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Original research article

Clinico-Radiological Profile in Peripheral Eosinophilia: a Pragmatic 2 year Retrospective Study from Eastern India

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Abstract

Background: Eosinophilic disorders represent a group of pathologic conditions with highly heterogeneous pathophysiology and clinical presentation and variable prognosis, ranging from asymptomatic or mild, to severe and complex cases, with fatal outcome.

Aims & Objectives: 1. To study the prevalence of Eosniophilia in our part of the country.
2.To study the demographic and clinico-radiological characteristics of cases-presenting with eosinophilia.

Materials and methods: It was a 2 year retrospective observational study conducted at a tertiary care center in Bihar. All patients coming to Hematology department with peripheral blood eosinophilia were studied with a sample size of 200 cases. All cases with normal eosinophil count are excluded from the study. Software used for data analysis was SPSS version 25 for statistical analysis .

Results: Among 200 patients 57.5% were males and rest 42.5% were females. Maximum number of patients belonged to age group of 11 to 20years (22.5%).52.5 % cases belonged to mild category whereas 39.5% and 8% cases belonged to moderate and severe categories respectively. Fever (46%) was the most common clinical symptom followed by skin rashes (44%) and cough (42.5%). Radiological findings were maximum in patients having severe eosinophilia (71.4%) followed by moderate eosinophilia cases (55.6%). Anemia was most commonly seen in patients with eosinophilia (57.5%) and hemoglobin level was statistically significant with eosinophilia severity with a P value of 0.028.

Conclusion: The study concluded that eosinophilia still is an under-reported public health problem in tropical settings with an estimated prevalence of 0.5-1-case/100,000 population in hospital settings and very few studies have been done so far highlighting the prevalence and etiopathoegensis of eosinophilia in developing countries like ours and many unseen folds still remain to be explored.

Keywords: eosinophilia, prevalence, clinico-radiological, etiopathogenesis, absolute eosinophil count.

Introduction

Eosinophilic disorders represent a broad spectrum of pathologic conditions characterized by various degrees of persistent blood and/or tissue hypereosinophilia, some of which can have potential for end-organ damage. Eosinophilic disorders are a group of pathologic conditions marked by varying degrees of chronic hypereosinophilia in the blood and/or tissues.

The prevalence of a particular category of illnesses has lately risen, and this trend is expected to continue. Understanding of pathologic mechanism, diagnostic criteria, classification and molecular biology as well as assessment of therapeutic management has increased in the recent years but many unknown facts still need to be explored. Symptoms might range from asymptomatic to severe.as well as lethal, with a variety of time course layouts.[1]

There are considerable geographical differences in the most common causes of hypereosinophilia, with parasite infections and allergy disorders being documented in tropical settings. Many non-hematologic (reactive) and other hematologic (primary) hypereosinophilic syndromes (primary or secondary) and illnesses, as well as related or idiopathic types, have all been identified.[2,3]

Normal eosinophil percentage is 1%-6%. Absolute eosinophil count (AEC) is determined by multiplying total white blood cell count by percentage of eosinophils. Eosinophilia is defined when AEC count exceeds 500/µl in the peripheral blood. Eosinophilia can be categorized into mild (AEC ranges from 500-1500/ µl), moderate (AEC ranges from 1500-5000/µl) or severe (AEC>5000//µl).[4]

The 2010 revision of Hypereosinophilic syndrome (HES) diagnosis criteria recommended that a peripheral AEC > 1500/mm3 may not be a requirement for diagnosis, as previously considered, due to possible discrepancies between blood and tissue eosinophilia.[5]Eosinophilic disorders are defined by organ dysfunction induced by activated eosinophils and this can be single-organ disease or multiple-organ disease, accompanied by variable degree of blood eosinophilia.[6] The same revision of diagnostic criteria is recommended for provisional diagnosis of idiopathic eosinophilic disorder for the subgroup of patients who have blood eosinophilia > 1500/mm^3, but without end-organ dysfunction, since they may benefit from regular monitoring .[7]

From etio-pathogenic point of view, eosinophilic disorders are classified as secondary (or reactive) to a broad range of causal factors, such as infections and allergens, or primary, when no causal factor can be identified. Other terms have been used in the previous classifications, to define less well characterized eosinophilic syndromes, such as idiopathic associated, overlap or hypereosinophilia with uncertain or undetermined significance.[8]

There are no data available regarding incidence and prevalence of all types of eosinophilic disorders, which should be probably evaluated based on geographic regional approach. The reported age-adjusted incidence rate of hypereosinophilic syndromes, including chronic eosinophilic leukemia, based on the International Classification of Disease (ICD) for Oncology

(version 3), was about 0.036 per 100.000, as resulting from the Surveillance, Epidemiology and End Results (SEER) database between 2001 and 2005.[5]

2. Aims and objectives:

1. To study the prevalence of eosniophilia in Eastern India.
2. To study the demographic and clinico-radiological and hematological characteristics of cases-presenting with eosinophilia .

3. Materials and methods:

3.1 Study design: a retrospective observational study conducted at a tertiary care center in Bihar.

3.2 Duration of study: August 2019 to August 2021.

3.3 Study Population: all patients coming to the Hematology department of a tertiary care hospital with peripheral blood eosinophilia. Sample size would be approximately 200 cases. It may increase or decrease depending on the availability of cases.

3.4 Place of study: Department of Hematology.

3.5 Inclusion criteria: All patients presenting with eosinophilia either on complete blood count or on peripheral blood smear.

3.6 Exclusion criteria:

All cases with normal eosinophil count are excluded from the study.

3.8 Procedure of data collection:

The retrospective analysis was performed using medical records of 2 years (August 2019 to July 2021). The clinical features, laboratory findings, treatment and follow up details were retrieved from the clinical record files. Patients were evaluated with detailed history, clinical examination, complete hemogram, serological tests (anti-nuclear antibody/ANA, anti-neutrophil cytoplasmic antibody/ANCA, IgE levels, parasite serology), skin hypersensitivity test for aspergillus, stool examination, morphological evaluation of peripheral blood. Bone marrow, flow cytometry and ancillary tests like molecular studies were also analysed in certain cases wherever required. Patients were investigated in a stepwise manner to exclude reactive or secondary causes of eosinophilia followed by evaluation for clonal conditions. Complete blood count (CBC) was performed by collecting blood samples in EDTA vacutainers and CBC was performed by hematology analyser SIEMENS ADVIA 2120i. The eosinophil % was determined by manually counting a minimum of 200 leukocytes in the Leishman stained peripheral smears. AEC was calculated by multiplying total WBC count with eosinophil percentage.

3.7 Statistical analysis:

Discrete categorical data are presented as *n* (%); continuous data given as median, range and interquartile range (IQR). The comparison of categorical data between two groups was performed by Chi-square test and Fischer's exact test. Results were recorded as frequencies, means ± standard deviations (SD) and P values. For all purposes, a P value of < 0.05 (95% confidence level) was considered as the criteria of significance.

Statistical analysis was performed using SPSS for Windows (version 25.0; SPSS Inc., Chicago, IL, USA). All procedures followed were in accordance with the ethical standards of the

responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Results:

1. Prevalence of eosinophilia according to age group and sex:

Among 200 patients 57.5% were males and rest 42.5% were females.(Table 1) Maximum number of patients belonged to age group of 11 to 20years (22.5%) followed by 0-10 years (22%) and 21-30 years (17.5%) respectively with age range included in the study population being 8 months to 73 years.(Table 2)

Table 1: Showing gender wise breakup of eosinophilia cases.

Gender	No. of cases (n)	%age
Male	115	57.5
Female	85	42.5

Table 2: showing distribution of eosinophilia in various age groups.

Age range	Males (n,%)	Females (n,%)
0-10	29(14.5)	15(7.5)
11-20	25(12.5)	20(10)
21-30	19(9.5)	16(8)
31-40	15(7.5)	11(5.5)
41-50	15(7.5)	04(2)
51-60	09(4.5)	07(3.5)
61-70	11(5.5)	12(6)
>70	07(3.5)	0(0)

2. Prevalence of different categories of eosinophilia as per AEC:

52.5 % cases belonged to mild category whereas 39.5% and 8% cases belonged to moderate and severe categories respectively.(Table 3)

Table 3: showing prevalence of various categories of eosinophilia.

Grading of eosinophilia	No. of cases (n) ; %age
Mild(500-1500 cells/cumm)	105(52.5)
Moderate (1501-5000cells/cumm)	79(39.5)
Severe(>5000cells/cumm)	16(8)

3. Comparison of clinical characteristics in different categories of eosinophilia:

Fever (46%) was the most common clinical symptom followed by skin rashes (44%) and cough (42.5%). Pain abdomen and allergy was complained by 34% and 13% cases respectively. 15.5 % cases were asymptomatic. Skin rashes were most frequently seen in mild eosinophilia cases (53.3%) whereas cough was mostly seen in severe eosinophilia cases (71.4%).85.7% severe eosinophilia cases presented with fever. Pain abdomen was commonly seen in moderate eosinophilia cases while lymphadenopathy was uncommon overall and mostly seen in severe eosinophilia cases, making all these clinical symptoms statistically significant with a p value of <0.05 as calculated by Fischer's exact test.(Table 4)

Table 4: showing frequency of various clinical manifestations in eosinophilia cases.

Clinical features	Frequency (n;%)
Skin rashes, eczema, skin nodules	88(44)
Cough, dyspnea, wheezing	85(42.5)
Fever	92(46)
Pain abdomen	34(17)
Altered bowel habits(loose motion, constipation)	18(9)
Allergy	26(13)
Joint pain	12(6)
Lymphadenopathy	03(1.5)
Asymptomatic	31(15.5)

4. Frequency of radiological findings:

Radiological findings were maximum in patients having severe eosinophilia (71.4%) followed by moderate eosinophilia cases (55.6%). Among the radiological manifestations, presence of broncho-vascular markings prominence was most commonly noted (42.6%) followed by ground glass opacity (23.8%) .Pleural effusion and nodular opacity was seen in 2.9% cases each. Radiological findings were found to be statistically significant to degree of eosinophilia with a P value of 0.000 estimated by Fischer's exact test.(Table 5)

Table 5 : showing frequency of radiological findings in eosinophilia cases.

Radiological findings	No.of cases (n,%age)
Increased bronchovascular markings	33(16.5)
Ground glass opacity	16(8)
Consolidation	9(4.5)
Pulmonary pneumonitis	6(3)
Pleural effusion	2(1)
Splenomegaly	6(3)
Hepatomegaly	10(5)
Any lymphadenopathy	05(2.5)
Unavailable	38(19)
No radiological findings	75(37.5)

6. Hematological features in different categories of eosinophilia:

36.5% cases had normal hemoglobin levels whereas 57.5% cases had anemia. Anemia was most commonly seen in patients with eosinophilia (57.5%) and hemoglobin level was statistically significant with eosinophilia severity with a P value of 0.028.

Total WBC count was maximally raised in moderate eosinophilia cases (71.6%) followed by severe eosinophilia cases (52.5%). One case of severe eosinophilia had a total leucocyte count of 1.23lacs/cumm with 72% eosinophils on peripheral blood smear. His bone marrow evaluation also revealed marked myeloid proliferation with increased eosinophil and its precursors with few dyspoietic forms and occasional blasts. Molecular studies (PDGFRA and PDGFRB and FGFR1) were positive confirming it to be Chronic eosinophilic leukemia.

Majority of patients had normal platelet count where as 9.5 % cases had low platelet count
These hematological parameters (total WBC count and platelet count) were found to be statistically significant by Fischer's exact test with a P value of < 0.05.(Table 6)

Table 6: showing frequency of various hematological parameters in different categories of eosinophilia

RBC parameters	Total number,n (%)	Degree of severity Mild	Moderate	Severe	P value
Hemoglobin					0.0000
Normal	94(47)	53	37	04	
Anemia	97(48.5)	51	35	11	
Increased hemoglobin	09(4.5)	01	07	01	
Platelet count					0.0000
Normal	168(34)	94	63	11	
Increased	13(6.5)	03	05	05	
Decreased	19(9.5)	08	11	00	
WBC count					0.0000
Normal	170(85)	96	63	11	
High	92(46)	24	53	15	
Low	05(2.5)	05	00	00	
Eosinophil % Increased					0.0000
Absolute eosinophil count (AEC)	200	105	79	16	

Discussion:

The estimation of prevalence of eosinophilia is difficult due to the lack of clear consensus and according to SEER database of the National Cancer Institute, the age-adjusted incidence of HES is 0.18 per 100000.[5] These may not represent the true incidence in tropical countries with high prevalence of parasitic infections; and unfortunately, there is no data regarding the same from several tropical countries including India.

The evaluation of a patient with eosinophilia can be lengthy, expensive, and time-consuming, requiring a multidisciplinary approach with hematopathologists, physicians and infectious diseases specialists.

Due to varied clinical picture and various genetic factors, evaluating eosinophilic disorders is difficult clinically . The degree of eosinophilia may indicate the aetiology as well as the likelihood of a severe illness outcome. While mild and moderate eosinophilia are common in allergy disorders and infections, extreme eosinophilia can signal more serious illnesses including malignant hypereosinophilic syndrome. Because of the many possible abnormalities, unknown elements, and the necessity for highly specialised additional testing, haematological evaluation of eosinophilia is complex.[7,9]

Causes of reactive eosinophilia have a significant regional influence worldwide and regional large epidemiologic studies would be needed for a global evaluation of the problem. Despite the general perception that parasitic infections are the main cause of eosinophilia in tropical regions, few recent studies found that an underlying malignancy was diagnosed with nearly equal frequency compared with infections.[10,11] Another important epidemiological aspect is the continuous increasing prevalence of allergic diseases in developed countries, with

respiratory, drug and food allergies estimating to affect a large part of the population in the near future. There is a clear need for harmonization of terminology and classification of eosinophilic disorders for better quantification of eosinophilia related end-organ damage.[12]

The proposal to implement a category of B symptoms for eosinophilia -related organ damage, similar to that already used in lymphoma disease stratification, seems of practical value.[13]

Despite remarkable progress in understanding pathophysiologic mechanisms of eosinophilic disorders, there are still many unclear aspects, confusing terminology and gaps in diagnosing this very heterogeneous group of diseases.

Beside an agreement upon clear and useful classification for disease phenotypes, there may also be an increasing need for disease endotyping and novel biomarkers, which may improve understanding of the disease pathophysiology. Classification based on disease endotypes can also have a direct impact on disease management and prognosis, considering personalized medicine.[14] There is a clear need for specialized centres in eosinophilic disorders and for multidisciplinary teams, in order to implement international multicentric registries, updated diagnosis criteria and management guidelines. With the refining of therapeutic options and introducing of more targeted molecules, the prognosis of eosinophilic disorders might be significantly improved in the near future.[15]

Eosinophilia appears to be an under-reported public health problem in tropical settings with an estimated prevalence of 0.5-1-case/100,000 population in hospital settings. [16]

Infections especially helminths are the commonest cause of hypereosinophilia in our study, and the spectrum of infections is so wide that the demonstration of the specific infective agent is often difficult in resource-limited settings; necessitating an empirical course of anti-helminths in most of the patients. In contrary to the general perception in tropical countries, an underlying malignancy is diagnosed with nearly equal frequency compared to infections. An underlying malignancy is highly likely in patients with presence of blasts in peripheral blood, >5% blasts in bone marrow and bone marrow fibrosis. But there are no hematological or serological parameters, which can reliably be used to exclude an underlying malignancy, necessitating a thorough follow-up and comprehensive work-up in patients with eosinophilia.[17-20]

Conclusion:

Eosinophilia appears to be a common occurrence in tropical countries like ours with a high incidence in Eastern India due to poor socio-economic and hygiene status. Most common etiologies identified in this study were parasitic, protozoal or fungal infestations and infections. Allergy related problem also constituted a significant health problem in the local population. In a significant proportion of patients a definite etiology of eosinophilia could not be zeroed upon. Individuals of all ages can be affected by eosinophilia. Children and young adults usually had mild eosinophilia. Severe eosinophilia was seen in middle aged or elderly patients. The evaluation of unexplained eosinophilia in an asymptomatic individual is a challenging problem that requires knowledge about a wide variety of potential pathogens. Nevertheless, the prevention of morbidity by the diagnosis and prompt treatment of parasitic helminth infection is also an important task in these patients. This study also highlighted that despite of high prevalence of eosinophilia in tropical countries ,unfortunately, there is no data regarding the same that undermines the clinical relevance of this entity and many such studies are required in near future to find out the exact scenario of eosinophilia in India.

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