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Editorial

WHO & World Health Day

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Origin of WHO :

The International sanitary conferences originally held on 23 June, 1851 was the first predecessor of the WHO. A series of 14 conferences from 1851 to 1938 of international sanitary conferences worked to combat many diseases chief among of them are cholera, yellow fever and the bubonic plague. In 1892 the international sanitary conference dealt with cholera and in 1897 the convention for plague was signed. As a result of successes of the conferences, the Pan American Sanitary Bureu and the office International d'Hygiene Publique were soon founded in 1902 and 1907 respectively. When the League of Nations was formed in 1920, they established the Health organisation of the league of Nations. After world war II the united Nations absorved all the other Health organisations to form the WHO.

The use of the "World" rather than "International" emphasized the truly global nature of what the organisation was seeking to achieve. The constitution of the world Health Organisation was signed by all 51 countries of the united Nations and by 10 other countries on 22nd July 1946. It thus became the first specialised agency of the United Nations to Which every member subscribed. Its constitution formally came into force on the first world Health day on 7th April 1948, when it was ratified by the 26 member state.

Over all Focus :

The WHO's constitution states that its objective is the attainment by all people of the highest possible level health.

The WHO fulfills the objective through its functions as defined in its Constitution.

(a) To act as the directing and coorditinating authority on international health work. (b) To establish and maintain effective collaboration with the United Nations, specialized agencies, government health administrations, professional groups and such other organisations as may be deemed appropiate. (c) To assist Government, upon request, in strengthening health services. (d) To furnish appropriate technical assistance and, in emrgencies, necessary aid upon the request and acceptance of the Governments. (e) To provide or asist in providing, upon the request by United Nations, health services and facilities to special groups, such as the peoples of trust territories. (f) To establish and maintain such administrative and technical services as may be required, including epidemiological and statistical services. (g) To stimulate and advance work to eradicate epidemic, endemic and other diseases. (h) To promote, in co-operation with other agencies when necessary, the improvement of nutrition, housing sanitation, recreation, economic or working conditions and other aspects of enviornmental hygiene. (i) To promote cooperation among scientific and professional groups which contribute to the advancement of health. (j) To propose conventions, agreements and regulations and make recommendations with respect to international health matters and to perform.

Membership :

As of 2016, the WHO has 194 member states. A State becomes a full member of WHO by ratifying the treaty, known as the constitution of World Health Organisation. There are also some associate members like Puetro Rico and Tokelou. Several countries have been granted observer status like Palestine.

The Executive Board is composed of members technically qualified in health and gives effect to decision and policies at Health Assembly. WHO has official relations with International committee of the Red Cross, International Fedaration of Red Cross and Red Crescent societies.

World Health Assembly (WHA) is the legislative and supreme body of WHO, based on Geneva. It meets in May to appoint the Director General every five years. The assembly elects 34 members technically qualified in the field of health to the Executive Board for three year terms.

Head Office : Geneva, Swizerland

Regional Office :

Africa — Brazzauiles, Republic of Congo. Western Pacific — Manila, Philippines. Eastern Mediterranean — Cairo, Egypt.
South East Asia — New Delhi, India. Europe — Copenhagen, Denmark. Americas — Washington D.C., U.S.A.

The constitution of world Health Organisation had been signed by 61 countries on 22nd July, 1946, with first meeting world Heasith Assembly finishing on 22nd July 1946. It incorporate the official International d'hygiene Publique and the League of Nations Health organisation. Since its establishment, it had played a leading role in the eradication of small pox. Its current priorities include communicable disease, in particular HIV / AIDS, malaria, & tuberculosis. In each year since the inception of the world Health day in 1950, 7th April WHO select a Theme for public awareness in support of human right for health.

It will not be unwise to name some of the theme of WHO year wise :

1994 - Global Polio Eradication. 1997 – Emerging infectious diseases. 1998 – Safe motherhood.
2004 – Road Safety. 2009 – Save lives, make hospitals safe in emergencies.
2011 – Antimicrobial resistance : no action today and no cure tomorrow.
2014 – Vector bourne disease : small bite big threats.
2015 – Food safety. 2016 - Halt the rise, beat diabetes. 2017 – Depression : let's talk.
2018 & 2019 – Universal Health Coverage : everyone everywhere.

The world health Day in held to mark WHO's founding, and is seen as an opportunity by the organisation to draw world wide attention to a subject of major importance to global health each year. The WHO organizes international, regional and local events on the Day related

to a particular Theme. WORLD Health Day in acknowledge by various governments and non governmental organisations with interest in public issues. WHO also organize activities and highlight their support in media reports, such as global Health Council.

World Health Day is one of eight official global health conpaigns marked by WHO. along with World Tuberculosis Day, World Immunisation week, World Malaria Day, World no Tobacco Day, World AIDS Day, World Blood Donor Day and World Hepatitis Day.

This year 2019 the who's theme is 'Health Coverage for everyone and every where'. The slogan is 'Health for all'. This theme is for doctor and for the common people of the world to make the community health concious.

"Health coverage for every one and every where"

Key Facts

(i) Al least half of the world's population do not have full coverage of essential health services.

(ii) About 100 million people are still being pushed in to extreme poverty because they have to pay for health care.

(iii) One 800 millions people (about 12% of world population) spent 10% of their household budgets to pay for health care.

(iv) All UN member States have agreed to try to achieve universal health coverage (UHC) by 2030, as a part of sustainable development goals.

What is UHC?

UHC means all individuals and communities receive the health services they need without suffering financial hardship. It includes the full spectum of essintial, quality health services from health promotion to pevention, treatment, rehabilitation and palliative care.

UHC enables every one to access the services that address the most significant causes of disease and death and engases that the quality of those services which are good enough to improve the health of the people who receive them.

Protecting people from the financial consequence of paying for health services out of their own pockets reduces the risk that people will be pushed in to poverty because unexpected illness requires them to use up their life savings, self assets or barrow, destroying their futures and often those of their children.

Achieving UHC is one of the targets of the nations of the world set when adopting the sustainable Development Goals in 2030. Countries that progress towards UHC will make progress towards the other health related, and towards other goals. Good health allows children learn and helps people escape from poverty and provides the basis for long term economic development.

What UHC is not :-

There and many things that are not included in UHC.

(i) It doesnot mean free coverage for all possible health interventions, regadless of the cost, as no country can provide all services free of charges on a sustainable basis.

(ii) UHC is not just health financing; it encompases all components of the health system : health service delivery system, the health workforce, health facilities and communications net work, health technologies, information systems, quality assurance mechanism and governance and litigation.

(iii) UHC is not only about ensuring a minimum package of health services, but also ensuring a progressive expansion of coverage of health services and financial protection as more resources become available.

(iv) UHC is not only about individual treatment services, but also includes population based services such as public health compaign, adding floride to water, arsenic poisoning of drinking water, controlling insects breeding and so on.

(v) UHC is composed of much more than just health, taking steps towards equility, development priorities and social inclusion and cohesion.

What is primary health care?

Primary health care is an approach to health and wellbeing centered on needs and circumstances of individuals, families and comminutes. It addresses comprehensive and interrelated physical, mental and social wellbeing.

Who has developed a cohesive definition of primary health care based on three components:-

(i) People's health problems are addressed through comprehensive promotive, protective, curative, preventive, rehabilitative and palliative care throughout the life course, with the key stem functions aimed at individuals, famities and of community by a centrally integrated service delivery across all levels of care.

(ii) Systematically addressing the broader determinant of health including social, economic environmental as well as people's characteristict and behaviours.

(iii) Empowering individuals, families and communities to optimise their health as advocates for policies that promote and protect health and wellbing.

Primary health care is the most efficient and cost effective way to achieve universal health coverage (UHC) around the world.

WHO uses 16 essential health services in 4 catagories as indications of the level and equity of coverage in countries.

(A) Reproductive, maternal, newborn and child health :-

- Family planning
- Antenatal and delivery care
- Full child immunisation.
- Health seeking behaviour of pneumonias.

(B) Infections couses :-

- Tuberculosis treatment
- HIV antiretroviral treatment
- Hepatitis treatment
- Use of insecticide – bed sets for malaria prevention
- Adequate sanitation.

(C) Non communicable disease :-

- Prevention and treatment of hypertention.
- Prevention and treatment or diabetes.
- Cervical cancer screening.
- Tobacco smoking.

(D) Service capacity and access :-

- Basic hospital access
- Health worker density
- Access to essential medinines.
- Health security compliance with the international health regulations.

Each country in unique and each country may focus on different areas or develops their own ways of measuring progress toward UHC. But there is also value in a global approach that used standerised measures used internationally, as it given the chances to compare with others.

Original Article

Drug induced liver injury due to anti tuberculous chemotherapy in directly observed daily therapy in fifty patients : a retrospective study in Western India

Subramanian Natarajan[1], Poonam Subramanian[2]

Drug induced liver injury (DILI) is the most common adverse drug reaction leading to interruption of treatment in tuberculosis (TB). There are limited guidelines and treatment strategies on DILI due to anti TB drugs. (1) To study whether rapid reintroduction of drugs in DILI has any adverse outcome. (2) Rates of recurrent drug induced hepatitis. (3) Does DILI predispose a patient for drug resistant TB. Case record forms (CRFs) of 2113 patients were analyzed for the incidence of DILI. A total of 148 patients were diagnosed with hepatotoxicity and after careful exclusion 50 patients were diagnosed with DILI. All patients were reintroduced with all the drugs together once the hepatitis was resolved. A written informed consent was taken. Incidence of hepatotoxicity was 7%. Incidence of DILI was 2.4%. Female predominance was seen (68%). Majority of patients were suffering from pulmonary TB (72%). A mean of 14.2 days were lost before reintroduction. Recurrent DILI was seen in ten percent of patients (n=5). Six patients developed drug resistant tuberculosis due to interruption of treatment. (p value 0.031). Rapid reintroduction of drugs was well tolerated with recurrence rates of 10%. DILI predisposes a patient to develop MDR TB. [*J Indian Med Assoc* 2019; **117**: 9-12]

Key words **: Hepatitis, anti tuberculosis treatment, multi drug resistant tuberculosis.**

Drug induced liver injury (DILI) is the most common adverse drug reaction leading to interruption of treatment in tuberculosis (TB). DILI may sometimes be fatal. The incidence of DILI is increasing steadily. However there are limited guidelines and treatment strategies on hepatotoxicity due to anti TB drugs. DILI remains one of the most challenging disorders faced by pulmonologists during the course of treatment for tuberculosis. The biochemical mechanism and pathogenesis of DILI due to anti TB medications is not entirely clear. It is very difficult to predict which patient will develop DILI. Idiosyncratic DILI is less common as compared to intrinsic DILI and has inconsistent dose response relationship and is more varied in its presentation. Metabolic idiosyncratic reactions appear to be responsible for most responsible for most DILI from anti TB medications. The tuberculosis control program in India has defined DILI as an area which requires priority research. Guidelines for management of DILI due to anti TB medications have been published by the American Thoracic Society (ATS)[1], the British Thoracic Society (BTS)[2] and the Task Force of the European Respiratory Society, the World Health Organization (WHO)[3] and the International Union Against Tuberculosis and Lung Disease[4]. However, there aren't any consensus guidelines or Cochrane reviews on the reintroduction strategies.

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Aim :

(1) Rates of recurrent drug induced hepatitis.

(2 To study whether the rapid reintroduction of drugs in patients with DILI has any adverse outcome.

(3) Does DILI predispose a patient for drug resistant tuberculosis ?

Materials and Methods

A retrospective observational study from a Tuberculosis (TB) outpatient department was conducted in two tertiary care private clinics in the city of Mumbai and Thane. The duration of the study was from March 2010 to December 2016. Patients diagnosed with tuberculosis were put on a weight based standard four drug regimen consisting of isoniazid(H), rifampicin(R), pyrazinamide(Z) and ethambutol(E) as per WHO guidelines. All patients were monitored for liver enzyme (LFT) derangements after the initiation of the drugs with the onset of symptoms of nausea and vomiting and repeated subsequently whenever they had symptoms or routinely weekly after the initiation of the anti – TB drugs. Once a patient was detected to have deranged LFTs, then H, R and Z were stopped. These drugs were withheld till the time liver enzymes returned to less than twice the upper normal limit. Once the enzymes came back to normal, all the three drugs, viz H, R and Z were reintroduced at the full dosage on day one itself[5]. This reintroduction regimen was chosen based on the findings

of a randomized trial published in 2010[5].

Clinical Data :

Accurate history of medication exposure and onset and course of liver biochemistry abnormalities was noted. History of other drug reactions as certain cross-reactivities may exist (eg, anti-epileptics). History of other liver disorders for eg, chronic viral hepatitis, nonalcoholic steatohepatitis, hemochromatosis, alcoholic liver disease, primary sclerosing cholangitis, primary biliary carcinoma, liver cancer was noted. Time interval from initiation of anti-TB drugs to occurrence of DILI was taken as the latency period. The R -value was defined as serumalanine aminotransferase / upper limit of normal (ULN) divided by serum alkaline phosphatase / ULN. Time interval from stopping is oniazid, rifampicin and pyrazinamide and achieving these parameters was taken as the normalization period. Patients were continued with ethambutol (E) and fluoroquinolones (FQ) till the transaminase levels returned to less than twice the upper normal limits[6]. Patients who developed recurrence in liver enzyme elevation after reintroduction of the drugs were again subjected to safe anti TB medications, viz E and FQ, and H, R, Z were sequentially reintroduced to determine the offending agent. All the patients were followed closely for any further increase in tuberculosis symptoms and development of multi drug resistant TB (MDR TB). Liver biopsy was performed in patients in which the elevated transaminase levels (more than 50% from the baseline values) persisted in spite of stopping the offending drug at the end of sixty days[7,8].

Laboratory Data Collection :

Tests to detect markers of acute viral hepatitis (Immunoglobulin M [IgM] anti–hepatitis A virus, Hepatitis B surfaceantigen [HBsAg], IgM anti–hepatitis C virus antibodies, and IgM anti-hepatitis E virus) were performed for all patients who developed features suggestive of DILI while receiving anti-TB drugs[1].An enzyme-linked immunosorbent assay (ELISA) to test for HIV type1 and type 2 was also performed. An abdominal ultrasonography was obtained for each patient to rule out fatty liver or chronicliver disease.

The Diagnostic Criteria for DILI were as follows :

(1) An increase of more than five times the upper limit of the normal levels (>250 IU/L) of serum aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) on 1 occasion without symptoms or more than thrice the upper limit of normal (>150 IU/L) with symptoms of anorexia, nausea, vomiting, and jaundice.

(2) An increase in serum total bilirubin more than 1.5 mg/dL[1,6].

During reintroduction of anti-TB drugs, liver function testing was done every fourth day after all the drugs were reintroduced[2]. After the successful reintroduction of anti-TB drugs, regular monitoring of liver function was performed by determination of serum bilirubin level, AST level, ALT level, and serum ALP level every week for the first month. From the second month, laboratory measurement was performed only when patient had recurrence of symptoms.

Exclusion Criteria :

Exclusion criteria observed were serological evidence of acute viral hepatitis, evidence of chronic liver disease on ultrasonography, human immunodeficiency virus (HIV) infection, longterm alcoholism [defined as consumption of more than 48 g of alcohol per day for at least 1 year[9]], concomitant consumption of other potentially hepatotoxic drugs (eg, methotrexate, dapsone, phenytoin, valproate, and fluconazole), pregnancy, and up to three months postpartum.

Statistical Data :

Chi square and paired T test was used. Medcalc version 17.1 was used with the help of a statistician.

Results :

A total of 2113 patients' case record forms were reviewed. Majority of our cohorts were in the age group less than 35 years (65%, n=1370). Of these, 148 patients had hepatitis during the course of the disease (7%). After careful exclusion, 2.4% patients were diagnosed as drug induced liver injury (DILI) (n=50). Mean age was 37.18 (SD 17.62). Age range was 16 to 84 years. Sixty percentage of our study patients were below the age of 35 years (n=30). Percentages of DILI were 2.2 in age less than 35 years and 2.7 in persons more than 35 years (p value 0.42). Female predominance was seen in our study. Two thirds of the participants were females(n=32, 68%). Pulmonary tuberculosis was seen in 72% (n=36) of cases. Only one disseminated TB was seen. Rest 26 % (n=13) were extra pulmonary TB. Of these extra pulmonary TB cases, 90% (n=11) were cervical lymph node tuberculosis. Rest two, were spine TB and abdominal TB, one each. Latency period varied between 02 to 120 days, the average being 18.12 days. (SD 21.03). All patients (n=49) had a latency period within a span of two months. Only one patient had a delayed latency period (120 days). R value was greater than five in 76% of the patients (n=38), between 2 and 5 in 12% of patients (n=6) and less than 2 in 12% of patients (n=6) (Fig 1). The average ALT was 336.16 (SD 303.95), AST was 422.12 (SD 384.48) and total bilirubin was 2.11. In 56% of the patients (n=28), the highest total bilirubin was less than 2.0 g/dL. In these patients, the mean AST

was 519 and ALT was 385. The rate of decline of AST was faster as compared to ALT (Fig 2). The rate of decline of bilirubin was the slowest as compared to all the liver enzymes. The normalization period varied between 05 to 90 days, the average being 14.2 days (SD16.98). Only two patients took more than two months for the liver enzymes to normalize. Of these, one underwent liver biopsy and died during the course of illness. Patients in whom the R value was less than 2 (cholestatic type) took a longer time for the enzymes to come back to normal. Recurrence of DILI was seen in 10 % (n=5) of patients in whom the drugs were reintroduced. Of these, three patients developed MDRTB subsequently. A total of six patients developed MDRTB (12%). Analysis revealed a statistically significant chance of developing MDRTB in patients with DILI as compared to those without DILI (p value 0.031). Death was seen in one patient.

Discussion

Hepatotoxicity during the course of treatment with Anti TB medications may be multi factorial. Factors like alcoholism; viral hepatitis and HIV are amongst commonest confounding causes in any study on DILI. Of all the patients diagnosed with hepatotoxicity (n=148) in our cohorts, only 35% (n=50) were included in the study. The incidence rates varied between 2% to 28% in various studies[10,14]. Majority of our study group were below the age of 35 years (60%) as TB is known if affect the younger productive age group population in developing countries, more so in India. Most of the studies and literature suggest that DILI increases with increasing age. As in our study, none of the studies have demonstrated any statistical significance[11,12,13]. Most of the studies have quoted female predominance. In the Singaporean study by Teleman et al, the risk of hepatotoxicity was four times in women as compared to the male cohorts[11]. The extent of tuberculosis including cavitory disease, multi-bacillary TB and extra-pulmonary organ involvement have been incriminated as positive predictors for TB DILI by some authors[15] while others have failed to note any significant association[16]. In our study, the majority of the patients were pulmonary tuberculosis. This may be due to referral bias.

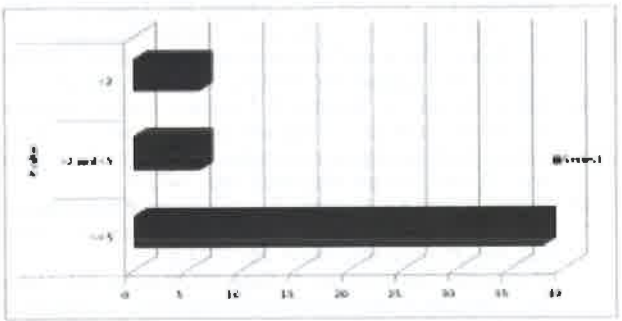

Fig 1 — Number of patients classified according to the R value.
X axis : Number of Patients

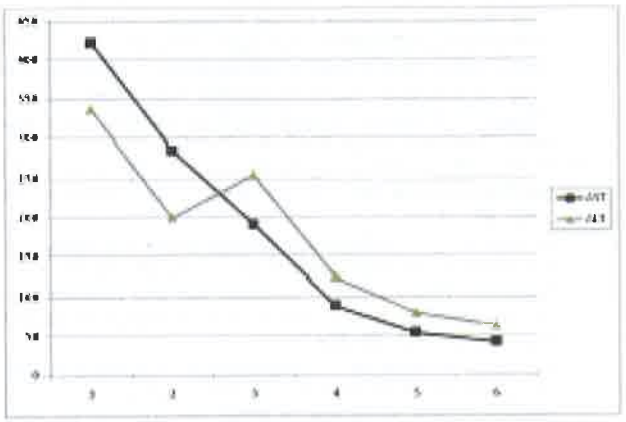

Fig 2 — Enzyme variation over days.
X axis: Number of days. Y axis: Enzyme levels in IU/L. ASt: Aspartate transaminase, ALT: Alanine transaminase

On the basis of the R-value at presentation, DILI can be categorized into hepatocellular,cholestatic, or mixed types. This categorization allows testing for competing etiologiesin asystematic approach[8]. Our study showed majority of the patients being classified as hepatocellular type based on the R value. However, in approximately one fourth of the patients (24%) we could find the other types also suggesting that DILI due anti TB medications had differing presentations. In the study done by Naqvi *et al* in Pakistan, 63% of their patients had hepatocellular pattern while mixed and cholestatic was found in 23 and 13% respectively[17].

Cholestatic DILI takes longer to resolve than the hepatocellular DILI[8].

There are no studies validating the utility of liver biochemical tests in prevention of DILI or assessing its severity. Such monitoring is often seen as inconvenient, expensive and inefficient by both patients and doctors, and thus the monitoring recommendations are poorly followed[18,19]. However, monitoring with liver tests is recommended in the following groups: patients who consume alcohol, individuals with chronic hepatitis B or C, and those on concomitant hepatotoxic drugs, have elevated baseline transaminase levels, and suffer from underlying liver disease and those with HIV[1,19].

In general, persistence of biochemical abnormalities lowers the threshold for liver biopsy. The majority of DILI cases show steady decline in liver biochemistries after the presumed drug is stopped. This observation is often referred to as "washout" or "de-challenge" and is a major factor in DILI diagnostic scoring algorithms[8,20]. Persistence of elevations weakens the case for DILI, thereby strengthening the possibility of other diagnoses[8]. The cut-off time for a significant decrease in alanine aminotransferase is 60 days[20]. For cholestatic injury, lack of significant drop in alkaline phosphatase or bilirubin (>50% drop in peak-ULN or drop to less than twice ULN) at 180 days

is considered significant. Liver biopsy at 60 days for unresolved acute hepatocellular and 180 days for cholestatic DILI is recommended[8].

Various guidelines[1,8] mention avoidance of reintroduction of offending drugs whenever possible. They also advocate complete stoppage of pyrazinamide in the regimen. Considering that first line anti-TB drugs are highly effective and relatively in expensive, benefits of re-challenge must outweigh its risks; it is unwise to discard these drugs from the regimen. Therefore, it is acceptable to attempt reintroduction of these medications[4,21].

In the study by Sharma *et al*, 11%–24% of patients, re-exposure to the same drug regimen led to recurrence of DILI[5] and positivere-challenge was not affected by the degree of initial injury[5]. Our study showed a recurrence of 10%.

Our study also showed higher incidence of MDR TB in patients with DILI, more so in patients with recurrent DILI. Our study showed a statistically significant increased chance of MDR TB in these patients of DILI. We couldn't find any studies which showed increased incidence of MDRTB in patients with DILI.

Drawbacks of the Study:

It was not clear which drug caused the hepatotoxicity as all the drugs were reintroduced simultaneously. It was possible that many study patients might have had hepatic adaptation or indeterminate unrelated hepatic events[22]. In this study, treatment interruption might have been done because of a concern of evolving hepatotoxicity rather than established hepatotoxicity as in the original study[5]. Excluding patients with preexisting liver disease or who were at greater risk for hepatotoxicity could have resulted in some observation bias.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.Written informed consent was obtained from all patients.

Conflict of Interest : None

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Original Article

Determination of safe anti-tubercular therapy regimen following anti-tubercular drug induced hepatitis in patients with active tuberculosis

Atanu Ghosh[1]

To determine the safety of restarting isoniazid and rifampicin and etambutol or isoniazid pyrazinamid and ethambutol in patients who develop antitubercular drug induced hepatitis. In 22 tuberculosis patients, who developed antitubercular drug induced hepatitis were analysed, for reintroduction of antitubercular drugs, isoniazid, rifampicin and ethambutol in 11 patients (Group A) and isoniazid, pyrazinamide and ethambutol in another 11 patients (Group B), following clinical and biochemical (liver function test) normalization. During antitubercular drug induced period, hepatotoxic antitubercular drugs were withdrawn till clinical and biochemical normalization and non-hepatotoxic antitubercular drugs like streptomycin, ethambutol were given. Jaundice appeared at variable interval of 2-13 weeks after starting the antitubercular treatment and before enrolling into the study. All 22 patients with abnormal liver function on close followup, came back to normal within 2 weeks of stoppage of antitubercular drug. On rechallange, 4 out of 11 patients receiving isoniazid and rifampicin developed hepatitis within 2-4 weeks of restart of therapy and 1 out of 11 developed (receiving isoniazid and pyrazinamide) in 4th week. Though the study sample size was small, the combination of isoniazid and pyrazinamide was apparently safer compared to isoniazid and rifampicin combination though it was statistically insignificant (p<0.155). [*J Indian Med Assoc* 2019; **117:** 13-9]

Key words : **Anti-tubercular agents, hepatitis, restart safe anti-tubercular regimen, active tuberculosis.**

Tuberculosis (TB) continues to be a major public health problem in India. Globally TB has remained a therapeutic challenge. Prevalence of TB cases per 1,00,000 population is 12-20 in developed countries, as against 250-500 in developing countries, so also is the mortality due to TB 1-2 per 1,00,000 population in the developed countries, as against 60-100 in developing countries. Nearly 5,00,000 people die of this disease in India every year[1]. According to conservative estimate, there are 15-20 million cases of infectious TB in the world. This infectious pool is maintained by the occurrence of 4-5 million new cases and 3 million deaths per year[1]. Inspite of these deluding statistics, TB is a curable disease. With modern chemotherapy cure rates of upto 99% can be achieved. However, unfortunately almost all the antitubercular drugs can cause hepatitis. Among these drugs, hepatitis is more common with isoniazid, rifampicin, and pyrazinamide when used either alone or in combination.

The risk of hepatitis with 2 months of isoniazid administration is about 5.2 per 1000 subjects having an age less than 35 years to 7.7 per 1000 for those aged 55 years or more[2]. The risk is similar in both sexes and the cumulative risk increases during the first 15-20 weeks of isoniazid administration[2,3]. About 15% of cases of symptomatic isoniazid induced hepatic injury appear within the first month of therapy and about 50% within first two months. In the remaining 50% of cases it may be delayed from three to twelve months[4-6].

Clinically isoniazid induced hepatitis resembles viral hepatitis[4,7-10]. If treatment is continued in patients with isoniazid induced hepatitis, fulminant hepatic damage can result; this has a very high mortality[2]. The fatality rate for clinically jaundiced patients is in the excess of 10% and most fatal cases have bilirubin level over 20mg/dl[16]. There are reports of patients of developing cirrhosis and portal hypertension following isoniazid induced hepatitis[2,11].

Rifampicin alone also can cause hepatocellular damage besides aggravating isoniazid toxicity through activation of hepatic microsomal enzyme systems[2]. Though rifampicin is well tolerated, transient elevation in AST levels are common (14-40% of patients) and of no clinical significance. Rifampicin induced hepatic injury usually appears, during the first month of therapy[30]. Major elevation of AST >150 units occurs in 4% and hepatitis with jaundice in about 1%[12]. Although considerable evidence exists regarding the rifampicin and isoniazid together causing more hepatotoxicity than either drug alone, lack of potentiation has also been reported[13-15].

Hepatotoxicity is not enhanced when pyrazinamid is

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added to isoniazid and rifampicin[16]. Reports from Madras indicate that a combination of isoniazid and rifampicin causes biochemical hepatitis in over 8% of patients[18]. The incidence of hepatitis was higher ie, 16-30% when treatment was given on daily basis as compared to 5% with twice a week regime[2]. Ramakrishna CV *et al* while reviewing the adverse effect of rifampicin, quoted the report of Asim Dutt *et al* in which chemical hepatitis observed in 12 (1.5%) of 781 patients receiving short course antitubercular chemotherapy, attributed to rifampicin in daily phase in four, and to isoniazid in six and could not assign a reason in two[19].

Pyrazinamide hepatotoxicity is dose related, it is around to 6% when the pyrazinamid dose is 40mg/kg. Pyrazinamide toxicity in lower doses (30mg/kg body weight), prescribed today shows no report of hepatitis (Fox 1978). Hepatitis is more common when higher doses of the drug are used[2].

Continuation of drug after symptoms of hepatic dysfunction have appeared tends to increase the severity of damage. Stoppage of antitubercular drugs and institution of supportive therapy are mandatory, if the patient on antitubercular treatment develops drug induced hepatitis[2,21].

The literature is silent as to which antitubercular drug should be started after liver function tests become normal following antitubercular drug induced hepatitis. Girling mentions that treatment with same drugs which caused hepatitis can often be resumed uneventfully[2,21-25] with close monitoring of liver function. Richard J O'Brien advocates stoppage of all drugs in a setup of serious hepatotoxicity eg. high transaminases and symptoms of hepatitis and to continue ethambutol and streptomycin and rechallenge the patients after introducing one drug at a time, preferably rifampicin first and then isoniazid and later followed by pyrazinamid[26].

Data regarding the safety of restarting antitubercular therapy after drug induced hepatitis is scanty. Since for any effective bactericidal antitubercular drugs like isoniazid, rifampicin, and pyrazinamide are essential, this study was proposed to determine safe readministration of isoniazid, ethambutol and rifampicin and its comparison with isoniazid, ethambutol and pyrazinamide after drug induced hepatitis.

Aim and Objective

To determine the safety of restarting isoniazid and rifampicin and ethambutol or isoniazid, pyrazinamide and ethambutol in patients who develop antitubercular drug induced hepatitis.

Materials and Method

This study was conducted on twenty two patients who developed antitubercular drug induced hepatitis. On the basis of international consensus meeting on definitions on drug induced liver disorders (Paris 12-13 June,1989),63 the patients were considered to be having drug induced hepatitis if there was :- (1) An increase above twice the upper limit of normal of alanine aminotransferase OR (2) An increase in conjugated bilirubin twice above the normal upper limit OR (3) Combined abnormality of aspertate aminotransferase, alkaline phosphatase and total bilirubin provided one of them is above the twice of the upper limit of normal.

Inclusion Criteria — Patients who develop hepatitis within three months of start of antitubercular drugs, were included in the study. Hepatitis was considered to be due to antitubercular therapy if the liver functions return to normal within 2 weeks of stoppage of drugs.

Exclusion criteria — (1) Hepatitis B surface antigen positive patients. (2) Patients with history of chronic alcoholism. (3) Patients with chronic liver disease. (4) Patients with previous history of jaundice. (5) Pregnancy. (6) Patients with history of blood transfusion within 2 weeks to 6 months of onset of hepatitis. (7) Patients with recent episode of hypotension. (8) Patients suffering from gall stones, choledocholithiasis or pancreatic disease.

Methodology

After the patients developed antitubercular drug induced hepatitis, all drugs were stopped and nonhepatotoxic drugs injection streptomycin and tablet ethambutol were started. Patients were closely monitored clinically and biochemically with liver functions till these became normal, then patients were randomly allocated to the following groups of antitubercular regimen.

Group A- Isoniazid, Rifampicin and Ethambutol.
Group B- Isoniazid, Pyrazinamide and Ethambutol

Doses (daily)

- Isoniazid	300 mg
- Rifampicin (for patients)	<50 kg - 450mg, >50kg - 600mg
- Pyrazinamid (for patients)	<50 kg – 1.5gm, 50-74kg – 2 gm, >75 kg – 2.5 gm

The doses were given to the patients according to the recommendations of International Union against tuberculosis and lung diseases[25].

As soon as the liver functions became normal, tablet isoniazid was added to each group of patient gradually increasing doses, starting 100 mg per day to reach maximum dose of 300 mg within seven days, after liver function monitoring. If liver function test remained normal after 300 mg of isoniazid, rifampicin and pyrazinamide, in the above mentioned doses was added to isoniazid, ethambutol in group A and group B respectively. The liver function tests were monitored every two weeks for a total period of three months and the group with highest hepatotoxicity following resumption of antitubercular therapy was determined. The drugs were stopped once patient observed

evidence of hepatitis either clinically or biochemically and restarted on injection streptomycin, tablet ciprofloxacin with continuation of ethambutol.

The liver function tests done, were (a) Aspertate amino transferase (SGOT). Normal value (2-20) IU (by the method spectrophotometry, Reitman and Frankel). (b) Alanine amino transferase (SGPT). Normal value (2-15) IU. (by the method of spectrophotometry, Reitman & Frankel). (c) Alkaline phosphatase. Normal value (70-140 IU / 3-13 KAU). (d) Serum bilirubin, total and conjugated. Normal value (0-0.8 mg%) (by the method of Vandenbergh & Muller). (e) Serum protein, total, albumin and globulin. Normal value- total protein- 5.5-7 gm%, albumin- 3.5- 5 gm%, globulin- 2- 3 gm%, (by the method of Biuret). Hepatitis B surface antigen from blood by ELISA was done when the patient was first detected to have hepatitis. Ultrasound study of liver, gall bladder, biliary tract and pancreas was done at the time of hepatitis to exclude extrahepatic biliary obstruction as a cause of jaundice.

Statistical Analysis

Comparison of safety between two antitubercular therapy groups was done by Chi-sqare test and fisher table.

Ethical Consideration

The study involved taking 5ml of blood in the beginning and 5ml of blood every 2 weeks or more frequently as was necessary, over a period of 3 months by venepuncture from the subjects. Study also included doing an Ultrasound study of abdomen, a non-invasive procedure. The ethical justification for restarting the same regimen ie, Isoniazid, Rifampicin, Ethambutol and Isoniazid, Pyrazinamid, Ethambutol, was based on the recommendation from the Committee on Treatment of the International Union against Tuberculosis and Lung Disease[25]. In all cases, informed consent were taken.

Observation

(A) The demographic profile of the two groups of patients are as

(1) Group A had a total of 11 patients, (4 males & 7 females) with an age range of 15-65 years (34.18 ± 15.33). Out of these 11 patients, 4 had pulmonary parenchymal lesion, 3 had pleural effusion (2 had associated pneumothorax), 1had skin TB (Tubercular verrucus cutis, lymphnodal tuberculosis), 2 had tubercular meningitis (1 had associated pulmonary parenchymal lesion), 1 had parietal lobe tuberculoma. These group of patients were rechallenged with rifampicin and isoniazid.

(2) Group B had a total of 11 patients, (male 5 & 6 female), with an age range of 15-60 years (30.09 +- 14.20). Out these 11 patients, 3 had pulmonary parenchymal lesion, 2 had disseminated tuberculosis (1 had associated pulmonary parenchymal lesion and 1had pleural effusion), 1 had TB spine (spinal TB), 1 had cold abscess back, 2 had lymphnodal tuberculosis (1 had associated pulmonary parenchymal lesion), 2 had abdominal TB.

Clinical profile of patients in 2 groups.

	Group A (n-11)	Group B (n-11)
Age in years :		
Mean ± SD	34.18±15.33	30.09±14.20
Range	18-65 years	15-60 years
Below 50 years M:F	3:6	3:6
50 years or above M:F	1:1	2:0
Icterus	9	9
Liver enlargement	5	4
Splenomegaly	0	0
Ascites	0	0

Liver function test of patients in 2 groups at the time of antitubercular hepatitis.

	Group A (n=11)	Group B (n=11)
Serum Bilirubin (Mean+-SD) (mg%)	3.5± 1.8	2.12±2..04
Range	0.8-7.7	0.8-5.7
SGOT	44-136	21-127
SGPT	21-141	26-127
Alkaline phosphatase	N-43	N-35
n = number of patients, N = normal		

(B) Hepatotoxicity to antitubercular drugs started from different specialities in the 22 patients, developed over a variable period of time i.e. 4-13 weeks. The drugs used in these patients before they were registered in this study were taking rifampicin, isoniazid, pyrazinamide, ethambutol, streptomycin. 4 patients (18.18%) developed hepatotoxicity within first week, 9 patients (40.9%) in second week, 2 in third week (9.08%), 1 in fourth week (4.54%), 1 in 8th week (4.54%), 4 in 12th week (18.18%), 1 in 13th week (4.54%).

(C) Time taken for the liver function test to come to normal.

	Group A(n=11)	Group B(n=11)
Duration taken to come back to normal	.5-14 days (11.27 ± 3.69)	4-14 days 12.09 ± 3.23)

(D) Recurrence of hepatic biochemical abnormality on rechallenge

In Group A 4 patients (36.36%) out of 11 (2 M & 2 F) developed hepatic biochemical abnormalities. All showed an increase above 2 folds in SGOT/SGPT levels while 2 patients showed an increase in serum bilirubin level after 2-4 weeks of restart of isoniazid and rifampicin (1 patient in 2nd week & 1 patient in 4th week).

Group B only one male patient (9.09%) out of 11 developed hepatic biochemical abnormalities, in the form of raised bilirubin and SGOT/SGPT after 4 weeks of restart of isoniazid ($p<0.0155$).

None of the patient developed liver function abnormalities after 1 week of initial restart of isoniazid. All these patients who developed hepatic biochemical abnormality on rechallenge had anorexia, 4 of them had vague epigastric discomfort and dull pain over the right upper quadrant.

Correlation of time of onset of hepatotoxicity following rechallenge with drugs with time of onset of the initial hepatotoxicity.

				On rechallenge		On initial treatment	
Pt No	Sex	Gr	SB mg%	SGOT/ PT level IU	Duration of onset of increase	SGOT/ SGPT level IU	Duration of onset of increase
4	F	A	0.9	41/22	2nd week	44/30	2nd week
6	M	A	2.7	64/85	4th week	57/77	4th week
7	M	A	1.7	98/99	2nd week	65/28	3rd month
10	F	A	0.7	62/60	22nd week	65/21	9th day
4	M	B	2.7	98/124	4th week	102/127	End of 3rd month

p>0.5; SB- Serum Bilirubin

Occurrence of rechallenge hepatitis in pulmonary and extra-pulmonary tuberculosis patients.

Group A (n=11) :

8 (72.72%) patients were suffering from pulmonary tuberculosis – out of which 3 (27.27%) patients developed hepatitis on restart. 3 (27.27%) patients were suffering from extra-pulmonary tuberculosis – out of which one (9.09%) patient developed hepatitis on restart.

Group B (n=11) :

6 (54.54%) patients were suffering from pulmonary tuberculosis – out of which no patient had hepatitis on restart. 5 (45.15%) patients were suffering from extra-pulmonary tuberculosis – out of which one (9.09%) patient developed hepatitis on restart. In 3 patients developed hepatotoxicity after the same duration of rechallenge with antitubercular drug, compared with initial antitubercular therapy, before the patients were registered into the study.

Ultrasound abdomen study revealed no evidence of chronic liver disease, Gall bladder, biliary tract or pancreatic abnormality, though one patient had fatty liver and another had Gall bladder polyp.

Follow up after rechallenge hepatotoxicity.

The drugs were stopped as soon as the liver function showed an abnormality and second line antitubercular drugs started and ethambutol continued. These liver function abnormality reverted back to normal again within two weeks and patients instructed not to restart isoniazid, rifampicin and pyrazinamide again. No patients developed either prolonged hepatitis, subacute hepatic failure or fulminant hepatic failure.

Discussion

Rifampicin, isoniazid and pyrazinamide constitute the main armamentarium of anti-tubercular chemotherapy, although their potential hepatotoxicity in combination or alone, is well known. To evaluate the hepatotoxic potential of rifampicin, isoniazid versus pyrazinamide and isoniazid combination, when rechallanged following recovery of anti-tubercular drug induced hepatitis, the study was conducted on 22 patients. There is scanty literature on the restart of anti-tubercular drug following drug induced hepatitis, although Girling et al in his study had mentioned the safety of restart of these drugs[21]. Citron *et al* also mentions that "all drugs following antitubercular hepatotoxicity, must be stopped. It is usually safe to restart all drugs after liver functions have returned to pretreatment levels. If symptoms recur the drug should be introduced individually once the liver function test have returned to normal, at a lower dose, initially together with at least one drug that unlikely to cause hepatic dysfunction (streptomycin and ethambutol)[24].

All the patients in this study, who had initially had antitubercular drug induced hepatotoxicity had their liver functions returning to normal within 2 weeks of stoppage of all the offending drugs. There may be confusion whether this jaundice is due to viral hepatitis or chronic liver disease. To exclude these diseases the following test done like HbsAg, Ultrasonographic study of abdomen.

While the start of initial hepatotoxicity before the patients were entered into the study, was after variable interval of 4 days to 13 weeks, majority (40.9%) developed hepatotoxicity in the end of 2nd week of starting treatment. Ramesh R *et al* reported mean onset of jaundice in 4 patients out of 50 patients of tuberculosis treated with rifampicin and isoniazid of 16 days (range 1-22 days) and complete recovery within two weeks[55]. Rugmini *et al* reported the duration of hepatotoxicity in 32 (24.7%) of the 130 children treated isoniazid and rifampicin. In majority of patients this was recorded mostly within 2 months. Similar duration of onset of hepatotoxicity have been reported by O'Brien *et al* and Riska *et al* when these patients were initially put on anti-tubercular treatment[26,48].

Rechallenge of isoniazid and rifampicin lead to hepatotoxicity in 4/11 (36.36%) patients which was accompanied by vague ill health, anorexia, and dull ache in right hypochondrium. This was more, than in patients given a combination of isoniazd and pyrazinamide (1/11) (9.09%) though the difference was statistically insignificant ($p<0.155$). Three of the above five patients had pulmonary tuberculosis as against 2 with extra-pulmonary tuberculosis. The ages of these patients who on rechallenge developed hepatotoxicity was 18-55 years with no predilection for old age. (33.8±4.8 years). Onset of hepatitis on rechallenge occurred in 2 weeks to 4 weeks after start of drugs.

Purohit et al reported 40.3% of patients of pulmonary tuberculosis receiving isoniazid and rifampicin showed abnormal ALT levels and 70% had clinical hepatitis within first three months and resumption of therapy was possible within 7-10 days. On resumption of isoniazid and rifampicin following recovery of anti-tubercular drug induced hepatitis, was possible without hepatotoxicity in all 4 patients who had an abnormal ALT level with clinical symptoms as reported by Purohit *et al*. Ramesh *et al* also re-

ported no increase in serum bilirubin or enzymes after re-introduction of isonoazid. Rugmini et al reported in children suffering from different forms of tuberculosis, 16 out of 32 cases who had transient elevation of transaminase did not show further problem on continuing therapy, although later in one children drug had to be stopped due to jaundice. In the remaining 16 out of 32 children on reintroduction isoniazid in same or other combination was possible in 9 cases.

In this study it is unique that liver function tests have been serially followed up for period of atleast three months. Three patients who developed hepatitis on restart, developed hepatitis at the same time as was the initial hepatitis, while 2 patients had it earlier compared to 3 months in the earlier episode of hepatotoxicity. The findings of this study could be subtle pointer against hypersensitivity type of adverse reaction with isoniazid and rifampicin / pyrazinamide, otherwise hepatotoxicity should have occurred faster and earlier and should have more severe[4].

None of study patients either on initial hepatotoxicity, at the time of entry into the study or on rechallenge, developed serious liver disease like fulminant hepatic failure or subacute hepatic failure. This strengthens the belief and general recommendation of stopping the drug as soon as the patient becomes symptomatic for liver disease or has abnormal liver function, which should be monitored for the initial 2 -3 months at least after the start of anti-tubercular therapy.

Hepatotoxicity complicates antituberculur chemotherapy mostly with rifampicin, isoniazid and pyrazinmide, which are bactericidal drugs and are essential for the effective short term treatment of tuberculosis. Mechanism of isoniazid induced hepatitis remains unclear and ambiguous but proposed mechanism is either metabolite induced immunoallergy or presence of toxic metabolite. Though it is reported that monoacetylhydrazine, an initial metabolite of isoniazid causes hepatic injury producing reactive acetyl radical following further acetylation, there are variable reports regarding the possible potentiation of hepatotoxicity of acetylator phenotype of patients (rapid or slow acetylator). Rifampicin, a hepatic microsomal enzyme inducer may alone itself cause hepatotoxicity or may potentiate the hepatotoxicity of isoniazid by increasing the level of isoniazid metabolite. Pyrazinamide hepatotoxicity, though uncommon, is usually dose related to high dose.

All 22 patients in this study, had normalization of liver function after stopping the drugs within 2 weeks which is consistent with the international consensus held in Paris 12-13 June 1989[63]. It may be concluded that while restarting isoniazid, rifampicin and pyrazinamide, isonazid combination, close monitoring of patients both clinically and biochemically, is necessary to avoid any serious untoward hepatotoxicity. From this study of small number of patients a conclusion could be drawn that on rechallenge isoniazid combinations have hepatotoxic potential. Liver function tests must be monitored every week or fortnightly for about 2 months.

Summary and Conclusion

There is scanty of literature on the safety on reintroduction of isoniazid and rifampicin / pyrazinamide, once the patient developed anti-tubercular drug induced hepatitis. In 22 patients of anti-tubercular drug induced hepatitis with the primary being pulmonary tuberculosis in 14 patients and 8 extrapulmonary tuberculosis patients were included in the study. The jaundice appeared in variable interval of 2-13 weeks after starting the anti-tubercular treatment and before enrolling into the study. All these 22 patients with abnormal liver function on close followup, came back tonormal within 2 weeks of stoppage of anti-tubercular drug. 22 patients were rechallanged with initially for a week with isoniazid (starting with 100 mg increase to reach maximum of 300 mg over a period of seven days monitoring liver function tests) and if the liver function was normal they were randomly allocated to either rifampicin or pyrazinamide (11 in Group A and 11 in Group B). The liver functions were assessed every weekly / fortnightly for a period of 3 months or / and the drugs discontinued if patient developed evidence of clinical or chemical hepatitis.

4 out of 11 patients receiving isoniazid and rifampicin developed hepatitis within 2-4 weeks of restart of therapy and 1 out of 11 patients, receiving isoniazid and pyrazinamide, developed in 4th week. This hepatitis was mild and subsided after discontinuation of the drug and these patients were put on non-hepatotoxic second line of drugs. They were continued on ethambutol and injection streptomycin during the recovery phase of initial and restart therapy.

In conclusion, this study sample size was small, the combination of isoniazid and pyrazinamide was apparently safer compared to isoniazid and rifampicin combination though it was statistically insignificant ($p<0.155$). None of this study patients with recurrence of hepatitis following rechallenge with isoniazid and rifampicin / pyrazinamide combination either developed prolonged hepatitis or subacute hepatic failure or fulminant hepatic failure.

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Review Article

Efficacy of triclosan-coated sutures for reducing risk of surgical site infection in adults : a retrospective real-world study of 306 patients from Northern India

Raj Kamal Jenaw[1], Bharat B Agarwal[2], Devendra Talera[3]

Surgical site infections (SSIs) are associated with an increased risk of morbidity, readmission, intensive care unit stay, and mortality. The present study aims to assess the efficacy of triclosan coated sutures (TCS) in reducing the incidence of SSI in a tertiary care setting in Northern India and the risk factors associated with it. This is a retrospective 'real-world' study of 306 patients who underwent surgery and wound closure with triclosan-coated suture from July 2016 to Jan 2017 at SMS Hospital, Jaipur. Association of factors with SSI incidence was analyzed using the χ^2 test. During the study, wound infection developed in 13.4 % as superficial/incisional SSI and 1.3% cases as deep incisional SSI. None of the patients had SSI 10 days after discharge. Thus, use of triclosan coated sutures could reduce the incidence of SSI by 85.3%. Significant association of incidence of SSI was observed with 'wound Class 1' and 'age group 58-67 years'. 12 patients of 50 (24%) in class II wound category has SSI with uncoated sutures whereas only 2 of 50(4%) patients had SSI in class II in coated vicryl category. Similarly, 16 patients of 29 (55%) had SSI in class III category which was on 2 of 25 (8%) for vicryl coated suture. There was no case of adverse effect reported in our study. With use of Triclosan coated sutures, SSI could be prevented in 85.3 % cases and class II and III wounds could be effectively prevented. Our study presents a compelling case for using TCS in routine clinical practice.

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Key words **: Triclosan coated suture, antibiotic coated sutures, surgical site infection, age, gender, wound class.**

Epidemiology of SSI :

Surgical site infection (SSI) is defined as microbial contamination of the surgical wound within 30 days of an operation or within 1 year after surgery if an implant is placed in a patient[4]. There have been many technical advances in infection control and surgical practices, still SSI continue to be a challenge, even in hospitals with modern infrastructure[5]. SSIs are the third most common hospital-acquired infection (14%-16%)[6]. In India, the rate of SSI varies from 6.1% to 38.7%[7-10]. However in comparison to the Indian hospitals the rate of infection reported from other countries is quite low, for instance in USA it is 2.8% and in European countries it is reported to be 2-5%[11]. A recent surveillance conducted worldwide by International Nosocomial Infection Control Consortium across 82 hospitals of 66 cities in 30 limited-resource countries including India revealed an overall SSI rate of 2.9% as compared with the incidence rate of 2.0% for the US hospitals[12]. The lack of attention towards the infection control measures, inappropriate hand hygiene practices and overcrowded hospitals can be the major contributory factors for high infection rate in India.

- **Wound contamination following surgery often involves both deep and superficial incisional sites. Therefore, to maximize benefit from antimicrobial sutures, triclosan coated sutures should be used for both superficial and deep musculofascial layers.**
- **The expected potential beneficial effects of triclosan coated sutures extend beyond merely the prevention of infection. In 2007, Gómez-Alonso *et al* demonstrated the efficacy of these sutures in preventing bacterial colonization and modulating the inflammatory response, which allowed better tissue healing[1].**
- **There are some unanswered areas with triclosan coated suture for instance, to evaluate the risk of antimicrobial resistance to triclosan and the long degradation time of triclosan[2] and its impact on potential risk for bioaccumulation in the environment[3].**
- **Previous studies have shown that the use of conventional antibiotics in patients with SSI can be reduced with triclosan-coated sutures.**

Health-economic Burden of SSI :

SSI impose a substantial burden in terms pharmacoeconomic loss. A cost comparison in India revealed total expenses incurred by patients with SSIs was INR 29,000 (average) as compared to INR 16,000 (average) incurred by non-infected patients[13]. The incidences of mortality were also higher in infected patients (12.8% to 19.9%) as compared to the controls (1.1% to 3.8%)[5,14].

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Clinical features of SSI :

SSI are usually caused by exogenous and/or endogenous microorganisms that enter the operative wound either during the surgery (primary infection) or after the surgery (secondary infection). The risk of SSI is markedly increased when a surgical site is contaminated with $>10^5$ microorganisms per gram. However, when foreign material is already present at the site (ie, 100 Staphylococci per gram of tissue introduced on silk sutures), the dose of contaminating microorganisms required to produce infection is much lower. Majority of SSIs are uncomplicated involving only skin and subcutaneous tissue but sometimes can worsen to necrotizing infections. Clinically, SSI present as an infected surgical wound can be characterized by pain, tenderness, warmth, erythema, swelling and pus formation[15].

Factors Impacting SSI :

Many preventable causes of SSI have been identified, and if proper measures are implemented, the incidence could be reduced. A number of patient related factors (old age, preexisting infection, co-morbid illness, nutritional status) and procedure related factors (poor surgical technique, pre operative part preparation, inadequate sterilization of surgical instruments, prolonged duration of surgery) can influence the risk of SSIs significantly[2]. In addition to these risk factors, the virulence and the invasiveness of the organism involved, physiological state of the wound tissue and the immunological integrity of the host are also the important factors that determine whether infection occurs or not[16].

SSI can be controlled by optimal preoperative, intraoperative and postoperative patient care. This encompasses meticulous operative technique, timely administration of appropriate preoperative antibiotics, and a variety of preventive measures aimed at neutralizing the threat of bacterial, viral, and fungal contamination posed by operative staff, the operating room environment, and the patient's endogenous skin flora. Another measure to support the above interventions is use of antibiotic impregnated sutures.

Place of Triclosan Coated Sutures :

Several products have been introduced into the market, including triclosan-coated polyglactin 910 antimicrobial suture (Vicryl Plus; Ethicon, Johnson & Johnson), triclosan-coated poliglecaprone 25 antimicrobial suture (Monocryl Plus; Ethicon, Johnson & Johnson) and triclosan-coated polydioxanone antimicrobial suture (PDS Plus; Ethicon, Johnson & Johnson). It has no toxic, teratogenic, or irritating effects at the standard concentration[17]. Triclosan targets the e Fab I gene, which blocks bacterial fatty acid synthesis (particularly the enzyme enoyl-acyl carrier protein reductase [ENR])[18]. Whilst many randomized controlled trials have supported the evidence of beneficial effect of TCS in the prevention of SSIs[19-21], but some studies have shown inconclusive results[22-24].

The present study aims to assess the efficacy of TCS in reducing the incidence of SSI in a tertiary care setting in Northern India and the risk factors associated with it in the General Surgery.

Material and Methods

Patients :

From July 2016 to Jan 2017, a total of 306 patients underwent surgical wound closure with triclosan-coated sutures at SMS Hospital, Jaipur.This retrospective study was approved by the Institutional Ethics Board. Written informed consent was not applicable as it was a retrospective study. Preoperative and demographic characteristics of the patients are mentioned in Table 1.

Some confounding factors like American Society of Anesthesiologists (ASA) score,elective or emergency surgery, antibiotic prophylaxis, blood loss and presence or absence of drain were noted. CDC criteria were used to define the type of surgical wound ie, Class I- Clean, Class II- Clean contaminated, Class III- Contaminated, Class IV- Dirty. The ASA score was used for classification of the patients in terms of risk for the development of a surgical site infection.29.1% had ASA score of 1, 34.3% patients had ASA score of 2, 17% patients had score of 3, 3.3% patients had score of 1, and 19.6 % had ASA score of 4. The mean duration of surgery was 57.50± 39.41 min.

Profile of wound condition at the time of discharge

Table 1 — *Pre-operative and demographic characteristics of patients*

Parameter	Number	Parameter	Number
No of Cases	306	Wound class :	
Age (years) :		Clean	202 (66%)
Mean	39.63	Clean contaminated	48 (15.7%)
SD	17.52	Contaminated	27 (8.8%)
Range	4-85 years	Dirty	29 (9.5%)
Height (cms) :		Blood loss :	
Mean	158.94	Yes	31 (10.1%)
SD	13.60	No	275 (89.9%)
Range	90-174	Need for blood transfusion :	
Weight (kgs) :		Yes	24 (7.8%)
Mean	64.77	No	282 (92.2%)
SD	11.33	Use of drain :	
Range	15-85	Yes	129 (42.2%)
Sex (%) :		No	177 (57.8%)
Male	204(66.7)	Mean duration of surgery (mins):	
Female	102(33.3)	Mean	57.5
Type of surgery :		SD	39.41
Elective	188 (61.4%)	Range	30 - 190
Emergency	118 (38.6%)		
ASA score :			
1	89 (29.1%)		
2	105 (34.3%)		
3	52 (17%)		
4	60 (19.6%)		
5	0 (0 %)		

was evaluated. 66% evaluated cases were found to be 'clean' at the time of discharge, 15.7% were clean contaminated, 8.8% were contaminated and 9.5 % were dirty. 24.5% of cases had serous discharge followed by 15.0% cases had purulent discharge and 60.5% had clean wound condition at the time of discharge (Fig 1, Table 2).

Exclusion criteria were any severe disease that might influence wound healing or known allergy to triclosan.

Surgical Closure :

Wound closures were performed by experienced surgeons as per centre's protocol. Prophylactic antibiotics were administered to all patients within one hour after the start of the operation. Surgical areas were shaved just before the operation only in required cases and were aseptically scrubbed with chlorhexidine (5%, soap). The wounds were closed subcutaneously with a 3.0 Coated Vicryl Plus Antibacterial (polyglactin 910) Suture (Vicryl Plus®, Johnson and Johnson, India Ltd,) and intracutaneously with a 4.0 triclosan-coated Monocryl® Plus Antibacterial (poliglecaprone 25) Suture(Monocryl Plus®, Johnson and Johnson, India Ltd,). All wounds were then covered with drape, compresses and elastic bandages. The drape was removed on the fourth postoperative day. We used drainage at the site of surgery in 42.2 % cases. Prophylactic antibiotic treatment was performed according to the anesthesiology unit protocol. Postoperative anticoagulation was performed if found necessary depending on wound and comorbidity. In cases of poorly healed wounds and the presence of discharge for a long period bacterial culture was considered.

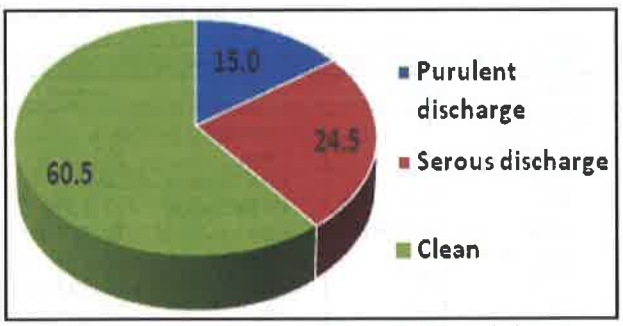

Fig 1 — Profile of wound condition at the time of discharge

Table 2 — *Profile of details of wound condition at the time of discharge and follow-up period*

Type of Wound Condition	At discharge (N = 306)		10th day after discharge (N = 306)	
	No	%	No	%
Purulent discharge	46	15.0	-	-
1 + Purulent discharge	14	04.6	-	-
2 + Purulent discharge	29	09.5	-	-
Mild Purulent discharge	02	00.7	-	-
Minor D/C Purulent (1+)	01	00.3	-	-
Serous discharge	75	24.5	-	-
1 + Serous discharge	37	12.1	-	-
2 + Serous discharge	35	11.4	-	-
Mild Serous discharge	03	01.0	-	-

Outcome Measures :

Patients were daily inspected by attending surgeons for any wound discharge, exudates, wound integrity, and signs of inflammation. In case of a suspected infection, wound swabs for cultures were taken, and evaluation for potential surgical revision was done. Association of occurrence of SSI with age, gender and class of wound was analyzed.

After discharge, if a patient reported any type of wound healing problems including dehiscence, swelling, redness or exudate, they were seen at the outpatient clinic, and the wounds were evaluated. Bacterial cultures were only collected from patients with symptoms of infection and no surveillance cultures were collected. SSI within the 30 first days after surgery were considered to be related to surgery and classified in terms of severity of the infection

Statistics :

Data are presented in descriptive manner for this single arm study as mean ± standard deviation, median and range or number and percentage. Association of factors with SSI incidence was analyzed using the χ^2 test and reported with risk ratio (RR) with 95% confidence interval (CI). A P-value of <0.05 was considered statistically significant. The treatment was considered efficient if observed probabilities were lower than previously reported in literature, not efficient if they were equal, and harmful if the observed rate of complications was greater than the predicted rate. Statistical analysis was done using Statistical Package for the Social Sciences software program version 20 (SPSS Inc, Chicago, IL).

Results

During the study, wound infection developed in 13.4% as Superficial/Incisional SSI and 1.3% cases as deep incisional SSI (Table 2). None of the patients had SSI 10 days after discharge. Thus, use of triclosan coated sutures could reduce the incidence of SSI by 85.3% (Tables 3-5).

In 2.2% cases with Wound Class 1 had SSI and the association was significant. SSI incidence was 10.5%, 32.7 and 25.0% cases with Wound Class 2, 3 and 4 respectively (non-significant) (Table 6).

Table 6 shows 36 patients of 156 (23%) had SSI in the uncoated sutures group. 10 patients of 149 (6.7%) had SSI in the vicryl coated suture category. In 12 patients of 50 in class II wound category has SSI with uncoated whereas only 2 of 50 patients had SSI in class II in coated vicryl category. Similarly, 16 patients of 29 had SSI in class III category which was on 2 of 25 for vicryl coated suture (Table 7).

In 4.9% cases who belongs to age group 58 – 67 years had SSI and the association was statistically

Table 3 — *Profile of surgical site infection at the time of discharge in study cases*

Surgical site infection	At discharge (N = 306)		10th day after discharge (N = 306)	
	No	%	No	%
Yes	45	14.7	-	-
No	261	85.3	306	100.0

Table 4 — *Profile of SSI type at the time of discharge in study cases*

Types of SSI	At discharge (N = 306)		10th day after discharge (N = 306)	
	No	%	No	%
Deep Incisional	04	01.3	-	-
Organ/Space	-	-	-	-
Superficial Incisional	41	13.4	-	-

Table 5 — *Association between wound class and SSI*

Wound Class	N	SSI	
		No	%
Class 1	89	*02	02.2
Class 2	105	11	10.5
Class 3	52	17	32.7
Class 4	60	15	25.0
Class 5	-	-	-
Unknown	-	-	-
By Chi – Square Test		*P =0.001, Significant	

Table 6 — *Profile of SSI for uncoated and coated sutures*

Class of wound	Non-coated suture (total)	Non-coated suture (non-infected)	Non-coated suture (infected SSI)	Vicryl coated suture (total)	Vicryl coated suture (non-infected)	Vicryl coated suture (infected SSI)
Class I	49	48	1	40	39	1
Class II	50	38	12	52	50	2
Class III	29	13	16	27	25	2
Class IV	28	21	7	30	25	5
Total	156	120	36	149	139	10

significant.Rest no age group showed a statistical correlation (Table 8).

In 12.7% of male cases had SSI which was numerically less as compared to 18.6% of female cases but the difference was not statistically significant.

There were no signs of wound dehiscence. There was not a single case of intraoperative complications in our cohort. There was no case of adverse effect reported in our study.

Discussion

As SSIs continue to pose a challenge within healthcare in India, further studies are required to substantiate the efficacy of TCS in Indian population along with a detailed identification of the factors associated with its prognosis. Infection of the surgical site results mainly from the imbalance between the amount of the microorganisms inoculated, their virulence, and the ability of the immune system to clear them. Therefore, it is logical that creating an

Table 7 — *Association between age groups and SSI*

Age groups	N	SSI	
		No	%
≤ 17	18	03	16.7
18 - 27	80	12	15.0
28 - 37	51	06	11.8
38 - 47	51	08	15.7
48 - 57	46	10	21.7
58 - 67	41	*02	04.9
≥ 68	19	04	21.1
By Chi – Square Test		*P =0.023, Significant	

Table 8 — *Associationbetween gender and SSI*

Gender	N	SSI	
		No	%
Male	204	26	12.7
Female	102	19	18.6
By Chi – Square Test		P =0.171, Not Significant	

antibacterial environment within the wound by virtue of suture material impregnation would be a targeted intervention to reduce the risk of SSIs.Suture materials play an important role in the development of SSIs by providing a local surface for the adherence of microorganisms. At the same time it is a criteria that can be easily changed[25].

Correlation with RCTs :

Ford HR *et al*[26] conducted a prospective, randomized, controlled, open-label, comparative, single-center study in pediatric patients undergoing various surgical procedures. TCS received more "excellent" scores (71% *versus* 59%) by surgeons.Significantly fewer patients treated with TCS reported pain on day 1 than patients who received the other suture (68% *versus* 89%, p = 0.01). Okada n *et al*[27] authored a controlled clinical trial of 198 consecutive patients undergoing pancreaticoduodenectomy. The rates of SSI were significantly less (4.5%) in the TCS group and (14.5%) in the control group (p=0.037). There are few other randomized control trials by Nakamura *et al* and others[28-30] which demonstrated a significant beneficial effect of TCS in the prevention of SSIs after surgery.

Correlation with Meta-analysis :

There are many level 1A evidence to support our results. Wu X *et al*[31] conducted a meta-analysis of 13 randomized controlled trials and 5 observational studies. Antimicrobial sutures significantly reduced SSI risk (for RCTs: OR 0.72, 95 % CI 0.59-0.88, p=0.001, I^2=14%; for observational studies: OR 0.58, 95 % CI 0.40-0.83, p=0.003, I^2=22%). Another meta-analysis by De Jonge *et al*[32] analyzed 21 RCTs including 6462 patients. Pooled effects showed a RR of 0.72 (95% CI 0.60 to 0.86; P<0.001). The trial sequential analysis confirmed a RR reduction of 15 per cent for the use of TCS.

Daoud *et al* meta-analyzed 15 randomized controlled trials and obtained a risk ratio of 0.67, 95% CI 0.54–0.84 (p=<0.00053), demonstrating a highly statistically significant, lower risk of SSI following operative procedures in incisions which were closed with TCS compared to non-antimicrobial closure technology. They had a similar inference to ours in terms of 'class of wound' association. A statistically significant reduction could be expected in clean-contaminated and contaminated incisions but these results were not robust when considered separately from the clean incisions. No conclusions could be drawn based upon this analysis on the impact of triclosan sutures as a risk reduction strategy for SSIs involving dirty incisions. Jonge et al also reiterated the same evidence that the effect of TCS appears to be more robust in clean procedures. On the same line Diener *et al*[33] concluded that efficacy of TCS in a population with mostly non-clean procedures was non statistically significant.

Limitation and Strength :

As a limitation, this was a retrospective historical controlled study having an observational nature conducted in a single institution. Although the big sample size of 306 patients was the study's strength and provides for good reliability. Another strength of the study is its generalizability and robustness due to inclusion of heterogeneous case-mix of patients.

Conclusion

SSIs are associated with an increased risk of morbidity, readmission, intensive care unit stay, and mortality. Hence the need to prevent SSIs is ubiquitous. Several earlier publications have alluded to the benefits of using triclosan coated sutures. Our study adds to the wealth of evidence from an Indian perspective and presents a strong case for implementing such technologies into routine clinical practice. The incidence of SSI in our cohort was 14.7% and SSI could be prevented in 85.3% cases.Triclosan antimicrobial sutures should be considered for superficial and deep layer closure after all surgical operations. Also, recognition of factors associated with SSI allows for having targeted approach.Our study demonstrated a significant protective effect of triclosan-coated sutures on the occurrence of SSI after elective and emergency surgery, in particular for wound class 2 & 3 and age group 58 – 67. We hope that our current study may generate enthusiasm for future prospective studies, with more robust designs, in order to back or negate our results.

Conflict of Interest : We hereby declare that the authors have no conflicts of interest related to this manuscript

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Review Article

A comparative study of onlay and pre-peritoneal mesh repair in the management of ventral hernias in our hospital

Tapan A Shah[1], Yogendra S Modi[2], Mukesh S Suvera[3], Rajesh H Parmar[4], Khyati C Vaja[4], Jemish B Patel[4], Shireesh M Ninama[4], Sachi P Sankhala[4]

A Ventral hernia includes both spontaneous and incisional hernias after an abdominal operation. Meshplasty can be onlay (over anterior rectus sheath) or sublay (pre-peritoneal). Controversy exists regarding use of the type of either meshplasty, due to differences in ease in performing the surgery, time of surgery, complications occurring in post-operative period and recurrence. Aim of our study was to compare the outcome of onlay versus sublay mesh repair for ventral hernia. A total number of 180 patients with ventral hernias (with defect size ≤4 inches), admitted in surgery dept. in Smt SCL General Hospital & Sheth VS Hospital, Ahmedabad from July 2016 to June 2017, were divided into two groups; A- onlay mesh repair and B- sublay mesh repair. Patients were evaluated for operating time, postoperative seroma formation, wound infection, drain duration, post-op hospital stay and recurrence of symptoms. Among 180 patients, 90 patients underwent onlay and 90 patients underwent pre-peritoneal meshplasty. Out of 90 cases of onlay, only 28 cases took >1 hour for operating. Out of 90 cases of pre-peritoneal meshplasty, hospital stay was > 5 days for 11 cases and seroma was found in 3 cases and wound infection was found in 4 case and post-operative pain score was less in most cases. On analysis of results and five variables, pre-peritoneal mesh repair is comparatively good option even though duration of surgery is longer than onlay mesh repair. [*J Indian Med Assoc* 2019; **117**: 25-8]

Key words **: Ventral hernia, onlay, pre-peritoneal, mesh repair.**

A ventral hernia is a bulge through abnormal opening in the anterior abdominal muscles. Ventral hernias include incisional hernia through previous surgical incision site, umbilical and paraumbilical hernia, epigastric hernia[1]. Repair of ventral hernias with mesh as opposed to suture has substantially improved long-term outcomes. However, many studies demonstrate an increased risk for wound complications with mesh placement including infections, seromas, and mesh erosions[2,3]. Mesh can be placed over anterior rectus sheath (onlay) or pre-peritoneal space. With onlay repair, skin flaps must be created, which increases the risk of wound complications and mesh infection[2,4]. The risks of postoperative complications are affected by where the mesh is placed. For example, mesh exposed to intra-abdominal contents potentially increases the risks of adhesions, bowel obstruction, and fistula formation[4,5,10].

Pre-peritoneal space potentially protects the mesh from both superficial wound complications and intraperitoneal contents. In addition, it also allows for load-bearing tissue in-growth from two directions[5]. Due to excess mobilization of fat and disruption of perforators immediate post-operative complications like seroma and wound infection rate will be more in onlay mesh technique[3,5]. This comparative study was to focus on advantage and disadvantage of two types of meshplasty and to provide information regarding benefits of one over another[6].

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Aims and Objectives of the Study :

The aim of this study was to compare the outcome of the onlay versus sublay mesh repair for ventral hernia.

Materials and Methods

A combined prospective and retrospective study was carried out on 180 patients of ventral hernias (epigastric, umbilical, para-umbilical and incisional hernias excluding very large hernias with defect more than 4 inches) admitted in the Department of Surgery, Smt SCL Hospital and VS Hospital, Smt NHL Municipal Medical Collage, Ahmedabad over a period of 1 year from July-2016 to june-2017. All patients were grouped alternatively as ;

- Group A : Onlay mesh plasty (mesh over the anterior rectus sheath, 90 cases)
- Group B : Sublay mesh plasty(pre-peritoneal, 90 cases)

Observations

In both the groups were made with regards to duration of surgery, postoperative complications like seroma formation, wound infection, duration of drain placement, postoperative stay and recurrences, if any.

• All the patients were given 1gm 3rd generation cephalosporin antibiotic preoperatively at the time of induction and continued till the 5th postoperative day twice daily, and then changed to oral antibiotic (cefixime/ amoxicillin + clavulanic acid) twice daily for the next 5 days. Early mobility was strongly encouraged as cultural attitudes towards surgery in the setting are prohibitors to early ambulation for several days in postoperative period[7,8].

Follow up every monthly for 12 months was done to see late wound complications like sinus, neuralgia and recurrence of hernia etc. Conclusions were drawn using unpaired student t-test.

• **Duration of Study :** 1 year (July-2016 to June-2017) Sample Size : 180.

• **Type of Study :** A CombinedProspective and Retrospective study.

• **Inclusion Criteria :**All patients of age group more than 18 years who were presented with ventral hernias (epigastric, umbilical,para-umbilical and incisional hernias) and undergone surgery, were taken and analysed.

• **Exclusion Criteria :** (1) Patients, less than 18 years, (2) Groin hernia, (3) Divarication of recti, (4) Patients, medically not fit for surgery, (5) Patients, not giving consent.

Surgical Technique :

(A) Onlay mesh repair : The onlay repair was done under general anaesthesia with skin incision over the bulge or the defect. The hernia sac was clearly dissected and the contents were removed and the margins of the defect were held by Kocher forceps. The sac was dealt with and its contents were reduced into the abdominal cavity. With non-absorbable suture, the defect in the linea alba was closed and a proline mesh of adequate size was placed on the rectus sheath and fixed with stitches[9,10]. Hemostasis was secured. A dose of broad-spectrum antibiotic was given prior to anesthesia.

(B) Sublay mesh repair : The principles of the pre-peritoneal or sublay mesh repair included two main steps; mesh placement deep to the recti muscles and mesh extension well beyond the hernia defect. After the sac was being dissected and delineated, the defect is opened and the pre-peritoneal plane is created between the posterior rectus sheath and the rectus muscle for the placement of the mesh. The posterior rectus sheath along with the peritoneum is closed with zero prolene suture.

A proline mesh tailored to the size is placed in the already created plane behind the recti. The mesh is secured with few interrupted 2-0 polypropylene sutures. A suction drain is placed over the mesh. The anterior rectus sheath is closed with continuous 1-0 polypropylene sutures[9,10]. Another drain is placed in the subcutaneous plane and the skin closed. Drains were removed when drainage was <20 ml in 24 hours.

All the patients were given 1gm 3rd generation cephalosporin antibiotic preoperatively at the time of induction and continued till the 5th postoperative day twice daily, and then changed to oral antibiotic (cefixime / amoxicillin + clavulanic acid) twice daily for the next 5 days. The hospital stay of the patients was also recorded down (Fig 1).

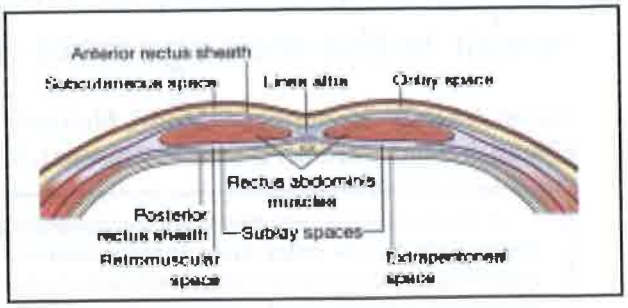

Fig 1 — Showing various layers into which mesh is placed in ventral hernia repair

Results

Among the 180 patients, 90 patients underwent onlay and 90 patients underwent pre-peritoneal mesh repair. Out of 90 cases of onlay, only 28 cases took more than one hour for operating. Out of 90 cases of pre-peritoneal mesh repair, hospital stay was more than five days for only 11 cases and seroma was found in only 3 cases and wound infection was found in only 4 case and postoperative pain score was less in most cases.

Percentage Distribution of Ventral Hernias:

In this study of 180 patients of ventral hernia, the most common type of ventral hernia was incisional hernia (47.22%). Epigastric hernia was the least common type (05%) (Table 1).

Table 1 — *Types of ventral hernias*

Type of Hernia	Frequency	Onlay	Sublay
Umbilical	63 (35%)	27	36
Paraumbilical	23 (12.78%)	11	12
Incisional	85 (47.22%)	45	40
Epigastric	09 (05%)	07	02
Total	180	90	90

Age and Sex Distribution :

Out of 180 patients, 98 patients were male and 82 patient were female. Most of cases are from middle age group (Table 2).

Table 2 — *Age and sex distribution*

Age group (in years)	Male	Female	Total	Percent
18 to 30	13	12	25	13.9 %
30 to 40	30	11	41	22.8 %
40 to 50	17	24	41	22.8 %
50 to 60	30	26	56	31.1 %
> 60	08	09	17	9.4 %
Total	98	82	180	100%

Postoperative Course :

The most common complication observed was seroma formation in 26 patients. Out of 26 patients, 3 were in pre-peritoneal and 23 in onlay mesh repair group (Table 3). This complication was managed with seroma drainage. Onlay technique had more of seroma formation, due to the fact that onlay techniques require significant subcutaneous dissection to place the mesh, which can lead to de-

vitalized tissue with seroma formation or infection.

Table 3 — Postoperative complications

Complications	Group A (Onlay) (90)	Group B (Sublay) (90)	Total (180)
Wound infection	23 (25.5%)	04 (4.4%)	27 (15%)
Seroma formation	23 (25.5%)	03 (3.3%)	26 (14.4%)
Flap necrosis	02 (2.2%)	00 (0.0%)	02 (1.1%)
Recurrence in 1 year	03 (3.3%)	00 (0.0%)	03 (1.66%)

Wound infection was found in 27 cases. Out of these 4 in pre-peritoneal group and 23 were in onlay group (Table 3). These patients were treated with appropriate antibiotics and regular dressing. No patient required removal of mesh because the infection was superficial and responded well to antibiotics.

Chronic pain was a complaint of 18 patients in all. Out of these 15 were in onlay group while 3 in pre-peritoneal mesh repair group.The reason for chronic pain in onlay mesh repair may be because mesh is placed below subcutaneous plane over the muscle and sutured over it that causes chronic muscle irritation and because of the fact that the closure is in tension (Table 4).

Table 4 — Postoperative pain

Postoperative pain	Group A (Onlay) (90)	Group B (Sublay) (90)
0 (no pain)	00 (00%)	00 (00%)
1-3 (mild)	05 (5.6%)	33 (36.6%)
4-7 (moderate)	46 (51.1%)	55(61.1%)
7-10 (severe)	39 (43.3%)	02 (2.3%)

Mean duration of hospital stay post operatively in sublay group was 4.8±1.51 days, whereas it was 6.68±1.46 days in onlay group (Table 5).

Table 5 — Duration of hospital stay

Duration of hospital stay	Group A (Onlay)	Group B (Sublay)
<5 days	07 (7.78%)	79 (87.78%)
> 5 days	83 (92.22%)	11(12.22%)
Total	90	90

Duration of Surgery :

In group A (onlay), the operative time ranged from 50 to 90 minutes with a mean operative time of 67.04±13.19 minutes, while in group B (sublay), the operative time ranged from 60 to140 minutes with a mean operative time of 93.26±24.94 minutes (Table 6).

Table 6 — Duration of surgery

Duration of surgery	Group A (Onlay)	Group B (Sublay)
<1 hour	62 (68.9 %)	00 (00%)
>1 hour	28 (31.1 %)	90 (100%)
Total	90	90

Discussion

Ventral hernia in the anterior abdominal wall includes both spontaneous and, most commonly, incisional hernias after an abdominal operation.Small hernias less than 2½ cm in diameter are often successfully closed with primary tissue repairs. Primary tissue repair is associated with higher unacceptable recurrence rate, now-a-days, tension free mesh repair is ideal hernia repair. Mesh placement in the pre-peritoneal, retro muscular sublay position with overlapping the hernia defect in all directions was introduced in the late 1980s[11]. The refinement of sublay technique decreased the recurrence rates and gave better outcome making it to be declared the standard of care of ventral hernias[11].

Most important comparable factors are duration of hospital stay, postoperative complications, recurrence and resume to routine work[12-14]. At the end of analysis, results mentioned above are compared. Based on the above results, duration of surgery was less in case of onlay mesh repair compared to pre-peritoneal mesh repair. In case of onlay mesh repair, 68.9% of cases took less than an hour for operating. But 100% of pre-peritoneal mesh repair took more than an hour for operating. In 87.78% pre-peritoneal mesh repair, hospital stay was less than five days. In 92.2% of onlay mesh repair, hospital stay was more than five days. 25.5% of onlay mesh repair cases developed seroma. But only 3.3% of pre-peritoneal mesh repair developed seroma. 25.5% of onlay mesh repair cases developed wound infection. But only 4.4% of pre-peritoneal mesh repair cases developed wound infection. Postoperative pain score was 4 and 5 for more than 60% of the pre-peritoneal mesh repair cases. But pain score was more than 5 in most of the cases in onlay mesh repair.

Conclusion :

Sublay mesh repair is a good alternative to onlay mesh repair that may be applicable to all forms of ventral hernia.The mesh related overall complication rate is low in sublay mesh repair such as drainage time, seroma formation and wound infection as well as the low recurrence rate.

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Case Report

Diaphyseal aclasis : study of imaging pattern and associated deformities

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Hereditary multiple exostosis, also known as Diaphyseal aclasis is characterised by development of multiple exostosis. We report two cases of diaphyseal aclasis who presented to the outpatient orthopaedics department of our institution with clinico-radiological correlation of the diagnosis with due emphasis on the associated deformity as encountered. The multiplicity of lesion and associated deformity makes the diagnosis of diaphyseal aclasis at an early stage than its solitary counterpart. Most of the patients presented with short stature as the chief complaint. The spectrum of the radiological features of osteochondroma, its variants and complications are a direct refelction of its pathological appearances. Identification of these features are important in guiding therapy and thus improving the patients management.

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***Key* words : Osteochondroma, hereditary multiple exostosis, diaphyseal aclasis.**

Osteochondroma is the most common benign tumor or tumour-like condition with characteristic radiological features. It may be solitary or multiple with latter being associated with Hereditary multiple exostosis or diaphyseal aclasis. Treatment of hereditary multiple exostosis is complex and is often directed to correct the associated deformities rather than restricted to exostosis alone (Figs 1-5).

Case 1 :

A twenty-five year old male patient presented with chief complaints of short stature and multiple bony swellings around the joints of upper and lower extremity since childhood. There was no history of similar complaints in the family. General and systemic physical examination was normal. On Local examination, multiple hard bony outgrowths fixed to the underlying bone were noted in the region of bilateral wrist joint, bilateral knee and ankle join with deformity at bilateral wrist joint and forearms with shorening of right lower extremity. Skeletal survey of the patient was done which revealed multiple sessile and pedunculated bony outgrowths continuing with the underlying bones at multiple sites. Radiograph of bilateral wrist with forearm revealed sessile bony outgrowths composed of cortical and trabeculated component continuing with the underlying shaft of the forearm bones. There was shortening of the bilateral ulna with outward bowing of radius and subluxation of bilateral radiocarpal joints classically termed as the Bayonet hand deformity. Radiograph of bilateral knee joint in frontal and lateral preojections shows undertubulation of ends of femur termed as Erlenmeyer flask deformity. Multiple pedunculated bony outgrowths from bilateral lower end of femur and upper end of tibia and fibula projecting away from the joint space, a deformity termed as coat hangers exostosis at the distal end femur. Radiograph of bilateral ankle joint, frontal projection showed similar pedunculated exostosis at the distal end of tibia and fibula with pressure erosion over the medial end of distal right fibula with formation of interlocking exostosis. Diagnosis of Diaphyseal aclasis was confirmed on the evaluation of the skeletal survey of the patient which revealed characteristic sessile and pedunculated multiple exostosis with associated deformities. The patient was treated with reconstructive operation for bilateral bayonet deformity.

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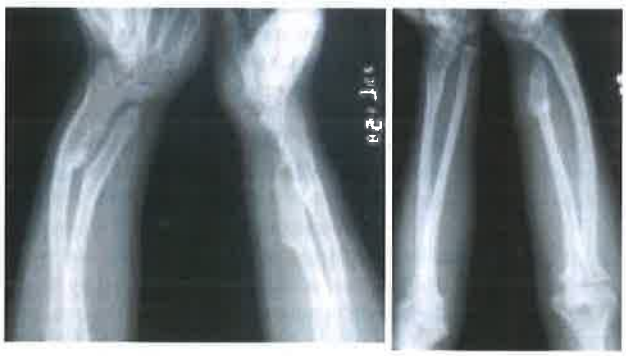

Fig 1(a) Fig 1(b)

Figs 1a & 1b — Radiograph bilateral forearms with wrist joint (Frontal projection):Multiple sessile bony outgrowths continuous with the undelying long bone noted at the lower end of bilateral radius-ulna with shortening of ulna and outward bowing of radius with subluxation of radio-carpal joint ,classically termed as Bayonet deformity

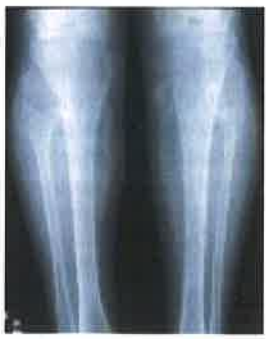

Fig 2 — Radiograph bilateral knee joint, frontal projection: Multiple sessile and pedunculated bony outgrowths consistent with multiple exostosis

Case 2 :

A thirty two year old male patient presented with chief complaints of multiple hard bony swelling around wrist and knee joint, associated with swelling over the back on the left side since childhood. There was no associated pain. Family history of similar swellings in elder brother was also noted. On examination, multiple bony swellings fixed to the underlying bones were noted in the region of wrist, bilateral knee, right shoulder and left scapular region. Radiograph of the right shoulder

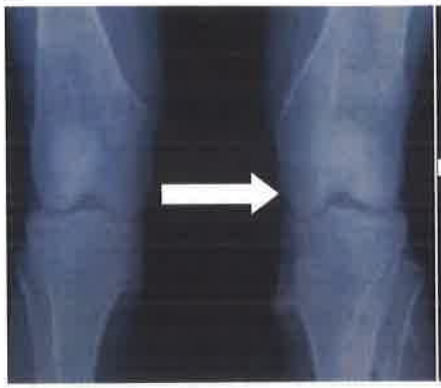

Fig 3 — Radiograph ,bilateral Knee : Undertubulation of lower end of bilateral femur(Erlenmeyer flask deformity) with multiple pedunculated exostosis growing away from the joint space (Coat hangers exostosis)

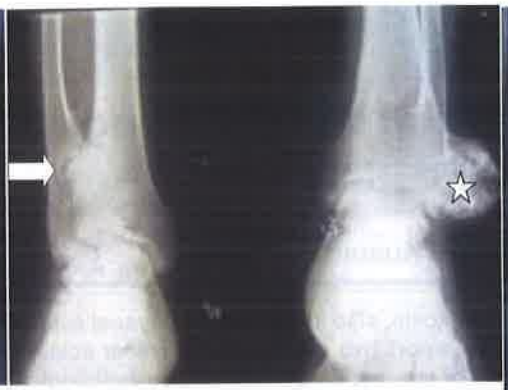

Fig 4 — Radiograph bilateral ankle joint : Multiple pedunculated exostosis noted at with calcified hyaline cap ,Cauliflower exostoses(star).Interlocking exostosis of right sided distal tibia-fibula with pressure erosion on distal medial shaft of right fibula.(arrow)

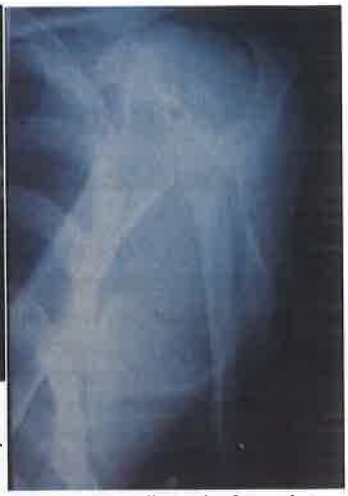

Fig 5 — Radiograph of scapula : Pedunculated exostosis arising from the infero-medial margin of left scapula

and humerus showed multiple sessile bony outgrowths from the proximal half of right humerus. Radiograph of the left scapula revealed similar exostosis arising from the lower medial border of the scapula. Radiograph of bilateral wrist with forearm revealed similar bony outgrowths with right sided bayonet deformity. Radiograph of bilateral knee joints showed multiple bony exostosis with undertubulation of the ends of femur and tibia-fibula. Diagnosis of hereditary multiple exostosis was made. The patient underwent reconstructive operation for the right side bayonet deformity with excision of the associated exostosis under general anaesthesia. Post-operative period was uneventful and physiotherapy was started on 4th postoperative day.

Discussion

Hereditary multiple exostosis, also known as familial osteochondromatosis or diaphyseal aclasis, is characterised by the development of multiple osteochondromas. It has an autosomal dominant inheritance with incomplete penetrance in females. The number of exostosis, the degree and type of deformities and the risk of complications varies significantly even within the family[1].

The genetic basis of HME is on chromosome[8], the locus being EXT-1 and additional locus on chromosome 11 and 19, referred as EXT2 and EXT3[2].

The skeletal distribution of lesions of HME is characteristically described as bilaterally syymmetric involvement with involvement of any bones developing from enchondral ossification with most frequent involvement of bilateral lower extremity in 50% cases.

On imaging, the individual osteochondromas in HME is identical to that of solitary lesions. Carroll *et al* noted that the amount of involvement and deformity of the forearm and distal leg is a measure of the overall disease extent. In addition, they found that the percentage of sessile osteochondromas correlated with the extent of deformities[3].

Cosmetic deformity caused by an osteochondroma is the most common clinical presentation. Bony deformities include both growth sequelae as a result of failure of normal tubulation and local effects such as osseous bowing and malalignment. Extrinsic pressure erosion of an adjacent osteochondroma is commoner with large lesions where paired bones lie juxtaposed. Other complications include Fracture of the osteochondral fragment, Vascular compromise, Neurological sequelae, bursal formation and rarely malignant degeneration, most commonly into chondrosarcoma. The risk of malignant degeneration is about 1% in solitary osteochondroma to upto 25% in HME.

Radiographic features suggestive of malignant degeneration include[4].

(1) Growth of osteochondroma in a skeletally mature patient.

(2) Irregurity of the surface of the lesion.

(3) Focal regions of radiolucency in the interior of lesion

(4) Erosion or destruction of adjacent bone. And

(5) Significant soft tissue mass with irregular calcification.

(6) A cartilage cap thickness of more than 1.5 cm should be considered suspicious for malignant transformation.

Treatment of patients with HME is complex and controversial. Most of the surgical treatment is directed to correct the associated deformity along with excision of exostosis[5]. Patients with HME require continuous surveillance for the progression of deformity and development of complications. The overall recurrence rate of osteochondromas is estimated to be 2% with most of these related to inadequate excision of the overlying perichondrium.

Fig 6 — Radiograph of right shoulder with proximal humerus: Multiple sessile exostoses noted arising from proximal humerus

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Case Report

Gaucher's disease — diagnostic value of bone marrow examination and genetic study

Tushar Vithlani[1], Jiten Vadher[2], Ashish Sheth[3], Bhavya Vora[4]

Gaucher's Disease is a rare Genetic Autosomal Recessive Lysosomal Storage disorder caused by inherited deficiency of acid-ß-Glycosidase (Glucocerebrocidase-GBA) which results in glycosphingolipid Glucosylceramide to accumulate within lysosomes of Macrophages[12]. Out of Three types of this disease type I is most common form of the disease and it does not involve CNS and can be present at Adulthood. In Present case 22 years old Female presented with weakness and abdominal fullness and pain. Hemogram shows Pancytopenia and USG revealed Hepatosplenomegaly. On Bone marrow examination Gaucher's Cells found and Gaucher's Disease (Type 1) diagnosis was made. Treatment of this disease is enzyme supplementation and Bone marrow transplantation.

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***Key* words : Gaucher's disease, bone-marrow examination, genetic study.**

Gaucher's Disease named after the French Doctor Philippe Gaucher, who originally described it in 1882. Storage of glucocerebroside was first recognized by Epstein in 1924 This disease presents with Symptoms of Pancytopenia, Hepatosplenomegaly, skeletal disorders, painful bone lesions, neurological complications, lymphadenopathy, and yellow deposition on the sclera[14] and can be diagnosed by Bone Marrow examination, Enzyme estimation and Definate diagnosis by Genetic Testing. Treatment of this disease is Enzyme Replacement therapy (ERT) and Bone marrow Transplantation[14].

Case Report

A 22 year old female came to OPD with complains of weakness, Abdominal Pain. No any other complains were present.

Examinations — The patient's Vital signs were within normal limits. There was pallor, Hepatosplenomegaly. There was no lymphadenopathy, Sternal tenderness or any skeletal abnormalities.

Investigations — Routine Hemogram shows Hb : 5.4g/dl ,Total RBC count : 2.85 mil./cmm Total Leukocyte Count: 2500/cmm, Diffential Count $P_{52}\ L_{42}\ E_{03} M_{03} B_{00}$, ESR : 65 mm/ 1st hour, Platelet count : 1,10,000 /cmm. Her Ferittin was 368 ng/ml and Vit. B-12: >2000 pg/ml, SGPT: 78.52 U/ml, total Billirubin: 0.73 mg%, Direct Billirubin: 0.60 mg%, Alkaline Phosphatase 91.25 IU/ml. Her peripheral smear shows Dimorphic Anemia with Leucopenia and Thrombocytopenia (Pancytopenia). Angiotensin Converting Enzyme (ACE) was 118.0 u/l.

Her USG examination shows Liver enlargement of 18 cm with Splenic Enlargement.

From the history, clinical examination and investigations it was evident that patient is suffering from Pancytopenia with high ESR and Hepatosplenomegaly. So Bone-Marrow aspiration examination was planned.

On Bone marrow examination many large Histiocytic cells having eccentric or centrally placed nuclei with fibrillary or striated pattern pale blue to grey 'crumpled cigarette paper' like cytoplasm. (Gaucher's cells) were present and Gaucher's Disease Diagnosis was made (Fig 1).

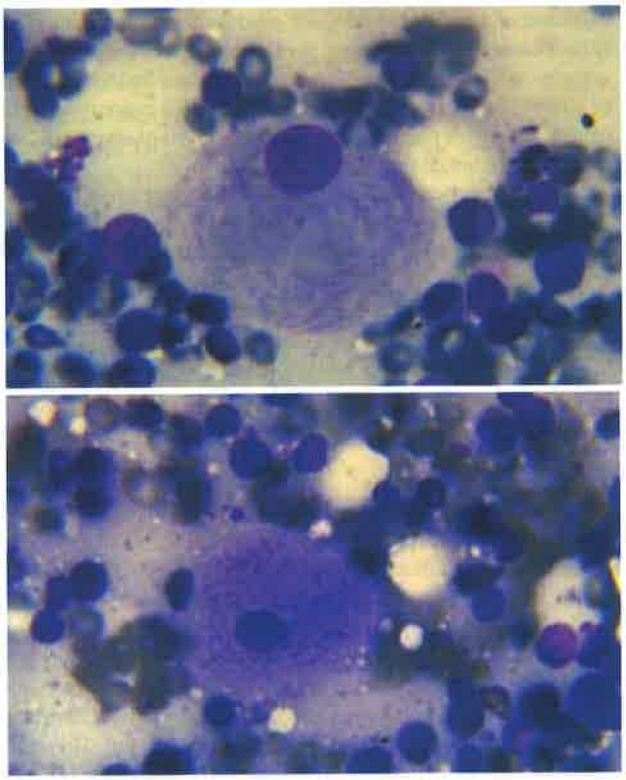

Fig 1 — Gaucher's cell (50x, field's stain)

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Discussion

Gaucher's Disease is a genetic disease and the most common of Lysosomal Storage Disease. It is a form of Spingolipidoses caused by deficiency of acid- ß -glucosidase enzyme which acts on glucosylceramide fatty acid, so there is accumulation of this fatty acid in macrophages. This can collect in Liver, Spleen, Kidneys, Brain and Bone marrow[11].

Epidemiology and Genetic Aspects :

The disease is affecting an estimated 1 in 50,000 to 1 in 100,000 people of the general population[6]. Persons of Eastern and Central European (Ashkenazi) Jewish heritage are at higher risk for the disease with incidence rate of approximately 1 in 500 to 1000[13]. There is inadequate information on the prevalence of this condition in the Indian population due to its rarity in this part of the world[2]. It is Autosomal recessive so mother and father must both pass one abnormal copy of the gene to the child in order for the child to develop the disease[3].

Located on long (q) arm of chromosome 1, GBA gene codes for production of enzyme Beta glucocerebrocidase[4]. However, the mutations in this gene leads to reduction in the activity of this enzyme causing toxic level accumulation of the glucocerebrosides in the cells which in turn damages the tissues and organs leading to the onset of characteristic features indicating Gaucher's Disease[3]. Most of these mutations are mis-sense mutation related with variable severity observed in the phenotype of the condition, for example the mutation c.1226A>G (N370S) on the GBA gene is often associated with certain degree of neuro-protection causing Type 1[5]. Whereas the homozygosity for the c.1448T>C (L444P) mutation on the GBA gene presents with neurological symptoms[4]. The complexity of identification and characterization of mutations in the gene of GBA is caused by a great amount of mutated alleles. The existence of a highly homologous psudogene and its location on chromosome 1, a highly gene rich region promotes the presence of complex alleles. Based on the mutations present and the numbers of alleles affected, the disease is classified into 3 major types indicating the variable phenotype and different levels of severity[1]. Each type has been linked to particular mutations:

Type I (Non-neuropathic) (N370S homozygote) most common form and does not involve CNS, Clinical manifestation are heterogenous and can come to attention from infancy to adulthood with median age at diagnosis is 28 years of age , range from very mildly affected individuals to those having rapidly progressive systemic abnormalities[4,12].

Type II (1 or 2 alleles L444P) is very rare, characterized by neurological problems in small children. The enzyme is hardly released into the lysosomes and prognosis is poor: most die before age of 3[3,12].

Type III (also 1-2 copies of L444P, possibly delayed by protective polymorphisms) presents in early child hood and most commonly in the Swedish population from the Norrbottern Region. This group develops the disease somewhat later, but most die before the age of 30[4,12].

Diagnosis

Diagnosis of this disease can be made by presence of Gaucher's cells in Bone marrow, Liver or Spleen Biopsy. The Gaucher's cells are having centrally or eccentrically placed nuclei with fibrillary, striated pale blue 'crumpled paper pattern' cytoplasm[5]. This cells show strong PAS and Tartrate Resistant Acid Phosphatase (TRAP) positivity with diffuse iron staining in cytoplasm[8]. Other key diagnosis is enzyme estimation which is decreased in the patient of this disease. It can be diagnosed by demonstration of deficient Acid- ß - Glucoside enzyme in isolated peripheral leucocytes or cultured fibrocytes. Confirmed diagnosis is made by molecular DNA assay which show mutation in GBA gene on chromosome 1. Mutation types N370S, L444p, 84GG, JVS2+1 and sequence analysis is useful for identifying rare mutant alleles associated with Gaucher's Disease[12]. Only Karyotyping will not be able to identify the array of mutation present[10]. Prenatal Diagnosis is available by determining enzymatic activity or specific mutation in chorionic villi or cultured amniotic fluid cells.

Treatment of this disease is Enzyme Replacement Therapy and Bone marrow Replacement. ERT has remarkable effects on Hepatosplenomegaly and anemia, increased growth velocity in children, weight gain and increased energy levels[7,13]. Treatment of patients with Type 1 with recombinant ß-Glucocerebrocidase (Imuglucerase) results in a decrease in the relative volume of bone replaced by Gaucher's cells and an increase in hemopoeitic and fat cells and decreased cortical bone structure[11].

Acknowledgment

We are very thankful to Dr BK Vora (MS, MCh) for his Kind support to Prepare Our Case Report

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Case Report

Leiomyoma of Hard palate — case report and review

Sushil Kumar Kashyap[1], Pallavi Agrawal[2], Sushil Kumar[3], Ravindra Kumar[3]

We report a rare case of Leiomyoma of The hard palate : Case Report and Review. A 42 year old male presented with a small 1 cm swelling over hard palate which was painless slow growing, non tender, smooth surface, overlying mucosa was reddish. Total excision was done with safe margins. The histopathological examination shown leiomyoma. This is rare tumour of hard palate which arise from unstriated muscle presented with slow growing swelling over hard palate. Treatment is total excision with safe margins followed by regular follow up.

[*J Indian Med Assoc* 2019; **117**: 33-5]

***Key* words : Leiomyoma, hard palate, smooth muscle.**

Leiomyoma is a benign smooth muscle tumor that may appear in any location, Though it is more common in the uterus, gastrointestinal tract and skin. It is rarely found in the oral cavity (0.065%), due to the scarcity of smooth muscle in this territory.

Oral leiomyoma is usually seen in adults and shows no gender predilection. The most frequent locations are the lips, tongue, hard and soft palate, and the cheeks. The tumor generally manifests as a slow-growing painless lesion, often of a purplish color.

The diagnosis is exclusively based on the histological findings. Clinically, a differential diagnosis must be established with lesions of the oral mucosa or connective tissue, such as fibromas, lipomas, salivary gland neoplasms, vascular tumors such as lymphangioma or haemangioma, etc. The differential diagnosis moreover must also include the malignant form of leiomyoma, ie, leiomyosarcoma. Treatment consists of complete resection, with dew safety margins and periodic controls to ensure early identification of possible tumor relapse. The present article describes a new case of oral leiomyoma, located in the palatal region, and evaluates the clinical and histological characteristics of the lesion, with a view to including the latter in the routine differential diagnosis of oral mucosal lesion.

Case Report

A 42-year-old male presented with a history of painless small swelling over hard palate on left side (Fig 1). The physical examination revealed a lesion measuring about 1 cm in diameter, located adjacent to the palatal surface of the upper premolars in the second quadrant. The lesion was a pale color with redness of adjacent mucosa, it was painless and non-hemorrhagic in response to palpation.

Treatment done with total excision of the lesion with a safe margin under local anesthesia and was sent for histopathology. The surgical wound was allowed to heal by second intention.

The histopathological study diagnosed oral leiomyoma (angioleiomyoma type). Hematoxylin-eosin staining (Fig 2, H&E x 100) revealed the presence of intermingling smooth muscle bands separated by cellular fibrous connective tissue.

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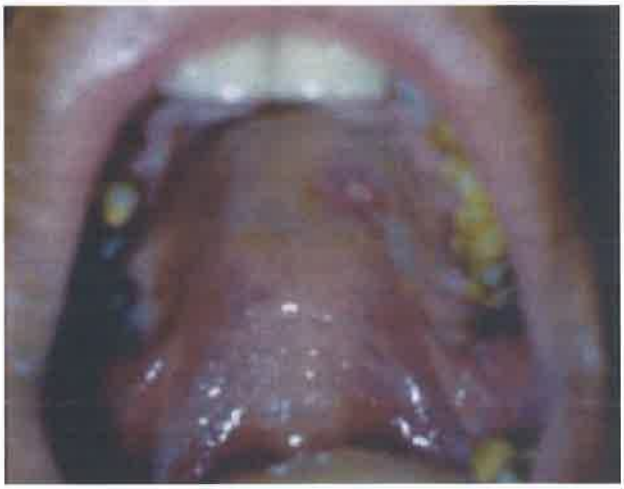

Fig 1 — Showing swelling over hrad palate

Discussion

Leiomyoma is infrequent in the oral cavity, due to the scarcity of smooth muscle in this territory. Stout suggested the smooth muscle of the tunica media of the arteries to be the probable origin of oral leiomyomas. Other authors consider leiomyomas to derive from the remains of embryonic tissue such as the lingual duct or circumvallate papilla of the tongue (Praal *et al*).

Leiomyoma of palate is rare tumour as reported. In the review published by Farman in 1975, involving 7748 smooth muscle tumors located throughout the body, only 5 cases (0.065%) corresponded to the oral cavity. The most common location was the female genitourinary tract. Hachisuga *et al* recorded 15 cases (2.7%) of oral angioleiomyomas in a series of 562 angioleiomyomas registered in a General Pathology Department. Brooks *et al* published a retrospective study of 12 angioleiomyomas, one solid leiomyoma and one leiomyosarcoma, out of a total of 76,412 biopsies/oral lesions registered in a Department of Oral Medicine in the period between 1963 and 2001. The incidence of angioleiomyoma was 0.016%, and represented 92.3% of all benign smooth muscle tumors located in the oral cavity.

Leiomyoma is usually seen in adults with the greatest incidence

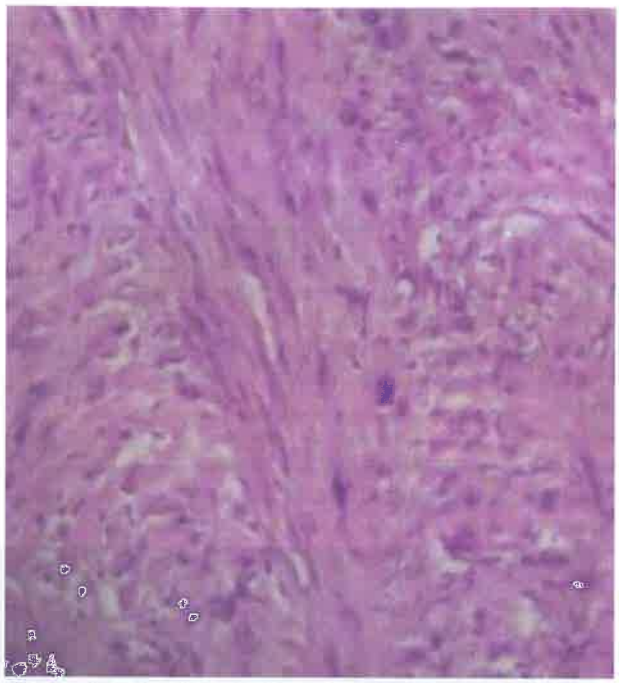

Fig 2 — Hematoxylin-eosin staining revealed the presence of intermingling smooth muscle bands separated by cellular fibrous connective tissue

corresponding to the 40-59 years age interval. Regarding gender distribution, some authors consider both males and females to be affected in equal proportion, though considerable controversy exists on this point. The present case was 45 years male, coincides with the typical presentations reported in the literature in relation to age distribution of leiomyoma.

The most frequent locations of oral leiomyoma are the lips, tongue, hard and soft palate, and the cheeks. Leung KW, *et al* reported a case of oral leiomyoma of buccal sulcus. In the series described by Svane *et al*, 21% of the leiomyomas were located in the palate. Out of these, angioleiomyoma represents 74%, solid leiomyoma 25%, and only one case of leiomyoblastoma has been documented. Brooks et al. recorded two angioleiomyomas at palatal level (16.7%) one in the hard palate and the other in the soft palate. The World Health Organization classifies leiomyomas into three histological types: leiomyoma (solid), angiomyoma (vascular leiomyoma) and epithelial leiomyoma (leiomyoblastoma).

According to Natiella *et al* the most frequent histological presentation of oral leiomyoma is angioleiomyoma (derived from smooth muscle of blood vessels). According to other authors, angioleiomyomas represent 64-66.2% of all types of oral leiomyomas. This is probably because the main source of smooth muscle tissue in the oral cavity is tunica media of the arteries. Duhig and Ayer suggested that vascular leiomyoma represents only a stage within a continuous process of smooth muscle maturation. The maturation sequence would be as follows: hemangioma, angioma, vascular leiomyoma, leiomyoma and solid leiomyoma. According to Damm and Neville, solid leiomyoma is histologically very different from angioleiomyoma, and the two entities therefore should be regarded as separate tumors. Leiomyoma tends to manifest as a smooth-surfaced submucosal nodule.

The overlying epithelium rarely ulcerates, though in some cases there is histological evidence of ulceration. The color of the lesions depends on their vascularization and depth. However, although their origin is related to the blood vessels, only 55.9% are red, blue or purple in color. The rest show the appearance of normal mucosa, or have a grayish tone. At palpation, the tumors appear firm and are generally well delimited, with free displacement within the lax tissues of the lip and oral mucosa. The lesions tend to grow slowly, with a size ranging from a few millimeters to 3 cm. In the cases described by Brooks *et al*, all the lesions were between 2-10 mm in size. Hemani DD *et al* presented a large leiomyoma of palate. The tumor in our patient was 1 cm in diameter, and presented a pink-purple color, as commented above. Most oral leiomyomas present as asymptomatic lesions, same in present case, though different authors have described clinical symptoms like pain on palpation, chewing and swallowing difficulties, and abnormal tooth mobility. The diagnosis of leiomyoma is relatively difficult to establish, due to the similarity with other fusiform cell tumors. The differential diagnosis must include other mesenchymal tumors (fibroma, neurofibroma, lipoma, etc), salivary gland neoplasms (mucocele, pleomorphic adenoma, etc), vascular tumors (lymphangioma, hemangioma, pyogenic granuloma, etc), and soft tissue cysts such as dermoid cysts. When located in the region of the hard palate, adjacent to teeth the tumor can be confused with a periodontal lesion.

The definitive diagnosis of leiomyoma is therefore based on the histological study of the lesion. Leiomyomas are composed of fusiform smooth muscle cells with elongated nuclei, similar to fibroblasts. The cells are distributed in parallel bundles, and the lesions are encapsulated or well delimited within the surrounding tissue. No fibrous stroma is noted only small capillaries among the tumor cells. In order to differentiate leiomyoma from the rest of fusiform cell tumors, specific stains are used to identify collagen and muscle cells, such as the Van Gieson, Masson trichromic and Mallory phosphotungstic acid-hematoxylin (PTAH) stains. Van Gieson staining is recommended for muscle. The Masson trichromic stain differentiates the cytoplasmic elements of the smooth muscle cells, which stain red, from collagen and fibroblasts, which stain blue or green. However, both the Van Gieson and Masson trichromic stains can give rise to false positive results for muscle and collagen fibers; it is therefore advisable to confirm the presence of myofibrils by using the Mallory PTAH stain. Immunohistochemical techniques can also be used. In this context, specific monoclonal antibodies for actin (a smooth muscle marker) are useful for confirming the diagnosis of leiomyoma (Gonzalez sanchez MA *et al*). Six cases diagnosed as leiomyoma were retrieved from the files of two oral biopsy were done with suitable controls. The haematoxylin and eosin and Masson's trichrome stains supported a diagnosis of leiomyoma in all 6 cases but PTAH was positive in only 3 of them. The immunohistochemical study confirmed the diagnosis of leiomyoma in 3 cases. The other 3 were identified as granular cell tumour, myofibroma and neurofibroma, respectively. Immunohistochemistry is a precise and reliable method for definitive diagnosis of oral leiomyoma (Baden E *et al*).

Leiomyoma must be carefully differentiated from leiomyosarcoma, particularly low-grade leiomyosarcoma. To this effect, a determinant factor is the presence of mitotic figures. In the presence of over 10 mitoses per high-magnification field (x40), the lesion is considered to have a malignant behavior, while fewer than two mitotic figures per 10 high-magnification fields is indicative of a good

prognosis. The presence of ulceration is also considered to be indicative of malignancy. Immunohistochemical techniques and molecular markers such as PCNA, bcl-2, CDK4, p53 and MDM2 are correlated to malignant lesions; the diagnostic procedure for differentiating muscle tumors is therefore based on these methods.

The treatment of choice is local resection, including an adequate safety margin of normal-appearing tissue. Despite the vascular origin of these lesions, important bleeding after excision is rare. Likewise, these benign smooth muscle tumors rarely relapse. Nevertheless, Brooks et al. documented relapse two weeks and 9 months after resecting two hard palate leiomyomas.

Conclusion

The leiomyoma is a rare benign tumor of the oral cavity, and with a good prognosis, though it must be included in the differential diagnosis of oral mucosal lesions. The treatment of choice is surgical resection with adequate safety margins in all cases, due to the high incidence of malignancy of this tumor within the oral cavity, when compared with the rest of anatomical locations. The possibility of relapse moreover requires periodic patient controls after resection. Histopathological examination should also include the immunohistochemical study.

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Letter to the Editor

CONGRATULATIONS !

Editorial, JIMA, Vol 117, No 03, March, 2019

Sir,

We are Dr Bhaskar Vyas and Dr Rajni Vyas, Octogenarian Life Members of IMA.We heartily congratulate you for your editorial article on ABC of stem cells, Vol 117, No 03, March, 2019. This is the need of the hour.

We further introduce ourselves as researchers in stem cells. We are a few amongst those who have been funded (twice) by DBT, GoI. You will be happy as an orthopedic surgeon to know that we have generated as original research to treat OA knee. We would like to contribute our research for publication to JIMA.

[1]MS, Plastic Surgeon — **Dr Bhaskar Vyas[1]**

[2]MD DGO, Obs & Gynae. — **Dr Rajni Vyas[2]**

Formally professors at Medical College, Baroda.

Activities Report

IMA Kunnamkulam Branch organised CME, International Women's day, Honouring Nurses, Charity, Health & Fitness activity, No Smoking Day, Table Tennis match, World Downs Syndrome day, BLS class, World TB day, IMA Telemedicine day in last month

IMA Madhya Kerala Branch Observed International Womens Day Celebrations, Zumba training for WDW members, International Women's Day Celebrations, Cancer detection camp, Awareness Class on Life style diseases in women, World Glaucoma Week, Eye camp, No Smoking Day, World TB day, Diabetes Detection camp

IMA Cochin Branch arranged, Blood donation camp, World Kidney day, IMA Sports Day, Drug Abuse awareness class, Monthly CME & Cultural Event, International Women's Day by WIMA, Talk & Awareness Class for ladies etc. in March, 2019

IMA Perinthalmanna Branch arranged Women's Day, BLS training, Walkathon, Dermatology camp, blood donation, awareness class, CME, World Down's Day

IMA Nemom Branch observed International Women's Day, "Kashmir to Kanyakumari Road Journey" - to spread the awareness about Diabetes.

IMA Thrissur Branch observed World Health Day

IMA Kumta branch arranged Pulse Polio Day & CME on Surgery in lung diseases

IMA Sirsi Branch arranged Kids health workshop, Holi celebrations, Blood donation camp & CME

IMA Hubballi Branch observed IMA State Level Athletic Meet

IMA Sullia Branch arranged free medical check up and treatment, Distributed the napkins to 19 poor village students, National Safe Motherhood Day, National Tuberculosis Day, World Health Day, Quiz competition etc

IMA-KGF Branch organised AIDS Day, CME, Free Cardiac and Pulmonary Camp

IMA Udupi Karavali observed World Health Day

IMA. Raichur Branch observed World TB day, Health Check-up camp & A Radio talk of World Health Day

IMA Jamkhandi Branch organised CME, Health talk at Albal Village, WHO Day Celebration at Savalagi, Dental check up Camp

IMA Yelahanka branch arranged National protest day against NMC and CME

IMA Mangaluru Branch organised World Health Day. Swatcha Mangaluru programme was conducted in Association with Shri Ramakrishna Mission's Mangaluru Branch

IMA-Nelamangala organised CME

IMA Mysuru Branch Organized Mega Health check Up Camp, The President Visit & Health Manifesto Press Meet Programme

KOLKATA

Dr

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