Multivariate Analysis of Prognostic Factors Affecting Egyptian Patients with Acute Myeloid Leukemia

Thesis

Submitted for partial fulfillment of

Master degree in internal medicine

By

Mohammed Salah Hamed Imam

M.B.B.Ch (Al Azhar university)

Supervised by

Prof. Dr: Fathy Ghamry Abdel-Razek

Professor of internal medicine

Faculty of Medicine – Al Azhar University

Prof. Dr: Essam Abdelwahed Hassan

Professor of internal medicine

Faculty of Medicine-Ain Shams University

Dr : Mahmoud Afifi El-Sayed

Lecturer of Internal Medicine

Faculty of medicine -Al Azhar University

Dr : Mahmoud Abdel-Rasheed Abdel-Khalek

Lecturer of Internal Medicine

Faculty of medicine -Al Azhar University

Dr : Amro Mohamed Sedky El-Ghammaz

Lecturer of Internal medicine and haematology

Faculty of Medicine – Ain Shams University

Faculty of Medicine – Al Azhar university

2014

Acknowledgement

First of all, I would to thank ALLAHmost gracious, most merciful for helping me to go through this work and for letting it come to an end.

I wish to express my heartily thanks and appreciation to**Prof.Dr.FathyGhamry Abdel-Razek**Professor of Internal Medicine, Faculty of Medicine, Al-Azhar University, for devising the plan of work and for his valuable supervision, suggestion, discussion, constructive criticism.

I would like to express my deepest thanks to **Prof Dr. EssamAbdelwahed Hassan**Professor of Internal Medicine and clinicalhaematology,Faculty of Medicine,Ain Shams University, for his kindness and suggesting study of this research.

I also would like to express my deepest thanks to **Dr. MahmouedAfifi El-sayed**lecturer of internal medicine,Faculty of Medicine, Al-Azhar University.

I am so grateful and deeply obliged to**Dr. Mahamoued Abdel-Rasheed Abdel-Khalek**lecturer of Internal Medicine, Faculty of Medicine,Al-Azhar University.

I would like to express, my deepest gratitude, thankfulness and appreciation to **Dr. Amro MohamedSedky El Ghammaz**

Lecturer of Internal Medicine and clinical haematology, Faculty of Medicine, Ain Shams University, for his infinite support, constructive criticism, valuable supervision, continual encouragement and sincere help during this work.

I would like to express my deepest thanks to my patients for helping me. Finally, my deepest thanks to all member ofmy family, they were always the supportive hand to me, without their kind care, continuous support and encouragement, this work would never been accomplished.

List of contents

Page numbersTitle

List of abbreviations

AP	Acid phosphatase.
ALL	Acute lymphocytic leukemia.
AML-NC	Acute myeloid leukemia with normal cytogenetics.
AMl	Acute myeloid leukemia.
APL	Acute promyelocytic leukemia.
ATRA	All trans retinoic acid.
BM	Bone marrow.
BAALC	Brain and acute leukemia cytoplasmic gene.
BRCP	Breast cancer resistance protein.
CBL	Casitas B-cell lymphoma.
CEBPA	CCAAT enhancer-binding protein alpha.
CAE	Chloro acetate esterase.
CEC	Circulating endothelial cells.
CD	Cluster of differentiation
CSF	Colony stimulating factor.
CGH	Comparative Genomic Hybridization.
CBC	Complete blood count.
CR	Complete remission.
CT	Computerized tomography.
CBF	Core binding factor.
CRP	C-reactive protein.
DNA	Deoxyribonucleic acid.
DIC	Disseminated intravascular coagulation.
EM	Electron Microscopy.
ERG	ETS-related gene.
ETS	*E-twenty six*.
EGIL	European Group for Immunological Characterization of Leukemia.

ELN	European Leukemia Net.
FISH	Florescence in-situ hybridization.
FLT3	FMS-like tyrosine kinase3.
FAB	French-American-British classification.
GVL	Graft-versus-leukemia.
GM-CSF	Granulocyte-monocyte Colony stimulating factor.
HSC	Hemopoietic stem cell.
INFs	Interferons.
IL-	Interleukin.
ITD	Internal Tandem Duplication.
Inv.	Inversion.
JMD	Juxtamembrane domain.
LIF	Leukemia inhibitory factor.
LDL	Low density lipoprotein.
MN1	Meningioma 1 gene.
MoAbs	Monoclonal antibodies.
M-FISH	Multicolor FISH
MDR-1	Multidrug resistance-associated protein.
MDS	Myelodysplastic syndrome.
MPO	Myeloperoxidase.
NSE	Non specific esterase.
NPM1	Nuclophosmine.
PTT	Partial thromboblastine time.
PAS	Periodic acid Schiff.
PB	Peripheral blood.
Pgp	P-glycoprotein.
PCR	Polymerase chain reaction.
+ve	Positive.
PT	Prothrombin time.
ROS	Reactive oxygen species.
RP	Retinoblastoma gene.
RBP-4	Retinol Binding protein -4

RNA	Ribonucleic acid.
SKY	Spectral Karyotype.
SCT	Stem cell transplantation.
SDF-1	Stromal derived factor 1.
SBB	Sudan black B.
TDT	Terminal deoxynucleotidyl transferase.
TLC	Total leukocytic count.
TGF	Transforming growth factor.
t(8;21)	Translocation between chromosome 8&21.
TSG	Tumor supressor gene.
TNF	Tumour necrosing factor.
TKD	Tyrosine kinase domain.
Wt-1	Wilms tumor-1 gene.
WHO	World health organization.

List of tables

List of figures

I) INTRODUCTION

Acute myelogenous leukemia (AML) is a malignant disease of the bone marrow in which hematopoietic precursors are arrested in an early stage of development. Most AML subtypes are distinguished from other related blood disorders by the presence of more than 20% blasts in the bone marrow (***Vardiman et al., 2002).***

Several factors have been implicated in the causation of AML, including antecedent hematologic disorders, familial syndromes, environmental exposures, and drug exposures. However, most patients who present with de novo AML have no identifiable risk factor (***Smith et al., 2004).***

Patients with AML present with symptoms resulting from bone marrow failure, symptoms resulting from organ infiltration with leukemic cells, or both. The time course is variable. Workup for AML includes blood tests, bone marrow aspiration and biopsy, flow cytometry, analysis of genetic abnormalities, and diagnostic imaging (***Larson et al., 1999).***

Most AML patients should be advised to undergo treatment promptly after diagnosis. The AML is the most common type of acute leukemia in adults. The condition is lethal within a few

months without treatment, but most young patients reach complete remission with chemotherapy. Many of them will relapse after a while, but an increasing number of young people survive for a long time **(Tangen et al., 2008).**

Although remission rates are lower in aged patients, a significant proportion enters remission **(Lichtman and Liesveld, 2006).** Therapy for AML consists of cytotoxic chemotherapy alone or stem cell transplantation (SCT) after chemotherapy **(Sievers et al., 2001).**

Aim of the work

The aim of this study is to show the impact of risk factors on the outcome of acute myeloid leukemia in Egyptian patients as regard remission and survival rates and consequently can modulate therapy for best outcomes.

II) GENERAL FEATURES ON ACUTE MYELOID LEUKEMIA

A) Definition:

Leukemia can be described as a cancerous change in the early cells from which mature blood cells develop. This precursor cell is called hemopoietic stem cell (HSC). Once leukemia arises, it results in an excessive accumulation of abnormal hemopoietic cells, called blast cells, in the bone marrow (BM) and peripheral blood (PB) **(Mughal et al., 2006).**

The term acute myeloid leukemia (AML) refers to a heterogenous group of marrow-based neoplasms that have clinical similarities but distinct morphologic, immunophenotypic and cytogenetic features **(Head, 2004).**

B) Epidemiology:

Incidence:

The AML is the most common type of leukemia in adults, as it accounts for approximately 25% of all adult leukemias in the Western world **(Greenlee et al., 2001).** The annual incidence rate of pediatric AML is now 10/1,000,000 in Japan, against 5 to

9/1,000,000 in the USA and Europe **(Tabuchi, 2007).** The incidence of AML in European standard population was 3/100,000 **(Phekoo et al., 2006).**

The lower rates of leukemia reported in sub-Saharan Africa probably represent failure of diagnosis or reporting to some extent ***(Parkin et al., 2005).***We should therefore use caution, when drawing conclusions based on the varying prevalence and incidence, as an indication of clustering of cases or an environmental or genetic effect, as this may simply be due to the deficiency of statistics in Africa. The disparity could also be a reflection of the research milieu and capacity of individual countries or research groups, which indeed seem to be the case as most of the current reports on leukemia emerges from countries with well established science capacities. Even with the scattered and available data, however, the difference from European and global trends could be observed as well as the evolution of the problem of leukemia.

In Egypt at the National Cancer Institute (NCI) Cairo University during the year 2002, out of a total of 19405 new cancer cases, 169 patients (1.8%) were diagnosed as AML(**Elattar I ,.2003**).