for minor trauma and one episode of fall and trauma on chin following which her family physician was unable to take suture as suture were cutting through the margin of wound. No family History of similar skin condition was elicited. Patient had history of full term normal hospital delivery with normal achievement of developmental milestone. There was no history of mental retardation, convulsion, breathlessness, dislocation of joint or any fracture,

On examination : Her skin was hyper extensible with doughy feel, Fraenulum underneath the tongue was absent.

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Joint examination revealed following findings

1. Bilateral passive dorsiflexion of palm $\geq 90^0$
2. Bilateral passive dorsiflexion of thumbs to forearm
3. Bilateral hyperextension of elbows beyond 10^0
4. Hyperextension of the knees beyond 10^0

(Patient scores more than 5 on Beighton's criteria) [(2)]

No Visible vessels, no varicose vain, no kyphoscoliosis, no flat feet were observed

Examination of Respiratory, Cardio-vascular, Central and peripheral Nervous system and Alimentary system revealed no abnormality.

Investigations :

Her blood counts and biochemistry profile like RBS, Liver profile, renal profile and coagulation profile were within normal limit.

ECG and Echocardiogram was normal

On the basis of History, clinical examination and Investigation she was diagnosed to having Ehler-Danlos syndrome type 1(Classical). Dentist was made aware of possible risk during tooth extraction and suture application and advised to use surgical glue if possible.

Counselling : Parents of the patient were made aware of her condition and advised to avoid trauma as far as possible, avoid consanguineous marriage, and possible high risk pregnancy (possibilities of uterine rupture)

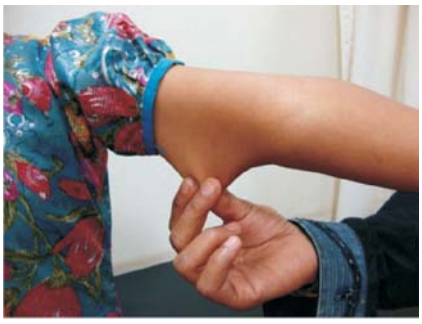

Figure : 1 Hyperextensible skin

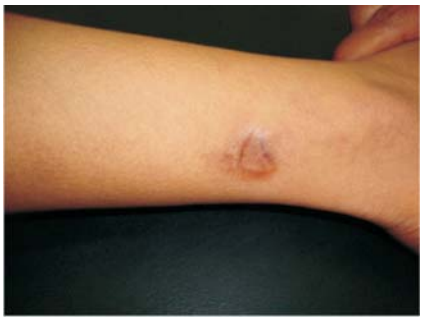

Figure : 2 Showing cigarrette paper scars at the site of trauma

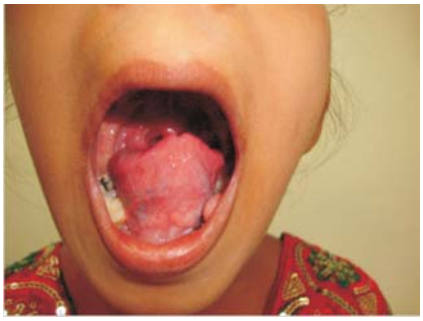

Figure : 3 Absent Frenulam

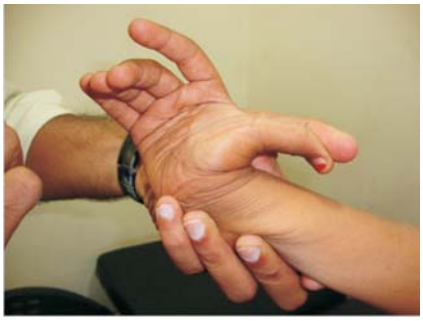

Figure : 4 Passive dorsiflexion of thumb to forearm

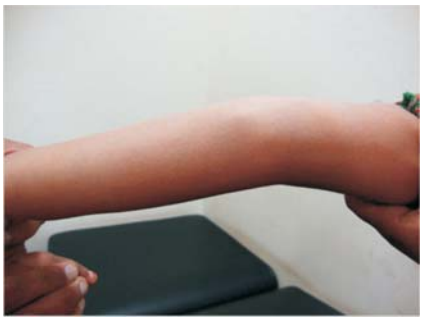

Figure : 5 Extension of Elbow more than 10

Discussion :

Dr. Ehler and Danlos Danish and French dermatologist respectively contributed to the clinical description of these conditions in early 1900 and this clinical constellation became known as the Ehler-Danlos syndrome. First molecular defect in collagen synthesis were described in 1972 and currently the molecular basis of most major forms of EDS is Known [4][5]

To date, 11 variants of Ehlers-Danlos syndrome are identified; all have genetic, biochemical, and clinical differences. More than one third of persons with Ehlers-Danlos syndrome do not fit exactly into a single type; overlap is common.

The collagen family is known to consist of as many as 28 distinct proteins with differential tissue distribution. Each collagen molecule is synthesis as precursor molecules pro-a-chain which may be either hetro or homo trimer, as a result, there are well over 40 genetically different pro a chain each being a distinct gene product[5]

The collagen defect has been identified in most of the types of Ehlers-Danlos syndrome. In Ehlers-Danlos syndrome types I and II, the classic variety, identifying the molecular structure in most individuals who are affected is difficult. Causative mutations may involve the *COL5A1, COL5A2,* and *tenascin-X gene* [7] significant portion of the mutations result in low levels of mRNA from the mutant allele as a consequence of nonsense-mediated mRNA decay. Transmission electron micrographs of type I collagen fibrils in a proband dermal biopsy specimen demonstrated heterogeneity in fibril diameter that was greater than that of a matched control sample. The proband was found to have a greater proportion of both larger and smaller fibrils, and occasional fibrils with a cauliflower configuration were observed.[8] Wenstrup and associates identified haploinsufficiency of the *COL5A1* gene that encodes the proalpha1 (V) chain of type V collagen in the classic form of Ehlers-Danlos syndrome. Eight of 28 probands with classic Ehlers-Danlos syndrome who were heterozygous for expressed polymorphisms in *COL5A1* had complete or nearly complete loss of expression of one *COL5A1* allele. One third of individuals with classic Ehlers-Danlos syndrome were estimated to have mutations of *COL5A1* that result in haploinsufficiency. These findings suggest that the normal formation of the heterotypic collagen fibrils that contain types I, III, and V collagen requires the expression of both *COL5A1* alleles.[9] Autosomal recessive type VI Ehlers-Danlos syndrome, also known as the kyphoscoliotic type is attribute to a deficiency in lysyl hydroxylase (LH), more than 20 mutation have been identified in LH gene. Yeowell and walker have reported two of them involving large duplication of exon 10-16 and nonsense mutation Y511X [10]. Tenascin-X is a large extracellular matrix protein, a deficiency of which causes a clinically distinct recessive form of this syndrome[11]. A novel

point mutation has been found in the vascular type of Ehlers-Danlos syndrome. The mutation took place in the second position of exon 24 of *COL3A1*.[12]

Common to all form of Ehler-Danlos syndrome are skin changes of white, soft skin in which underling vessels may be visible. Skin has doughy feel and hyper extensible and return to normal position immediately. Prolong healing time after trauma is common and suturing is difficult, wound dehiscence is common and may heal with cigarette paper type scar. Molluscoid pseudo tumour is common around scar. Subcutaneous spheroids are palpable free movable nodules over tibia and arms which may show calcification on radiography. Musculoskeletal features are easily found. These features include kyphoscoliosis, hallus valgus, pes planus (i.e., flat feet), and genu recurvatum. Cardiac defects, especially mitral valvular prolapse, are sometimes present. Dental finding includes hypodontia of permanent teeth, delayed eruption and dentin dysplasia.[13] Vascular type may present as splenic rupture due to peliosis.[14] Ehler-Danlos syndrome may be associated with cutaneous metaplastic synovial cyst.[15], multiple sclerosis[16], solitary rectal ulcer[17] and anorexia nervosa[18]. Beighton et al has described diagnostic criteria for classic form of Ehler-Danlos syndrome which include scores for joint Hypermobility[2].

It is important to identify Ehler Danlos syndrome type 4 which has worst prognosis and patient has considerable short life span due to spontaneous mitral valve prolapsed and perforation of large vessels most commonly splenic artery or other intra abdominal vessels or organ perforation and spontaneous pneumothorax. In this form skin is white translucent and shiny but not extensible and subcutaneous vessels are easily visible, joint hyperextensibility is rare or absent.

Limitation of study : Gold standards for the diagnosis of various types of Ehler Danlos Syndrome are combination of electron microscopy of dermal collagens, protein chemistry analysis from cultured fibroblast and mutation detection. Either of above was not available in our institute and was not performed outside because of finincial constrain. Though histopathology is of limited value in Ehler Danlos Syndrome, patient was counselled for skin biopsy but because of pre existing tendency of delayed wound healing and paper thin scaring patient was reluctant to undergo biopsy. Hence Histopathological evidence was not available.

Conflict of interest : None

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Unusual Presentation of Tuberculosis with Candida In Maxillary Sinus

Parimal Patel*, Sanjay Rathod**, Afroz Bloch, P.D.Shah*******

Abstract :

Tuberculosis is a common disease in developing countries with both pulmonary & extra pulmonary presentations with prevalence being 85% & 5% respectively. Tuberculosis of sinuses is a rare finding when the extra pulmonary tuberculosis cases are taken into consideration . In our case, a 40 yrs male patient presented with complain of repeated cold & left sided peri orbital swelling. Investigations revealed a mass in left maxillary sinus suspected to be a fungal growth which on microbiological examination showed *Candida glabrata* & acid fast bacilli as the etiological agents. The patient didn't have any underlying immunocompromised status. He was put on antifungals & Anti Kochs Treatment(AKT) for the same.

Key words : Extrapulmonary tuberculosis, maxillary sinus, Candida *glabrata*

Introduction :

Tuberculosis, one of the oldest diseases in man, is even today a leading cause of human suffering and loss of life. *Mycobacterium tuberculosis (humanis/bovis)* most frequently reaches the lungs through blood stream or lymphatics and rarely involves paranasal sinuses, nasopharynx, nose and facial bones. [1] It is sometimes confused with granulomatous or neoplastic processes for which diagnostic suspicion is important. Although the incidence of mycobacterial diseases, especially the extrapulmonary type is on the rise in many regions of the world, it still remains an underdiagnosed entity. It's because of occasional and uncommon clinical presentation with the involvement of atypical sites. [1] Mainly two types of tuberculous lesions of the antrum have been described. First type occurs less frequently and in this, there is an infection of the mucosa where the antrum is filled with a polypoidal thickened mucosa which presents boggy and pale appearance. The other type which has a tendency to spread shows bony erosion, fistula formation and caseation. Both types have tendency to be symptom free till the lesion is very much advanced. In cases with orbital involvement the only symptom may be epiphora and vision may be affected when the condition is very much advanced.[2]

Case Report : A 40 year old male patient from lower socio-economic class residing at rural region of Kutiyana, Porbandar, Gujarat, presented with C/O repeated cold & left sided periorbital swelling since 3 months, aggravated 1 week prior admission. He had past history of pulmonary tuberculosis. Locally the swelling was red, tender, periorbital & extending to the left cheek downwards up to the line joining the nasal ala & mastoid process leading to difficulty in speaking with history of weight loss. Nasal examination revealed purulent discharge and middle and inferior turbinates were absent. He was on oral antibiotics from last one month, but the swelling persisted. Haemogram report revealed. Total leucocyte count - 11600, Lymphocytes-21%, Monocytes-4%, Eosinophils-10%, Erythrocyte Sedimentation Rate(ESR) 20 mm after one hour by Westergreen method. X-ray of the paranasal sinus revealed haziness in the left maxillary sinus. CT-Scan revealed fungal sinusitis showing bilateral sphenoidal sinusitis. A soft tissues swelling was present over the left cheek and orbital region. For it, the patient was operated under general anaesthesia, brownish soft tissue mass was removed, through the left maxillary sinus .The specimen was sent for fungal examination, histopathological examination and for culture and sensitivity which revealed necrotizing granulomas with casseation, epitheloid cells and lymphocytes and on ZN stain it was **positive for AFB.** Specimen was also positive for fungi showing, budding yeast like cells and on culture *Candida glabrata* isolated.

Fig. 1 : Periorbital swelling

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Discussion : Most cases of tubercular involvement of the maxillary sinus are secondary to pulmonary tuberculosis.[1] Gleitsmann in 1907 reported that a search of literature revealed 20 cases of Maxillary Sinus Tuberculosis, other sinuses were infected less frequently.[3] The facial bones are unusual sites for tuberculosis and very few cases of maxillary sinus tuberculosis have been reported.[4] Clinically, the tuberculosis of maxillary sinus is characterized by lack of early symptoms and appearance of fluctuant swelling.

To conclude tuberculosis is not a foe to be forgotten. Sitting dormant in vivo for years, it can erupt suddenly as in this case. TB in tissue & specifically in the sinuses is a very rare finding. The clinician and microbiologist both may be tempted to search for fungus in this tissue sample provided, given the symptoms & the relative immunosuppressive frame of the patient due past history of Kochs & hypertension, but the pink color rods amidst the blue sea of pus cells on ZN stain, bacteria & even Candida lent a surprise to the clinical Microbiologist.

Because TB can affect almost all body organs & parts, it should always be kept in some of the grey cells of our brains while diagnosing so that we don't miss out this deadly disease.

This case calls for an all out, rationally planned & reasoned systemic diagnostic approach with regular follow up & proper history elicitation of the patient. You never know which single thing will provide you the bread crumbs you need to follow the trail of the pathogens.

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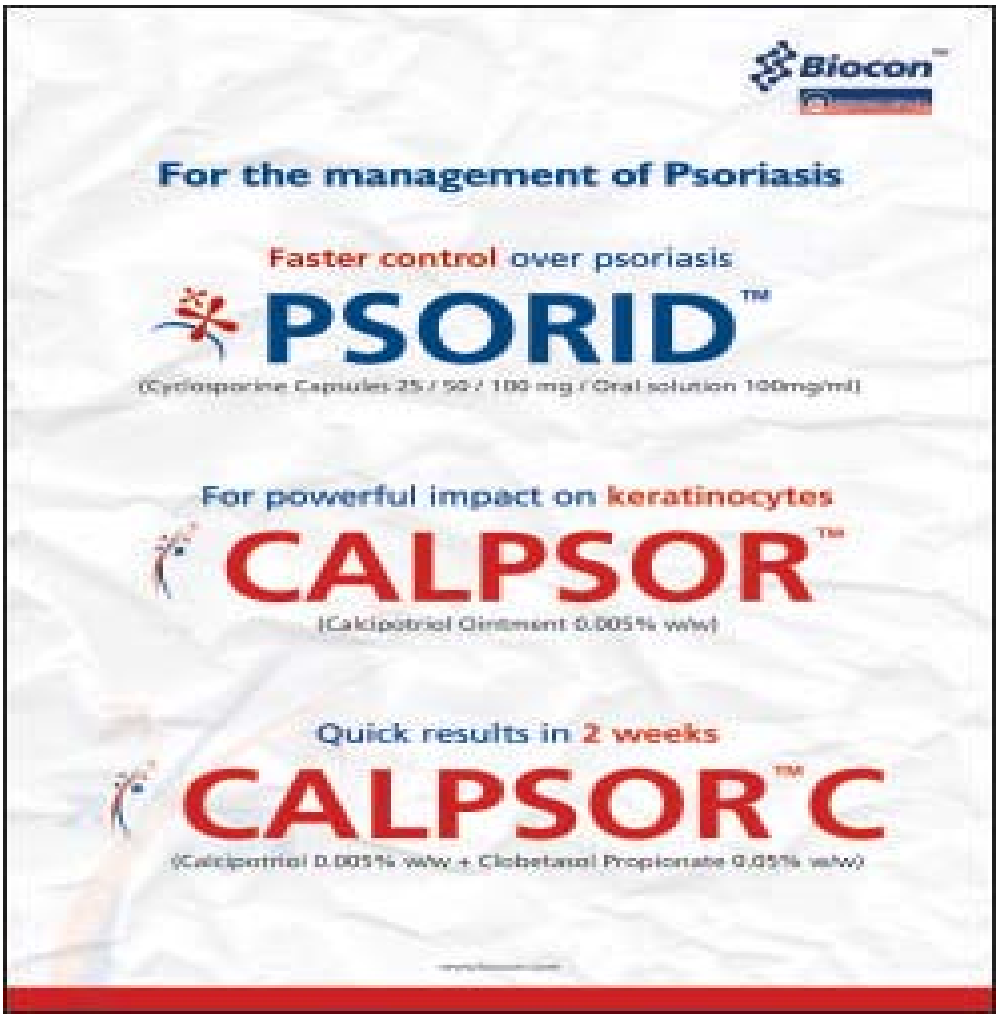


A Case Report on Absence of The Quadratus Femoris Muscle

Kiran Arora, Sudarshan Gupta***

Abstract :

The quadratus femoris is a rectangular muscle seen in gluteal region of lower limbs. Its upper border lies edge to edge with the inferior gemellus and its lower border with the upper margin of the adductor magnus. Action of the quadratus femoris muscle is lateral rotation of thigh at the hip joint. Unilateral absence of quadratus femoris muscle (QFM) was identified during routine dissection of 65 year old male cadaver at Anatomy Department of a Medical College.

Introduction :

Usually the origin of the quadratus femoris muscle is upper part of the external surface of ischial tuberosity. Quadratus femoris muscle extends laterally and is inserted on to the quadrate tubercle near middle of the inter trochanteric crest of the femur and from there extends vertically downward for a short distance. The lower border of quadratus femoris bisects the lesser trochanter. [1]

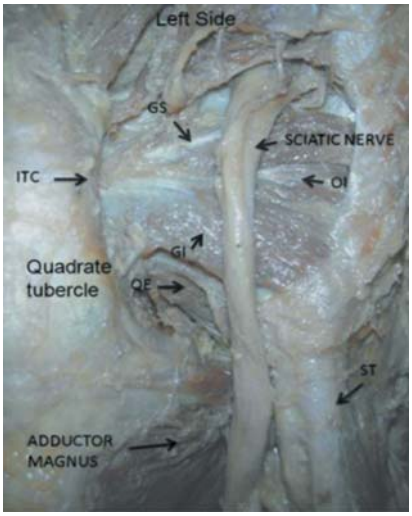
The elevation of quadrate tubercle represents the site of fusion of the epiphysis of greater trochanter and is not represented by pull of muscle. The cruciate anastmosis of arteries take place at the root of greater trochanter in the interval between the quadratus femoris and the upper border of the adductor magnus.

The quadratus femoris is supplied by the nerve to quadratus femoris which conveys fibers from the ventral branches of ventral rami of L4, L5 and S1 from sacral plexus. The nerve enter the gluteal region through the greater sciatic foramen below the piriformis and runs downwords deep to the sciatic nerve, the obturator internus , the gemelli and reaches the muscle from its deep surface. It also supplies twigs to the gemellus inferior and the hip joint.[2] Action of the quadratus femoris muscle is lateral rotation of thigh at the hip joint.

Case Report :

During routine educational dissection of gluteal region, lower limb of 65 years old male cadaver in Department of Anatomy in College of Medical sciences, Amargadh, (Gujarat) 2009, it was found that on left side quadratus femoris muscle was absent. There was a gap between left gemelli and left adductor magnus muscle. Some part of obturator externus was seen between these muscles. Nerve to quadratus femoris was present, normally it supplies to quadratus femoris and inferior gemellus and capsule of hip joint but in this case it was supplying to inferior gemellus and hip joint. There was no compensatory enlargement of any other muscle. Right side structures were normal. There was no other variation found.

Absence of quadratus femoris is occurring in 1% subject. [4]



ITC= Intertrochanteric crest, GS= Gemellus superior, GI = Gemellus Inferior, OI = Obturator Internus muscle, OE = Obturator externus muscle, ST= Semitendinosus

Figure 1 : Unilateral absence of quadratus femoris left side

Discussion :

As such many anatomists have observed various type of muscular variation. Like extra slip or head of origin or insertion of muscle. Absence of muscle is a rare finding other than the rudimentary muscles like psoas minor [3] and plantaris muscle [3] which are frequently found absent. In this case it was found that in the left side gluteal region, the quadratus femoris was absent. Such peculiarity in human being with absence of quadratus femoris is occurring in 1% subject.[4] E.P. Stibbe had observed absence of left side quadratus femoris while nerve to the quadratus femoris occupied its usual position under great sciatic nerve which supply inferior gemellus and capsule of hip joint. There were no other muscular abnormalities. [4]

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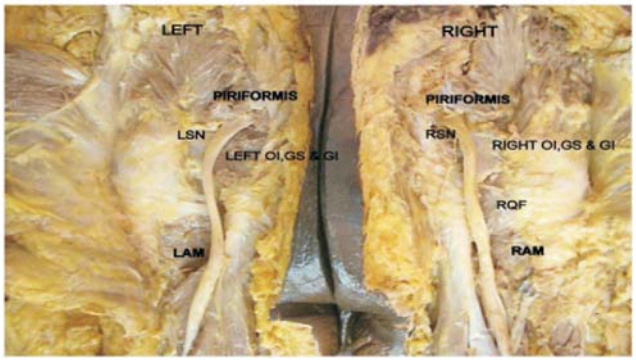

Figure 2 : Both side of gluteal region showing left Quadratus femoris muscle was absent (LSN - Left Sciatic Nerve, RSN - Right Sciatic Nerve, OI Obturator Internus muscle, GS Gemellus Superior, GI Gemellus Inferior, RQF Right Quadratus Femoris)

Hao LIU et al [5] observed bilateral absence of both quadratus femoris muscle and semimembranous muscles. Superior and inferior gemelli and tendon of obturator internus was not visibly enlarged to compensate the missing space. In present case similar findings were observed that there was no compensatory hypertrophy of surrounding muscles.

Bellamy E et al. [6] observed absence of quadratus femoris muscle while Hallett and Schwegel reported its absence and replaced by an unusually thick Obturator internus muscle. [7]

Other variations of quadratus femoris were also observed by other anatomist like it may be fused with the inferior gemellus or with adductor magnus, replaced by large inferior gemellus or obturator internus. It may be divided at its femoral insertion into two parts: one posterior, with the normal attachment and the other anterior, with insertion onto the inter trochanteric crest.

Quadratus femoris muscle is lateral rotator of hip joint. Obturator externus, obturator internus, superior and inferior gemelli, piriformis are also lateral rotator of hip joint. In case of absence of quadratus femoris muscle, others will laterally rotate the limb. Absence of quadratus femoris may be accompanied by compensatory hypertrophy of the other lateral rotator muscles of hip joint but not always. As such the compensatory hypertrophy may be developmental or acquired. We can say compensatory hypertrophy depends on the lifestyle of the person like powerful lateral rotation of the hip is required to throw a baseball, swing a bat or golf players.

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   The text of original articles amounting to up to 3000 words (excluding Abstract, references and Tables) should be divided into sections with the headings Abstract (structured - max. 200 words), Key-words, Introduction, Material and Methods, Results, Discussion, References (max. up to 25), Tables and Figure legends.

2. Case report:

   It should have max. limit up to 1000 words (excluding Abstract and references) and should have the following headings: Abstract (unstructured - max. 200 words), Keywords, Introduction, Case report, Discussion, Reference (max. up to 10), Table and figure legends.

3. Review article:

   It should have abstract (max. 200 words), introduction / historical background, discussion, conclusion, References, Tables and Figure legends.

4. Short communication:

   The length of it should not exceed 1000 words and references 10.

References

References should be numbered in the order of appearance in the text (not in alphabetic order). The titles of journals should be abbreviated according to the style used in Index Medicus. The commonly cited types of references are shown here, for other types of references please refer to ICMJE Guidelines

(http://www.nlm.nih.gov/bsd/uniform requirements.html).

1. Journals

   a. Shukla N, Husain N, Agarwal GG and Husain M. Utility of cysticercus fasciolaris antigen in Dot ELISA for the diagnosis of neurocysticercosis. Indian J Med Sci 2008;62:222-7.

2. Books and Other Monographs

   a) Personal author(s): Ringsven M and Bond D. Gerontology and leadership skills for nurses. 2nd ed. Albany (NY): Delmar Publishers; 1996.pp 616

   b) Editor(s), compiler(s) as author: Norman IJ, Redfern SJ, editors. Mental health care for elderly people. New York: Churchill Livingstone; 1996.pp 617.

   c) Chapter in a book: Phillips SJ and Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: pathophysiology, diagnosis, and management. 2nd ed. New York: Raven Press; 1995. pp. 465-78.

3. Electronic Sources as reference

   a. Journal article on the Internet

      Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [serial on the Internet]. 2002 Jun [cited 2002 Aug 1 2];1 02(6):[about 3 p.]. Available from:

      http://www.nursingworld.org/AJN/2002/june/Wawatch.htm

   b. Monograph on the Internet

      Foley KM and Gelband H, editors. Improving palliative care for cancer [monograph on the Internet]. Washington: National Academy Press; 2001 [cited 2002 Jul 9]. Available from: http://www.nap.edu/books/0309074029/html/

   c. Homepage/Web site

      Cancer-Pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources, Inc.; c2000- 01 [updated 2002 May 16; cited 2002 Jul 9]. Available from: http://www.cancer-pain.org/.

   d. Part of a homepage/Web site

      American Medical Association [homepage on the Internet]. Chicago: The Association; c1995-2002 [updated 2001 Aug 23; cited 2002 Aug 12]. AMA Office of Group Practice Liaison; [about 2 screens]. Available from: http://www.amaassn.org/ama/pub/category/1736.html

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