

**HIGH GRADE NON-HODGKIN'S
LYMPHOMAS RISK FACTORS AND
TREATMENT OUTCOME
(RETROSPECTIVE STUDY)**

Thesis

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clinical Oncology by

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Abstract

Key word: Diagnosis and investigation, B-cell aggressive, NHL, Non-hodgkin's, Rituximab, Vincristine, Prednisone, Cyclophosphamide

Establishment of computerized network to store and transfer the patient's records and information between clinics and admission ward is recommended for better documentation Proper documentation of patients management data in the records regarding chemotherapy protocol, dose specification, radiotherapy dose and fractionation and careful assessment of response and toxicity by addition of toxicity sheet to records. The usage of effective salvage treatment e.g HDCT/ASCR in chemotherapy sensitive relapsed patient is strongly recommended, and the use of molecular based prognostic models is recommended for discriminating patients especially with intermediate risk group in IPI

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List of Abbreviations

AA	Ann Arbor
aaIPI	Age-adjusted International Prognostic Index
ABC	Activated B-cell
ACVBP	Adriamycin, cyclophosphamide, vindesine, bleomycin, prednisone
AGMT	Arbeitsgemeinschaft Medikamentöse Tumortherapie
AITL	Angioimmunoblastic T-cell lymphoma
AIDS	Acquired immune deficiency syndrome
ALCL	Anaplastic large cell lymphoma
ALK	Anaplastic lymphoma kinase
ALL	Acute lymphoblastic leukemia
ALT	Alanine transaminase
AM L	Acute myeloid leukemia
ASCT	Allo-stem cell transplant
ATCL	Adult T-cell lymphoma
ATLL	Adult T-cell leukaemia/lymphoma
BCL-6	B-cell lymphoma-6
BCNU	Carmustine
BOB-1	B-cell-OCT binding protein-1
BEAM	BCNU + etoposide + Ara-C (cytarabine) + melphalan
BL	Burkitt lymphoma
BM	Bone marrow
BMT	Bone marrow transplant
C TCL	Cutaneous T-cell lymphoma/leukemia
CALGB	Cancer and Leukemia Group B
CAP	Cyclophosphamide + doxorubicin (Adriamycin) + prednisone
CBV	Cyclophosphamide + BCNU + etoposide
CHOP	Cyclophosphamide + Adriamycin + vincristine + prednisone
CHL	Classical Hodgkin lymphoma
CLL	Chronic lymphocytic leukemia
CLPD-NK	NK-cell chronic lymphoproliferative disorder
CNS	Central nervous system
CODOX-M	Cyclophosphamide + vincristine + doxorubicin + methotrexate

COPP	Cyclophosphamide + vincristine + procarbazine + prednisone
CR	Complete remission
CS	Clinical stage
CSF	Cerebrospinal fluid
CT	Computed tomography scan
CVAD	Cyclophosphamide + vincristine + adriamycin + dexamethasone
CVP	Cyclophosphamide + vincristine + prednisone
CytaBOM.	Cytarabine, bleomycin, vincristine, methotrexate
DFS	Disease-free survival
DHAP	Dexamethasone + Ara-C (cytarabine) + cisplatin
DICE	Dexamethasone + ifosfamide + cisplatin + etoposide + mesna
DLBCL	Diffuse large B-cell lymphoma
EATL	Enteropathy-associated T-cell lymphoma
EBV	Epstein-Barr virus
ECOG	Eastern Cooperative Oncology Group
EFS	Event-free survival
ENS	Extracapsular neoplastic spread
ENT	Ear, nose, and throat
EORTC	European Organization for Research and Treatment
ESR	Erythrocyte sedimentation rate
FAB	French-American- British Cooperative Group
FC	Fludarabine + cyclophosphamide
FDCS	Follicular dendritic cells
FDG	Fluoro-deoxy glucose
FEV1	Forced expiratory volume in one second
FNA	Fine needle aspiration
GCB	Germinal center B-cell
FND	Fludarabine + mitoxantrone + dexamethasone
G-CSF	Granulocyte-colony stimulating factor
GEP	Gene expression profile
Gem-cis	Gemcitabine + cisplatin
GELA	Groupe d'Etudes des Lymphomes de l'Adulte duSang
GHSG	German Hodgkin Study Group

GMAL L	German multicentre adult acute lymphoblastic leukemia
GOELAMS	Groupe Ouest—Est des Leucé mies et des Autres Maladies
GY	Gray
HAART	Highly active antiretroviral therapy
HAMA	Human anti-mouse antibodies
HDACI	Histone deacetylase inhibitors
HDCT	High dose chemotherapy
HDT-SCT	High-dose therapy with stem cell transplantation, ,
HHV	Human herpesvirus
HIV	Human immunodeficiency virus
HL	Hodgkin lymphoma
HLA	Human leukocyte antigen,
HPS	Hemophagocytic syndrome,
HSCT	Hematopoietic stem cell transplantation
HSTL	Hepatosplenic T-cell lymphoma
HTLV	Human T-lymphotropic virus
HVS	Hyperviscosity syndrome
ICE	Ifosfamide + carboplatin + etoposide
IFRT	Involved field radiation therapy
IgH	Immunoglobulin heavy chain
IMRT	Intensity-modulated radiation therapy
IPI	International Prognostic Index
IPID	Inflammatory proliferative intestinal disease
IV	Intravenous
IVAC	Ifosfamide + mesna + etoposide + cytarabine
JAK-2	Janus kinase -2 in tyrosin kinas pathway
KPS	Karnofsky Performance Status Scale
LBL	Lymphoblastic lymphoma,
LDH	Lactate dehydrogenase
LPL	Lymphoplasmacytic lymphoma
LVEF	Left ventricular ejection fraction
LyG	Lymphomatiod granulomatosis

MACOP-B	Methotrexate, doxorubicin, cyclophosphamide, prednisone, bleomycin
MACOP-B	Methotrexate + Adriamycin + cyclophosphamide + vincristine
	bleomycin + prednisone
MALT	Mucosa-associated lymphoid tissue
MAL	Mylin and lymphocyte gene
M-BACOD	Methotrexate, bleomycin, doxorubicin, cyclophosphamide,
	vincristine, dexamethasone
MCL	Mantle cell lymphoma
MDS	Myelodysplastic syndrome
MDR	Median duration of response
MEP	Mitomycin C + etoposide + cisplatin
MF	Mycosis fungoides
MHC	Major histocompatibility
MRI	Magnetic resonance imaging
MTD	Maximum transthoracic diameter
MTX	Methotrexate
MUGA	Multiple gated acquisition scan
MUM-1	Multiple myeloma gene -1
NHL	Non-Hodgkin lymphoma
ENK/TCL	Extranodal T-cell lymphoma, nasal type
NK	Natural killer
NLPHD	Nodular lymphocyte predominant Hodgkin disease
NF-kB	Nuclear factor Kappa-light chain enhancer of B-cell
NPV	Negative predictive value of Cancer
OCT-2	Organic cation transporter-2
ORR	Overall response rate
OS	Overall survival
PAX-5	Paired box-5 transcription factor
PB	Peripheral blood
PBL	Plasmoblastic lymphoma

PCNSL	Primary central nervous system lymphoma
PMLBCL	primary mediastinal large B-cell lymphoma
PET	Positron emission tomography
PEL	Primary effusional lymphoma
PFS	progression-free survival
PFS	Progression free survival
PFT	Pulmonary function test
PPV	Positive predictive value
PR	Partial response
PS	performance status
PTCL	Peripheral T-cell lymphoma
PTCL/L	Peripheral T-cell lymphoma/leukaemia
ProMACE	prednisone, methotrexate, doxorubicin, cyclophosphamide
PTCL-Nos	Peripheral T-cell lymphoma – not otherwise specified
PTLD	Post-transplant lymphoproliferative disorder
PUVA	Psoralen + ultraviolet A radiation
R	Rituximab
R-CHOP	Rituximab + cyclophosphamide + Adriamycin + vincristine +
	prednisone
R-CVP	Rituximab + cyclophosphamide + vincristine + prednisone
R-FCM	Fludarabine + cyclophosphamide + mitoxantrone + rituximab
RIT	Radioimmunoconjugate therapy
RICOVER60	Randomized controlled over 60 trail
RD I	Relative dose intensity
RR	Response rate
RT	Radiotherapy
RTOG	Research and Treatment oncology group
SCT	Stem cell transplant
SD	Stable disease
SLE	Systemic lupus erythematosus

SLL s	Small lymphocytic lymphoma
SOT	Solid organ transplant
SPTCL	Subcutaneous panniculitis-like T-cell lymphoma
SS	Sezary syndrome
SWOG	South western oncology group
TBI	Total body irradiation
TCL	T-cell leukaemia
TCR	T-cell receptor
TdT	Terminal deoxynucleotidyl transferase
T-LGL	T-cell large granular lymphocytic leukaemia
T-PLL	T-cell prolymphocytic leukaemia
TRAF-1	Tumor necrosis factor receptor –associated factor-1
TSH	Thyroid stimulating hormone
TTF	Time to treatment failure
VEGF	Vascular endothelial growth factor,
WBC	White blood count
WBRT	Whole brain radiotherapy
WHO	World Health Organization
WM	Waldenström macroglobulinemia

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Introduction

Non-Hodgkin's lymphomas (NHLs) are a heterogeneous group of cancers arising from B or T-lymphocytes, also rarely from natural killer cells (NK). This heterogeneity results from the numerous histological entities, lymphoma's location in nodal or extra nodal sites, its capacity to remain localized or to disseminate through the body, and patient's age and associated co-morbidities.^[1]

NHL accounts for more than 85% of the lymphomas. Aggressive lymphomas constitute approximately 60% of NHL series, while indolent lymphomas account for approximately 40% of new diagnoses. The vast majority of NHLs are of B-cell origin. Early stage lymphoma is curable in greater than 75% of patients; however, advanced stage disease is curable in only 50% of patients.^[2]

High grade Non-Hodgkin's lymphomas occur in all age groups and often present with symptoms progressing rapidly and can be cured. They are among the most sensitive malignancies to radiation and cytotoxic therapy.^[3]

Non-Hodgkin's lymphomas are the fifth and sixth most common malignancies in man and women, respectively and are among the most rapidly increasing malignancies. In 2007 there were 63,190 new cases of NHL in United States 4% of new cancers in males, 5% in females and ranks as the seventh most common cause of cancer-related death.^[3,4]

European cancer registry data suggest that the incidence of NHL increased until the mid-1990s, then began to plateau. In 2006, an estimated 72,800 new cases were diagnosed, increased from 62,300 in 2004. NHL accounted for 3.2% of new cancer cases and 2.8% of cancer deaths in Europe in 2006, making it the eighth leading cause of new cancer cases and the 10th leading cause of cancer death. The most

common form of NHL is diffuse large B-cell lymphoma (DLBCL), which accounts for 31% of NHL cases. The incidence of DLBCL increases with advancing age, such that the disease represents 54% of NHL cases among patients older than 75 years.^[5]

In Egypt NHLs represent the third most common cancer in males and the second most common cancer in females, accounting for 10.9% of all cancer in Egypt diagnosed every year.^[6] NHL is common Kuwait, Oman, and Saudi Arabia, accounting for about 10% of all cancers.^[7]

High grade NHL is the most common subtype in Egypt.^[8,9] The same result in Jordan ,Saudi Arabia, and Pakistan. ^[10,11] The high grade NHL represent more than 50% of NHLs diagnosed in western countries and more than 60% in Egypt , Jordan, Saudi Arabia, Pakistan and Hong Kong.^[12]

Treatment of aggressive NHLs is based on multiple factors, including histology, International Prognostic Index. Treatment is frequently curative for DLBCL, ALCL, Burkitt's lymphoma, and lymphoblastic lymphoma. Cure is uncommon in most peripheral T-cell lymphoma.^[13]

Aim of the work

The aim of the present work to study the different risk factors and treatment outcome of high grade non-Hodgkin's lymphomas among Egyptian patients treated in oncology department, faculty of medicine, Cairo University, during the period 2005—2009 inclusive, with comparison with what mentioned in literature.