

بسم الله الرحمن الرحيم



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**Detection KIT D816 Mutation and Its Association with
Outcome of Sudanese Acute Myeloid Leukaemia Patients at
Khartoum State.**

الكشف عن الطفرة الجينية كيت دال 816 وعلاقتها بنتائج التحاليل لمرض سرطان الدم
النخاعي الحاد لدى السودانيون في ولاية الخرطوم

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degree of M.SC in Hematology and Immunohematology .`

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Dedication

To my teachers

Who gave me the gift of sharing their minds and experiences.

To my father

Who gave me advices and support through the years, I am very grateful
for everything you have done for me.

To my mother

Who is encouraging and guiding me toward success, made me a best
woman and learned the meaning of love

To my brothers, sister, aunt, cousins and dear friends

Who always is being by my side through good and bad times.

Best wishes

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Abstract

This is a prospective and longitudinal cohort study carried out in Khartoum State in Radio Isotop Center Khartoum , Omdurman Military Hospital and Gafar Ibn Auf Paediatric Hospital in the period from (May 2015 to May 2017) to detect KITD 816 mutation and its association with outcome of Sudanese Acute Myeloid Leukaemia patients at Khartoum state under same chemotherapy treatment plan .Thirty diagnosed AML patients with different subtypes of AML FAB classifications (M0,M1,M2,M4,M5,M6) were selected 14 (46%) male and 16(53%) female. The age was range from(5-70 years) ,4.5 ml of venous blood was withdrawn from each patients placed in 1%EDTA container it was divided for two parts, 200ul of blood for DNA extraction and the other part for CBC analysis, which would be replicated to all patients monthly with monitoring the clinical findings to follow up of patient's outcome during this period (minimum period to follow up 5 months).The results was analyzed by SPSS version 19.They AML patients were enrolled for two study groups:23(76.6%) patients were KIT D 816 mutation positive as case group and the other group contain 7(23.3%) patients were KIT D 816 mutation negative act as control group .The results showed association of KIT D 816 mutation with AML disease (p.value=0.00) ,adverse patient's outcome if corresponded with some AML subtypes(M0,M4 and M5) (p.value=0.05) and males were high frequent than female (p.value=0.008) but no association between KIT D 816 mutation with patient's outcome generally and age of AML patients (p.value=0.666).

In light of this study results KIT D 816 mutation should be considered as diagnosed cytogenetic test of AML disease and to determine suitable treatment plan to benefit outcome.

الخلاصة

هذه الدراسة هي دراسة استطلاعية وطويلة أجريت في مدينة الخرطوم في مستشفى الذرة لعلاج الاورام ومستشفى السلاح الطبي ومستشفى جعفر بن عوف وبرج الامل في الفترة من مايو 2015 الى مايو 2017 للكشف عن الطفرة كت دال 816 وعلاقتها بنتيجة النشافي لدى المرضى السودانيون المصابين بسرطان الدم النخاعي الشوكي الحاد في مدينة الخرطوم، وعليه تم اختيار ثلاثون مريضاً مشخص بسرطان الدم النخاعي الحاد بمختلف تصنيفاته المقررة من قبل التصنيف الفرنسي الامريكي البريطاني (م0م، 2م، 3م، 4م، 5م، 6م) منهم 14 من الذكور و16 من الاناث وكانت الاعمار متفاوتة من (5اعوام-70 عام) وتم اخذ 4,5 مليلتر من الدم الوريدي من كل مريض وتم وضعه في وعاء يحتوي على 1% مانع تجلط حمض ثنائي أمين ايثيلين رباعي حمض الاستيك بحيث قسمت الى جزئين: 200 مايكروليتر من الدم تم استخلاص حمض نووي ريبوزي منقوص الاكسجين للكشف عن طفرة كت دال 816 بواسطة تحليل الاليل المحدد مانع التنافسية بوليميراز المتسلسل (ACB-PCR)، اما الجزء المتبقي من العينة تم استخدامه لتحليل خلايا الدم الشامل لمتابعة تقدم المرض لديهم مع مراقبة الاعراض السريرية، وتم تحليل النتائج بواسطة برنامج الحزم الاحصائية للعلوم الاجتماعية اصداره 19، وقد تم تقسيم مرضى سرطان الدم النخاعي الحاد الى مجموعتين: مجموعة تحتوي على 23 (76%) مريض حامل لطفرة كت دال 816 والمجموعة الثانية تحتوي على 7 (23%) مرضى خاليين من طفرة كت دال 816 وتم اعتبارها كمجموعة ضابطة، وقد اظهرت النتائج التحليلية ان طفرة كت دال 816 لها علاقة بحدوث مرض سرطان الدم النخاعي الحاد (بقيمة معنوية =0.00) وايضا لها علاقة عكسية بنتائج تحليل دم المريض اذا وجدت مرتبطة مع بعض التصنيفات الفرعية لمرض سرطان الدم النخاعي الحاد وخاصة (م، 4م، 5م) (بقيمة معنوية=0.008)، وكذلك وجد ان هناك علاقة بين هذه الطفرة وجنس المريض حيث اثبتت وجودها لدى الرجال اكثر من النساء (بقيمة معنوية =0.05)، ولكن في المقابل وجد انه لا توجد علاقة بين طفرة كت دال 816 ونتائج التحليل بصورة عامة كما انه لا توجد علاقة بين وجود الطفرة وعمر سرطان الدم النخاعي الحاد (بقيمة معنوية=0.666)

في ضوء نتائج هذه الدراسة يجب ان تؤخذ طفرة كت دال 816 في الاعتبار التشخيصي لسرطان الدم النخاعي الحاد ضمن الفحوصات الخلوية كفحص تأكيدي للمرض وومساعد لاختيار خط العلاج الانسب للشفاء .

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List of Abbreviations

ACB-PCR	Allel Specific Competitive Blocker –Polymerease Chain Reaction
ALK1	Activin Like Kinase
ALL	Acute Lymphoblastic Leukemia.
AMk	Acute Megakaryoblastic Leukemia
AML	Acute Myeloid Leukemia.
AMML	Acute Myelomonocytic Leukemia
APL	Acut Promyelocytic Leukemia
ARF	Acute Renal Failure
ASR	Age Standardised Rate
ATP	Adenosine Triphosphate
ATRA	Alltrans Retinoic Acid
CALGB	Cancer and Leukemia Group B
CBC	Cpmplete Blood Count.
CBF	Core Binding Factor.
cCD	Cytoplasmic Cluster of Differentiation
CD	Cluster of differentiation.
CLL	Chronic Lymphocytic Leukemia
CML	Chronic Myeloid Leukemia
CNS	Central Nervous System.
CR-Rate	Conversion Rate.
CSF	Cerebro Spinal Fluid.
DNA	Deoxyribo Nucleic Acid.
DN	De Novo
DIC	Disseminated Intravascular Disease
DS	Down Syndrom
EBP	Enhancer Binding Protein
EGIL	European Group for the immunological Classification of Leukaemia.
ET	Essential Thrombocythemia
ETO	Early Termination Option
FAB	French American British classification.
FISH	Fluorescent in Situ Hybridization.
FLT 3	Fims-Like Tyrosine Kinase 3
FPD-AML	Familial Platelet Disorder with propensity to Myeloid Malignancy.
G-CSF	Granyocyte Colony Stimulating Factor
GM-CSF	Granulocyte Monocyte Colony Stimulating Factor

HLA	Human Leukocyte Antigen
IMF	Idiopathic Myelofibrosis
IL	Interleukin
Inv	inversion.
ITD	Internal Tandem Repeat Duplication
JM	Juxtamembrane
kD	Killo Dalton
LDH	Lactic Dehydrogenase
MDP	Multidrug Resistance Protein.
MDR-AML	Myelodysplasia Related-AML
MDS	Myelodysplasia Syndrom
MLL	Mixed Lineage Leukemia
MPO	Myeloperoxidase
MYH1	Myosin Heavy Chain 1.
NCR	National Population-based Cancer Registry
NPM	Nucleophosmin
NSE	Nonspecific esterase
PCR	Polymearase Chain Reaction .
PDGF	Platelet Derived Growth Factor
PKC	Protein Kinase C
PML	Promyelocytic Leukemia
PTK	Protein Tyrosin Kinase
PV	Polycythemia Vera
RA	Retinoic Acid
RAR	Retinoic Acid Receptor
RARA	Retinoic Acid Receptor
RHD	Runt Homology Domain .
RICK	Radio Isotop Center Of Khartoum
RNA	Ribose Nucleic Acid .
RT-PCR	Real Time –Polymerase Chain Reaction
RUNX1	Runt Related Protein
SBB	Sudan Black B
SM	Systemic Mastocytosis
TdT	Terminal Deoxynucleotidyl transferase.
USA	United State of American
US	United State
WBCs	White blood cells .
WHO	World Health Organization
ZIP	Zipper

