

A STUDY ON CLINICAL PROFILE OF HIV AND AIDS PATIENTS AND FIND ITS CORRELATION WITH CD₄⁺ AND CD₈⁺ T LYMPHOCYTE LEVELSMoirangthem Ratankumar Singh¹, Suchitra Chongtham², Thongam Bhimo Singh³**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: OBJECTIVE: To Study clinical profile of HIV and AIDS patients and find its correlation with CD₄⁺ and CD₈⁺ T lymphocyte levels. **MATERIALS AND METHODS:** 104 HIV infected or AIDS cases were enrolled. Demographic and clinical data were recorded. General and systemic examinations with particular attention to presence of opportunistic infections was done. The diagnosis of HIV/AIDS was done bases on the criteria provided by National AIDS Control Organization (NACO). CD₄⁺ count was estimated by Fluorescent Activated Cell Sorter (FACS). Opportunistic infection (OI) was diagnosed based on clinical signs, symptoms supported by laboratory investigation findings. Serum total protein, serum SGPT were estimated using kit method. **RESULTS:** The data collected was analyzed statistically using SPSS version II. Out of 104 HIV/AIDS cases, most cases were in the age group (30 – 40) years. Tuberculosis was the commonest OI 40(38%) including 72(69%) extra pulmonary tuberculosis 16(15%) followed by oral candidiasis 22 (21%), cyptococcal meningitis 15 (14%) and others. Most patients had CD₄⁺ T lymphocyte count between (100 – 200) cells/μl and CD₈⁺ T lymphocyte in range (400 – 600) cell/μl. Hepatitis C and Hepatitis B co infections occurred in 24 (23%) and 11 (11%) of cases respectively. All had CD₄ count below 400 cell/ μl. A significant level of correlation was observed between CD₄ and serum total protein with Karl Pearson's correlation coefficient r=0.270, at 0.01 level of significance. **CONCLUSION:** IDU was the commonest route of infection. Tuberculosis including extra pulmonary tuberculosis being the most common OI. Co infections with Hepatitis –C and Hepatitis B occurred in many patients which could be attributed for the rise in SGPT levels. Most of the OIs occurred in patients having CD₄ count <100 cells/μl. Out of 104 cases, 68 cases were under antiretroviral drugs and 14 such cases developed OIS. Hence there is possibility of treatment failure on first line drug treatment and in these cases further study is required.

KEYWORDS: Clinical Profile, HIV, AIDS, CD₄⁺, CD₈⁺ T Lymphocyte, SGPT, Serum Protein.

INTRODUCTION: The chronic and incurable infection of the HIV causes insidious erosion of host immune system and gives vent for opportunistic infection and malignancies.^[1] As per WHO report 2014, 36.9 million people are living with HIV of which 2.0 million are newly infected cases and 1.2 million deaths. The United Nations population Division projects that by the year 2015 the life expectancy at birth in the seven countries in Africa with adult HIV prevalence rate >20% will be 32 years lower on average than the projected life expectancy in the absence of AIDS.^[2]

India has the third largest number of people living with HIV in the world- 2.1 million at the end of 2013 and accounts for 4 out of 10 people living with HIV in the region.^[3] Manipur is the sixth highest HIV prevalent state in India.

The current CDC classification is based on three ranges of CD₄⁺ lymphocyte count and three clinical categories, represented by a matrix of nine mutually exclusive categories. Any HIV infected individual with a CD₄⁺ T cell count of <200/ml has AIDS by definition regardless of the presence of

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symptoms on opportunistic disease. As the CD₄⁺ T lymphocyte count goes down different opportunistic infections (OTs) occur increasing the mortality and morbidity. The clinical spectrum of diseases caused by opportunistic infections is constantly changing from time to time.

The correlation of CD₄ T lymphocyte count and distribution of pathogenic or opportunistic infection most commonly found in HIV positive individuals differ from one area to another. Potent antiretroviral therapy (ART) has decreased the incidence, changed the manifestations and improves the outcome of opportunistic infections though Immune Reconstitution Syndrome (IRS) is encountered in some cases as per a report by MACS, HIV treatment coverage is only 36% in India, where 51% of AIDS-related deaths occur. The proportion of people who do not have access to antiretroviral therapy treatment is 64% in India.^[4]

So far, few systematic study on clinical profile of OIs and its correlation with CD₄⁺ and CD₈⁺ T lymphocytes among adolescents and adults of Manipur have been done. Therefore the study was taken up with a view to highlight the various modes of clinical presentations of HIV and AIDS with associated OIs with CD₄⁺ and CD₈⁺ lymphocyte levels.

MATERIALS AND METHODS: This hospital based cross sectional study was conducted in the Departments of Medicine, Microbiology, Biochemistry Regional Institute of Medical Sciences over a period of 21 months from Nov. 2004 to July 2006 on 104 HIV infected or AIDS cases above 13 years of age attending OPD and indoor wards of Medicine Department, FACS count center Microbiology Department and ART center of RIMS, selected randomly for the study.

Detailed demographic and clinical data were recorded, meticulous general physical and systemic examinations were done with particular attention to presence of opportunistic infections and the findings were entered in a predesigned Performa.

The diagnosis of HIV/AIDS was done based on the criteria provided by National AIDS Control Organization (NACO, 2000) ^[5]. After pretest counseling informed consent for HIV testing was taken. For unconscious patients counseling was given to the guardians or spouses of the patients.

3ml of blood was sent to the National Reference Laboratory (NRL) cum Voluntary Confidential Counseling and Testing Centre (VCCTC) Department of Microbiology, RIMS Hospital, Imphal.

Strategy III where 3 ELISA/Rapid/Simple Tests using different principles and Antigens were followed for diagnosis and confirmation of HIV infection. The posttest counseling was done with maintenance of full confidentiality.^[2]

CD₄⁺ count of the patient were estimated by Fluorescent Activated Cell Sorter (FACS) machine in Department of Microbiology. Relevant samples were sent to Microbiology, Pathology and Biochemistry Departments maintaining strict biosafety measures.

Opportunistic infections were diagnosed based on clinical signs/symptoms, supported by laboratory investigation findings. Supportive and specific treatments were given in each case and outcome recorded. ART was given as per ART guidelines of NACO. These cases were closely monitored and followed up. The discharged cases were followed up during the study period for any mortality.

RESULTS: The data collected was tabulated and analyzed using SPSS version 11.

In our study in 104 HIV/AIDS cases within a period of 21 months, maximum number of cases were in the age group (30-40) years [Table 1] predominantly males 72 (69%) [Table 2] The most common route of infection was injecting drug use (IDU) 64(62%) followed by sexual transmission 31(30%) as shown in [Table 3].

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Among the Opportunistic Infections (OIs) tuberculosis was the commonest 40(38%) cases including extra pulmonary tuberculosis contributing 16(15%) cases followed by oral candidiasis 22(21%), cryptococcal meningitis 5(14%), herpes zoster 14(14%), penicillium marneffei 5(5%), cerebral toxoplasmosis 5(5%), cryptosporidial diarrhoea 4(4%), pneumocystis carinii pneumonia (PCP) 3(3%), viral meningitis 2(2%), Kaposi's Sarcoma 1(1%), hairy cell leucoplakia 1(1%) respectively [Table-4].

Other diseases associated with HIV seropositive cases under study were acute gastroenteritis -15(14%), alcoholic liver disease-9(9%), portal HTN-9(9%), peptic ulcer syndrome-8(8%), focal neurological deficit-6(6%), cirrhosis-3(3%), type II diabetes mellitus-1(1%), drug induced hepatitis-1(1%), malena-1(1%), chronic sinusitis-1(1%), epilepsy-1(1%) and deep vein thrombosis of leg 1(1%) respectively [Table-5]. Most of the cases 65(63%) and predominantly males had serum protein in the range (6.1-8.0) gm% [Table -6].

The serum level of Alanine Transaminase (ALT/SGPT) of most of the cases 36(34%) were in the range (30-65) U/L; 26 (25%) cases had SGPT in the range (100-200)U/L and even 200 and above units in 5(5%) [Table7]. When categorized into different CD4 range groups majority of the cases had CD4+ T lymphocyte count between(100-200)cells/ of which 19(18%) were males and 10(9%) were females and 28(27%) predominantly males had CD4 count<50cells/ μ l. There was only 1 case with CD4 count>500 cells/ μ l [Table 8].

A look into the various levels of CD 8+T lymphocyte among the HIV seropositive cases showed that maximum no. of cases had CD8 levels in the range (400-600) cells/ul. There were (7%) cases with CD8 + lymphocyte count <200; 18(17%) cases had (200-400) cells/ul. We found 21(20%), 9(9%), 12(12%) 6(6%), 5(5%) and 4(4%) cases having CD8+ lymphocytes in the ranges (600-800), (800-1000), (1000-1200), (1200-1400), (1400-1600) and above 1600 cells / μ l respectively [Table-9]. A correlation is found to exist between CD4+ T lymphocyte and serum total protein with Karl Pearson's correlation coefficient ($r=0.270$), highly significant at 0.01 level of significance [Table-10].

The level of CD4+T lymphocytes were examined among the various study subjects when the OIs were manifested. It was observed that 15(14%) of the total cases were found to be suffering from cryptococcal meningitis and all of them had CD4 t lymphocytes <200; 14(13%) of the cases were even less with cell count <200. Extra pulmonary tuberculosis was occurred in 16(15%) cases and all of them had C4 +T lymphocyte below 400; 13(12%) of which with CD4+ T lymphocytes count <200. All subjects with pulmonary tuberculosis except 1(1%) case had CD4+T lymphocyte count below 400 out of which 21(20%) had count below 200. Herpes zoster case 14(14%) except for 1(1%) were found to have CD4+T lymphocyte count below 400 and out of which 10(10%) cases had cell count below 200. Oral candidiasis 22(21%) cases had CD4+T lymphocyte below 400 and 20(19%) of the cases had CD4+T lymphocyte below 200.

Hepatitis C co infection was present in 24(23%) of total cases and all had cell count below 400 and 22(21%) of the cases had even below 200. Hepatitis B co infection occurred in 11(11%) of cases. All cases were found to have CD4+T lymphocytes cell count below 400 and 9(9%) of the cases had even less than 200. 5(5%) of total cases had cerebral toxoplasmosis with cell count below 400 and 4(4%) of the cases had CD4+T lymphocyte below 200. Penicillium marneffei and lower respiratory tract infection were found to be equally common among the study subjects 5(5%) each. All patients with penicillium marneffei had CD4+T lymphocyte count below 400, 4(4%) of them had count even below 200, while the later 4(4%) of the cases was found to have CD4 count below 400 and even 200. Cryptosporidial diarrhea 4(4%), Pneumocystis carinii pneumonia (PCP) associated cases 3(3%) cases

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had cell count <200. Viral meningitis and cytomegalovirus (CMV) 2(2%) cases had CD4 count <200. Viral fever, Kaposi's sarcoma and Hairy cell leucoplakia 1(1%) each had CD4+ T lymphocyte count <400[Table-11].

Age (years)	No. of Cases (1%)
14-20	1 (1)
20-30	16 (15)
30-40	55 (53)
40-50	27 (26)
50 and above	5 (5)
Total	104 (100)

Table 1: Distribution of the HIV seropositive cases with respect to age

Sex	No. of Cases (%)
Male	72(69)
Female	32(31)

Table 2: Distribution of HIV seropositive cases with respect to sex

Total 104(100).

Risk factor	No. of Cases (%)
IDU	64(62)
Sexual transmission	31(30)
Blood transfusion (Before imposition of mandatory screening)	4(4)
Unknown	5(5)

Table 3: Distribution of HIV seropositive cases with respect to risk factors

Total 104(100).

Opportunistic Infection and Co-infection	No. of Cases (%)
Cryptosporidial diarrhea(C parvum)	4(4)
Cryptococcal meningitis	15(14)
Tuberculosis:	
(i) Extrapulmonary	16(15)
(ii) Pulmonary	24(23)
Pneumocystis carinii pneumonia(PCP)	3(3)
Cerebral toxoplasmosis	5(5)
Penicillium marneffeii	5(5)

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Herpes zoster	14(14)
Viral meningitis	2(2)
Oral candidiasis	22(21)
Hepatitis B virus	11(11)
Hepatitis C virus	24(23)
Cytomegalovirus infection (CMV)	2(2)
Kaposi's sarcoma	1(1)
Hairy cell leukoplakia	1(1)

Table 4: Distribution of HIV seropositive cases with respect to opportunistic infections(OI) and co-infection

Associated Diseases	No. of Cases (%)
Acute gastroenteritis(AGE)	15(14)
Alcoholic liver disease(ALD)	9(9)
Portal hypertension	9(9)
Peptic ulcer syndrome(PUS)	8(8)
Focal neurological deficit:	
(i) Rt VI nerve palsy	1(1)
(ii) VII nerve palsy	2(2)
(iii) VIII nerve palsy	1(1)
(iv) Right hemiparesis	2(2)
Cirrhosis	6(6)
Type II diabetes mellitus	3(3)
Drug induced hepatitis	1(1)
Malena	1(1)
Chronic sinusitis	1(1)
Epilepsy	1(1)
Deep vein thrombosis of leg	1(1)

Table 5: Distribution of HIV seropositive cases with respect to associated diseases

Total protein	Sex		Total(%)
	Male (%)	Female (%)	
≤6.0	17(16)	7(7)	24(23)
6.1-8.0	47(46)	18(17)	65(63)
Above 8.0	8(7)	7(7)	15(14)
Total	72(69)	32(31)	104(100)

Table 6: Distribution of HIV seropositive cases with respect to sex and total protein (gm %)

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Sex			
SGPT (U/L)	Male (%)	Female (%)	Total (%)
Below 30	8(8)	8(8)	16(16)
30-65	24(23)	12(11)	36(34)
65-100	16(15)	5(5)	21(20)
100-200	21(20)	5(5)	26(25)
200 and above	3(3)	2(2)	5(5)
Total	72(69)	32(31)	104(100)

Table 7: Distribution of HIV seropositive cases with respect to SGPT(U/L)

CD4+T- Lymphocyte count	Sex		total
	Male (%)	Female (%)	
Below 50	2(21)	6(6)	28(27)
50-100	20(19)	4(4)	24(23)
100-200	19(18)	10(9)	29(27)
200-300	7(7)	7(7)	14(14)
300-400	3(3)	3(3)	6(6)
400-500	1(1)	1(1)	2(2)
500 and above	-	1(1)	1(1)
Total	72(69)	32(31)	104(100)

Table 8: Distribution of HIV seropositive cases with respect to CD4+T lymphocyte count(cell/ul)

Total 72(69) 32(31) 104(100).

Sex			
CD8+ T-lymphocyte cell count	Male (%)	Female (%)	Total (%)
Below 200	4(4)	3(3)	7(7)
200-400	16(15)	2(2)	18(17)
400-600	15(14)	7(6)	22(20)
600-800	16(15)	5(5)	21(20)
800-1000	5(5)	4(4)	9(9)
1000-1200	6(6)	6(6)	12(12)
1200-1400	4(4)	2(2)	6(6)
1400-1600	4(4)	1(1)	5(5)
1600 and above	2(2)	2(2)	4(4)

Table 9: Distribution of the HIV seropositive cases with respect to CD8 +T-lymphocyte cell count

Total 72(69) 32(31) 104(100).

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	CD4	Total Protein
CD4 Pearson Correlation,r	1	.270(**)
t		2.941
Sig.(2-tailed)		.006
n	104	104
Total Pearson Correlation,r	.270(**)	1
Protein t	2.941	
Sig.(2-tailed)	.006	
n	104	104

Table 10: Correlation Table

** Correlation is significant at the 0.01 level (2-tailed).

Major OI and co-infection CD4+ T lymphocyte cell count					
	Below 100	100-200	200-400	400 and above	Total
Cryptococcal meningitis	11(10)	3(3)	1(1)	-	15(14)
Extrapulmonary tuberculosis	6(6)	7(6)	3(3)	-	16(15)
Pulmonary tuberculosis	14(13)	7(7)	2(2)	1(1)	24(23)
Herpes zoster	6(6)	4(4)	3(3)	1(1)	14(14)
Oral candidiasis	13(12)	7(7)	2(2)	-	22(21)
Hepatitis B	5(5)	4(4)	2(2)	-	11(11)
Hepatitis C	15(14)	7(7)	2(2)	-	24(23)
Cerebral toxoplasmosis	4(4)	-	1(1)	-	5(5)
Penicillium marneffeii	2(2)	2(2)	1(1)	-	5(5)
Cryptosporidial diarrhea	3(3)	1(1)	-	-	4(4)
Pneumocystis carinii pneumonia	1(1)	2(2)	-	-	3(3)
Cytomegalovirus infection (CMV)	1(1)	1(1)	-	-	2(2)
Kaposi's sarcoma	1(1)	-	-	-	1(1)
Hairy cell leukoplekia	1(1)	-	-	-	1(1)

Table 11: Distribution of the HIV seropositive cases with respect to CD4+T-lymphocyte cell count(cell/ul) and major OIs and co-infections

DISCUSSION: Out of a total of 104 HIV seropositive patients included in this 21 months study from November 2004 to July 2006 maximum number of cases were in the age group 30-40 years (55 cases) which is the sexually active and in reproductive age group. Unemployment, frustrations and habit of testing or abusing drugs could also be important additional factors.

The associated risk factors were IDUs 64(62%), sexual transmission 31(30%), blood transfusion 4(4%) and unknown 5(5%). Easy availability of such narcotic substances like heroin which can be abused intravenously and sexual transmission of the disease to their partners are causes of HIV infection. Pulmonary tuberculosis 24(23%) cases, oral candidiasis 22(21%) followed by extra pulmonary tuberculosis 16(15%) were the frequent OIs encountered. Our findings are in agreement with the findings of Ayyagari A et.al.^[6]

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The incidence of TB in HIV infected persons is more than 100 times that of the general population and unlike other opportunistic infections, TB can occur at an early stage of HIV infection with pulmonary features and also in late stages with more extra pulmonary presentations.^[7] Cryptococcal meningitis occurred in 15(14%) of the cases where as a greater figure was observed by Singh PN et.al where tuberculosis and Cryptococcus's were the first and second common OIs in the south East Asia.^[8]

Skin infections like Herpes zoster occurred in 14(14%) cases. The common co-infections seen were Hepatitis B-11(11%) cases and Hepatitis C-24(23%) cases. This is caused by sharing of needles by the IDUs. Alcoholic fatty liver and cirrhosis of liver were associated in 9(9%) cases and 3(3%) cases respectively. Cerebral toxoplasmosis occurred in 5(5%) of the cases which is a lower figure compared to findings of Nissapatron V et.al ^[9] where 226 out of 505 patients suffered from toxoplasmosis, 27 with toxoplasma encephalitis and 199 without encephalitis.

Penicillium marneffeii, an important OI accounts for 5(5%) of the study population though it was the third most common OI in South East Asia after TB and Cryptococcus's as reported by Singh PN et al.^[8] Pneumocystis carinii pneumonia (PCP) shared 3(3%) and it is supported by other authors,^[10] where PCP was the most common parasite and ubiquitous extracellular protozoa which proliferates easily in the immune compromised patients.

Cryptosporidial diarrhoea claims 3(3%) of the total cases which is comparable to other studies.^[11] Viral meningitis occurred in 2(2%) cases. This could be attributed to their immune compromised states during which viral infection was very common among the masses.

Cytomegalovirus (CMV) infection occurred in 2(2%) contrast to a larger figure found by other authors.^[12] where the most frequent OIs were mycobacterium avium complex, pneumocystis carinii pneumonia and cytomegalovirus retinitis.

Focal neurological deficit in the form of paralysis of one side of body (Hemiparesis) with cranial nerve palsy accounting for 6(6%) or one limb (Monoparesis) accounting for 2(2%). These patients had cerebral infections like cryptococcal meningitis and tubercular meningitis. Kaposi's sarcoma, hairy cell leukoplakia were other associated health problems.

The moderately raised SGPT level in many cases could be attributed to Hepatitis B virus, Hepatitis C Virus co-infection and chronic alcohol use. Further analysis showed 28(27) HIV seropositive cases has CD₄+ T lymphocyte cell count below 50/cumm which was the highest percentage. Lack of awareness, late diagnosis could be the reason. Maximum no. of cases 22(20%) had CD₈+ T lymphocyte range (400-600)/ μ l of blood.

A look into the distribution of HIV seropositive cases with respect to CD₄+T lymphocytes cell count and major opportunistic infections showed pulmonary TB and Hepatitis C virus 24(23%) stand highest followed by oral candidiasis 22(21%), Extra pulmonary Tuberculosis 16(15%) and Cryptococcal meningitis 15(14%). The maximum number of pulmonary tuberculosis patients manifest when CD₄+T lymphocyte count is below 100, indicating that higher incidence of OI occur with lower level of CD₄+T lymphocyte count although the opportunistic infections are different in various geographical regions.^[13] In America and Europe the pueumocystis carinii pneumonia, cryptococcal meningitis, CMV infection and toxoplasmosis are common but in developing countries like Africa and India tuberculosis and other tropical parasitic infections are predominant.

Analysis of CD₈+T lymphocyte count of HIV+ cases and major opportunistic diseases reveals that maximum number of cases with pulmonary tuberculosis have CD₈+T lymphocyte cell count less than 400 μ l and the most of oral candidiasis cases have CD₈+T lymphocytes cell count between (600-

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800)/ μ l. Next was extra pulmonary tuberculosis whose maximum number falls in the interval (400-600)/ μ l whereas cryptococcal meningitis cases had cell count below 400/ μ l. The relation between OI and CD8+T lymphocyte cell count is insignificant.

The serum level of total protein varies positively with the level of CD4+T lymphocyte cell count significantly as the value of t-statistics is (2.941) with $P < 0.01$ when $r = 0.270$ but the variation in the level of total protein may not be due to variation in the level of CD8+T lymphocyte cell count with the Karl Pearson coefficient of correlation $r = 0.043$. The value of 't' was found to be insignificant ($t = 0.435$).

CONCLUSION: In our study in 104 HIV/AIDS cases within 21 months maximum no of cases were in the age group (30-40) years and the most common route of transmission was IDU i.e. 64(62%) followed by sexual transmission 31(30%) tuberculosis was the most common opportunistic infection 40(38%) cases including extra pulmonary tuberculosis 16(15%) cases, followed by oral candidiasis, cryptococcal meningitis herpes zoster 14(14%), penicillium marneffeii 5(5%), cerebral toxoplasmosis 5(5%), cryptosporidial diarrhoea (*C. parvum*) 4(4%) pneumonystis carinii pneumonia (PCP) 3(3%), Kaposi's Sarcoma 1(1%), hairy cell leukoplakia 1 (1%). Co infection with Hepatitis B Viral and hepatitis C virus were 11(11%) and 24(23%) cases respectively as IDU is still the commonest route of transmission in Manipur. Most of the OIs occurred in patients having CD4 count less than 100/ml i.e 83(79%) cases except in a case of pulmonary tuberculosis and one case of herpes zoster with CD4+ T lymphocyte above 400/ml. Increase in serum SGPT could be due to Hepatitis B, Hepatitis C co infection and chronic alcohol use. A significant positive correlation exists between CD4+T lymphocyte and serum total protein. Out of 104 cases, 68 cases were under antiretroviral drugs and 14 of such cases developed OIs again. Hence, there is possibility of treatment failure on first line antiretroviral drug treatment and in these cases further study is required.

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AUTHORS:

1. Moirangthem Ratankumar Singh
2. Suchitra Chongtham
3. Thongam Bhimo Singh

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of General Medicine, Jawaharlal Nehru Institute of Medical Sciences, Imphal, East.
2. Assistant Professor, Department of Biochemistry, Jawaharlal Nehru Institute of Medical Sciences, Imphal, East.

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4. Professor, Department of General Medicine, Regional Institute of Medical Sciences, Imphal, West.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Moirangthem Ratankumar Singh,
Jawaharlal Nehru Institute of Medical Sciences,
Porompat-795001, Imphal East.
E-mail: drmratan2007@gmail.com

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