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Editorial

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ABC of Stem Cell

A stem cell is a cell with the unique ability to develop into specialised cell type in the body. In the future they may be used to replace cells and tissues, that have been damaged or lost due to disease. Our body is made up of many different types of cells/tissues. Most cells are specialised to perform particular functions, such as red blood cells, that carry oxygen around our body in the blood, but they are unable to divide, where as stem cells provide new cells for the body as it grows and replace specialised cells that are damaged or lost. They have two unique properties that enable them to do so; (1) they can divide over and over again to produce new cells. (2) As they divide, they can change into other types of cell that make up the body. There are three main types stem cells.

(1) Embryonic stem cells. (2) Adult stem cells. (3) Induced pluripotent stem cells.

Embryonic Stem Cell :

Embryonic stem cell supply new cells for an embryo as it grows and develops into a baby. These cells are said to be pluripotent, which means they can change into any cells in the body.

Adult Stem Cell :

Adult Stem Cells supply new cells as an organism grows and to replace cells that are damaged. Adult one are said to be multipotent, which means they can only change into some cells in the body but not any cells i.e.

Blood (or heamotopoietic) stem cells can only replace the various types of cells in the blood. Skin (or epithelial) stem cells produce the different types of cells that make up our skin and hair.

Induced Pluriopotent Stem Cells :

These are cells called 'IPS cells' that scientists make in the laboratory. Induced means they are made in the lab; by taking normal adult cells like skin or blood cells and reprogramming them to become stem cells; then just like embryonic stem cells they are pluripotent and develop into any type of cell.

The stem cells have several uses.

(i) In Research : to help us understand the basic biology of how living thing works and what happened when different type of cells are diseased.

(ii) Therapeutic : to replace lost or damaged cells that our bodies can't replace naturally.

Stem Cells Research :

(i) To understand how our bodies grow and develop.

(ii) To find ways of using stem cells to replace cells or tissues that have been damaged or lost.

(iii) If we understand stem cell development, we may be able to replicate this process to create new cells, tissues and organs.

(iv) The organ can be studied to find out how they function and how they react to stimulus nimbus like drugs.

Stem Cell Therapy :

Stem cells may be one way of generating new cells that can be transplanted in the body to replace those that are damaged or lost.

Adult stem cells are currently used to treat some conditions, for example :

(i) Blood cells are used to provide a source of healthy blood cells for people with some blood conditions, like thalassaemia and cancer patients who have lost their own blood stem cell.

(ii) Skin stem cells can be used to generate new skin for people with severe burns.

(iii) Age related macular degeneration (AMD) is an example of a disease where stem cells can be used as a new form by treatment in future.

(iv) Stem cells can be used to generate new organs for use in transplant. Induced pluripotent stem cells generated from patient themselves can be used to grow new organs.

How to Generate Induced Pluripotent Stem Cells ?

To generate induced pluripotent stem cells scientist reintroduce the signals that normally deal stem cells to stay as stem cells in the early embryo. These switch off any genes that tell the cell to be specialized, and switch on genes that tell the cell to be a stem cell.

Stem Cells in India :

According to Indian Council of Medical Research, all stem cell therapy in India are considered to be experimental with the exception of bone marrow transplant. Regardless, stem cell therapy is legalised in India. Umbilical cord and adult stem cell treatment are considred permissible. On 15 october 2017 in a move to curb rempent malpratice, India has banned commercial use of stem cell "as elements of therapy" and warned of punishment to erring climian claiming stem cells cure for diseases through direct or consumer marketing. As per the national guide lines for stem cell research, 2017, at present there is no approved indications for stem cell therapy other than Heamatopoietic stem cell transplantantion (HSCT) for heomatological disorder, like Blood cancer, Lukeamia etc.

According to FDA, there are currently only a limited number of stem cell therapies approved by the agency including ones involving bone marrow for bone marrow transplants in cancer care, and cord blood for specific blood related disorders. There is no approved stem cells treatment for other diseases.

FDA warns about stem cell therapies. Researchers hope stem cell will one day be effective in the treatment of many medical conditions and diseases for which few treatment exist.

Today a great hope is set on regenerative medicine in all medical fields. Leland Kaiper introduced the term 'Regenerative medicine" in 1992. He forecasted that "a new branch of medicine will develop that attempt to change the course of chronic diseases in many instances and will regenerate tired and failing organ systems". The so called induced pluripotent stem cells provide the possibility of autologus therapy, but it bears some essential safety problems.

Scientists now are in a position to treat medical condition; but they may cure or not

1. Spinal cord injury
2. Heart disease
3. Parkinsons disease
4. Alzheimer's disease
5. Lou gehnig disease
6. Lung disease
7. Arthritis
8. Sickle cell Anamia
9. Organ failure
10. Non union, delayed union and osteonecoris.

Side effects of stem cell therapy :

Decreased appetite, Diarrhea, Abdominal belly ramp, wight loss, yellowing of skin and eyes (Jaundice), Enlarged liver, Bloated abdomen, pain in right upper part of abdomen, increasd level of liver enzyme in blood, skin fells tight, dry buring eyes, dryness or painful shore in the mouth, burning sensation when eating acidic foods, bacterial infections, Blockage of smaller air ways of lungs, Autisum, Aids, Hair Loss and Eye diseases.

In India as well as globally, only blood stem cells from bone marrow to treat blood cancers and other different blood disorders are permitted. The clinical use in any other disease or use of stem cells other than this is still in research stage. But in India we see a marked contrast. Individuals and institution offer often new cell therapy to all patients. They claim successfull use of stem cells in treatment of diseases of heart, liver and other organs, spinal cord damaged by injury even cancer.

The stem cells have high oncogemic potentials.When injected undifferentiated they can cause 'Teratoma'. The use of adult stem cells raised less ethical concern. The adult stem cells can differentiate in cell types of the tissue in stem which they reside. Mesenchymal stem cells are most promising as they show good differentiations towards cartilage, tendon and bone cells; they are mainly bone marrow, fat, amniotic membrane, periosteum. There are two different strategies of this types of cell therapy.

(I) Cell therapy: The cell suspension is simply injected into the damaged tissue or into blood circulation.

(II) Tissue engineering- It is a complex one where cells are combined with a three dimensional matrix to compose a tissue like construct to substitute lost part of the tissue.

Editorial

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Stop TB — Partnership is the Key

Tuberculosis control has always been a serious challenge anywhere. First countrywide report of the epidemiological burden in India came from National Sample Survey (NSS) 1955-58. The survey confirmed the impression of high prevalence of tuberculosis with widely separated infection and disease rates, comparatively low mortality and morbidity rates, chronic disease more in elderly and lack of significant difference between urban and rural population. However, NSS had to make certain compromises on grounds of practicability and feasibility to get estimates for India as a whole as access and reach were not uniform all over the country. Pockets of extremely high morbidity were not considered separately.

The core challenge appeared to be delayed diagnosis and inadequate treatment. As per records, patients seeking care in the public sector had a better chance of treatment than from private providers but still 1/3rd were lost between care-seeking and successful cure. National TB Programme of India (NTP) was instituted in 1962 for this measure. NTP was originally designed for domiciliary treatment, using self administered standard drug regimen. Unfortunately the notion that time that patients with tuberculosis do not need to be hospitalized got wide acceptance and practice but the equally important finding of the need for supervised treatment was largely overlooked. NTP got marred by overreliance on chest X-ray for diagnosis at the cost of sputum smear and more stress on diagnosis rather than cure. This was compounded by inadequate funding and weak organizational support. A programme review after 30 years in 1992 revealed that only 30% of patients were being diagnosed and of these, only 30% completed treatment successfully. Revised National Tuberculosis Control Program (RNTCP) pilot project was the result, commissioned in 1993 and launched in 1997 adopting the internationally recommended Directly Observed Short Course (DOTS) strategy as the most systemic and cost effective approach to combat tuberculosis. The essential components were: political and administrative commitment to ensure the provision of organized and comprehensive TB control services; reliable and early diagnosis through smear microscopy of self-reporting chest symptomatic in the general health services; an uninterrupted supply of good quality anti-TB drugs; effective and patient-friendly treatment with Short Course Chemotherapy (SCC) given under direct observation; and accountability through proper recording and reporting. The objective of RNTCP were to achieve at least 85% cure rate among the new smear positive cases initiated on treatment and thereafter a case detection rate of at least 70% of such cases. RNTCP was scaled-up in 1998 and by 2004 more than 80% of country populations were covered. Entire country got covered by RNTCP by 2006 paving the way for the next step, Stop TB Strategy in 2006.

STOP TB Strategy 2006 :

While RNTCP was gathering momentum, the menace of HIV and drug resistant TB also assumed epidemiological proportions. In 2006, WHO introduced a six-point Stop TB Strategy building on the success of DOTS, but also incorporating new challenges and in particular HIV-related TB and MDR-TB. The Stop TB Partnership launched the Second Global Plan to Stop TB, 2006-2015 providing a roadmap and budget to reach the Millennium Development Goals (MDGs) and related Stop TB Partnership targets for TB control by 2015.

STOP TB strategy had additional six components. (1) Pursue high-quality DOTS expansion and enhancement. (2) Address TB/HIV, MDR-TB, and the needs of poor and vulnerable populations. (3) Contribute to health system strengthening based on primary health care. (4) Engage all care providers. (5) Empower people with TB, and communities through partnership. (6) Enable and promote research.

Public Private Mix (PPM) :

Even before the study of Uplekar in 1991 it was evident that significant proportions of the tuberculosis patients in India are managed by the private sector and RNTCP must involve the private health sector in general and private practitioners in particular in TB care and control. The Stop TB concept initiated a comprehensive approach to involve all relevant health-care providers in DOTS and ensure that they apply international standards for TB care. These included 'Private-for-profit qualified clinical providers' and 'Non Governmental Organization qualified clinical providers'. The PPM DOTS concept was expanded to encompass engagement with a range of providers, including some semi-qualified providers, traditional providers and public and private hospitals.

National Strategic Plan for Tuberculosis Control, 2012–2017 :

The central theme of this plan was the goal of universal access to quality TB diagnosis and treatment for all TB patients in the community. This entailed sustaining the achievements till date, finding unreached TB cases before they can transmit infection, and treating all of them more effectively, preventing the emergence of MDR-TB. The dossier laid out the next 5 year plan towards achievement of a "TB free India" considering the issues and challenges ahead and outlining the framework for tackling each of these. Integration of the private sector with RNTCP was deemed crucial for fight against TB. During 2012-17 RNTCP targeted to encompass, accept and improve TB care provided by the private sector at the national and state level. Involving private practitioners (PPs) through RNTCP- Indian Medical Association public-private mix (RNTCP-IMA PPM) project was a great step towards this direction. A Government order issued by the Government of India in May 2012 mandated all health care providers to notify every TB case and / or treated, to local authorities. To support TB notification and strengthen TB surveillance in general, a case based web based TB notification system NIKSHAY was established to provide platform for notification from both public and private sectors.

National Strategic Plan for Tuberculosis Elimination 2017–2025 :

India is now poised to address TB better than ever before. With advanced and effective interventions and technologies the National Strategic Plan 2017–25 (NSP) aims for TB elimination in India. The requirements for moving towards TB elimination have been integrated into the four strategic pillars of "Detect – Treat – Prevent – Build" (DTPB). DETECT: Find all DS-TB and DR-TB cases with an emphasis on reaching TB patients seeking care from private providers and undiagnosed TB in high-risk populations. TREAT : Find all DS-TB and DR-TB cases with an emphasis on reaching TB patients seeking care from private providers and undiagnosed TB in high-risk populations. PREVENT: Prevent the emergence of TB in susceptible populations. BUILD: Build and strengthen enabling policies, empowered institutions and human resources with enhanced capacities.

The National Stop TB Partnership :

Tuberculosis elimination is a daunting task and needs integrated effort from all the stakeholders. The National Stop TB Partnership in India is a consortium of civil society representatives and NGOs working with the Government for increased visibility and community ownership of the national TB program and to provide a platform for all to work together. Partnership of RNTCP with Indian Medical Association (IMA) is of paramount importance in this effort. IMA End TB Initiative 2018 project would provide impetus to private doctors with awareness campaign, training, streamlining TB treatment and reporting in all the states and Union territories of India.

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Original Article

Trends of CD4 count after initiation of antiretroviral therapy and the predictors of immunological non response in HIV infected patients in a tertiary care centre of Southern Bengal

Kripasindhu Gantait[1], Atanu Chandra[2], Puspendu Biswas[3], Indranil Sen[4], Rajat Goswami[5]

This retrospective cross sectional study was done by reviewing the records of 422 patients of HIV (who received ART from the ART clinic of Midnapore Medical College) to assess the trends in CD4 cell recovery among HIV patients after initiation of ART, the effect of different baseline characteristics on CD4 cell count response & to find out predictors of immunological non response (Rise of CD4 counts of <50 cells/µl after first 12 months of ART). Relationship of different variables like baseline CD4 counts, age etc with immunological non response were also assessed. The overall median change from baseline to the 48 months CD4 count was +359 cells/µl. The median changes at 48 months were +216 cells/µl,+35cells/µl & +59 cells/µl in the strata of baseline CD4 of >350, 201-350 & <200 cells/µl respectively. CD4 counts almost returned to normal at the end of 48 months in those with initial CD4 counts of >350 cells/µl. The patients with a lower baseline CD4 had lower peak CD4 counts. Patients with lower CD4 counts at the beginning had subsequent poor CD4 recovery & higher chances of immunological non response as well. Female patients & patients of WHO clinical stage 4 was also found to be at significantly higher risk of immunological non response. Our findings suggest that HAART should be initiated early for better immune recovery & female patients should be given more consideration regarding adherence to the therapy.

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Key words **: CD4 counts, ART, HAART, HIV.**

Infection with HIV is a common public health problem all over the world, especially in developing countries like India. Vital cells in the human immune system such as helper T cells (mainly CD4+ T cells), macrophages, and dendritic cells are primarily infected by HIV[1]. This gradual decline of CD4 T cells leads to general decline in immune functioning and is the primary determining factor in the clinical course of the HIV infected individual. The CD4+ T-cell count is the single best laboratory determinant of clinical outcomes[2]. The Antiretroviral Therapy (ART), results in reduction of plasma HIV-RNA that in turn allows increase in the CD4 cell count. In India, the availability of measurement of viral load is limited & CD4 cell counts is a very important marker of starting and monitoring of highly active antiretroviral therapy (HAART)[3]. Sustained increase in the CD4 cell response to HAART and suppression of HIV load were both associated with greater increases in CD4 cell counts[4]. Previous recommendation by the World Health Organization (WHO) was to start ART in patients with CD4 cell count <350 cells/µl[5]. But the current WHO recommendation is to initiate ART in everyone living with HIV at any CD4 cell count. This is based on evidence from clinical trials and observational studies released since 2013 showing that earlier use of ART results in better clinical outcomes for people living with HIV compared with delayed treatment[6].

The relationship between the recovery of CD4 counts with ART & baseline CD4 counts is still a matter of debate. The objective of the present study was to determine trends in CD4 cell recovery among HIV patients after initiation of ART and the effect of different baseline characteristics on CD4 cell count response in a sample of Indian patients. We also studied to find out predictors of immunological non response (increase of CD4 cell count <50 cells/µl from baseline after 12 months of therapy). To the best of our knowledge, there are no such studies before from the area on this topic.

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Material and Method

Midnapore Medical College & Hospital is one of the largest tertiary care centre in southern region of West Bengal, India. This retrospective cross sectional study was conducted by reviewing the medical records of HIV infected patients aged 16 years or more who received antiretroviral treatment at the ART Clinic of Midnapore Medical College & Hospital during the period of 2006 to 2013. Seriously ill patients & those who did not complete 4 years of antiretroviral treatment either due to death, transfer out or lost follow up were excluded from our study.

For the purpose of this study, a baseline and 6-monthly CD4 cell count(by flow cytometry) upto 48 months and basic information such as patients' sex, age, weight, presence of TB co infection, anemia and WHO clinical stage were collected from medical records.

Our study was approved by Institutional Ethics committee for human research, Midnapore Medical College & Hospital.

Sample size, sampling technique & Statistical analysis : 422 sample size. Formula Z^2pq/L^2.

Z=1.96, on 95% confidence interval, p= 50%, q=(1-p), L=absolute error of 5%. 422 records were evaluated at ART clinic from 2006-2013 those who completed 4 years ART.

Data were being entered and analyzed by using SPSS for Windows, version 20.0. The median (IQR) in the absolute CD4 cell count at baseline and every six months thereafter was determined. Changes in CD4 cell count every six months were also examined and stratified on the basis of baseline CD4 cell count (<200, 201–350, and >350cells/µl). Categorical variables were summarized as frequencies and percentages while numerical variables with non-normal distribution were summarized as median and IQR. To assess the factors associated with the risks of immunological non response, logistic regression analysis was applied. All tests of significance were two-sided, with $p<0.05$ indicating statistical significance.

Observations

Baseline characteristics of the patients :

A total of 422 medical records of the ART Clinic of Midnapore Medical College & Hospital were reviewed. Baseline characteristics of the patients are depicted in Table 1.

Trend of CD4 count after comencement of ART :

The changes in the median CD4 cell count at 6 months interval after the commencement of ART is plotted in Fig 1. The overall median CD4 Count & median CD4 count in different strata are depicted in Table 2. CD4 count Median IQR at 0 m was 132 (93-168), 265 (230-301), 380 (364-397) and at 48 m 191 (188-203), 300 (274-324), 596 (488-698) cells/µl of CD4 <201, 201-350, >350 cells/µl respectively (Table 2, Fig 1).

Baseline CD4 cell count was evaluated whether it was a risk factor associated with immunological non-response. The percentages of immunological non-response was 17.5% (74 out of 422 patients). The proportions of patients who had immunological non responses were 31% (23 out of 74), 46% (34 out of 74) and 23% (17 out of 74) among patients with baseline CD4 <200, 201–350 and >350 cells/µl respectively. Results of logistic regression analysis of baseline characteristics associated with the risk of immunological non-response are depicted in Table 3.

Table 1 — *Baseline characteristics of the patients (n=422)*

Baseline variables	Frequency	Percentage
Gender :		
Male	198	46.9
Female	224	53.1
Age (years) :		
<45	369	87.4
≥45	53	12.6
Mean±SD	34.05±8.459	
WHO clinical stage :		
1	95	22.5
2	146	34.6
3	139	32.9
4	42	10.0
Baseline CD4 count :		
≤200	191	45.3
201-350	204	48.3
>350	27	6.4
Weight (kg) :		
<40	77	18.3
40-60	323	76.5
>60	22	5.2
TB co-infection :		
Yes	117	27.7
No	305	72.3
Anemia :		
<12	354	83.9
≥12	68	16.1

Discussion

The overall median CD4 cell count had improved among HIV-infected patients over the period of 48 months in our study. It was also seen that the CD4 counts almost returned to normal at the end of 48 months in those with initial CD4 counts of >350 cells/µl. The patients with a baseline CD4 cell count <200 cells/µl had the lowest peak CD4 counts. So a lower CD4 cell count at the start of antiretroviral therapy was related to a lower plateau CD4 cell count. These findings are in accordance to the literature[7,8,12-15].

A study by Moore RD et al showed that, only patients with baseline CD4 cell counts >350 cells/µl returned to nearly normal CD4 cell counts after 6 years of follow-

Table 2 — *Distribution of CD4 median values among categories of CD4 count (n=422)*

	All	CD4≤200	CD4 201-350	CD4 >350
0m	219	132	265	380
6m	322	160	291	415
12m	365	181	301	453.5
18m	405	158.50	301	462
24m	449.50	168	286	490
30m	473.50	186	282	502
36m	501	146	287	544
42m	545	198	298	578
48m	578	191	300	596

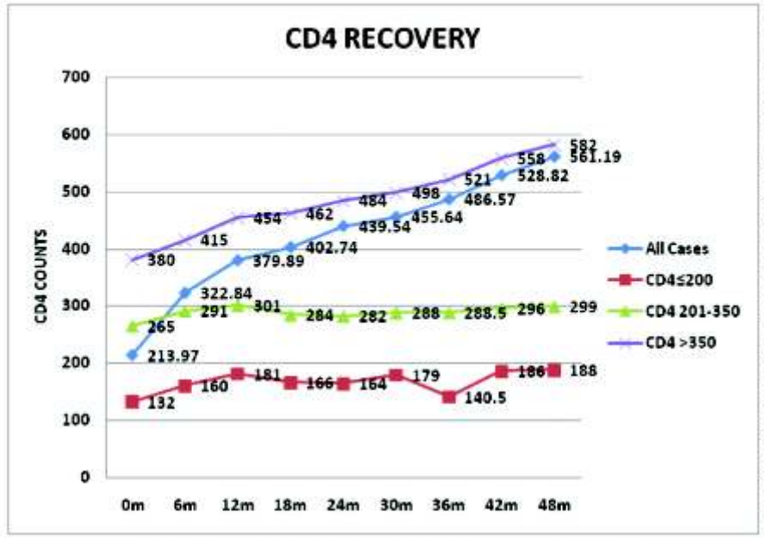

Fig 1 — Changes in the median CD4 cell count at 6 months interval

up[11]. Another study by Kelley CF *et al* revealed that a substantial proportion of patients who delay therapy until their CD4 cell count decrease to <200 cells/mm do not achieve a normal CD4cell count, even after a decade of otherwise effective antiretroviral therapy[7]. Palella FJ Jr *et al* found that survival rates in HIV-infected patients has been significantly improved by ART through its ability to increase the CD4 lymphocyte count in peripheral blood as well as reducing HIV load to undetectable levels[12]. In most of the studies it is seen that there is increase in CD4 counts for initial few years followed by a less pronounced increase or decline thereafter. A study by Kaufmann GR et al showed that the recovery of CD4 T lymphocytes occurs mainly in the first 2 years after the initiation of ART, and is associated with age and the pre-existing degree of HIV-1-related immunodeficiency, suggesting that the long-term exposure to HIV-1 infection has caused damage to the immune system that is difficult to correct[13]. Another study by Hunt DW *et al* showed that most patients who achieve and maintain viral suppression on HAART continue to experience CD4 T-cell gains through 4 years of therapy. The immune system's capacity for CD4 T lymphocyte restoration is not limited by low pre-therapy CD4 counts[8]. A longitudinal study was conducted in northern Ethiopia where the median CD4 lymphocyte count had improved over the five year period except at the 54th and 60th months where the median CD4 cell count showed a slight decline[14].

Table 3 — *Results of logistic regression analysis of baseline characteristics associated with the risk of immunological non-response (increase of < 50 cells/microlitre)*

Charecteristics	Risk of immunological non-response at 12 months	
	OR (95% CI)	P value
Gender :		
Male	1	
Female	1.901 (1.038, 3.481)	0.038
Age (years) :		
<45	1	
≥45	0.466 (0.203-1.072)	0.073
WHO clinical stage :		
1	1	
2	1.825 (0.873, 3.814)	0.110
3	2.094 (0.902, 4.865)	0.086
4	6.287 (1.352, 29.228)	0.019
Baseline CD4 count :		
≤200	1	
201-350	0.739 (0.389, 1.404)	0.355
>350	0.068 (0.025, 0.189)	0.000
Weight (kg) :		
<40	1	
40-60	1.403 (0.661, 2.978)	0.378
>60	2.818 (0.606, 13.113)	0.187
TB Co infection :		
Yes	0.592 (0.286, 1.226)	0.158
No	1	
Anemia :		
<12	1	
≥12	1.713 (0.758, 3.870)	0.196

Among the different predictors, immunological non-response was significantly observed among female patients. Patients of WHO Clinical stage 4 was associated with higher risk of immunological non response, whereas patients with baseline CD4 cell counts of >350 cells/µl was at significantly lower risk of it.

In most of the studies, male patients are seen at increased risk of immunological non-response. Higher rate of subsequent CD4 cell recovery was observed among female patients than males was also seen in those studies[15,16]. A study by Addisu A *et al* described that better immunological response in female could reflect the feminization of the HIV epidemic, better health seeking behavior of women and possibly the linkage of treatment sites with the antenatal clinics and the prevention-of-mother-to-child HIV programs resulting in better immune recovery & unimproved outcomes among male patients were because of poor health seeking behavior of men, lower rates of HIV testing, lower rates of repeat-testing and lower acceptance of linkage to HIV-care after a positive result[14]. Some other studies showed that gender was not related to initial & subsequent CD4 responses[4].

The poor initial CD4 recovery (immunological non response) among females in our study may be due to the fact that most of the patients belonged to lower socio economic & male dominated societies. As a result, females were much neglected, they had poorer adherence to the health seeking behavior & poorer general condition. We found in our studies that, patients with baseline CD4 cell counts of >350cells/µl had significantly lesser chances of immunological non response compared to those with lower baseline CD4 cell counts. These findings are in accordance to the previous studies.

A study by Florence E et all showed that a lower CD4 cell count was associated with a lower rate of CD4 cell recovery at 12 months of HAART[17]. In contrast, a study by Lawn SD *et al* showed that patients with baseline CD4 cell counts < 50 cells/µl have equivalent or greater capacity for immunological recovery compared to those with higher baseline CD4 cell counts[10]. Another retrospective study in Thailand reported that the outcomes of HIV patients did not differ by baseline CD4 cell count[18].

Therefore, our study findings suggest that HAART should be initiated early for better immune recovery & female patients should be given more consideration regarding adherence to the therapy.

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Original Article

Dignosis and declaration of death

K Sreenivasulu[1]

Diagnosis and declaration of death is the most important responsibility of a doctor. The diagnosis at various levels of hospitals is described along with confirmation tests. The modern concept of brain death is also detailed in relation to the organ harvesting and organ transplantation following the relevant Acts and Rules of India. Emphasis is laid on the rule of "No death-No Donation."

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Key words **: Death, diagnosis and declaration of death, Brain (stem) death, organ harvesting and organ donation.**

Diagnosis of death is the most important responsibility of a doctor and the declaration of death must be made only after the confirmation of death. If the diagnosis of death is wrongly declared and the patient shows signs of life after the declaration of death, the doctor will be solely held responsible and the consequences may be disastrous to the negligent doctor. Hence, an attempt is made in this article by the Author, as to how to make a correct diagnosis before declaration of death, as this subject of the diagnosis and declaration of death is not dealt in the medical books.

Definition of Death :

Death is the permanent termination of all vital biological functions or life processes, which sustain a living organism and as such is the end of life[1]. The Author defines death as the multi organ failure of the vital organs of brain, heart, lungs, kidneys and liver, as the failure of one leads to the failure of other organs in course of time leading to death.

Causes of Death :

They are different in different countries and different within the same country due to difference in the income. Injuries are the commonest cause of death to all age and income groups. Infections (tuberculosis, malaria, HIV) are common in low income groups. Ischaemic heart disease, stroke, diabetes, hypertension, COPD, cancer, dementia etc. are common in middle and high income groups[2].

History of Death :

Death is as old as humanity. Death has challenged the intelligence of humans since their origin and till today, in spite of great advances in science, medicine and technology, death is inescapable and every human being born is destined to die. Due to various causes, death can occur in children, adults and invariably in old age and all the efforts made to prevent death have failed and no human has lived beyond 200 years in the recorded history of human beings. The death of the national leader, Sri Jayaprakash Narayan, who actually died on 08.10.1979 in Patna, was earlier declared dead by a doctor, which was announced by the then Hon'ble Prime Minister of India, Sri Morarji Desai, who, later, on the same day apologised to the nation and announced in the Parliament, that Loknayak Sri Jayaprakash Narayan was alive, as first diagnosis was wrongly made by the doctor(the exact date is available in the records of Parliament). During my internship in 1975, the patient, who was declared dead by the assistant professor of medicine, got up when the body was cut during the autopsy in the pathology department and the live patient was returned to the hospital. As he was a destitute, there was no problem to the negligent doctor. The doctorhad not applied the criteria for diagnosis and failed to confirm death before declaration. In the past, there were several such Instances of misdiagnosis and wrong declaration throughout the world due to the failure of confirmation of death before declaration. The doctors, making wrong diagnosis were punished by the Governments and the courts in the event of litigation by the patients and their attending relatives. It was again due to the failure of confirmation of death before declaration. In this article, the clinical features of death, the investigations required to confirm death are detailed before the declaration of death.

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Process of Death :

The Author has studied death since his graduation in 1975, when death was the total death of the whole individual and the present concept of brain death was not evolved. Clinically, death was diagnosed by establishing cardiovascular failure and failure to revive. The author has found that in primary disorders of lungs, the respiration stops first followed by cardiac arrest in a few minutes and if the cardiac arrest is due to the cardiovascular disorders, the heart stops first followed by the stoppage of breathing in a few minutes. This is due to the reason that the heart and lungs act as one unit and hence, if heart stops beating, the lungs stop breathing and vice versa. Hence, the revival of heart and lungs is done simultaneously to save the life of critically ill patient. Before death, the Author observed the following about respiration: the respiration becomes abnormal, ie, slow and shallow, sometimes deep and slow or rapid and shallow; sometimes, the last respiration may be one deep inspiration followed by long and loud expiration, which is often described that the patient breathed his last respiration, which started as first breath after birth[3]. Before death, there may be tachycardia followed by bradycardia and cardiac asystole or bradycardia followed by cardiac arrest.

Author' Research and his Views About Death :

Death results if head and neck are seperatedby cutting through neck, but does not happen after bilateral forequarter and hind quarter amputations, while infected penetrating injuries of head, neck, chest and abdomen resulted in death. (Homicide was practised by the above methods from times immemorial). Hence, complete integrity is vital for preservation of life. The Author's best example of life is the glowing electric bulb, where the integrity of the physical bulb and the flow of electric energy are important to make the bulb glow. Similarly, the physical integrity of body, is vital to sustain life and its absence leads to death.Usually pain is caused by trauma and by all the diseases except the neurological disease affecting the sensory system. Coma precedes death, making death painless. Hence, the painful death is a myth.

(1) Diagnosis of death and its declaration at primary health centre, community health centre, or private doctor at or below the taluq level (primary care hospitals), where the facilities available are different from those of district and state headquarters: The diagnosis of irreversible cardio-respiratory failure is made by recording the complete cessation of respiration and cardiac arrest, the pupils are fully dialated and not reacting to light. Patient is in deep coma (total unconsciousness) without response to the deep painful stimuli. All the four limbs (upper and lower) are cold and clammy without any movements and lifted up and allowed to fall, they suddenly drop to the bed with a thud being lifeless, which is different in a living person. The cardio-respiratory resusciation consisting of mouth to mouth breathing, external cardiac massage, dopamine drip, parenteral or intra cardiac administration of adrenaline are tried to save the patient from the impending death. These measures to revive the patient are tried periodically, say, every 15 minutes, feeling carotid pulse, auscultating the heart, assessing the level of consciousness by the deep painful stimuli and noting the size of pupils for full dialatation and testing the reaction to light (pupillary reflex). All the attendants of the patient should be informed about the critical illness and impending death and doctor's attempts to revive the patient. Observations are made every 15 minutes and recorded in the case sheet along with the treatment given. This is continued for one to three hours or even more time, as the diagnosis of death, after declaration, cannot be reversed. The diagnosis of death is only clinical at this level of primary care hospitals, as there are no investigations like ECG or EEG for the confirmation of clinical diagnosis of death. If the death is non medico-legal, the body of the patient can be handed over to the relatives, without autopsy and if it is medico-legal, information should be given to the police by phone and in writing and the body is kept in the mortuary. If the doctor diagnosing the death is not the head of the medical institution, he should inform the head of the medical institution. If the relatives have taken away the body before the medico-legal post mortem examination, the same should be informed to the police immediately by phone and in writing, as failure to do so, attracts criminal action against the doctor declaring death after diagnosis. If the doctor has correctly diagnosed death, before declaration and the patient did not become alive after declaration of death, no doctor, accused of negligence of diagnosis is punished by the courts. But unfortunately, if the patient comes back to life, after the declaration of death, the doctor declaring death is in trouble and must settle the problem outside the court by paying compensation before litigation begins, as he cannot prove his innocence and his negligence in diagnosis will be proved and punished by the courts by fine or imprisonment or both. He will also lose his licence and job.

(2) The diagnosis at area hospital, (divisional level), district hospital (district level) in Government and private hospital (secondary care hospitals):

All the clinical features described above under the primary care hospitals, should be followed and the diagnosis of death can be confirmed by taking an ECG, demonstrating absence of electrical activity of heart.

(3) Diagnosis and declaration of death in the teaching and nonteaching general hospitals and other state level corporate private hospitals (tertiary care hospitals): All the clinical features and the ECG investigation are the same as described under the secondary care hospitals. The additional test for the confirmation of the diagnosis is the EEG and the absence of electrical activity of the brain indicates brain death of the patient and declaration of death can be done after ECG and EEG, which are isoelectric.

(4) Diagnosis of brain (stem) death in the hospitals permitted by government for organ harvesting for organ transplantation: When Brain (stem) functions stop due to trauma or other disorders, it is called Brain (stem) death. In a few minutes after brain death, the respiration stops with car-

(Continued on page 24)

Original Article

Dermatology referral of inpatients from other disciplines : pattern and impact on managent of patients in a tertiary care hospital

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Although dermatology has traditionally been practiced through outpatient consultation, hospitalized patients often have dermatologic problems. Along with common dermatological diseases hospitalized patients may have a wider spectrum of severe and serious dermatological conditions, associated with significant morbidity within hospitals which demands dermatological expertise. These often provide a clue to the future diagnosis, prognosis and treatment of patients. To analyze the causes of inpatient dermatology referrals, departments sending referrals, and impact of dermatology consultation on patient management. In this year-long prospective observational study of 398 patients we used a specific data collection form to record information on consultations for patients admitted between February 2017 and December 2017. The demographic details, specialties requesting consultation, cause of referral, and dermatological advice have been recorded and analyzed. General medicine requested the maximum number of referrals, and infections (43.46%) are the most common cause for referral. Most variable and interestng cases were referred from the department of Paediatrics, followed by General Medicine. Accurate diagnosis on referrals was provided by only 34.01% of nondermatologists. Common dermatological disorders were often misdiagnosed by these physicians. Our study revealed the importance of inpatient medical dermatology referral in terms of both service and education. While dermatologic referral leads to improved patient care, there is a need for better training of nondermatologists enabling them to recognize and treat common dermatoses. Apart from that, dermatologist also get enriched by evaluating different dermatological findings in patients suffering from systemic disease.

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Key words **: Referral, Dermatology, In-patient.**

Dermatologic consultations often have a huge impact on inpatient care and outcome, though Dermatology is primarily considered to be an outpatient-catering specialty although modern dermatology needs not only beds but operation theatre and 'ITU'. Most often, patients admitted in a different speciality with some specific medical complaints, show features of cutaneous signs and symptoms, which may be tell-tale sign specifying some internal disease. As skin diseases are often diagnosed clinically and without the support of objective tests, misdiagnoses by care givers other than specialists often happen. Thus, dermatologic referral should be mandatory when the clinical diagnosis is uncertain, particularly when there is an unexpected or unexplained cutaneous manifestation during the course of the disease.The interdepartmental referral not only helps in patient care but also improves the diagnostic accuracy and clinical knowledge of the clinician[1-5]. The present study was conducted to see the type of dermatological diseases encountered among patients admitted in other wards and its impact on patient management at a tertiary care teaching institute of West Bengal.

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Materials and Methods

This study was carried out at the tertiary care teaching institute of Kolkata for 1 year duration (Feb 2017 to Jan 2018). During this period all the inpatients referred from non-dermatology wards to dermatology unit were attended by one visiting consultant along with one or more residents. Where diagnostic intricacies existed, opinion of another consultant was sought. In case of diagnostic dilemma, specific investigations such as KOH examination,

Gram's smear, Tzanck smear, slit skin smear, skin biopsy, dermatosopy, nerve conduction velocity, and also blood and radiological investigations were undertaken to reach the diagnosis. Referral services were also provided to non-ambulatory sick patients in intensive care units or other wards. Details of the referring unit, patients' demographic profile, primary diagnosis for which patient was admitted, provisional diagnosis of dermatoses if made by the admitting consultant, and final diagnosis of dermatoses by specialist dermatologist were recorded in a proforma for analysis and interpretation. All the patients were examined within 24 hours of request for referral. Institutional Ethics Committee approval was obtained for the study and all the data have been preserved for future reference.

Result

A total of 398 referrals were received during the study period. The average number of patients seen per month was 31. There were 170 males (42.71%) and 228 females (57.28%), with a M:F ratio of 1:1.34 (Table 1). The spectrum of age of the attended patients ranged widely from 1 day to 87 years. Majority of the patients (212; 53.26%) were in 19-45 year age group at the time of consultation.

The referral service of the dermatologist was sought by almost all the specialties. The referral was most frequently sought by the inpatient department of General Medicine (214,53.76%), thus accounting for nearly half of the total patients, followed by those of Gynaecology and Obstetrics (52,13.06%), Pediatrics (38,9.54%) and Surgery (23,5.77%)(Table 2).

A total of 391 dermatological diagnoses were made among 398 patients other 7 patients were referred for some non-specific symptoms.

Infections and infestations were the most common (173,43.46%) cause of referral and included viral infections (76), fungal infections (45), bacterial infections (18), parasitic infestations (25), and mycobacterial infections (9) (Table 3). "Viral infections" accounted for almost half (43.93%) of the infective group. This was followed by and drug reactions (43,10.80%) and eczema (52,13.06%).

Table 1 — *Departmentwise referral list*

Department	Total no of patients	Male (%)	Female (%)
Medicine	214	98	116
Surgery	23	16	7
Gynae	52	NA	52
Orthopedic	19	11	8
Chest medicine	12	7	5
Eye	7	2	5
Ent	4	2	2
Psychiatry	16	9	7
Cardiology	4	3	1
Paediatric	38	16	22
Neuromedicine	5	2	3
Plastic surgery	3	3	0
Urology	1	1	0
TOTAL	398(100%)	170 (42.71%)	228 (57.28%)

Table 2 — *Probable Etiology of Referral (Total = 398)*

Medicine [Total patients 214 (53.76%) :			
Drug reaction	42	Viral exanthem	60
Collagen vascular disease	18	Vasculitis	9
Bullous dermatosis	7	Tinea	11
Non healing ulcer	5	Leprosy	5
Dermatitis	21	Oral ulcer	8
Pyoderma gangrenosum	1	Perforating dermatosis	1
Reiter's disease	1	Varicella	6
Diabetic dermatosis	6	Post inflammatory exfoliation	2
Erythema nodosum	7	Others	4
Surgery [Total patients 23 (5.77%) :			
Cellulitis	12	Non healing ulcer	2
Contact dermatitis	5	Herpes simplex	1
Scabies	2	Tinea	1
Gynae [Total patients 52 (13.06%) :			
Pregnancy dermatosis	17	Tinea corposis	11
Xerosis	7	Varicella	3
VDRL positive	2	Scabies	4
Genital LSA	1	Genital wart	3
Herpes simplex	1	Other	3
Orthopedic [Total patients 19 (4.77%) :			
Contact dermatitis	7	Herpes simplex	2
Tinea corporis	5	Cellulitis	3
Scabies	2		
Chest medicine [Total patients 12 (3.01%) :			
Tinea corporis	6	Scabies	2
Scrofuloderma	1	Post inflammatory exfoliation	1
Scleroderma	1	Lichen simplex chronicum	1
Eye [Total patients 7 (1.75%) :			
Herpes zoster	4	Seborrhoic bhepharitis	1
Contact dermatitis	2		
ENT [Total patients 4 (1.005%) :			
Oral LP	2	Aphthous ulcer	1
Herpes Zoster	1		
Psychiatry [Total patients 16 (4.02%) :			
Pediculosis capitis	10	Pediculosis corporis	3
Scabies	1	Xerotic eczema	2
Cardiology [Total patients 4 (1.005%) :			
Tinea corposis	2	Alopecia areata	1
Onychomycosis	1		
Paediatric [Total patients 38 (9.54%) :			
Prupura fulminence	3	Hypomelanosis of Ito	1
Neonatal pustulosis	3	Papular urticaria	8
Varicella	2	Candidal intertrigo	5
Miliaria rubra	4	Hemangioma	2
Carbon baby syndrome	1	Childhood Dermatomyositis	1
Tinea	4	Dermatitis	4
Neuromedicine [Total patients 5 (1.25%) :			
Leprosy	3	Scabies	1
Drug reaction	1		
Plastic surgery [Total patients 3 (0.75%) :			
Non healing ulcer	2	Eczema	1
Urology [Total patients 1 (0.25%) :			
Varicella	1		

The most common types of drug reactions were maculopapular rash, Stevens Johnson syndrome, and erythema multiforme. A total of 26 patients out of 43 diagnosed with drug reaction and in addition to 7 cases of immunobullous diseases, were transferred to our side for better management.

We found that 18 patients had dermatologic manifestations of systemic diseases.We diagnosed huge bulla on legs and ulcerated lesions on sole in cases of diabetes. We identified vasculitic lesions in patients subsequently diagnosed as a case of collagen vascular disease.Perforating dermatosis was seen in patients on dialysis for chronic renal failure.

Some dermatological conditions that include lichen planus, pigmentary disorders, lichen sclerosus et atrophicus, wart, reiter's diaease, nevus, alopecia were found to be less common, accounting for <3 cases each.

Table 3 — *Diseasewise referral list*

Diseases	No of patients	Percentages
Drug reaction	43	10.80%
Infection :		
Fungal	45	43.46%
Bacterial	18	
Viral	76	
Parasite	25	
Mycobacterium	9	
Dermatitis	52	13.06%
Collagen vascular disese	20	5.02%
Non healing ulcer	9	2.26%
Vasculitis	9	2.26%
Pregnancy dermatosis	17	4.27%
STD	5	1.25%
Bullous dermatosis	7	1.75%
Panniculitis :		
Erythema nodosum	7	1.75%
Oral ulcer	11	2.76%
Genetic disorders	1	0.25%
Nevus/ hemangioma	3	0.75%
Uncommon but specific dermatological diseases	24	6.03%
Others :		
Miliaria, hair fall, nail dystrophy, non-specific itching etc.	17	4.27%

We also got some uncommon dermatological diseases like carbon baby syndrome, reiter's disease, pyodema gangrenosum etc. which was getting treatment wrongly by the respective department and was diagnosed after dermatological referral.

Most variable and interestng cases were referred from the department of Paediatrics, followed by General Medicine (Table 2).

The different diagnoses made by the dermatologists after examining the referred patients have been tabulated in Table 2.

Our study showed that referring physicians could correctly mention the category of skin disorders in 34.01% cases on the dermatology referral sheets (eg, skin infections, immunobullous disorders), while in the remaining, only a vague diagnosis was provided (eg, "skin rash," "round lesion" "skin changes" etc). An additional investigations, specifically skin biopsy was performed in 18.32% of the referred cases to confirm the diagnosis.

Discussion

In our study, most of the patients referred for dermatology consultations were in 19-45 year age group (212; 53.26%) and a similar result was obtained in a study conducted in the USA[6]. In the said study, males have outnumbered females while in our study showed females were more commonly referred for dermatological opinion (M:F ratio of 1:1.34). Another study from India showed equal gender distribution in referral cases[7].

The referral pattern from different specialties has varied in different studies possibly due to differing pattern of dermatoses seen in different regions. In the present study, General Medicine accounted for the highest proportion of dermatological consultation (214,53.76%), as seen in several other published studies[2,3,8-15]. It is possibly due to higher admission rates in General Medicine wards and Dermatology is treated as an allied subject of General Medicine.

Gynaecology (13.06%), followed by Paediatrics (9.54%) specialities accounted for other common referrals in the current study. This result differs from other studies[2,3,8,10,11,14]. General Surgery requested maximum referrals (29.76%) in the study conducted by Walia and Deb from India. However we found only 5.77% referral from General Surgery indoor. Our finding in this resect is close to that of another study done in India[7,16]. Interestingly, in some studies, neurology unit has accounted for a significant number of referrals after Internal Medicine[5,12,13]. But the present study revealed only 5 cases (1.27%) from Neurology department. In an Indian study from Secunderabad, Surgery (29.8%) and Internal Medicine (29.7%) departments were responsible for more than half of the referrals to dermatologists[16].

Only 4.02% of referrals in our study were requested by the Psychiatry Department in contrast to some other studies, where Psychiatry accounted for almost 16% of the total referrals[6,17,18].

The pattern of dermatosesin referred cases seen in the reviewed studies is difficult to compare because the classification and quantification criteria were not uniform. However, in most of the studies,the frequent dermatological diagnoses were infections, dermatitis and drug reactions[8,10-13,16,19-25]. These were the most common diagnoses also observed in our study.

Drug rash, viral infections, dermatophytosis, connective tissue diseases, and dermatitis were the common dermatological diagnoses in patients referred from the Medicine Department whereas cellulitis or bacterial infection was most commonly found in patients from the Surgical wards. Most interestingly, we noticed that though we got a large number of referral from Paediatric department, it did not follow any pattern.

Before referral to the Dermatology unit, a tentative dermatological diagnosis was made in 57% patients only by the referring unit, and it was found to be correct in only 31% of the patients which is close to two Indian studies,

depicting 30.20% and 39% respectively[7,16]. Another Indian study from south Rajasthan showed it to be only 20%[20]. Other studies from Portugal,US,and Brazil have reported that a correct diagnosis was made in 23.9%, 48%, and 33% of the patients, respectively[3,8,13]. These studies also showed inability of many clinicians other than dermatologists to recognize simple cutaneous infections such as scabies,eczema, tinea or drug reactions, particularly drug hypersensitivity syndrome which is of serious concern, thus emphasizing the need for dermatological referral by non-dermatologist.

The final diagnoses made by the dermatologists revealed infections (43.46%), drug reactions (10.80%), and eczema/dermatitis (13.06%) to be the most common skin disorders. This finding coroborates with other studies[3,16,20].

In an Indian study conducted by Balai M *et al*, 26% of gynecological referrals were due to venereal disease research laboratory (VDRL) test positivity in a titer of <1:8. In our study we only found 2 patients of VDRL positivity with significant titre[20].

Conclusion

We may conclude that many common dermatological disorders cannot be diagnosed or are misdiagnosed by the non-dermatologists in our setup. A proper dermatological evaluation aids in the diagnosis and management of several conditions and in addition, makes the treatment less time-consuming and more cost-effective. Apart from that,dermatologist also get enriched by evaluating different dermatological findings in patients suffering from systemic disease. The clinical findings and course of such diseases get modified with proper advice from dermatologist. Dermatologist also get acquainted with the improvised and modified management of dermatological conditions in those patients of systemic diseases. Further, such referral is essentially required for medicolegal aspect.So, referral system is a very appreciable practice and is beneficial for both doctors and patients.

Conflict of Interest : NIL

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diac asystole. The reflexes that should be absent in brain death are: (a) Pupillary reflex (b) The corneal reflex (c) Pain response in the distribution of 5 th cranial nerve. (d) The occulocephalic reflex (e) The vestibulooccular reflex (f) The gag response and cough reflex. (g) Rebreathing test: this is performed using 100% oxygen given through the endotracheal tube to maintain satisfactory oxygenation to the patient, which cause a rise in pCo2, which would normally act as a stimulus for respiration. Failure of this indicates brain (stem) death[4].

Confirmation Tests of Brain Death : They are:

(1) Cerebral Angiography,
(2) Electroencephalography
(3) Transcranial Doppler Ultrasonography
(4) Cerebral Scintigraphy

All the above tests are conducted by trained personnel and interpreted by the experienced specialist doctors. The general medical officers have no role in the conduct or interpretation of the above tests.

The diagnosis of brain (stem) death is made by an experienced neurophysician or neurosurgeon and neuroanesthesiologist experienced in neurocritical care, examining separately, at least on two occasions and who are not part of the organ transplantation team for the obvious reasons of selfish pre declaration of Brain (stem) death in the vested interest of procuring the precious organs which are in great demand for the waiting transplantation individuals. Hence, "No Death-No Donation" rule should be followed, ie, organ harvesting should be done only after the occurrence of the actual death followed by organ donation[5].

From legal and ethical aspects, it is always better for the honest specialist doctors diagnosing and declaring brain death belong to a separate hospital and the harvested organs are transported to the other hospital, where organ transplantation is undertaken. Where ever possible, the informed and written permission (consent) of the prospective brain death donor should be taken during the state of full consciousness of the patient. When the patient is unconscious, say after a major accident, the written and explicit consent of the immediate relatives must be taken without making any monetary incentives by the honest doctors and the organ donation must be voluntary and free of monetary considerations. The transplantation act[6] with amendments and transplantation of human organ rules[7] must be followed in India. Brain dead individuals are the potential donors of multiple organs for transplantation, ie, two eyes, two lungs, two kidneys, a heart and a liver. Brain is spared as the successful technique of brain transplantation is currently not possible. There should not be racketsin harvesting the multiple organs for the transplantation[8].

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Review Article

Understanding Nutritional Issues in Cirrhosis of Liver

Anup Kumar Das[1]

Cirrhosis of liver is a huge health burden in our country. It has a multitude of problems arising out of hepato-cellular damage and portal hypertension. Although the curative treatment remains liver transplant in cases which are usually advanced when first seen, the majority of cases need multipronged conservative treatment. Being a catabolic condition, malnutrition is very common but often under-evaluated and not adequately treated. It is now established that malnutrition, which has a number of etiologies in this disease, is deleterious in cirrhosis of liver. Understanding the mechanism, extent and degree of malnutrition in cirrhosis is essential to evaluate the condition for formulating a better management strategy as far as nutritional support is involved. This is very important as macro and micro nutrient deficiencies are very common which should be corrected as far as possible in a rationale manner at the earliest, with the help of a qualified nutritionist. Western guidelines exist wherein specific and succinct protocols are detailed. In cirrhosis of liver a compact evaluation of nutritional status should be undertaken so that a better quality of life and disease prognosis is achieved.

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Key words **: Cirrhosis, malnutrition, nutritional support, nutritional assessment, sarcopenia, nutritional deficiencies, impact of malnutrition**

Nutrition involves assimilation of enteral or parenteral food by a living organism for maintenance, growth, reproduction, and tissue repair, both in health and disease. When the food and nutrient intake is inadequate or unbalanced; or assimilated or utilized improperly, malnutrition results. It can lead to either under or overnutrition, both with adverse health effects, altering body composition and it's biological functions.

Prevalence of malnutrition ranges from 20% in compensated liver disease to >80% after decompensation occurs[1]. In advanced liver disease irrespective of cause, the prevalence reportedly varies from 50%-90%[2,3]. Even in early stages of cirrhosis, malnutrition occurs, and has a poor prognosis and higher mortality[4,5]. Nonetheless, it is under-recognized and possibly under-treated, and the extent of nutritional assessment and support in routine clinical care is unknown[6]. There are few studies on nutritional issues in cirrhosis, especially in Asian population[7].

Macro and micro nutrient deficiency, especially sarcopenia in cirrhosis is multifactorial, yet very common even in early stages of the disease. Proper understanding of the condition is important so that these deficiencies can be assessed and corrected since malnutrition worsens the prognosis. Correction of malnutrition should be routine part of management protocol but often overlooked and expert dietary consultations should be sought, particularly in advanced stages. Indian guidelines don't exist in this regard which is a necessity now keeping in view of the increasing number of patients.

Impact of Malnutrition in Cirrhosis of Liver :

Malnutrition in patients with liver cirrhosis during hospitalization is associated with increased morbidity including hepatic encephalopathy, variceal bleeding, refractory ascites, spontaneous bacterial peritonitis (SBP) and hepatorenal syndrome (HRS)[8]. Carvalho and Parise[2] found that 21% of Child A patients had moderate or severe malnutrition, versus approximately 52% of Child B and 58% of Child C patients in non hospitalized patients. Therefore, it occurs early in the natural history of cirrhosis and frequently recognized late in chronic liver disease. In cirrhosis, the decompensation risk is 58% over 10 years[9], and 12% per year[10]. The decompensated states involve higher mortality. But it is important to note that prognostic assessments in cirrhosis (especially in early stages) is difficult because several factors influence the natural history, eg, the etiology, the effect of treatment in decreasing the underlying hepatic necro-inflammation/fibrosis, the extent of hepatic dysfunction, the presence/degree of portal hypertension, and the presence of hepatocellular carcinoma[11].

Still, malnutrition is acknowledged as an independent predictor for survival, as shown by a study on 212 hospi-

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talized cirrhotics followed up for 2 years[12]. It is interesting to note that the two prognostic scores for chronic liver disease (Child-Pugh and MELD) do not include nutritional status as a parameter.

Pathogenesis of Malnutrition in Cirrhosis :

The aetiology of malnutrition is multifactorial[13]. Basically three mechanisms are important : Decreased intake, Malabsorptive and Metabolic.

(a) Decreased intake of macronutrients have both disease related and iatrogenic factors[14]. The former include any of a GI symptom like nausea, anorexia, bloating, pain, belching or diarrhea present in upto 80% in cirrhosis. Upregulation of TNFa and leptin can also cause anorexia in cirrhosis, in addition to ascites, lactulose, psychological stress and low serum testosterone, and complications like HE and SBP. Delayed gastric and intestinal transit in cirrhosis has been demonstrated in 25% and 35% cases respectively; and may lead to anorexia or bloating via decreased gastric accommodative power and bacterial overgrowth (SIBO)[15]. Zinc deficiency is common in advanced liver disease and can contribute to anorexia by causing loss of taste and smell. Zinc and magnesium deficiency can occur due to diuretic use and restricted animal protein intake. In-hospital fasting for procedures like endoscopy, radio-imaging and during variceal bleed also contribute to calorie deprivation since the diseased liver has a low glycogen reserve.

(b) Malabsorptive factors develop due to altered bile flow (causing fat malabsorption), SIBO and pancreatic insufficiency (especially in alcoholics with an 18% prevalence), which are common in cirrhotics. These anomalies also impair food intake. SIBO is 4 times more common in patients with HE than in those without[16]. Another interesting but under-recognized condition is celiac disease which shows a prevalence of 1 in 40 in cirrhosis as compared to controls[17] and needs further studies to recommend a gluten free diet in them. Porta-systemic shunting can lead nutrients to bypass the liver, thus depriving their metabolism and assimilation. Particularly, long-chain fatty acids enter portal circulation instead of micelles (due to bile acid deficiencies) leading to increased hepatic triglyceride concentration which may hamper liver function further in an already diseased liver. 90% of cirrhotics also have Vitamin D deficiency and 29% of them being severe[18]. Use of steroids exacerbates Vitamin D deficiency in autoimmune cirrhosis.

(c) Metabolic factors Hypermetabolism occurs in 15% – 30% cirrhotics, probably due to stimulation of sympathetic system (tachycardia, increased cardiac output, hyperglycemia) and release of pro-inflammatory cytokines like TNF-a, IL1 or IL6[19] which induce high energy expenditure. Hypermetabolism is defined as Resting Energy Expenditure (REE) >120% compared to the predicted value and is the amount of energy an individual uses to perform vital organ functions, without activity and digestion. This sympathic overactivity may result from gut bacterial translocation, chronic inflammatory state, or central neuro-circulatory dysregulation. Insulin resistance, increased neoglucogenesis, protein catabolism and decreased glycogenolysis, are characteristic. These cause a significant depletion of protein and fat reserves, in about 50% of cirrhotic patients[20]. Decreased glycogen reserve in a diseased liver implies that with a short overnight fast, the amount of fat and protein catabolism in cirrhosis is equivalent to 2 to 3 days of fasting of a normal individual. Because in the absence of glycogen, neoglucogenesis uses protein and fats as alternate fuel leading to sarcopenia and adipopenia respectively, defined as hepatic cachexia. In cirrhosis sarcopenia is the primary and predominant consequence, especially in skeletal muscles whose fibers in adults are composed of terminally differentiated myocytes that do not replicate. Overweight and obesity are now endemic in many parts of the world. Cirrhosis may result in simultaneous loss of skeletal muscle and increased adipose tissue,a condition called sarcopenic obesity.This is characterized by a reduction in muscle size but increased proportion of inter- and intra-muscular fat. This is uncommon in Indians[7].

(a) SARCOPENIA (defined as a muscle mass two standard deviations below the healthy young adult mean) leads to a low functional capacity. After the age of 50 years, approximately 1% of skeletal muscle loss occurs per year and therefore is a feature of aging and many chronic diseases including malignancy. It is common in end-stage liver disease and increases it's morbidity and mortality[21]. The factors responsible for cirrhotic sarcopenia includes decreased total energy intake and reduced availability of substrates for muscle mass due to malabsorptive/malnutritional factors mentioned earlier. The skeletal muscles play an important part in controlling raised blood ammonia (due to hepatic dysfunction and porta-systemic shunts) by increasing glutamine synthesis in skeletal muscles and brain which binds to ammonia. This is however, a stop-gap, short term process. If continued, glutamine accumulation occurs which is metabolized again by a (normal) liver. If the liver is dysfunctional, then excess glutamine will be broken down by glutaminase in kidneys and intestines which re-converts one molecule of glutamine to two ammonia molecules, thereby promoting further ammonia generation and HE. Branch Chain Amino Acids (BCAA) is important here, as they act as a substrate of muscles to convert glutamine to glutamate in the muscles. In cirrhosis, serum BCAA is decreased and long-term supplementation of BCAA has been shown to improve nutritional status and prolong event-free survival and quality of life[13]. Myostatin, a member of the TGF ß superfamily expressed in the skeletal muscle, inhibits protein synthesis. It is increased in cirrhotics. It also inhibits satellite cellular differentiation and proliferation, and found to be increased in muscles of cirrhotics, and may contribute to muscle wasting. Satellite cells are myogenically committed precursor cells that contribute nuclei to the myocytes for maintenance and growth of mature skeletal muscle. In cirrhosis, skeletal muscles may also play a part in release of cytokines like TNF-a by a proteolytic pathway involving ubiquitin leading to sarcopenia[22]. In addition, muscular autophagy and IGF1 anomalies (involved in protein synthesis or degradation in skeletal muscles) are seen in cirrhotics[23]. It may be noted that sarcopenia is not universal in underweight cirrhotic patients, and can be present in patients with any BMI.

(b) MICRONUTRIENTS In addition to micronutrient deficiencies mentioned above, rates of deficiencies of fat-soluble vitamins vary among studies, although frequent in primary biliary cirrhosis. Vitamin A,D,E,K deficiency in upto 33%, 13%, 2%, and 8% respectively was reported in one study.24 Hepatitis C virus and its therapy with peg-interferon/ribavarin therapy competes with human cells for vitamins and may disturb nutrient utilization leading to folate, B1, B2 and B6 deficiencies.

Prognosis :

Several studies have consistently shown that malnutrition, especially sarcopenia, in cirrhosis adversely affects the survival and the development of various complications of cirrhosis[23]. It is interesting to note that till date no study has proven that reversal of malnutrition improves survival. After TIPS (to reverse portal hypertension), however, some patients show reversal of sarcopenia and they show better survival than those whose sarcopenia did not show improvement. Pre-transplant malnutrition shows a statistically significant increased mortality after transplantation, including prolonged ICU stay in a metaanalysis of 13 studies involving 1187 patients[23]. As regards quality of life based on existing data, it is worse in cirrhosis with sarcopenia and adipopenia. Episodes of HE, even after complete recovery, impact the quality of life in patients with cirrhosis[25]. Seven studies[23] (n = 751) studied the impact of malnutrition (prevalence 6.1% to 67.0%) on the complications of cirrhosis (ascites, SBP, portal hypertension, hepatorenal syndrome, and HE). There was a statistically significant increase in complications in those with malnutrition. Alcoholics are significantly more malnourished than non-alcoholics. Irrespective of etiology, comparatively males show more muscle mass depletion, while female cirrhotics have more fat depletion[1]. This is probably due a larger fat reserve in females, which are utilized before the muscles to meet the catabolic demands of cirrhosis as compared to male counterparts[7].

Nutritional Assesment in Cirrhosis :

A thorough history and physical examination are imperative (changes in weight, appetite, GI symptoms, peripheral edema, ascites, muscle wasting and subcutaneous fat loss). Various clinical tools are available to assesss nutrition (Table 1). Although Dual-Energy X-ray Absorptiometry (DEXA) is the gold standard, the European Society of Clinical Nutrition and Metabolism (ESPEN2006) guideline recommends the use of the subjective global assessment (SGA), anthropometry, or the handgrip strength test to identify patients with cirrhosis who are at risk of malnutrition[26]. The SGA is commonly used because it is simple and cost-effective but requires clinical judgement, consistency and is time consuming. SGA is a bedside assessment of dietary intake, weight change, and gastrointestinal symptoms; it includes an examination for subcutaneous fat loss, muscle wasting, edema, and ascites. Being essentially a "nutritional review", SGA may underestimate nutritional status in early stages of the disease. Traditional anthropometric measures like weight, midarm circumference, and triceps skin-fold thickness in patients with cirrhosis should be routinely performed. The handgrip test (classified as malnourished if their grip strength is <2 SD from the mean of the age and sex groups), compared to SGA in cirrhosis was found to be superior in predicting occurrence of complications (65% *versus* 35.7%)[5]. Therefore, there is a need for a comprehensive analysis of patients' nutritional status that should include a combination of subjective and objective tools before nutritional intervention. Biochemical tests for liver function, serum micronutrients, lymphocyte count and serum cholesterol (indicating calorie depletion) can be help-

Table 1 — *Showing different nutritional assessment tools*

Tool	Advantage	Disadvantage
BMI	Easy to perform	Inaccurate in edema/ ascites
Mid–arm circumference (MAC)	Low cost	Not a strong predictor of malnutrition
Skin fold thickness	Low cost, easy	Unclear accuracy
Hand Grip strength	Better at predicting complications, simple, quick	Correlates with MELD but not with CP score
Bioelectrical impedence	Not limited by compliance	Inaccurate in edema
Subjective Global Assesment (SGA) eg, RFH-GA	Systematic and bedside multifactorial tool, simple	Subjective in nature, time consuming
DEXA	Gold Standard	Expensive, technically complex

ful. It must be noted that frequent nutritional assessment is required in any patient with chronic liver disease, as the dynamic nature of the disease may warrant adjustments for different nutrients over time.

Nutritional Interventions :

The basic goals in cirrhosis are to meet estimated energy requirement and prevent protein catabolism by frequent feeds by the least invasive route. Specialist dieticians review should be sought whenever possible.

Both the American and European Societies of parenteral and enteral nutrition (ASPEN/ESPEN) have their own recommendations (Table 2). The ESPEN guidelines stresses more on prevention of malnutrition and is followed commonly. The patient's "dry weight" needs to be determined first because of edema and ascites can affect the actual weight. This is done roughly by subtracting from the patient's total weight by an amount of 2.2 kg, 6 kg and 12 kg (in mild, moderate, severe ascites respectively) and 1kg, 5 kg and 10 kg (in mild, moderate and severe edema respectively). Protein restriction, even in HE, do not confer any benefit and cirrhotics require more protein than normal. BCAA are essential for protein synthesis and turnover, and regulation of energy metabolism. It may be beneficial in improving CP score, improving quality of life and reduced hospital stay[27]. A late night high BCAA diet has recently been reported to improve mortality[28]. Leucine-enriched essential amino acids may be useful in the treatment of sarcopenia as Leucine is a substrate for protein synthesis, plays a key role in the skeletal muscle anabolism, protein synthesis and autophagy regulation[29].

Nocturnal oral supplementation can shorten the length of overnight fasts and improve protein stores. Carbohydrate restriction is not recommended although cirrhosis is associated with insulin resistance. However, glucose should not be given in doses of more than 5-6 gm/day. Long chain fatty acid containing foods are best avoided as they can not be metabolized in cirrhosis and may lead to steatosis, and many patients also have associated exocrine pancreatic deficiency.

All should receive a multivitamin. Diet supplementation with higher doses fat-soluble vitamins (A,D,E, and K), zinc, and selenium are recommended in advanced disease but deficiencies in these are frequently found in patients with compensated liver disease as well[23]. Alcohol abuse warrants long term folic acid and thiamine supplementation. Due to presence of SIBO, probiotics have been used, but long-term use seems to be useful in HE, and more research is needed to find out the appropriate strains and the dosage.

When indicated, cyclical or continuous nasogastric or nasojejunal feeding is recommended in upright position or with a pro-kinetic to prevent aspiration[30]. Varices are no contraindication of tube insertion, but percutaneous route is best avoided because of possible bleeding or infection, in those with gastric varices or ascites. Generally, high-energy whole protein formulation are recommended in ascetic patients. Diarrhea/malabsorption may result in many, where a trial of medium-chain fatty acids can be given.

Total parenteral nutrition (TPN) is indicated when there are contraindications to oral or enteral nutrition and when adequate oral or enteral caloric intake is inadequate. The formulation contains protein, carbohydrate, fat, electrolytes, minerals and vitamins. Risk of potentially fatal infection, central venous thrombosis and deterioration of hepatic function(cholestasis) increases with TPN. Infection occurs due to endotoxemia, immunodepression, altered intestinal permeability, high glucose infusion and catheter related. TPN is recommended in very advanced disease, for end of life care and after surgery or liver transplant but the lipid content should be <1gm/kg/day.

Table 2 — *Nutrition Recommendations*

Energy requirement, based on dry weight or determined ideal body weight, for patients with ascites	25–40 kcal per d
ASPEN :	
Without encephalopathy	25–35 kcal/kg per d
With acute encephalopathy	35 kcal/kg per d
Stable and malnourished	30–40 kcal/kg per d
ESPEN :	
All stable cirrhosis patients	35–40 kcal/kg per d
Macronutrients :	
Carbohydrate	45%–65% of daily caloric intake per DRI
Protein :	
All patients, except acute encephalopathy	1.0–1.5 g/kg per d
Acute encephalopathy	0.6–0.8 g/kg per d
Fat	25%–30% of daily caloric intake per DRI
Micronutrients :	
Fat-soluble vitamins (vitamins A, D, E, and K); all patients with compensated liver disease	Up to RDA levels[a]
Zinc	Up to RDA levels[a]
Selenium	Up to RDA levels[a]
Folic acid and thiamine; patients with history of alcohol abuse	Up to RDA levels[a]
Sodium; patients with ascites and edema	Restricted to <2 g per d

Summary :

Malnutrition, especially sarcopenia in cirrhosis, is present in all grades which decreases quality of life, increases mortality and complications. It is multifactorial. Although the inclusion of sarcopenia into cirrhosis prognostic scores has been limited by lack of dependable, simple and objective method to quantify muscle wasting, it should be assessed routinely in clinical practice and corrected. Addition of nutritional indices will add significantly to the presently used CP and MELD scores for prognosis in cirrhosis and needs further research. Although malnutrition progresses with worsening liver function and CP score, it is not yet established that improvement of nutrition, particularly sarcopenia will improve survival. Hence early nutritional intervention in cirrhosis is more practical rather than in advanced stages. However, novel therapy like myostatin antagonists are being tried in animal models.

Conflict of Interest : NIL

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Case Report

Posterior reversible encephalopathy syndrome and spontaneous spinal epidural hematoma with pregnancy induced hypertension : a rare association

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Posterior Reversible Encephalopathy Syndrome (PRES) is reversible condition characterised by typical neurological and radiological features. Spontaneous spinal epidural hematoma (SSEH) is a rare entity, mostly associated with bleeding disorders, anticoagulant therapy, arteriovenous malformation, arteritis, and sometimes iatrogenic. We report a young pregnant female with a rare association of atypical PRES and SSEH along with pregnancy induced hypertension.

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Key words **: Posterior Reversible Encephalopathy Syndrome, Spontaneous spinal epidural hematoma, Pregnancy induced hypertension.**

Posterior Reversible Encephalopathy Syndrome (PRES), a condition which is usually reversible, is characterised by typical neurological and radiological features associated primarily with severe hypertension, preeclampsia/eclampsia, treatment with immunosuppressive drugs and renal disease[1]. Spontaneous spinal epidural hematoma (SSEH) is a rare entity, associated with conditions like bleeding disorders, anticoagulant therapy, vascular malformation, and arteritis[2]. Hypertension has also been reported as a rare cause of SSEH[3]. We report an uncommon case with PRES and SSEH in the setting of pregnancy induced hypertension.

Case Report

A 32 year old female with 8 months pregnancy developed acute, severe back pain, weakness of both lower limbs along with decreased sensations below waist and retention of urine. Few hours later she developed headache, irrelevant talking and inability to recognise family members. This was not associated with fever or seizures. She was admitted to a nearby hospital, where her blood pressure was recorded 210/130 mm Hg and was treated with antihypertensives. MRI brain revealed T2 and FLAIR hyperintensities in bilateral fronto-parietal and periventricular white matter, bilateral basal ganglia, thalami, brainstem and cerebellum (Fig 1). MR angiogram of brain was normal. MRI dorsal spine showed epidural hematoma at D9 to D12 level, compressing the cord (Fig 1). There was no evidence of any well formed nidus, abnormal bunch of vessels, any prominent vein or arterial feeder which could have raised suspicion of arteriovenous malformation. Her coagulation profile was normal. After 3 days of treatment, her sensorium and headache improved but deficit in lower limbs persisted. Next day she delivered a still born child with caesarean section and was referred to our centre for further management, but she reported after 3 months. Her past history revealed recurrent neurological deficits during peripartum period in each of her previous three pregnancies which developed acutely and were accompanied by high blood pressure and moderate intensity headache. These deficits resolved completely over next 3-7 days with antihypertensive and supportive treatment. Previous treatment record or scans were not available. She was normotensive between her pregnancies and did not have history of foetal loss or still birth before the present illness. There was no past history of seizures, diminution of vision, prolonged or excessive bleeding or repeated blood transfusions, anticoagulant drug intake, orogenital ulcers, joint pain, weight loss, any spinal procedure or trauma.

Her general physical examination showed pallor, blood pressure was 130/80 mm Hg. She was conscious and oriented with normal higher mental functions. Cranial nerves' examination including fundus was normal. Motor system examination in upper limbs was normal, while she had hypotonia, power of MRC grade 0/5, absent deep tendon reflexes, and extensor plantar response in both lower limbs. All sensory modalities were impaired below waist.

She had microcytic hypochromic anemia (Hb- 7.2 gm %). Her coagulation profile was normal. Serum chemistry reports were within normal limits. CRP was positive, while tests for RF, ANA antiphospholipid antibodies, HIV and treponemal serology were negative.

Repeat MRI brain revealed near complete resolution of signal abnormalities except for few small circumscribed hyperintensities in periventricular white matter (Fig 2). Repeat MRI of dorsal spine showed myelomalacia at D10, D11 level (Fig 2). There was no evidence of any abnormal vessel in this scan too which could have suggested the possibility of spinal AVM. So CT angiogram of dorsal spine was not ordered. In view of the reversible clinical and radiologic affection of brain, associated spinal epidural hematoma and subsequent myelomalacia, and the presence of pregnancy induced hypertension, a diagnosis of PRES with SSEH was made.

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Poor prognosis regarding neurologic deficit in lower limbs was explained to the patient.

Discussion

PRES is a reversible clinico-radiological syndrome which is prevalent worldwide, and is seen in persons of all age and sex[4]. There are several hypotheses proposed to explain the poorly understood pathogenesis of PRES[4] which includes (1) breakdown of cerebral autoregulation due to a sudden rise in blood pressure leading to disruption of the blood–brain barrier, (2) endothelial dysfunction due to circulating toxins which affect the blood–brain barrier leading to subsequent extravasation, (3) focal vasospasm leading to decreased blood flow and ischemia with resultant edema.

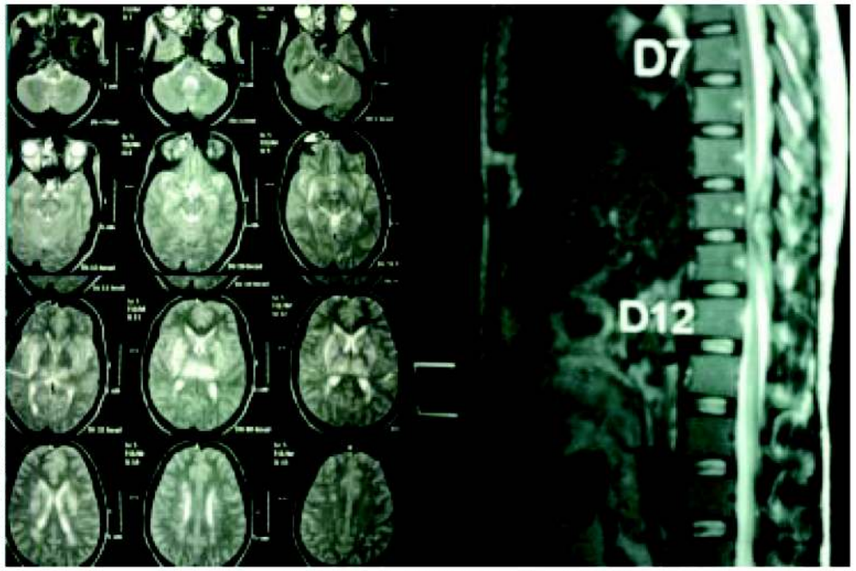

Fig 1 — MRI brain and dorsal spine at the onset of illness

Encephalopathy and seizures are the main presenting symptoms in PRES followed by headache, visual abnormalities and focal neurological deficits[5]. Acute hypertension is reported in more than 80% of patients with PRES[1]. It is classically associated with subcortical vasogenic edema, with preferential affection of the occipito-parietal regions of brain[5]. Frontal lobe involvement is seen in 51-77% of cases[5,6]. Lesions in temporal lobe, cerebellum, brainstem, basal ganglia and corpus callosum are also reported, though these locations are considered atypical for PRES[5,7]. Diagnosis of PRES in our patient was quite evident in the presence of reversible clinico-radiologic findings and pregnancy induced hypertension. Reversible cerebral vasoconstriction syndrome (RCVS) was also considered as a differential diagnosis, but ruled out on the basis of absence of characteristic thunderclap headache and normal brain angiogram. The recurrence of reversible focal neurologic deficits in our patient can be explained by recurrent PRES. Only few cases of recurrent PRES have been reported in literature, the possible triggers for recurrence being infection and hypertension[7].

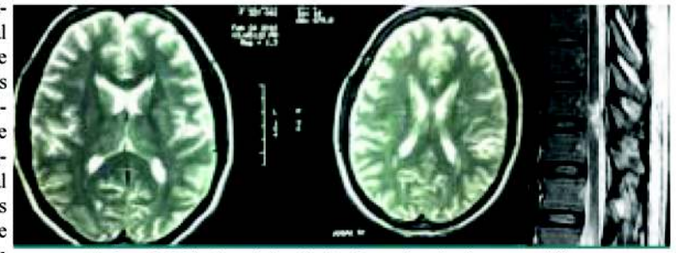

Fig 2 — MRI brain and dorsal spine 3 months after the onset of illness

SSEH is a rare condition, responsible for less than 1% of the spinal epidural lesions. Mostly it is associated with anticoagulant therapy, inherited or acquired bleeding disorders, arteritis, vascular malformation and rarely with hypertension[3]. Neurological signs and symptoms include sharp, radiating back or neck pain, progressive sensorimotor affection, and bowel-bladder disturbances, which develop acutely within minutes to hours, corresponding to the level of the spinal cord affection. The pathogenesis of SSEH is not clear. Most authors accept epidural venous plexus as the source of hematoma while others believe that the spinal epidural artery is the ruptured vessel[2]. The gold standard management is emergency evacuation of the hematoma and spinal cord decompression. Prompt surgical decompression is associated with favourable outcome. Conservative treatment may be sometimes successful in cases with minimal neurologic deficits or patients showing rapid spontaneous improvement[8,9]. In our case, the possibility of coagulation disorder and spinal vascular malformation was ruled out appropriately. The spinal epidural hematoma and the reversible cerebral lesions were probably the consequence of hypertension. Pregnancy induced hypertension overwhelmed the cerebral autoregulatory mechanisms leading to brain edema and similarly led to the extravasation of blood in spinal epidural space[3]. Functional deficit could not be improved because of the lack of surgical decompression at appropriate time.

This case is being reported due to the rare association of recurrent PRES with SSEH, in the setting of pregnancy induced hypertension.

Conflict of Interest : No financial interests, direct or indirect, exist for any of the individual contributor in connection with the content of this paper. There were no sources of outside support for the project.

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(Continued on page 33)

Case Report

If rapunzel were a boy : a rare presentation of trichobezoar — a case report

Nandini Kaul Bedi[1], Alka G Grewal[2]

A trichobezoar with an extension into the small bowel is known as 'Rapunzel syndrome'. It is very rare in boys. We present a 9 year old boy with Rapunzel syndrome. He presented with vomiting and a palpable abdominal mass which was a trichobezoar. It was successfully removed by surgery. It was over 6 ft in length and extending from the stomach into the jejunum. In the paediatric age group a trichobezoar should be suspected even in boys presenting with a palpable upper abdominal mass.

[*J Indian Med Assoc* 2019; **117:** 32-3]

Key words **: Trichobezoar, Pica, Intestinal obstruction.**

Trichobezoar is a condition seen predominantly in girls between the ages of 5 and 15 years. It is the result of eating hair (trichophagia), usually one's own. These patients, after management of the acute condition, will require psychological analysis and support and should be under psychiatric care over a period of time. If not actively controlled, the habit continues and causes further problems of malnutrition and even recurrence of trichobezoar.

Case Report

A 9 year old boy presented to casualty with a history of vomiting for 2-3 days and inability to hold down even water. He weighed 15 kg, had a puffy face with pitting oedema over limbs and abdominal distension with free fluid detected on ultrasound. He was suffering from anaemia and hypoproteinaemia. He had a broad forehead with short, broken hair and generalized alopecia.

Examinations — On examination a palpable mass in the left upper abdomen at the site, and in the shape of, the stomach was noticed which was indentable- known as Lamerton's sign[1]. Contrast enhanced CT scan of the abdomen showed a mass of alternating density, suspected to be a trichobezoar, extending from the stomach through duodenum till the early part of the jejunum.

On explorationa trichobezoar was removed from the stomach via laparotomy and anterior gastrotomy. It consisted of hair and, in the distal part was intertwined with thread (Fig 1). The gastric part was 30 cms in length, and its extension was about 158 cms long. The total length of the trichobezoar was 188 cms (74 in).

Postoperative recovery was uneventful. He is currently on follow up with a psychiatrist and a child psychologist.

Discussion

The mechanism of formation of a trichobezoar is by continuous trichophagy. The mass of hair, acid, pepsin and mucin form clumps with ingested food particles. Hair does not move forward easily with peristalsis and tends to stick to the mucosal lining till a large enough hair-ball forms which is aided by ingestion of other particles including food[2]. In our patient's case, his mother gave a history of the child eating his handkerchief in school; hence she would try not to give him one. The cotton threads were a major part of the bezoar towards the distal end. Laparotomy remains the approach of choice[2].

Fig 1 — Trichobezoar removed at surgery showing the distal end (black arrow) with threads intertwined in hair – this end was lying in the jejunum.

Trichobezoar is seen mostly in girls between the ages of 5 and 15 years. Hair length is required to form a bezoar, which is probably why it is seen and reported mostly in girls. When the bezoar is long and extending into the jejunum – it earns the name "Rapunzel syndrome" - after a fairytale character with very long hair. It was first described by Vaughan in 1968[3]. There are very few cases reported of a trichobezoar in a boy, particularly the 'Rapunzel syndrome'. Our patient, a 9 year old boy, had very short hair, which was patchy in distribution. His mother gave a history of the boy picking his own hair as well as those discarded by others from the streets and eating them. Trichophagy and trichotillomania are considered the result of a disturbed psyche and are seen mainly in girls.

Conclusion

The Rapunzel syndrome can present even in boys. All patients treated for trichobezoar should be referred for psychiatric evaluation and support to avoid recurrences.

Competing Interest : The authors declare that they have no competing interests.

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Case Report

A wandering foreign body — ingested fish bone migrating to thyroid gland

Sunil Deshmukh[1], Kalpana Patil[2], Shrinivas Chavan[1], Chaya Diwan[3]

An interesting case of an accidently ingested foreign body ie, a sharp fish bone which has travelled to the left lobe of thyroid gland without causing any complication like oesophageal perforation or tear is reported here. Many People frequently eat fish as their food and accidently fish bone gets embeded in either tonsils or throat which can be removed safely by an ENT surgon. Many times it usually passes through the gastrointestinal tract without any complication, but here in our case when pt. came to us for the first time with Complaints of pain in throat at that time she was having no radiological and endoscopic evidence of FB and hence was send home but the same pt.came to us after 12 days with left lobe thyroid swelling which radiologically showed evidence of a radio opaque FB which was removed successfully by opening left thyroid lobe without doing lobectomy. The incidence of such type of complication without any mishap is very rare, hence we are reporting this case.

[*J Indian Med Assoc* 2019; **117**: 34-5]

Key words **: Fish bone, foreign body, oesophagus, thyroid gland.**

Case Report

Esophageal penetration resulting from foreign body ingestion is uncommon, with the incidence reported to be between 1% and 4%[1]. A wide variety of objects were retained in the esophagus but fish bones were the most common (60%) and chicken bones the second most common (16%). Owing to their fine, linear and sharp structure fish bones have tendency to stick and penetrate the mucosa, which occasionally can lead to severe complications. Prompt recognition and retrieval of ingested fish bones can reduce the morbidity and mortality.

A middle aged female of 40 years s came to us with chief complaints of :- A/H/O Foreign body (? Fish Bone) ingestion 12 days back, C/O difficulty in swallowing and C/O swelling (lump)over left side of neck x 5 days[2]. She gave H/O accidental ingestion of fish bone 12 days back. So she presented to our emergency department with C/O pricking sensation in throat and dysphagia and some pain during swallowing. She was again presented in emergency deptt. with C/O swelling over left side of neck since 5 days and pain during swallowing and over the swelling (lump) also (Fig 1).

There was No H/O Fever, Headache, Cough with or without expectoration. No H/O Blood in Sputum or Vomitus.- No H/O Drooling of Saliva.- No H/O Chocking sensation in chest.- No H/O Difficulty in breathing.- No H/O Nausea, Vomiting.There was no significant H/O any major disease like DM,TB,or recurrent sinus or throat infections.

L/E : A swelling over anterior neck on left side measuring approximately 2 cm by 2 cm, smooth surface, with normal skin over it, ill defined margins, tender firm swelling moving on deglutition,

Fig 1 — Showing lump in front of neck (Lt) side of Preoperative photograph of patient

but not with protrusion of tongue, non pulsatile and non reducible.

Investigations

Haematological —

- Hemoglobin- 11.2 gm %. Total leucocyte count: 14,000/mm^3
- Differential leucocyte count: P 85 L 12 M 03 L 00. Platelet count: 2.1 lakh/mm^3. Random blood sugar: 126 mg%
- USG Neck showed A linear hyperechoic foreign body is noted in a 4x2.8 cms sized collection in left paratracheal region adjacent to left lobe of thyroid gland (Figs 2&3).

CT Neck Findings —

- Hypodense lesion of size 4.5 x 1.8 cms noted adjacent to the heterogeneously appearing left lobe of thyroid with hyperdense linear structure within S/O? Foreign body. The above lesion is at the level of C5-C6 vertebrae.Right lobe of thyroid normal.
- Parotid glands appear normal. Both submandibular glands appear normal.

Provisional Diagnosis : A radio-opaque FB in neck? in left lobe of thyroid gland.

- Final Diagnosis : Foreign body oesophagus migrating to left lobe of thyroid .
- Treatment : systemic antibiotics followed by surgical exploration.

Surgery —

- Under GA, under AAP, PPD.

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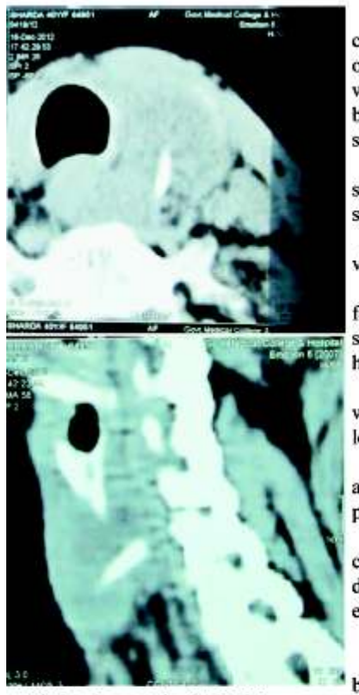

Fig 2 — Preoperative CT Neck Images, showing FB of Axial Image (Top) and Sagittal Image (Bottom)

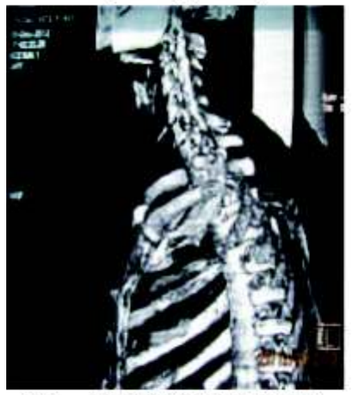

Fig 3 — Reconstructed image – sagittal : showing FB in front of T1 Vertebra

- A horizontal coller incision taken over anterior neck midway between upper border of thyroid and supra-sternal notch.
- Strap muscles separated by blunt dissection.
- Thyroid gland visualised.
- Left lobe found to be enlarged swollen and haemorrhagic.
- Foreign body was palpated inside left lobe of thyroid, which
- Was explored and removed completely.
- Incision closed and dressing done. procedure uneventful (Figs 4&5).

Discussion

Ingestion of a fish bone is a common otolaryngological emergency. This occurs frequently in Asian populations, where it is common to eat fish that has not been deboned. Although fish bones will spontaneously pass though the digestive tract, most fish bones are impacted at the tonsils or base of the tongue and can be removed easily with minimal morbidity. Fish bones retained in the oesophagus can result in complications such as retropharyngeal abcess, perforation of oesophagus, mediastinitis,or vascular complications all of which can morbidity or even cause death. The mechanism of perforation is thought to be a combination of local inflamation of oesophageal wall and direct pressure necrosis.

- The rarity of an esophageal foreign body migrating to the thyroid gland may be attributed to the fact that each thyroid lobe is attached to the trachea by a dense consolidation of connective tissue, called Berry's ligament[3]. X-ray is not conclusive in most such cases so we can't visualize the F.B. in first instance. Ultra-

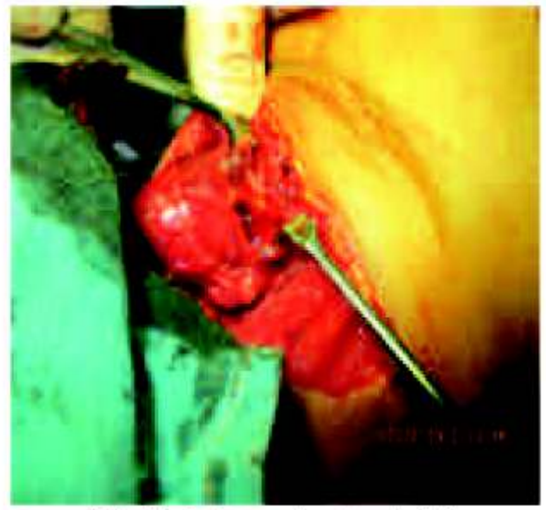

Fig 4 — Showing intraoperative photograph of left thyroid lobe explored

Fig 5 — Approximately 2 x 0.25 cms fish bone is retrieved

sonography and a CT scan of the neck are considered the most helpful diagnostic tools to determine the size, type, location and orientation of a migrated fish bone and its relationship to the other structures of the neck[4]. Exploration for a migrated F.B. from oesophagus in thyroid gland is a challengig task. Here in our case fish bone was removed after careful splitting of thyroid lobe without doing lobectomy[5].

- Exploration for a migrated esophageal foreign body in the thyroid gland is a challenging task.
- Fish bones was identified and removed after careful splitting of the thyroid lobes, without the need for thyroid lobectomy[5], because the damaged thyroid lobes was easily repaired with vicryl and drain left postoperatively (Fig 6).

Conclusion

- One must be aware of the changing nature of the patient's complaints. A case involving an enlarging thyroid mass and a history of foreign body ingestion should alert the physician to the possibility of a penetrating, migrating foreign body in the thyroid gland[1], with subsequent infection and inflammation[6,7]. Ultrasonography and CT scan should be performed to investigate if in doubt and surgical removal of FB in thyroid gland can be achieved with minimal tissue ablation.

Letter to the Editor

Fibrolipoma of the back of neck — a rare entity

SIR,

Fibrolipoma is an extremely rare variant of lipoma[1]. And it usually presents clinically as a slowly growing mass with a firm or soft consistency and usually occurs in middle-aged person. The authors report an unusual case of fibrolipma with slow-growing speed, which was misdiagnosed as amelanocytic nevi in local hospital. The diagnosis of nevi was ruled out by dermoscopy in authors' clinic Operation was performed in authors' clinic and diagnosis of fibrolipma was made on histopathology.

Fibrolipoma unlike lipoma is a rare variant of lipoma, usually benign with mild pain occasionally and very slow growing.The basis of suspicion were fine needle aspiration cytology,ultrasound B mode and confirmation on histopathology which shows mature adipose tissue in upper dermis ,lying in a sea of fibrous tissue. Normally there are prominent bundles of mature fibrous tissue traversing fat globules[2].

We report a case of fibrolipoma of neck with duration of 10 years, slow growing,diagnosed as amelanocytic nevi, we did a dermoscopy and found fat cells (yellowish cigar shaped structures probably fibrous tissue arranged radially with balloon structures in between.On histopathology from excision biopsy, the mature adipocytes was seen in upper dermis amongst fibrous tissue.The first case was published in Edinborrough Medical Journal way back in 1927[3] and only a few cases are reported in literatureand it was first diagnosed by dermoscopy.

We presented the case owing to rarity and establishing dermoscopy can be a good tool to diagnose it.

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Activities Report

Dr Santanu Sen, MP & National President in IMSCON 2019 conference in Kolkata

Dr Santanu Sen, MP & National President in Orissa

IMA Cochin Branch organised Protest Day, Mega Medical Camp, Awareness class for students, oil free cooking

IMA Kunnamkulam Branch Branch organised Christmas, All India Protest day, Medical Camp, Community Service day, Republic day

IMA Palakkad Branch Branch organised Anti Leposy Day, CMEs & Distict Committee Meeting in previous month

IMA AKN Sinha Institute & IMA Bihar State Branch organised Inaugural function of
Basic Life Support Certificate Course (BLS) on 18th February, 2019, in presence of
Hon'ble Health Minister Shri Mangal Pandey; Dr Santanu Sen, MP (Rajya Sabha) & National President, IMA;
Dr R V Asokan, Hony Secretary General, IMA,
Dr Sahajanand Pd. Singh, Imm Past President, IMA Bihar State Branch and other leaders of IMA

IMA Trivandrum Branch organised World Cancer Day, World Leprosy Day, Anemia Detection Camp, Medical Camp, Health Awareness Class etc.

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