

## Approach to the Patients with Monocytosis

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### Abstract:

**Background:** The approach to the identifying the cause of monocytosis is a challenging problem. Moreover, the prevention of morbidity by identifying the cause of monocytosis and intervening therapeutically is an important task that must be approached systematically. There were several studies about monocytosis in different diseases and these studies suggested that monocytosis was associated with different causes, in which either monocytosis was important indicator for prognostic significance in some diseases or it was valuable for diagnostic importance in some diseases. So, study of monocytosis can give some clues and exact diagnosis will be achieved after doing appropriate history taking, physical examination and investigations.

**Methods:** A total of one hundred cases of monocytosis were obtained from 4210 cases those who came to the hospital laboratory for examination of blood for full blood count, then differential monocyte count was done by peripheral blood film examination. History taking, clinical examination and evaluation of investigations were recorded according to proforma.

**Results:** There were seventeen clinical conditions associated with monocytosis. They were tuberculosis (16%), acute viral infection (14%), dengue haemorrhagic fever (10%), malaria (9%), diabetes mellitus (8%), very severe pneumonia (8%), non-haemopoietic malignancy (6%), appendicitis (6%), chronic obstructive pulmonary disease (4%), HIV infection (3%), acute myocardial infarction (3%), bronchial asthma (3%), enteric fever (3%), non-Hodgkin lymphoma (2%), chronic myeloid leukaemia (2%), aplastic anaemia (2%), pyrexia of unknown origin (1%).

**Conclusion:** The most common disease associated with increased monocyte count was found to be tuberculosis which constitutes 16 %.

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## I. Introduction

### Background

Modern study of mammalian phagocytes began with Metchnikoff in the nineteenth century. The justification of designating the monocyte-macrophage system as the functional system for merely referred to as the reticuloendothelial system includes the finding that tissue macrophages have important functional characteristics (particularly, pronounced phagocytic ability in vivo and adhesiveness to glass or plastic surfaces in vitro) and kinetic studies that identify a marrow cell as the precursor of the blood monocyte, and the monocyte as the precursor of the tissue macrophages. (1)

The monocyte responds to inflammation and chemotatic stimuli by active diapedesis across the vessel wall into the inflammatory focus, where it can mature into the macrophage, with greater phagocytic activity and increased content of hydrolytic enzymes. Free macrophages also are present in pleural, peritoneal and synovial fluid. (1)

Monocyte and macrophages cells an important role in the integrity of the immune system. As in the main part of the phagocyte cell system monocyte-macrophage cells perform diverse functions including phagocytosis of microorganisms, killing of antibody-coated erythrocytes or tumor cells (antibody dependent cellular cytotoxicity), spontaneous killing of unsensitized tumor cells, antigen presentation to helper T lymphocytes, secretion of different biologic substances, they also serve as a reservoir for human immunodeficiency virus. (1)

## II. Methods

This study is hospital & laboratory based, cross-sectional descriptive and analytical study. Patients who show monocytosis, that is, absolute monocyte count  $>0.8 \times 10^9/L$  in full blood count by automatic coulter counter (SYSMEX KX-21 Automatic Haematological Analyzer) are selected. Then differential monocyte count was done by peripheral blood film examination. Absolute monocytosis cases were reviewed and followed for further investigation. Clinical data collection such as history taking, clinical examination and evaluation of investigations were recorded according to proforma.

### Ethical Consideration

The patients were explained about the detailed procedure and written informed consent was obtained before the assessment of study. Patients who do not wish to participate or request to withdrawal from the study at anytime doing this research period would be allowed without effecting the current or further treatment. Ethical issue approved by board of University of Medicine 2, Yangon.

### Prevalence

In this study, 100 cases of monocytosis were obtained during the period of August 2007 to March 2008. They were selected from 4210 in-patients for whom examination of blood for full blood count was requested at NOGH Pathology Department. Out of 4210 cases, 133 cases showed monocytosis in differential count. Among them 100 cases were obtained for the study. Thirty three out of 133 cases were from out-patient department. Thus, overall prevalence of monocytosis cases in this study was 3.1% (133/4210x100).

They came from various wards of NOGH. They were admitted for diseases other than causes of monocytosis, which was an accidental finding. Among them fifty nine cases were from the medical ward, twenty cases from the child ward, fourteen cases from the surgical ward, three cases from cardiac medical ward, two cases from orthopaedic ward and two cases from O.G ward.

### Age and sex distribution

The youngest patient in this study was 1/12 year old male and the oldest patient was eighty six years old male. Fifty-one cases (51%) were male and forty-nine cases (49%) were female.

## III. Results

Seventeen possible causes of monocytosis were detected in this study. Majority of them were due to infection. Sixteen out of hundred cases (16%) were associated with tuberculosis: twelve cases of pulmonary tuberculosis, two cases of tuberculous osteomyelitis, one case of tuberculous meningitis and one case of miliary tuberculosis. Fourteen cases out of hundred cases (14%) were associated with acute viral infection. Ten cases (10%) were associated with Dengue Haemorrhagic Fever (DHF): seven cases of DHF grade I, two cases of DHF grade III and one case of Dengue Shock Syndrome (DSS). Nine cases (9%) were associated with malaria infection: eight cases of clinical malaria and one case of cerebral malaria. Eight cases (8%) were associated with diabetes mellitus. Eight cases (8%) were found to have associated with very severe pneumonia.

Six cases (6%) were associated with non-haemopoietic malignancy: two cases of malignant ovarian tumour, two cases of carcinoma of breast and two cases of carcinoma of rectum. Six cases (6%) were associated with appendicitis: four cases of acute appendicitis, one case of appendicular abscess and one case of appendicular mass. Only six haematological disorders were identified as associated with monocytosis: two cases of Non-Hodgkin lymphoma, two cases of chronic myeloid leukaemia and two cases of aplastic anaemia.

Three cases (3%) were associated with HIV infection and another three cases (3%) were associated with enteric fever. Three cases (3%) were associated with acute myocardial infarction. Four cases (4%) were associated with chronic obstructive pulmonary disease and three cases (3%) were associated with bronchial asthma. Only one case (1%) out of hundred cases was associated with pyrexia of unknown origin found in two years old girl.

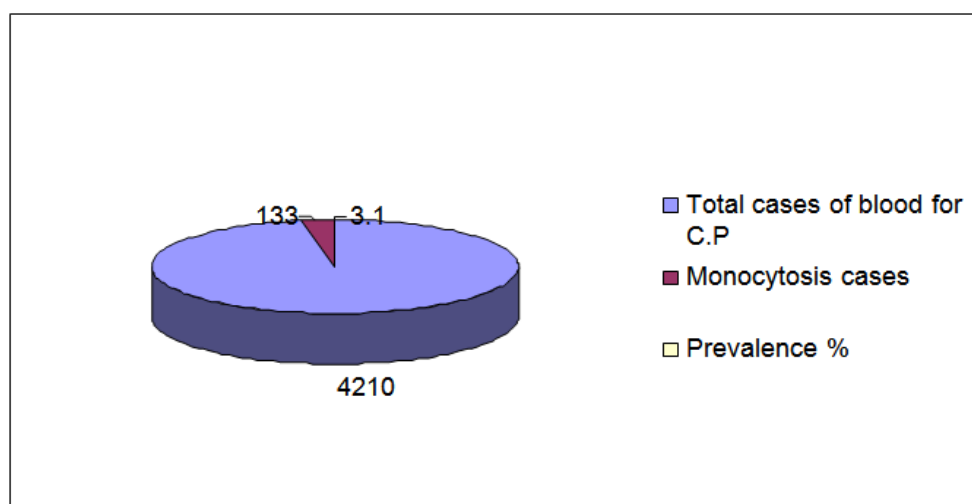


Figure (1) Prevalence of monocytosis

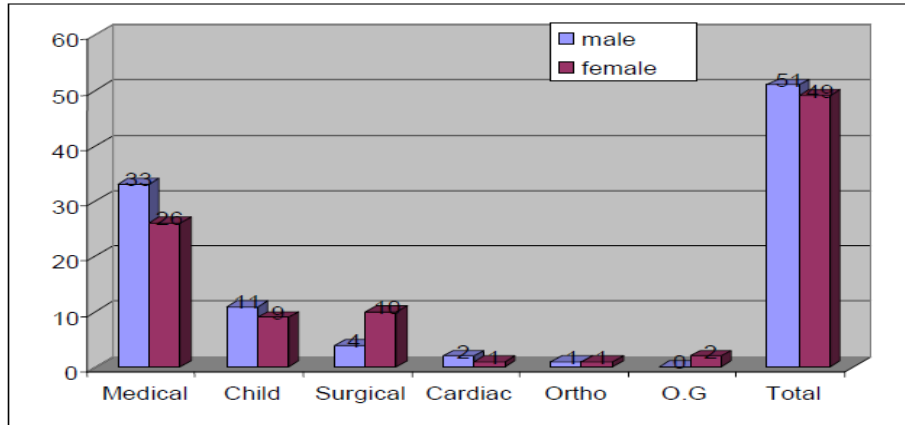


Figure (2) Case distribution in various wards of NOGH

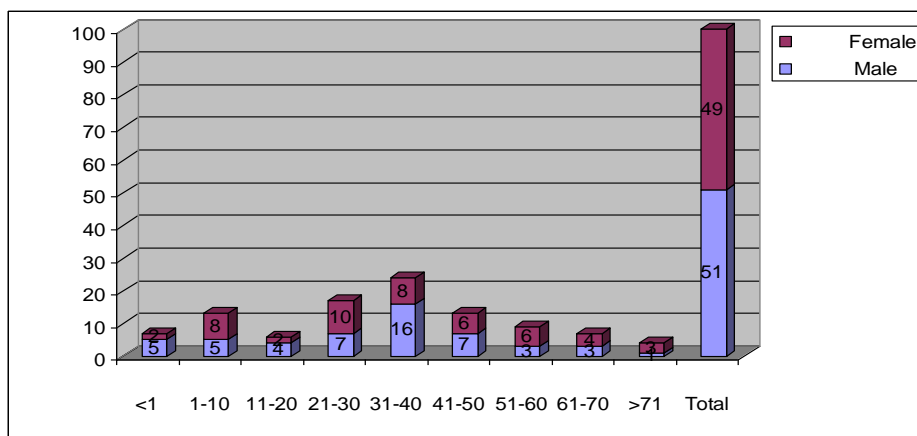


Figure (3) Age and sex distribution in various wards of NOGH

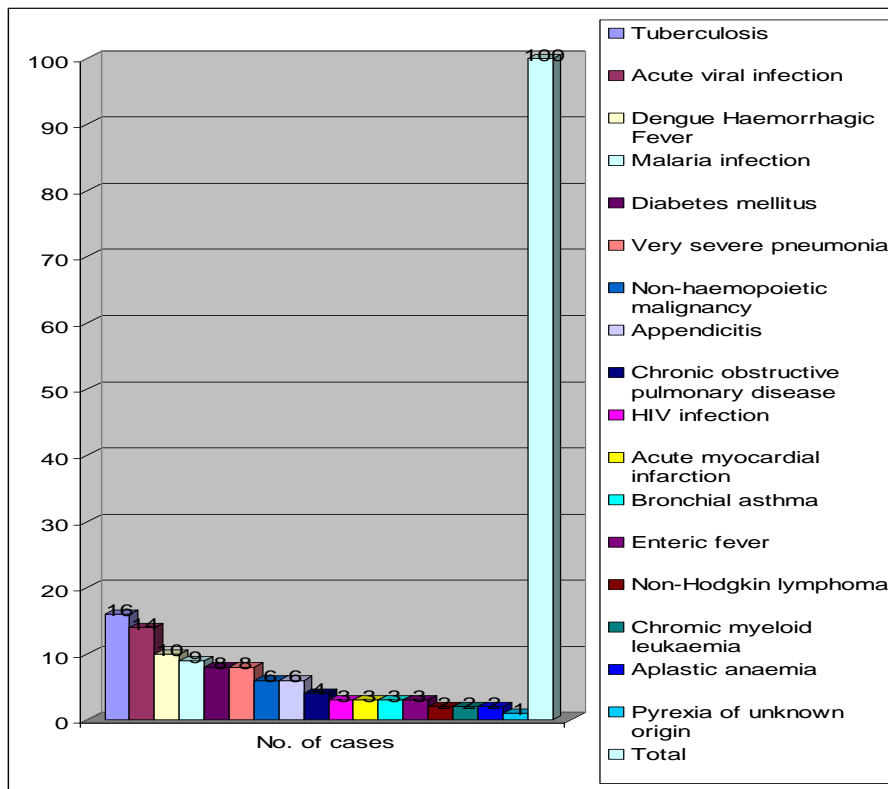
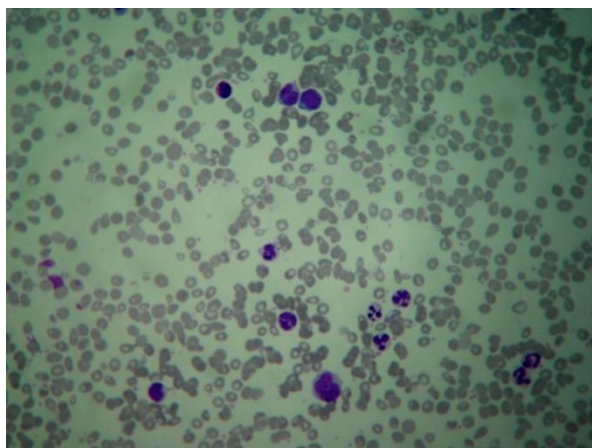
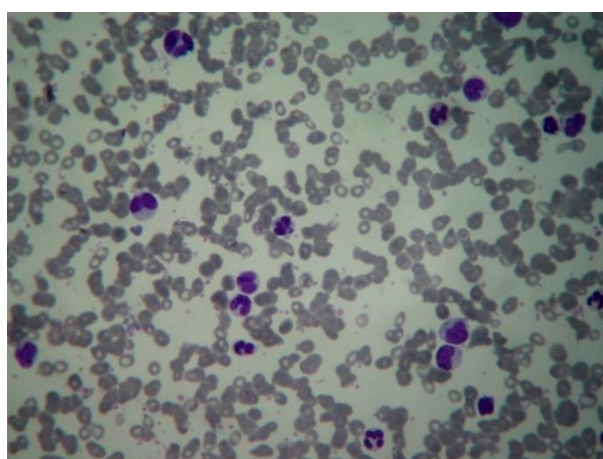


Figure (4) Causes of monocytosis



**Figure (5) Monocytosis in peripheral blood film of tuberculosis case (Leishman stain x 400)**



**Figure (6) Monocytosis in peripheral blood film of chronic myeloid leukaemia Case (Leishman stain x 400)**

#### IV. Discussion

This study showed the monocytosis can occur in all ages and there was no significant difference in sex incidence (51% of male and 49% of female). Thus, the age and sex distribution of the monocytosis is mainly depends on underlying causes. In this study, the main cause of monocytosis was tuberculosis, which can affect all age and sex group.

In this study seventeen possible causes of monocytosis were detected. Among them, tuberculous infection was the most common causes, which constituted sixteen cases (16%) because tuberculosis is common in this country. Lichtman stated that tuberculosis was one of the leading cause of monocytosis, because of the role of monocytes in granuloma (tubercle) formation and monocyticleukemoid reaction have been reported in this disease. (2)

The next common cause of monocytosis was acute viral infection, which constituted fourteen cases and dengue haemorrhagic fever which constituted ten cases. Ravandi stated that microorganisms responsible for macrophage activation through macrophage activation factor (MAF), identified as INF- $\gamma$ , as well as IL-2, IL-4, M-CSF and GM-CSF either directly or indirectly. They stimulate monocyte/macrophage proliferation, increase adhesive receptor expression and they stimulate the production of proteolytic agents responsible for pathogen clearance. (3)

There were nine cases of malaria infection and it is also common in this country. The study of Halim et al (2002) stated that monocytosis observed in malaria patient especially those on antimalaria therapy. Thus monocytosis, may enhance the predisposition to a favourable clinical outcome. (4)

There were nine cases of diabetic mellitus were associated with monocytosis. The possibility is that the diabetic mellitus patients are immunocompromised and they prone to get infection. So due to underlying infection in somewhere, their blood picture will have monocytosis.

There were six cases of non-haemopoietic malignancy. Beutler et al stated that sixty percent (60%) of patients with non-haematologic malignancy exhibit a monocytosis, which is independent of the presence or absence of metastatic disease. (5)

There were three cases of HIV infection associated with monocytosis. Costello explained that in many of the patient with HIV infection who shows increased numbers of marrow histiocytes, there is no obvious infective cause and it is likely that HIV itself is probably by initiation of cytokines production, resulting in macrophage stimulation. (6)

There were three cases of acute myocardial infarction from cardiac medical ward associated with monocytosis. The study of Maekawa et al stated that the peripheral monocytosis is associated with pump failure, left ventricular aneurysm and long-term outcome after reperfused acute myocardial infarction, suggesting a possible role of monocytes in the development of post-infarct left ventricular remodeling. (7)

There were six cases of haematological disorders. Lichtman stated that most of the haematological disorders can be associated with monocytosis. Monocytosis can occur in Non-Hodgkin lymphoma and can increase with exacerbation of disease activity. Patients with chronic myeloid leukaemia may have an increased proportion of monocytes and in variants of CML, monocytosis may be striking. (2)

There was one case of pyrexia of unknown origin found in two years old girl from child ward associated with monocytosis and the underlying cause has not been detected. The study of Cunha BA et al found that fever of unknown origin due to underlying preleukaemia or myelodysplastic syndrome is associated with monocytosis. (8)

## **V. Conclusion**

This is a prospective study of monocytosis cases based on hospitalized patients in North Okkalapa General Hospital. This study mainly emphasized of various causes of monocytosis among in-patients.

In this study, seventeen possible causes of monocytosis were identified. Most of them are as described in literature, for example, tuberculosis, malaria, non-haemopoietic malignancy. But some cases which are not consistent in causes of monocytosis such as diabetic mellitus, HIV infection and bronchial asthma.

Tuberculosis is very common in this country and hence a major cause of monocytosis as in other developing countries. The second common cause in this study population is acute viral infection which is also common in our country. Other causes such as dengue haemorrhagic fever, malaria, diabetic mellitus and very severe pneumonia in child patients are common in the population.

Non- haemopoietic malignancy, haematological disorders were found to have associated with monocytosis. In appendicitis, chronic obstructive pulmonary disease, bronchial asthma, and pyrexia of unknown origin which were identified as the main cause of admission and they were associated with monocytosis. In these cases, because of the short duration of study and limited facilities, we were unable work up in detail to identify the exact cause of monocytosis.

However, monocytosis is an interesting topic, which associated with a wide variety of disease. It is related with body's immune system and many cytokines and chemokines are involved in their accumulation and function. The knowledge of monocytosis and their function in various diseases are still developing and further research should be directed in those aspects.

If we can develop advanced technology such as cytokine analysis, immunophenotyping, molecular biology technique and genetic study, we hope to give more valuable information about the monocytosis and improve the management.

In conclusion, to our knowledge, this is the first report of causes of monocytosis in Myanmar. A limitation of this study is its small sample size in a single hospital.

### **Author's contribution**

SS was principal authors who conceptualized the manuscript, wrote background and methods sections, results and discussion sections of the manuscript, performed data analysis, interpretation of the results, and revised the final drafts of the manuscript.

LLW, TYA, TMM, and KKS assisted in conceptualization of the manuscript and data analysis.

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**Competing interests:** none

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