Myeloperoxidase Index distribution in acute myeloid leukemia patients of Northwest Iran

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2016,April

Introduction

Myeloperoxidase

- Myeloperoxidase (MPO) is a peroxidase enzyme that in humans is encoded by the MPO gene on chromosome17.

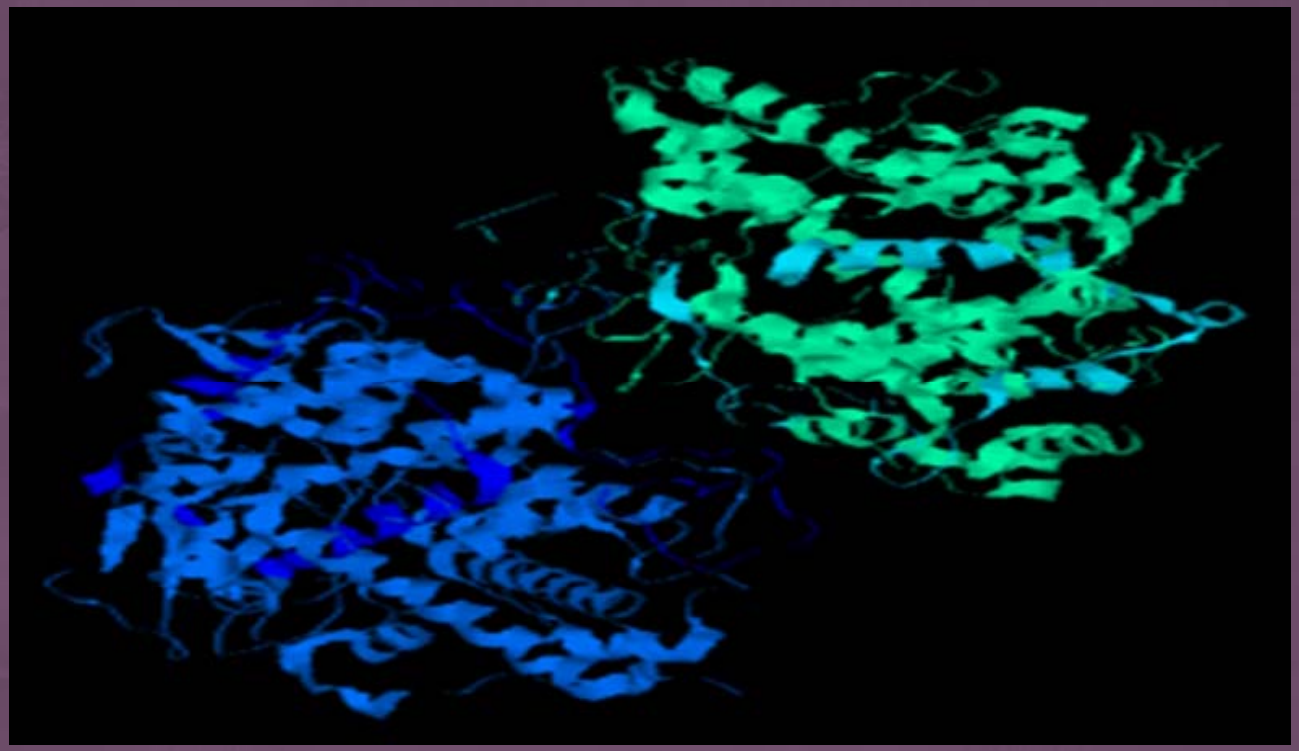
- MPO is most abundantly expressed in neutrophil granulocytes, and produces hypohalous acids to carry out their antimicrobial activity.

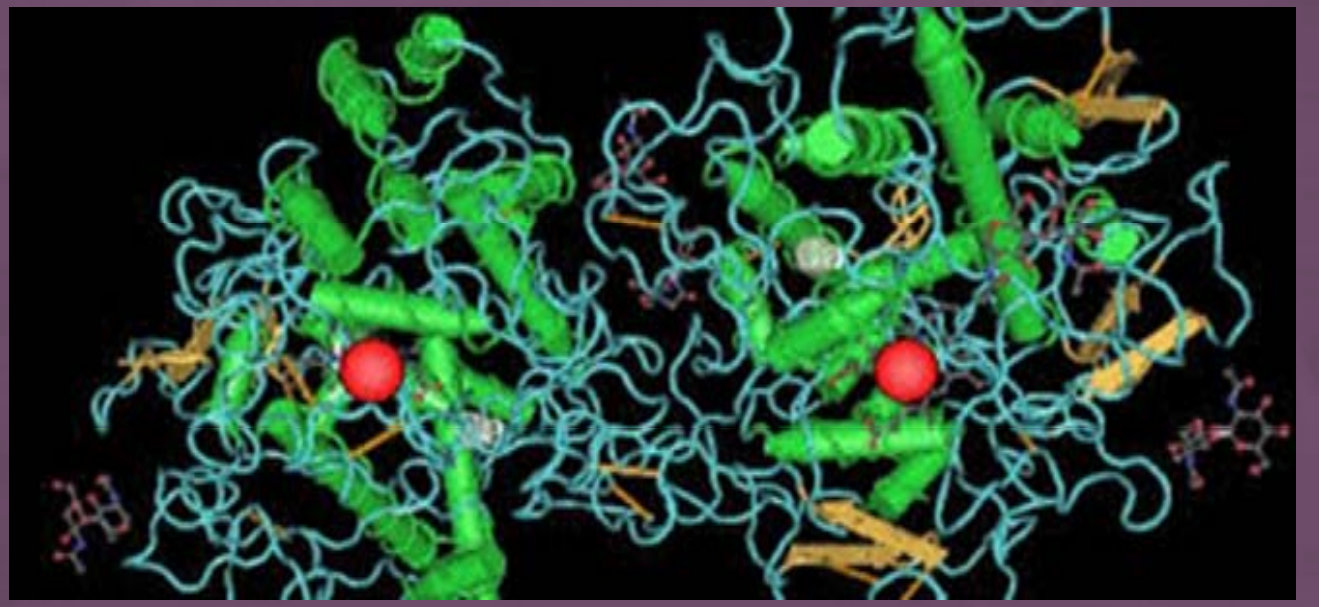
- It is a lysosomal protein stored in azurophilic granules of the neutrophil and released into the extracellular space during degranulation.

Introduction

- MPO has a heme pigment, which causes its green color in secretions rich in neutrophils, such as pus and some forms of mucus.
- The 150-kDa MPO protein is a cationic homo dimer consisting of two 15-kDa light chains and two variable weight glycosylated heavy chains bound to a prosthetic heme group.
- Together, the light and heavy chains form two identical 73-kDa monomers connected by a cystine bridge at Cys153.

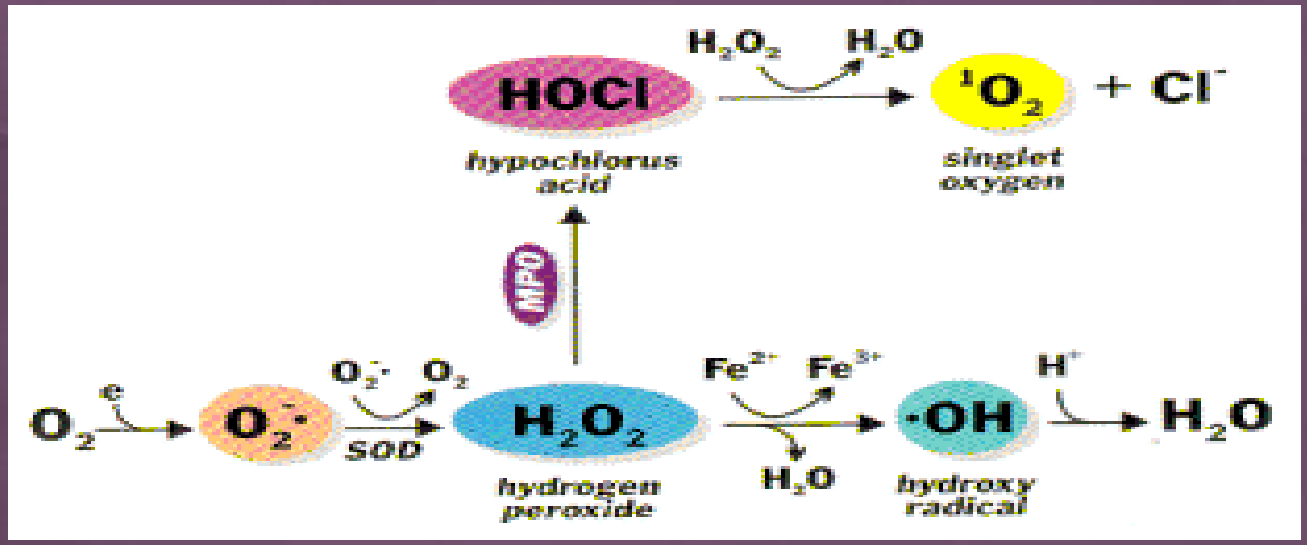
Introduction





Introduction

- MPO is a member of the XPO subfamily of peroxidases and produces hypochlorous acid (HOCl) from hydrogen peroxide (H2O2) and chloride anion (Cl−) (or the equivalent from a non-chlorine halide) during the neutrophil's respiratory burst.



- It requires heme as a cofactor.

Introduction

- Furthermore, it oxidizes tyrosine to tyrosyl radical using hydrogen peroxide as an oxidizing agent.
- Hypochlorous acid and tyrosyl radical are cytotoxic, so they are used by the neutrophil to kill bacteria and other pathogens.
- However, this hypochlorous acid may also cause oxidative damage in host tissue.
- Moreover, MPO oxidation of apoA-I reduces HDL-mediated inhibition of apoptosis and inflammation.

Introduction

- Myeloperoxidase deficiency is a hereditary deficiency of the enzyme, which predisposes to immune deficiency.
- Antibodies against MPO have been implicated in various types of vasculitis.
- Antibodies are also known as anti-neutrophil cytoplasmic antibodies (ANCAs).

Introduction

- Recent studies have reported an association between elevated myeloperoxidase levels and the severity of coronary artery disease.
- And Heslop et al. reported that elevated MPO levels more than doubled the risk for cardiovascular mortality over a 13-year period.
- It has also been suggested that myeloperoxidase plays a significant role in the development of the atherosclerotic lesion and rendering plaques unstable.

Introduction

- An initial 2003 study suggested that MPO could serve as a sensitive predictor for myocardial infarction in patients presenting with chest pain.
- The 2010 Heslop et al. study reported that measuring both MPO and CRP (C-reactive protein; a general and cardiac-related marker of inflammation) provided added benefit for risk prediction than just measuring CRP alone.

Introduction

- Immunohistochemical staining for myeloperoxidase used to be administered in the diagnosis of acute myeloid leukemia to demonstrate that the leukemic cells were derived from the myeloid lineage.

- Myeloperoxidase staining is still important in the diagnosis of myeloid sarcoma,contrasting with the negative staining of lymphomas, which can otherwise have a similar appearance.

Introduction

- Myeloperoxidase is the first and so far only human enzyme known to break down carbon nanotubes, allaying a concern among clinicians that using nanotubes for targeted delivery of medicines would lead to an unhealthy buildup of nanotubes in tissues.

Introduction

Acute myeloid leukemia

- Acute myeloid leukemia is a clonal heterogenic disorder of hematopoietic progenitor cells that is most common in adults.
- AML constitutes less than 1% of all cancers and 25% of all leukemia. It is more common in adults and its prevalence increases with age.
- It was estimated that among 52,380 new cases of leukemia in the United States in 2014, 18,860(36%) of them were AML cases and among 24,090 estimated leukemia death, 10, 460 (43%) instances were due to AML.

Material and Methods

Patient Selection

- In this descriptive study, forty-six new cases of adult denovo AML, who diagnosed in Shahid Ghazi hospital (Tabriz, Iran), from 2012-2014 was included.
- AML diagnosis confirmed, according to bone marrow aspiration and peripheral blood smears, total blood count, cytochemistry and immunophenotyping.
- Two oncologists classified patients based on French-American-British (FAB) cooperative group criteria, in eight subtypes (M0-M7).
- Cases, which had received any treatment and with present or past other related diseases history, were excluded.

Material and Methods

- MPXI analyzed using the first blood samples of patients with the automatic analyzer (H1, Tecknicon, USA).

Results

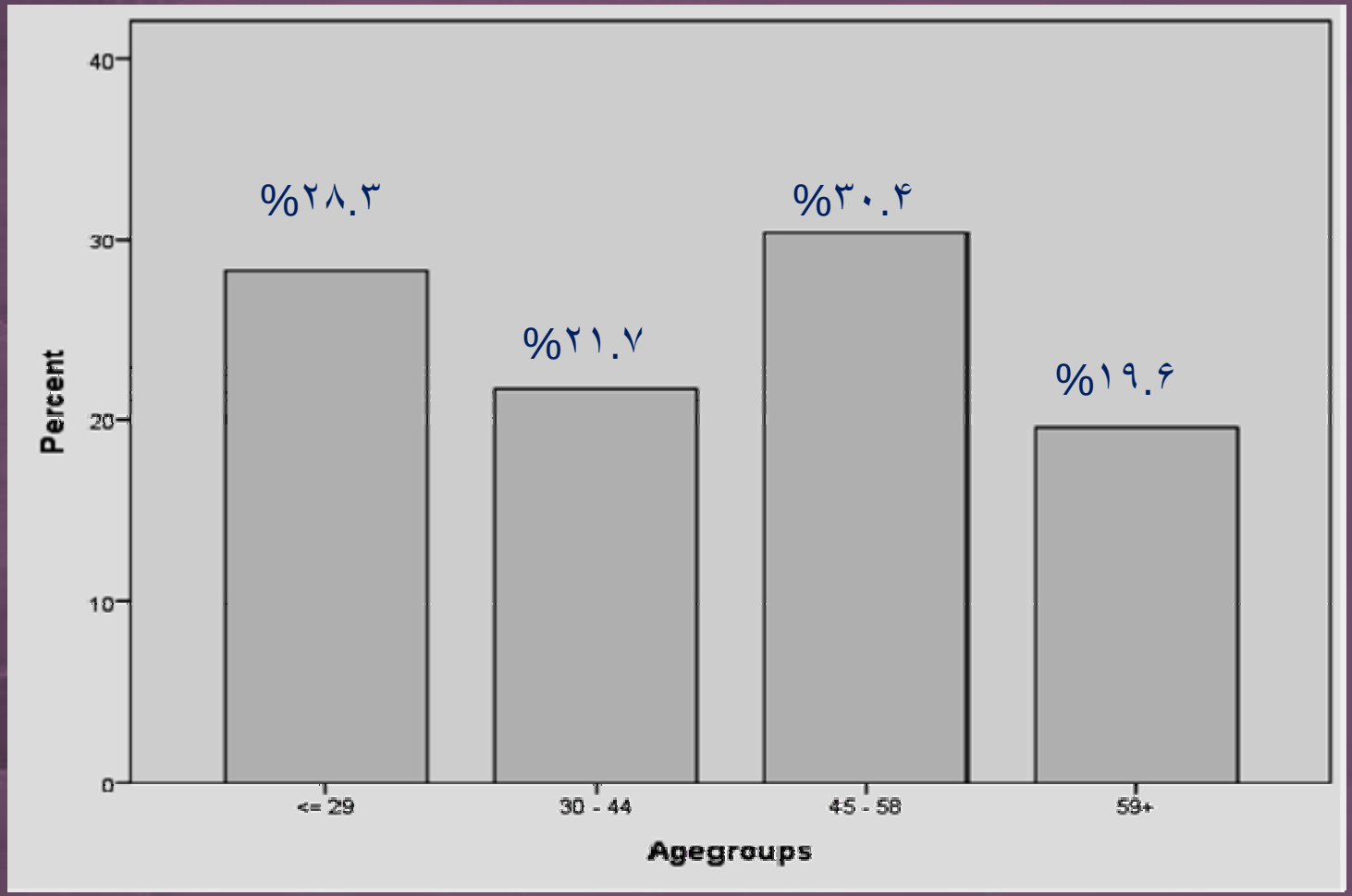
Clinical, Morphologic and Hematologic Characteristics

Summary of Clinical, Hematologic and Morphologic Characteristics for total Acute Myeloid Leukemia Patients

	Number (%)	Mean(SD)	Range(min-max)
Age		44(16.59)	64(16-80)
Male/Female	21(45.7%)/25(54.3%)		
FAB	M0 1(2.2%) M1 5(10.9%) M2 16(34.7%) M3 4(8.7%) M4 8(17.4%) M5 4(8.7%) M7 1(2.2%) Unknown 7(15.2%) Total 46(100%)		
WBC ($\times 10^3$ /μl)		35.65(49.19)	201.43(0.57-202)
Hb(g/dl)		8.5(1.68)	6.7(4.9-11.6)
PLT ($\times 10^3$ /μl)		73.08(92.97)	493(12-505)
Blast (%)		28.14(20.03)	85(3-88)

Results

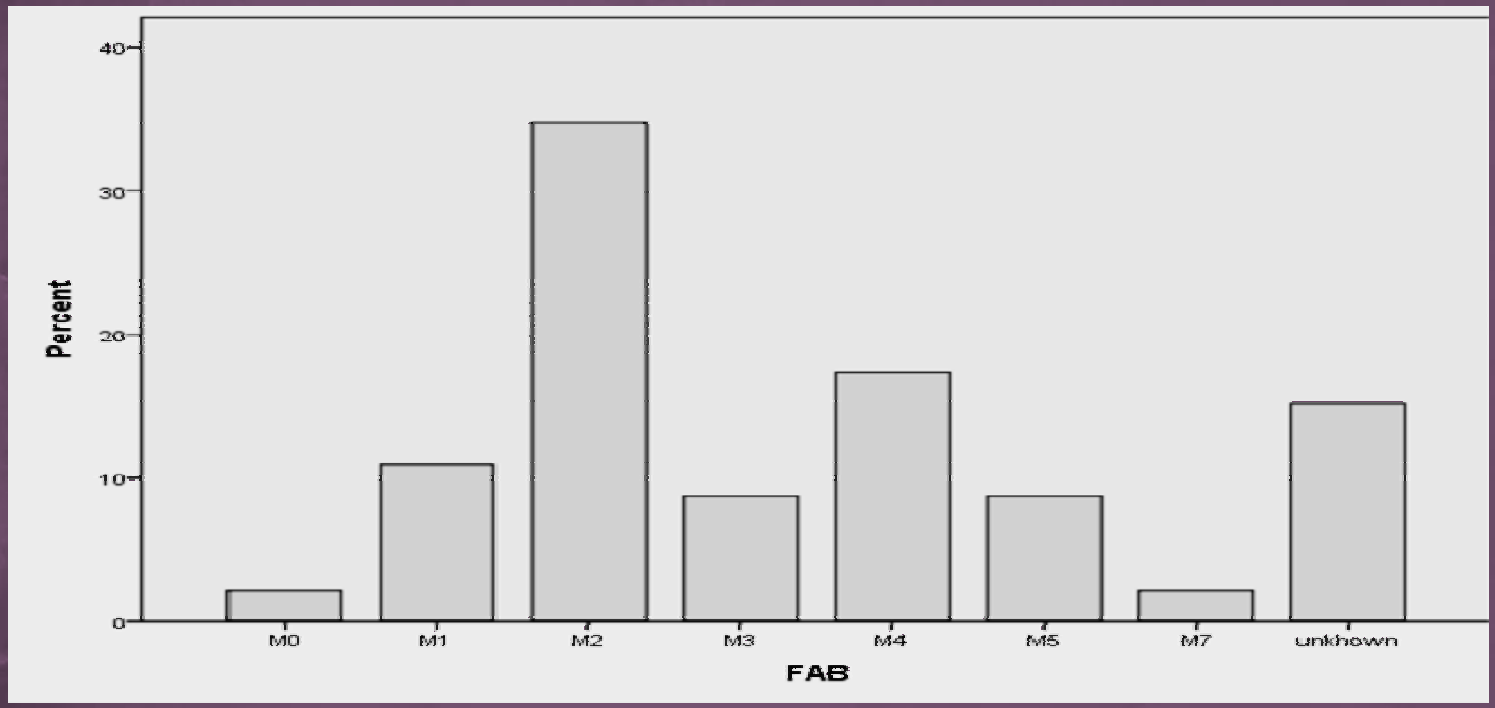
Age group distribution



- Most patients are in 45-58 age group and all patients are relatively young.

Results

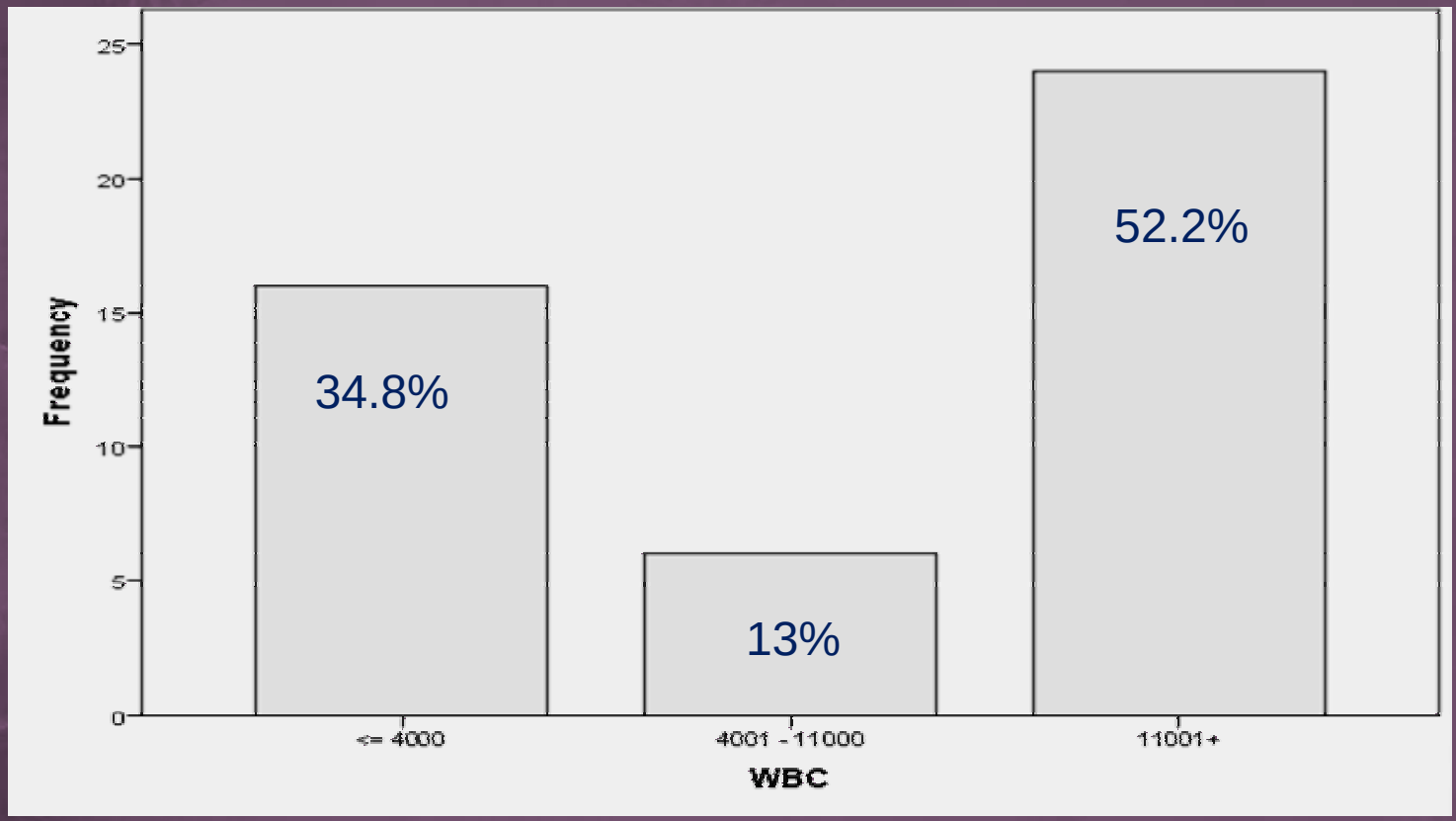
Frequency of patients in FAB classification



- Frequency of M2,M4,M1,M3,M5 are higher respectively.

Results

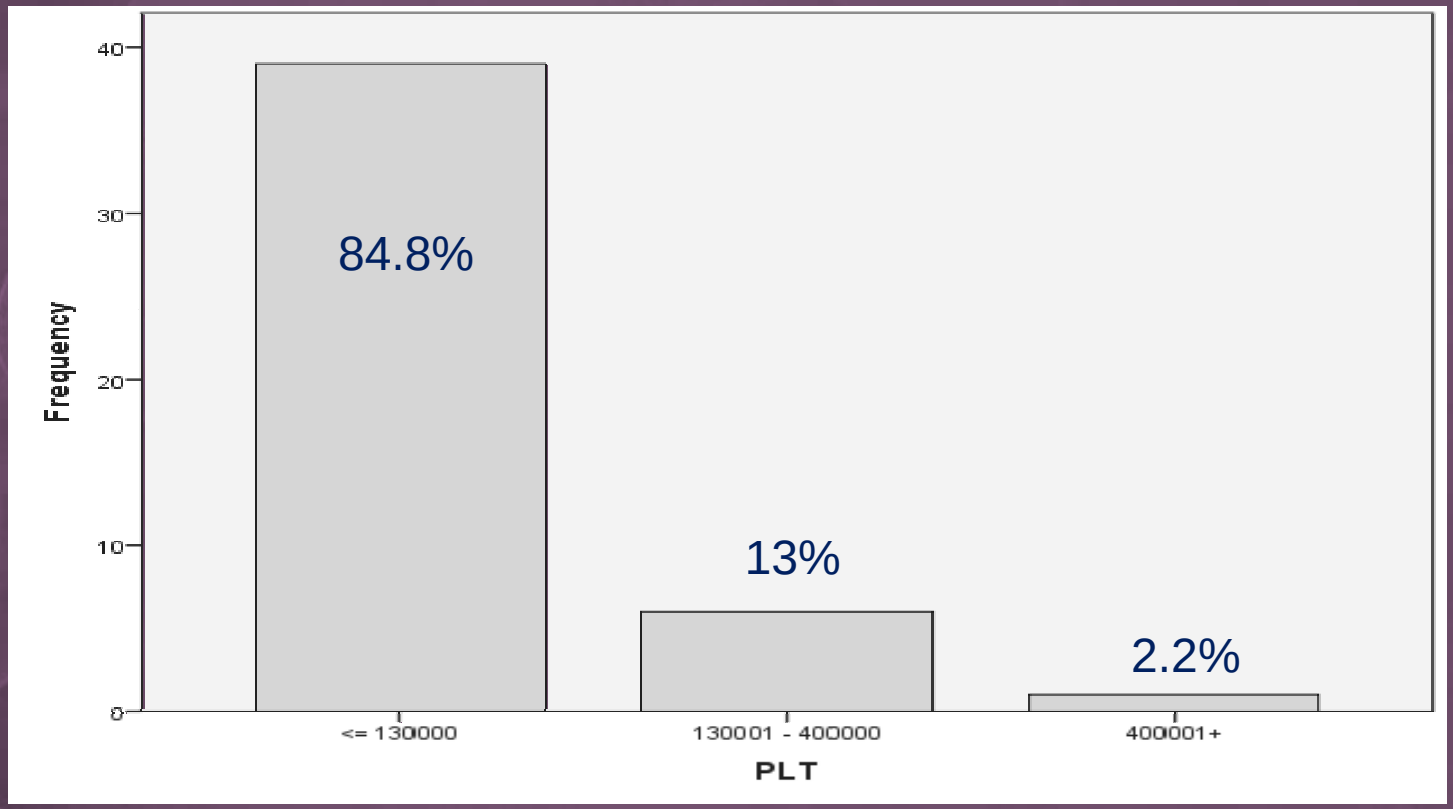
Distribution of white blood cell



- Most of the patients have leukocytosis and 34.8% of patients have leukopenia.

Results

Distribution of platelets

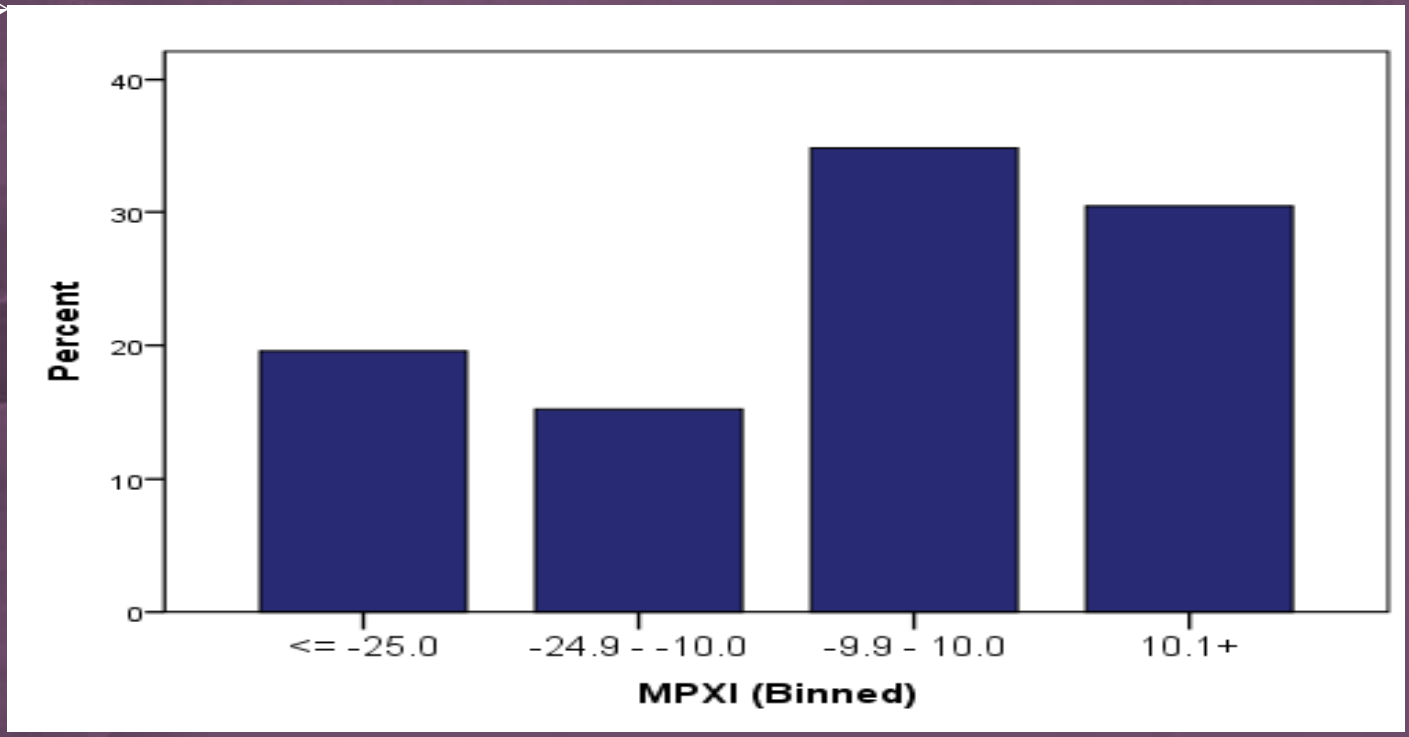


- Most patients with platelet count less than 130000 /µl, have thrombocytopenia.

Results

Distribution of MPXI

- Most of the patients are in normal range (-10 - +10), after that 30.4% of patients have high value of MPXI (> 10) and 19.6% of patients with values below -25 have myeloperoxidase deficiency and autosomal recessive anomaly.



Results

- Based on FAB classification most of the patients with high value of MPXI are in M3 and M4 subtypes and most of the patients with myeloperoxidase deficiency are in M2 subtype.

		MPXI (Binned)				Total
		<= -25.0	-24.9 - -10.0	-9.9 - 10.0	10.1+	
FAB	M1	2	0	2	1	5
	M2	5	3	6	2	16
	M3	0	0	0	4	4
	M4	1	1	2	4	8
	M5	0	1	2	1	4
	M7	0	1	0	0	1
	unknown	1	0	4	2	7
	M0	0	1	0	0	1
Total		9	7	16	14	46

Discussion

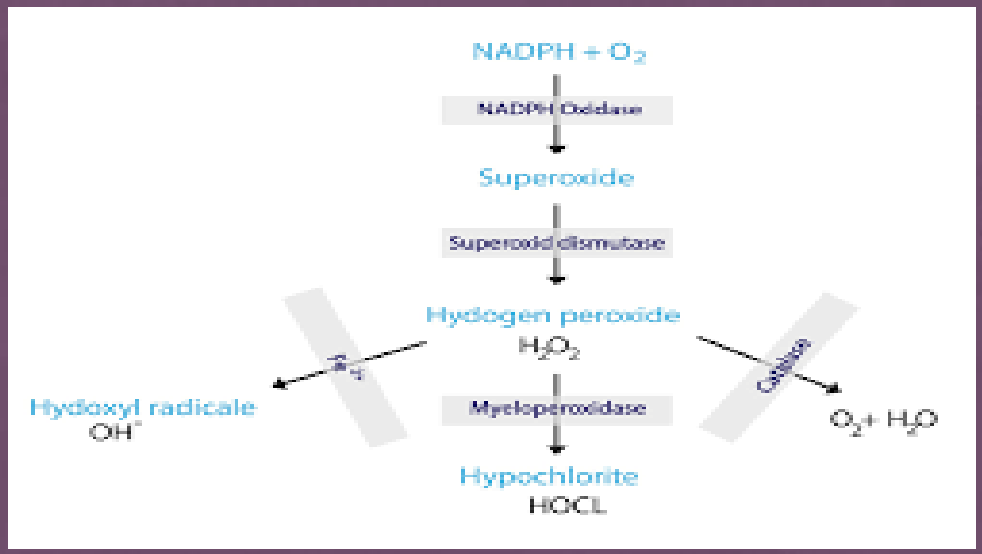
- Taylor and Bain2 have reported that an elevated neutrophil myeloperoxidase index (MPXI) may be indicative of a diagnosis of megaloblastic anemia.

- Study in Tabriz concluded that MPXI >20 denoted megaloblastic and MPXI <-11.6 denoted aplastic anemia.

Discussion

- In the other study in Tabriz researchers concluded that mean MPXI is almost always negative in M1,M4 and M5 subtype but it may be positive in M3.

- All of our patients in M3 subtype have high value of MPXI but in other subtypes results are different and especially in M2 subtype, result are interesting and result don't reject relationship of AML subtypes and MPO ,but other studies with higher number of patients are recommended.


NADPH + O_2
NADPH Oxidase
Superoxide
Superoxid dismutase
Hydrogen peroxide
H_2O_2
Hydroxyl radicale
OH^-
Catalase
O_2+ H_2O
Myeloperoxidase
Hypochlorite
HOCL