بسم الله الرحمن الرحيم

Republic of Sudan

Ministry of Higher Education and Scientific Research

Shendi University

Faculty of Graduate Studies and Scientific Research

Assessment of Complete Blood Count Among Patients Receiving Chemotherapy at Tumor Therapy and Cancer Research Center in Shendi Town

A thesis submitted in partial fulfillment of the degree of Msc in medical laboratory sciences (heamatology)

By:

Amal Abdellah AbdEl-Rahaman Awad

(Bsc Shendi Unversity -2009)

Supervisor

Dr: Hamza Ahmed Hassan Mohammed

Assistant professor in Haematology, Medical Laboratory Science , Shendi University

August-2018

الآيـة

بسم الله الرحمن الرحيم

قال تعالي

﴿ اقْرَأْ بِاسْمِ رَبِّكَ الَّذِي خَلَقَ * خَلَقَ الْإِنسَانَ مِنْ عَلَقٍ * اقْرَأْ وَرَبُّكَ الْأَكْرَمُ * الَّذِي عَلَّمَ بِالْقَلَمِ * عَلَّمَ الْإِنسَانَ مَا لَمْ يَعْلَمْ ﴾

صدق الله العظيم

الآية 1–5 في سورة العلق

Dedication

-To dear my mother,

Who taught me the meaning of life.

-To my dear father,

Who gave me love and respect.

-To my husband,

Who give me love and support.

-To my son and daughter,

Whom give my life happiness

-To my brother,

Who bring happiness to my life.

-To my teachers,

whom led me to the way of success

-To my friends and colleagues,

I dedicate this study.

Acknowledgement

First of all I thank the Almighty Allah who helped me to complete this study.

I would like to express endless thanks to my supervisor,

Dr: Hamza Ahmed Hassan

For his great efforts and guidance.

I would like also to thank **Dr. Awad Altayb Ali** and **Dr. Nada Mahadi** for their great helps and endless support.

I thank the staff of tumor treatment and researches centre.

I thank the staff of the Faculty of Medical Laboratory specially **Dr. Ibrahim Bakhet**

I would also like to thank all the participants (patients) who gave the allowance to give me samples of this research and many others whom I could not mention here, but their direct and indirect supports had already contributed in this study.

Abstract

Background:

Cancer is the abnormal cells divide in uncontrolled way which may eventually spread into other tissues in the body

It can begins when genetic changes interfere this orderly process ,that treated by chemotherapy, radiotherapy, hormonal therapy and immune therapy.

The aim of the study is to assessment of complete blood count among patients treated by chemotherapy by comparing the *CBC* parameters pre and post chemotherapy dose in haematological and non haematological type of cancer.

Methods:

This is a cross-sectional study conducted at tumor treatment and researches center in Shendi town in the period between (March to August 2018).

The study included (50) patients who were diagnosed as cancer patients and blood is collected from them to estimated the complete blood count by using Mindray Haematology Analyzer (Mindray -3000 plus) pre and post chemotherapy dose.

Data was collected using questionnaire and the (SPSS) (version 20) programm was used for data analysis.

Results:

The study showed that the cancer patients were (80%) of non haematological cancer and (20%) of haematological cancer, frequency of six (50%) male and (50%) female, frequency of their age group (20-50) years old was (30%), their age group (51-80) years old was (56%), and their age group of more than 80 years old was (14%).

The (40) blood sample collected from non haematological cancer patients include frequency of sex was (45%) male and (55%) female, frequency of age group (20-50) years old was (27.5%), age group (51-80) years old was (60%) and age groups more than 80 was (12.5%).

-The *CBC* of non haematological cancer showed reducing in the mean values of *Hb, RBCs, PCV, MCV, MCH and MCHC* in post chemotherapy were (10.0 g/dl), ($3.5x10^{12}$/l), (31.9%), (84.6 fl), (26.3 pg) and (30.7 g/dl) respectively from their mean values pre chemothearapy were (11.8 g/dl) ($4.1x10^{12}$/l), (35.7%), (84.7fl), (27.7pg) and (31.8 g/dl) respectively.

-Also showed reducing in mean values of TWBCs and platelet count in post chemotherapy were (13.900 x 10^9 /l) and (180.0 x 10^9 /l) respectively from their mean values of pre chemotherapy were (30.20 x 10^9 /l) and (323.0 x 10^9 /l) respectively.

-Also (10) blood sample collected from haematological cancer patients were (70%) male and (30%) females, frequency of age group (20-50) years old (40%), age group (51-80) years old (40%) and age group more than 80 years old(20%).

-The *CBC* showed reducing in the mean values of *Hb, RBCs, PCV, MCV, MCH and MCHC* in post chemotherapy were (8.1g/dl), ($3.2x10^{12}$/l), (27.3%), (72.3 fl), (25.9 pg) and (30.0 g/dl) respectively From their mean values pre chemotherapy were (9.9 g/dl), ($3.6x10^{12}$/l), (31.2%), (86.9 fl), (26.6 pg) and (30.8g/dl) respectively .

Also showed reducing in the mean values of *Twbcs and* platelet count in post chemotherapy were (8.0 x 10^9 /l) and (108.0 x 10^9 /l) respectively from their mean values pre chemotherapy were (159.0 x 10^9 /l) and (205.7 x 10^9 /l) respectively

المستخلص

مدخل:

السرطان هو عبارة عن انقسام غير منظم للخلايا ويمكن ان ينتشر الي بقية أنسجة جسم الإنسان وهو يحدث نتيجة لبعض التغيرات الجينية التي تؤثر علي تنظيم العمليات الحيوية، ويتم علاجه عن طريق العلاج الكيميائي والإشعاعي والمناعي.

وتهدف هذه الدراسة إلى لتقيم فحص الدم الكامل *CBC* للمرضي الذين يتعالجون بالعلاج الكيميائي وذلك بمقارنه نتيجه ال CBC قبل وبعد جرعه العلاج الكيمائي بالنسبة لمرضي سرطان الدم والانواع الأخرى من السرطانات.

منهجية الدراسة:

أجريت هذه الدراسة المقطعية في مركز علاج وابحاث السرطان بمدينة شندي في الفترة من مارس الي اغسطس 2018م.

وقد تضمنت هذه الدراسة 50 مريضاً بالسرطان بأخذ عينات دم لفحص الدم الكامل بواسطة جهاز Mindray Haematology Analyzer (Mindray -3000 plus) قبل وبعد جرعه العلاج الكيميائي تم جمع المعلومات بواسطه الاستبيان ومن ثم استخدام برنامج الحزمة الإحصائية للعلوم الاجتماعية الذي يعرف (SPSS) ببرنامج التحليل الإحصائي

النتائج:

أظهرت الدراسة أن مرضي السرطان وهم (20%) سرطان الدم و (80%) من الأنواع الأخرى من السرطان (50٪) ذكور و (50٪) اناث وكان متوسط أعمارهم (30٪) للأعمار من (20–50) سنة و(56%) للأعمار من (51–80) سنه ,و (14%) للأعمار الأكثر من 80 سنة.

– كما أظهرت الدراسة أن مرضي السرطان ماعدا سرطان الدم (45٪) ذكور و (55٪) إناث وكان متوسط أعمارهم (27.5٪) للأعمار من (20–50) سنة و(60%) للأعمار من (51–80) سنة، و (12.5%) للأعمار الأكثر من 80 سنة.

أظهر تحليل الدم الكامل ان متوسط الهيموغلوبين، وتعداد كريات الدم الحمراء ،الحجم الحشوي للدم ،متوسط حجم الخلية الحمراء، متوسط الهيموغلوبين في الخلية الحمراء ،متوسط تركيز الهيموغلوبين في الخلية الحمراء قد نقصت بعد جرعة العلاج الكيميائي (10.0 g/dl) ($3.5x10^{12}$/l) (31.9%) (84.6 fl) (26.3 pg) (30.7 g/dl) علي التوالي عن متوسطها قبل جرعة العلاج الكيميائي ((27.7 pg) (31.8g/dl g/dl) (11.8 g/dl) ($4.1x10^{12}$/l) (35.7%) (84.7 fl) على التوالي.

وأظهرت أيضاً أن متوسط تعداد كريات الدم البيضاء والصفائح الدموية بعد جرعة العلاج الكيميائي (13.900 x 10^9 /l) و (180.0 x 10^9 /l) علي التوالي قد نقصت عن متوسطهم قبل جرعه العلاج الكيميائي (30.20 x 10^9 /l) و (323.0 x 10^9 /l) علي التوالي.

– كما أظهرت الدراسة أن مرضي سرطان الدم (70٪) ذكور و (30٪) إناث وكان متوسط أعمارهم (40٪) للأعمار من (50–20) سنة و (40%) للأعمار من (51–80) سنه، و(20%) للأعمار الأكثر من 80 سنه.

أظهر تحليل الدم الكامل ان متوسط الهيموغلوبين ، وتعداد كريات الدم الحمراء ،الحجم الحشوي للدم، متوسط حجم الخلية الحمراء ، متوسط الهيموغلوبين في الخلية الحمراء، متوسط تركيز الهيموغلوبين في الخلية الحمراء بعد جرعة العلاج الكيميائي(8.1g/dl) ($3.2x10^{12}$/l) (27.3%) (72.3 fl) (25.9 pg) (30.0 g/dl) علي التوالي قد نقصت عن متوسطهم قبل جرعة العلاج الكيميائي (9.9 g/dl) (31.2%) ($3.6x10^{12}$/l) (86.9 fl) (26.6 pg) (30.8 g/dl) على التوالي.

وأظهرت أيضاً أن متوسط تعداد كريات الدم البيضاء والصفائح الدموية بعد جرعه العلاج الكيميائي (8.0 x 10^9 /l (108.0 x 10^9 /l)علي التوالي قد نقصت عن متوسطهم قبل جرعة العلاج الكيميائي 159.0 x 10^9 /l) و (205.7 x 10^9 /l) على التوالي.

List of Contents

List of Tables

List of abbreviations

Abbreviation	Mean
ABC	Adenine triposphate binding cassette
ATP	Adenine triphosphate
BC	Before century
BCRP	Breast cancer resistance protein
CBC	Complete blood count
DIC	Disseminated intravascular coagulation
EDTA	Ethylene diamine tetra acetic acid
fL	Femtoliter
FN	Febrile neutropenia
g/ dL	Gram per deceliter
HB	Haemoglobin
H.CA	Haematological cancer
HCT	Haematocrit
HIF	Hypoxia inducible factor
IARC	International agency for researches on cancer
Km	Kilometer
MCH	Mean cell haemoglobin
MCHC	Mean cell haemoglobin concenteration
MCV	Mean cell volume
mmol/l	Millimol per liter
MRP1	Multidrug resistance protein 1
M.Sc	Master of sciences
NH.CA	Non haemtological cancer
NK	Natural killer
NRBCs	Nucleated red blood cells
PCV	Packed cell volume
Pg	Pico gram
P.gp	P.glycoproptein
PIH	Pregnancy induced hypertension
RBCs	Red blood cells
RF	Radio frequencies
RNA	Ribonucleic acid
SLS	Sodium lauryl sulphate
Yrs	Years

Chapter one

Introduction

Rationale

Objectives

1-1 Introduction

There is some truth to the old adage that cancer is as old as the human race, but paleopathologic findings indicate that tumors existed in animals in prehistoric times, long before men appeared on Earth.

In medicine, the earliest written description of diseases and cancer, a breast cancer, is found in the Edwin Smith Papyrus that was written approximately 3000 BC [(1).]

The Ebers Papayrus, dated circa 1500 BC, contains the first reference to a soft-tissue tumor, a fatty tumor, and includes reference to possible cancers of the skin, uterus, stomach and rectum [(2)]

Cancer is a leading cause of death worldwide. An estimated 12.7 million new cancer cases occurred in 2008, of which about 715,000 new cancer cases resulted in 542,000 deaths in Africa [(3)]

there will be an estimated 1,688,780 new cancer cases diagnosed and 600,920 cancer deaths in the US american socitaty of cancer.

Cytotoxic chemotherapy drugs primarily damage proliferating cells and we now know the molecular target of most of the drugs in clinical use.

Even so, non-specificity of cytotoxic agents is a major drawback and potential to damage normal tissues means that cure with chemotherapy is not often achieved. With advances in science, rational drug design is now becoming a reality, but these mechanism-driven, targeted agents are likely to be additions to, rather than substitutes for, conventional chemotherapy drugs.

As cancer treatment becomes increasingly complex, the challenge for clinicians and scientists now is to manipulate our treatments to maximize benefit and minimize harm for the individual patient.

There are a number of strategies in the administration of chemotherapeutic drugs used today.

Chemotherapy may be given with a curative intent or it may aim to prolong life or to palliate it is the use of anti-cancer drugs to destroy cancer cells.

In combination chemotherapy a number of drugs may be given at the same time. Sometimes only one drug is used Chemotherapy may be used before or after surgery or radiation therapy, or together with radiation therapy [4]

The CBC can help detect blood diseases and disorders, such as anemia ,infections, clotting problems, blood cancers, and immune system disorders. This test measures many different components of blood. [5]

Red blood cells carry oxygen (O_2) from lungs to the rest of the body. Abnormal red blood cell levels may be a sign of anaemia, dehydration (too little fluid in the body), bleeding, or another disorder. [6]

White blood cells are part of the immune system, which fights infections and diseases. Abnormal *WBC* levels may be a sign of infection, blood cancer, or an immune system disorder [7]

1.2 Rationale

In last year's increased prevalence of many type of cancer which needs to attempt draw a more organized and update picture of affect of their treatment by chemotherapy on the body , and to know the affect of chemotherapy treatment on HB, RBCs, PCV, MCV, MCH, MCHC and Platelet count in meaning of reduced these side effects. So that in this study attempt to determine the effect of chemotherapy on blood count.

1.3 Objectives

1.3.1 General objective

To Assessment of complete blood count among patients receiving chemotherapy**.**

1.3.2 Specific objectives:

1- To detect the affect of chemotherapy on *CBC* parameters of haematological malignancy and for another type of malignancies .

2- To perform complete blood count (*Hb, PCV, RBCs, RBCs* indices, *WBCs*, platelet count) and correlate them pre and post chemotherapy dose.

Chapter two

Literature review

Previous studies

2. Literature review

2.1 Cancer:

Cancer is the abnormal growth of cells. Cancers arise from any organ or body structure and are composed of tiny cells that have lost the ability to stop growing. Occasionally, cancer may be detected "incidentally" by a laboratory test or radiological routine test or for an entirely different reason. In general, cancer must reach a size of 1 cm, or be comprised of 1 million cells, before it is detected. At this point, it may be referred to as a "'mass," a "growth," a "tumor," a "nodule," a "lump," or a "lesion." Exceptions to this general rule include cancers of the blood and bone marrow (leukemia's and lymphomas) – which frequently do not produce a "mass," but will be evident on laboratory tests.[8]

2.1.1 Categories of cancer:

Cancer cells continue to grow unless one of four things occur:

(1) The cancerous mass is removed surgically.

(2) using chemotherapy or another type of cancer-specific medication, such as hormonal therapy.

(3) using radiation therapy.

(4) the cancer cells shrink and disappear on their own. This last event, while extremely rare, can occur with some melanomas or some kidney cancers[9].

2.1.2 Hallmarks of Cancer Cell

Hanahan and Weinberg (2000) [10][11] listed the seven attributes of cancer:

1- Self sufficiency in growth signals.

2- Insensitivity to anti-growth signals.

3- Evading apoptosis.

4- Limitless replicative potential, telomerase and telomeres.

5- Sustained angiogenesis.

6- Tissue invasion and metastasis.

7- Genome instability.

All seven attributes have received great attention in the past decade. Growth and anti-growth signaling are really complex [25].

Protein-protein interaction and signaling networks, growth signaling pathways, the role of ubiquitination and protein degradation, and dysfun2ctional protein networks [12][13] and interactions are complex, described as hubs, modules and motifs [25].

Information on cancer cell death and provocation by drugs and irradiation now requires all cell death types to be considered- apoptosis, necrosis, autophagy [14][15]

We now must include the pivotal role of micro*RNAs* [16][17], and methylation patterns [18] for example, micro*RNA*-185 suppress cancer growth by interfering with Six1; when absent in cancers leads to increase growth and progression [19].

Recent efforts have uncovered the role of transposons in the induction of cancer in mouse models; the studies are generating previously unknown cancer related genes [20],class II (*DNA* transposons) and class I retrotransposons contribute to *DNA* instability [21].

Cancer cells use aerobic glycolysis to meet energy needs (Warburg effect) and presumed to be a response to hypoxia and tumor micro-environment; changes in metabolic needs of cancer cells such as need for glutamine and activation of hypoxia-inducible-factor (*HIF*) are interconnected to oncogene activation [22][23].

These interacting functionalities of cancer cells impact prognostic and predictive models based on one or two functional attributes of cancer [24].

2.1.3 Tumours (lumps) can be benign or malignant.

2.1.3.1Benign tumours:

Are not cancerous and rarely threaten life.

They tend to grow quite slowly, do not spread to other parts of the body and are usually made up of cells quite similar to normal healthy cells.

They will only cause a problem if they grow very large, becoming uncomfortable or press on other organs - for example a brain tumour inside the skull.

2.1.3.2 Malignant tumours

are faster growing than benign tumours and have the ability to spread and destroy neighbouring tissue. Cells of malignant tumours can break off from the main (primary) tumour and spread to other parts of the body through a process known as metastasis. Upon invading healthy tissue at the new site they continue to divide and grow. These secondary sites are known as metastases and the condition is referred to as metastatic cancer [26]

2.1.4 Cancer can be classified according to the following categories:

2.1.4.1 Carcinoma

- A cancer that arises from the epithelial cells (the lining of cells that helps protect or enclose organs). Carcinomas may invade the surrounding tissues and organs and metastasise to the lymph nodes and other areas of the body.

The most common forms of cancer in this group are breast, prostate, lung and colon cancer.

2.1.4.2 Sarcoma

A type of malignant tumour of the bone or soft tissue (fat, muscle, blood vessels, nerves and other connective tissues that support and surround organs). The most common forms of sarcoma are leiomyosarcoma, liposarcoma and osteosarcoma

2.1.4.3 Lymphoma

Lymphoma is a cancer of the lymphatic system, which runs all through the body, and can therefore occur anywhere. The two main forms are non-Hodgkin's which begins with uncontrolled growth of the - white blood cells -lymphocytes - of the immune system) and Hodgkin's lymphoma in which cells of the lymph nodes become cancerous.

2.1.4.4 Leukaemia

Leukaemia is a cancer of the white blood cells and bone marrow, the tissue that forms blood cells. There are several subtypes; common are lymphocytic leukaemia and chronic lymphocytic leukaemia

2.2 Chemotherapy:

Chemotherapy is one of the principal modes of the treatment of cancer patients it was first used to treat advanced lymphoma in the late 1940s after it became known that the use of mustard gas in the world wear I caused leukopenia [27]

Although the role of chemotherapy in the treatment of common, epithelial malignancies was limited to the treatment of symptomatisc metastatic disease for almost 30 years.

2.2.1 Chemotherapy applications:

1- **curative** for a small number of malignancies including childhood leukaemia, Hodgkin's and non-Hodgkin's lymphoma, and germ cell malignancies.

2- **a palliative role** for most metastatic epithelial malignancies.

3- **an adjuvant role** in several types of resected epithelial malignancies.

By definition, chemotherapy treatment should interfere with the biochemical program that is involved or committed to cellular replication and cause selective cell death.

At that, the host cell should be able to adapt and recover from toxicity many chemotherapeutic agents kill cancer cells oxidatively via the production of reactive oxygen species and the induction of either apoptosis or necrosis of tumorous cells [28][29], whereas others act on various components of cellular metabolism influencing activities of different enzymes needful for cell division.

Cancer treatment is targeted at its proliferation potential and its ability to metastasise; hence, the majority of chemotherapy drugs take advantage of the fact that cancer cells divide rapidly [30]

Chemotherapy agents can be divided into several categories based on the factors such as how they work, their chemical structure, and their relationship to another drug.

2.2.2 Categories of chemotherapeutics include:

-Alkylating agents (e.g., cyclophosphamide, ifosfamide, melphalan, busulfan).

-Antimetabolites (e.g., 5-fluorouracil, capecitabine, methotrexate, gemcitabine).

-Antitumour antibiotics (e.g., daunorubicin, doxorubicin, epirubicin).

- Topoisomerase inhibitors (e.g., topotecan, irinotecan, etoposide, teniposide

- Mitotic inhibitors (e.g., paclitaxel, docetaxel, vinblastine, vincristine). [31][32]

Most chemotherapeutic drugs target the cell cycle machinery relying on the difference in the frequency of cell division to differentiate between the cancer clones and normal cells.

In fact, the more chemotherapy is given, the higher is the aggressiveness of relapse. In these cases, chemotheray may indirectly select the most resistant mutant cell for clonal expansion.

Cancer is a highly heterogeneous disease, especially in its advanced forms [27]

Moreover, the unique characteristics of tumour microenvironment (hypoxia, low extracellular pH, high interstitial fluid pressure), developed at least in part as a result of the malformed tumour vasculature, act as barriers to chemotherapy impairing the transport and delivery of circulating therapeutic molecules in tumour tissue [33][35]

Some tumours are intrinsically resistant to certain drugs, whereas others can acquire resistance after treatmen [37].

Cancer cells can often develop resistance not only to the agent, which they have been exposed to, but also to other drugs and chemicals that they have not encountered.

There are a number of mechanisms mediating such multidrug resistance [27][37][38].

Upregulation of drug efflux *ATP*-binding cassette (*ABC*) transporters, such as P-glycoprotein (*P-gp),* multidrug resistance protein 1 *(MRP1),* and breast cancer resistance protein (*BCRP*), may be responsible for the resistance to many chemotherapeutics affecting disposition of these drugs in the tumour cells and modifying seriously the clinical outcome [37] [29][40].

2.2.3 Effectiveness of Chemotherapy:

Effectiveness of chemotherapy depends on various factors, including:

2.2.3.1 Properties of cancer cells:

If tumour is hypoxic or Mitochondrial function is severely compromised, or the number of mitochondria within the cancer cell is low, chemotherapy will be of limited value, only increasing the clonal selection of the most resistant and possibly also the most aggressive cancer phenotype.

2.2.3.2 Tumour size:

The microscopic form of tumour is much more successfully treated than macroscopic cancer. [27]

2.2.3.3 Number of chemotherapy cycles

(polychemotherapy may be more active than single agent, whereas the order of administration of drugs as well as their time schedule is also important combining drugs with different modes of action may lead to enhanced or even synergistic antitumour effects without injuring the host [41][43]

Cancer is a systemic and not a local disease metastatic spread of tumour cells may take place already at an early stage of the malignancy; however, little is known about the tumour-biological parameters of such disseminated cells [27].

Metastatic foci might vary with genotype, phenotype, and drug response [47], whereas expression profiles and signalling pathways between primary tumour and metastatic tissue can be different [42]namely, the latest would be the real targets for

any systemic therapy to prevent them forming a clinically relevant metastatic disease [38]

2.2.4 Side Effects of Chemotherapy:

Although the desired goal of chemotherapy is to eliminate the tumour cells, diverse ranges of normal cell types are also affected, leading to many adverse side effects in multiple organ systems [28][51] such debilitating effects are a major clinical problem ,whereas the toxicity often limits the usefulness of anticancer agents [52]

Knowing how the chemotherapy agent works is important in predicting its side effects, for instance, treatment with alkylating agents and topoisomerase II inhibitors increases the risk of secondary cancer (acute leukaemia); anthracyclines (like doxorubicin) induce cardiotoxicity; and mitotic inhibitors have the potential to cause peripheral nerve damage [29].

The most common acute complaints of cancer patients undergoing cytotoxic therapy are:

Fatigue, nausea, vomiting, malaise, diarrhea, mucositis, pain rashes, infections, headaches, and other problems [27][53][54]

Through the induction of nausea and vomiting, difficulties in swallowing, dry mouth, alterations in taste and smell, depression, poor energy, and aversion to food cytotoxic drugs affect also the nutritional status of patients [27][54] showing that chemotherapy is a sufficient stressor in causing malnutrition.

It must be appreciated that malnutrition is the reason why majority of the cancer patients die [27][55]

Most cytotoxic drugs have immune suppressive side effects, many chemotherapeutics kill dividing haematopoietic cells manifesting as profound neutropenia and cytopenia resulting in decreased immunity, increased susceptibility to infections, and elevated risk of bleeding [27]coming from the requirement of the bone marrow to repopulate white cells and platelets in the

blood, drugs are often administered episodically followed by the drug-free intervals of 2-3 weeks, such scheme helps to minimise the chance of infection or bleeding but allows also the tumour to recover[56][57], most chemotherapy drugs are genotoxic likely causing epigenetic and genetic damage [27] many cancer patients encounter thus the problem of developing second malignancies as a result of treatment.

The common secondary tumours are a variety of acute leukaemias and non-Hodgkin's lymphomas, less common are carcinomas of the urinary bladder and other malignancies, which are usually refractory to treatment.

Secondary leukaemias constitute approximately 10% of all leukaemias having the average latent interval from the diagnosis and treatment of the primary neoplasm to development of acute leukaemia for four to six years.

The(International Agency for Research on Cancer) *(IARC*) has identified 20 single chemotherapeutic agents or regimens which cause cancer in humans and about 50 others that are suspect [27].

Chemotherapy-associated immunosuppression can result in an increased rate of infection by oncogenic viruses which further increase the risk of secondary cancers [27] current treatment protocols often apply multiagent chemotherapy and this may even increase the extent of adverse side effects [44]

Several serious complications can cause discontinuation of therapy, prolong the duration of stay in hospitals, and may affect the overall prognosis and outcome of the disease [55].

It is important to bear in mind that, in general, older cancer patients are more susceptible to treatment-related complications than younger individuals [53]

These malignancies share the characteristics of a high proliferative rate, large tumour burden, or high sensitivity to cytotoxic therapy and in principle, any tumour that is highly responsive to chemotherapeutic drugs, particularly if the

cancer cells die through the necrotic pathway, can give rise to this severe metabolic syndrome [27].

2.3 CBC:

The Complete blood count (*CBC*) is one of the more common laboratory tests ordered during the neonatal period. The *CBC* may be obtained to evaluate for anemia, infection, and thrombocytopenia the test offers a wealth of clinical informastion about the hematopoietic system, including erythrocyte, leukocyte, and thrombocyte values.establishing normal neonatal ranges has been difficult because blood has not been drawn on healthy neonates of similar ages.[60]

Reference ranges that consist of the 5th to 95th percentile compiled from various studies have been used to approximate normal neonatal values.

A variety of factors such as sample site, timing of the sample, gestational age, and the neonate's degree of health can affect the *CBC* therefore, the astute practitioner must be able to recognize the clues and nuances of the *CBC* to guide the diagnostic assessment[61].

2.3.1 Components of the *CBC:*

The CBC provides information on the following

-Erythrocyte, or red blood cell (*RBC*), count

-Measure of hemoglobin (*HB*)

-Hematocrit (*Hct)* (percentage)

-Mean corpuscular hemoglobin (*MCH*) measurement

-Mean corpuscular hemoglobin concentration(*MCHC*)

-Mean corpuscular volume (*MCV*)

-Leukocyte, or white blood cell (*WBC*) count

-Thrombocyte count

Several factors can affect *CBC* values. Postnatal fluid shifts can alter the hemoglobin and hematocrit levels, and late clamping of the umbilical cord may result in an elevated hematocrit and transitory polycythemia[61]

values can vary between sample sites. For example, capillary samples have approximately an 82 % correlation with venous samples and approximately a 77 % correlation with arterial samples, with the capillary site having a higher hemoglobin concentration and hematocrit value due to the sludging of *RBCs* in the low-flow capillaries and transudation of plasm.[63], the sample site must be taken into consideration when the practitioner reviews the *CBC* because it can impact the intervention. For example, acapillary sample may reveal an elevated hemoglobin level and hematocrit percentage, an indicator of polycythemia.

In this situation, an arterial or venous sample would give a more accurate value[64]

Neutrophil counts can be affected by the type of delivery the infant experienced and the timing of the sample.

Neutrophil values peak at approximately six to eight hours of age in neonates born at >28 weeks gestation.

2.3.2 Hematopoiesis:

Blood cell development begins in the earliest weeks of gestation.

Cell differentiation appears to begin from a population of progenitor or stem cells located within the yolksac, liver, and bone marrow of the developing fetus.

The microchemical environment of the developing stem cells determines the differentiation of at least two cell lines:

- Myloid hematopoietic system

-Lymphoid hematopoietic system ,[61] the myloid hematopoietic cell line leads to the roliferation and differentiation of stem cells into the:

-Erythroid

-Myeloid

-Megakaryocyte precursors

2.3.2.1 Erythrocytes:

Red blood cells, first appear in the yolk sac during the Mesoblastic period; this period begins at approximately two weeks gestation and peaks at approximately six weeks gestation.

The RBC count measures the number of circulating erythrocytes.

a mature *RBC* is a nonnucleated ,biconcave disc, surrounded by a flexible membrane. Fetal (and neonatal) RBCs differ from adult RBCs in that they are larger in size, have a shorter life span, altered shape and deformability, and they contain a high fetal hemoglobin concentration RBCs transport oxygen to the organs and tissues; it is the protein, hemoglobin, in erythrocytes that carries oxygen.

The hematocrit is the proportion of blood volume that consists of the rbcs. It is expressed as a percentage on the *CBC*

Hemoglobin in blood is measured in grams per one deciliter of whole blood and is expressed as *g/dL (mmol/L)* on the *CBC*

Two conditions that can be identified by evaluating the rbcs count are anemia and polycythemia. Anemia is a deficiency in the concentration of erythrocytes and hemoglobin in the blood.

Neonatal anemia can be caused by acute, chronic, or iatrogenic blood loss; decreased erythrocyte production; increased destruction of erythrocytes, as with hemolysis; or shortened erythrocyte survival [(63).]

Because *RBCs* concentration directly impacts blood viscosity, neonates with polycythemia may exhibit symptoms as a result of increased viscosity they may be plethoric with occasional cyanosis or may exhibit neurologic symptoms of lethargy, irritability, and hypotonia, there are other indices that can provide

estimates of the average size of the erythrocytes and the average concentration and quantity of hemoglobin in the erythrocytes.

These indices can be measured directly or calculated electronically using modern hematology analyzers.

They can be useful in further classifying anemia according to the hemoglobin quantity in the *RBCs* or the size of the *RBCs* or in identifying the pathologic process causing the anemia.

The erythrocyte indices include the *MCV*, the *MCH*, and the *MCHC*.

The *MCV* measures the average size of circulating erythrocytes. It can help to quantify anemia as microcytic (small cells) or macrocytic (large cells).

An elevated *MCV* is seen with hyperviscosity/polycythemia and also in anemia caused by folate or vitamin *B12*deficiency.

The *MCHC* measures the hemoglobin concentration in a given volume of red blood cells. The *RBCs* described as normochromic, hypochromic, or hyperchromic depending on their color, which is determined by the amount of hemoglobin present in the *RBCs*.

The *MCH* measures the average amount of hemoglobin per *RBCs* in a sample of blood.

The *MCHC* can be used to identify anemia due to an acute or chronic blood loss

Many changes in erythrocyte morphology can be identified using the *CBC,* a few include:

- Anisocytosis (variation in cell size), macrocytosis, microcytosis, schistocytes (fragmented cells and spherocytes (rounded cells). Anisocytosis can be seen on a peripheral blood smear and may indicate a normal variation in the size of the RBCSs.

-Macrocytosis is a condition of abnormally large-sized mature *RBCs* and may be used in the classification of anemias.

-Microcytosis describes *RBCs* of small size and may be seen with anemias caused by chronic blood loss or an iron deficiency.

Schistocytes or fragmented red blood cells are indicative of intravascular hemolysis and can also be seen in cases of disseminated intravascular coagulation(*DIC*)

-Spherocytes, or rounded red blood cells, may indicate congenital spherocytosis, a condition in which the red blood cell lacks a protein critical to the cell membrane. Without this Protein red blood cells maintain a rounded rather than spherical shape

.

2.3.2.2 Leukocytes:

Leukocytes, or WBCs, are the body's main defense against invading organisms. Leukocyte formation begins in the liver at approximately weeks gestation[64].

By approximately 20 weeks gestation, the bone marrow becomes the primary site of leukocyte hematopoiesis.

Leukocytes may be classified as granulocytes or agranulocytes, depending on the presence of granules in the cytoplasm.

The three types of granulocytes are the neutrophils, eosinophils, and basophils.

These cells are the most active in defending the body, with the neutrophils having the primary role.

- Neutrophils are phagocytic cells capable of recognizing, ingesting, and digesting foreign particles; they are generally the first to arrive at the infection site [65].

The neutrophil progresses through six stages of development before it reaches a mature state.

These stages are the myeloblast, promyelocyte, myelocyte, metamyelocyte, band, and finally the polymorphonuclear neutrophil or segmented mature neutrophil.

The release of immature neutrophils from the bone marrow storage pool into the bloodstream is not fully understood.

It is thought that certain substances regulate the production and movement of the neutrophils.[66]

When mature neutrophils leave the storage pool and move into the bloodstream, approximately half circulate freely in the bloodstream, constituting the circulating pool.

The remainder adhere to the vessel walls as the marginating pool.

The neutrophils move constantly between the circulating pool and the marginating pool.

Neutrophils circulate in the blood stream for about 6–8 hours before they migrate to the tissues, where they can live for an additional 24 hours[67]

A small number of bands, immature neutrophils, are normally released into the bloodstream with the mature neutrophils.

If these circulating cells cannot meet the body's demand and the storage pool is depleted, more bands and other immature cells are released from the storage pool into the bloodstream.

-Mature eosinophils have a bi-lobed nucleus with distinctive granules in the cytoplasm.

They have immuno-enhancing and immunosuppressive functions and play a role in selective tumor response, helminthic (parasitic) infections, and allergies.

-Mature basophils have a bi-lobed nucleus with metachromatic granules in the cytoplasm that contain heparin, histamine, and several other proteins[64].

Basophils mature and differentiate in the bone marrow before they are released into the circulation.

They function in chemotaxis; phagocytosis; granule release of histamine, perioxidase, and heparin; and in factor synthesis.

-Basophils also participate in hypersensitivity reactions.

The two types of agranulocytes are lymphocytes and monocytes. -Lymphocytes function in the immune response.

There are three types of lymphocytes:

B cells, T cells, and the natural killer (*Nk*) cells.

Lymphocytes are small, round cells with blue-black nuclei after staining; they are not phagocytes, but are migratory cells[68].

-Monocytes are large cells with a horseshoe-shaped nucleus.

They are specialized phagocytes that are able to release cellular mediators.

They can circulate in the bloodstream for approximately eight hours, after which they migrate to the tissues to become macrophages.

They defend against intracellular parasites; remove cellular debris; participate in iron metabolism; present antigens to lymphocytes during an immune response; and secrete various enzymes, factors, and interferons[64][68].

2.3.2.2.1 Abnormalities of the WBCs:

The CBC measures the number and types of circulating leukocytes.

The differential count identifies the types of leukocytes according to their morphology and categorizes the types as a percentage value on the CBC[61].

Leukocytosis refers to an elevated *WBC* count; it may be seen with infections, leukemias, or leukemoid reactions. If the *WBC* count is determined using an automated cell analyzer, it can be falsely elevated because this machine frequently counts/misidentifies nucleated red blood cells *(NRBCs*) as *WBCs* because they are similar in size, routinely, this is corrected in the laboratory by a manual count of all the cells on a peripheral smear; however, it can also be calculated Leukopenia refers to a decreased *WBC* count; it can be seen with viral or bacterial infections as well as in infants born to women with pregnancy-induced hypertension (*PIH*), morphologic or degenerative changes that may be seen in granulocytes include

vacuoles (visible openings), Dohle bodies (cytoplasmic inclusions), and toxic granulation (larger-than-normal granules).

These are nonspecific changes that can be found in approximately 63 percent of neonates with confirmed sepsis [61].

In 1979, Manroe and coleagues from the University of Texas Southern Medical School published reference values for blood neutrophil concentrations [66].

This landmark study has been used as a baseline to identify and study neutrophil ranges during the first 60 hours after birth.

Neutrophilia is an increase in the number of neutrophils in the bloodstream and can result from inflammation, certain malignancies, or the presence of corticosteroid drugs.

Neutropenia is a decrease in the number of neutrophils in the bloodstream and can result from infection, impaired bone marrow production, or abnormal distribution, itis more predictive of neonatal sepsis than is neutrophilia, but it can also be associated with *PIH* ,birth asphyxia, intrauterine growth restriction*, Rh* hemolytic disease, or periventricular hemorrhage.

Neutropenia associated with *PIH* is a result of diminished production and generally resolves in three to five days [68].

Eosinophilia is frequently overlooked because its significance and causative factors are not clearly understood, it may be caused by infection, antibiotics, exposure to antigens in parenteral nutrition, catheters, and blood products; it may also be seen in preterm infants experiencing an anabolic growth period .

2.3.2.3 Thrombocytes:

Thrombocytes, or platelets, are produced in the bone marrow by polyploidy cells called megakaryocytes.

Megakaryocytes become giant cells and undergo a process of fragmentation that creates approximately 1.000 platelets/megakaryocyte. Platelets are tiny [69] microns in size.

They are disc-shaped, noncellular, anuclear, containing cytoplasmic granules and can survive for approximately nine to ten days in the bloodstream [70].

The major function of platelets is to promote primary emostasis. During a healthy state, platelets circulate in the bloodstream without adhering to the walls of blood vessels or other cells.

When the endothelial lining of the blood vessel becomes njured, platelets are activated. In response to injury, they transform their shape, adhering to and aggregating at the injury site to form a primary hemostatic plug [71].

Platelet Abnormalities Thrombocytopenia and thrombocytosis can be identified on a CBC Thrombocytopenia is a condition of reduced platelets, It is one of the most common hematologic problems in sick neonates [72] it can be caused by decreased production or by increased destruction, sequestration, or loss as a result of many conditions. The differential diagnosis includes bacterial and viral sepsis, hypoxia, *DIC*, necrotizing enterocol it is, persistent pulmonary hypertension of the newborn, erythroblastosis fetalis ,polycythemia, congenital infections, congenital anomalies/syndromes, neonatal alloimmune thrombocytopenia, maternal immune thrombocytopenic purpura, and pre eclampsia[73].

Depending on the severity of the thrombocytopenia, the symptoms may vary, but can include petechiae; purpura; gastrointestinal, cutaneous, and mucosal bleeding; hematuria; and central nervous system hemorrhage [74].

Neonates rarely display signs of thrombocytosis, it may be physiologic or associated with infection, inflammation, iron deficiency, medications such as the cephalosporins, asplenia syndrome, vitamine deficiency, congenital neoplasms, Down syndrome, or congenital adrenal hyperplasia. [75]

2.4 Previous studies

- Study done by Goldberg GL1, Gibbon DG, Smith HO, et al . about Clinical impact of chemotherapy-induced thrombocytopenia in patients with gynecologic cancer [76].

- Study done by Chul Won Choi, Hwa Jung Sung,Kyong Hwa Park ,
About risk factor of chemotherapy-induced febrile neutropenia. [77]

- Study done by Walter Cj, Bell TO L, Parsons S R,et al .Prevalence and significance of anemia in patients receiving long-course neoadjuvant chemoradiotherapy [78].

- Study done by Jerome E, Groopman Loretta M. Itri , about Chemotherapy-Induced Anemia in Adults incidence and treatment . [79]

-Study done by Crawford J ,Dale DC, Lyman GH. 80-Crawford J ,Dale DC, Lyman GH. about Chemoherapy induced neutropenia ,risk consequences ,and new directions for its management .[80]

s

Chapter three

Materials and Methods

3. Materials and methods

3.1 study design:

This is a cross sectional study conducted to assessment the complete blood count among patients receiving chemotherapy in tumor treatment and researches center during the period from (march to august 2018).

3.2 Study area:

This study was conducted in Tumor Therapy and Cancer Research Center which located in the Rever Nile State in Shendi town. The center was established in 2016 and contain chemotherapy unit , radiotherapy unit, Radioiodine Therapy unit, Atomic survey of members unit and Early detection of Breast Cancer unit.

3.3 Study population:

A total of 50 samples collected of study group of cancer patients under chemotherapy treatment.

3.4 Inclusion criteria:

Patients of both sexes with cancer taken chemotherapy treatment (had one dose of chemotherapy were included).

3.5 Exclusion criteria:

Patients of cancer treated by other type of treatment other than chemotherapy.

3.6 data collection tools :

Data was collected using questionnaire which specifically designed to obtain information that helped in study.

3.7 Blood sampling:

Venous blood collected using sterile disposable plastic syringe after cleaning the venipuncture area with (70%) ethanol, the blood added to the EDTA anticoagulant.

3.8 Methods:

3.8.1CBC was done by using Mindray Haematology Analyzer (Mindray -3000 plus):

3.8.1.1 Principle:

Blood cells can be broadly divided into three categories .red blood cells, White blood cells and platelets.

The analyzer measures the number of cells and distinguishing between their types according to size using sheath flow *DC* detection. Electrical current is passed through a solution; this method measures the changes in electrical resistance that occurs when blood cells pass through detection aperture.

This instrument performs haematology analyses according to the *RF/DC* detection method, Hydro Dynamic Focusing (*DC* Detection), and sodium lauryl sulphate (*SLS*) haemoglobin method. The radio frequencies and direct current (*RF/DC* detection method) detects the volume of blood cells by changes in direct- current resistance.

3.8.1.2 Procedure:

RBCs count, Hct, Hb concentration, haematimetric indices *(MCV, MCH, and MCHC), WBCs* and platelets counts were measured by using an automatic blood cell counter (Mindray -3000 analyzers). The assay was performed according to the instructions provided by the manufacturer.

The analyzer was controlled by normal control, abnormal high and abnormal low.

The EDTA blood samples were aspirated into analyzer through a sample probe, and the counting was started automatically, the results were displayed on the screen within (20) second, the print key was pressed to print out the results.

3.9 Ethical consideration:

The consent of the selected individuals to the study was taken after being informed with all detailed objectives of the study and it is health emphasis in the future.

3.10 Data analysis:

The collected data code in master sheet and proceed for analysis using SPSS version (20) (mean, standard deviation, P.value by using Paired test).

Chapter four

Results

4. Results

4.1 Demographic and clinical data of haematological cancer (H.CA) and non haematological cancer (NH.CA):

-The (10) blood sample collected from haematological cancer patients under treatment by chemotherapy pre and post chemotherapy dose include frequency of sex was 7 males (70%) and 3 females (30%), frequency of age groups 20-50 years 4 (40%), age groups 51-80 years 21 (40%) and age groups more than 80 is 5(20%) .

-Also (40) blood sample collected from non haematological cancer patients under treatment by chemotherapy pre and post chemotherapy dose include frequency of sex was 18 males (45%) and 22 females (55%), frequency of age groups 20-50 years 11 (27.5%), age groups 51-80 years 21 (60%) and age groups more than 80 is 5(12.5%) .Table (4-1)

Table (4-1) : Distribution of study population according to sex and age for haematological cancer (H.CA) and non haematological cancer (NH.CA):

Characteristic		H.CA		NH.CA	
		Frequency	percent %	Frequency	Percent %
Sex	Male	7	70%	18	45%
	Female	3	30%	22	55%
	T0tal	10	100%	40	100%
Age/ yrs	20-50 yrs	4	40%	11	27.5%
	51-80 yrs	4	40%	24	60.0%
	>80 yrs	2	20%	5	12.5%
Total		10	100%	40	100%

4.2 Laboratory Data of haematological cancer (H.CA) and non haematological cancer (NH.CA) for Hb , RBCs and RBCs indices pre and post chemotherapy:

-The mean values in haematological cancer for Hb, RBCs, PCV, MCV, MCH, MCHC, in pre chemothearapy were (9.9 g/dl), ($3.6x10^{12}$/l), (31.2%), (86.9 fl), (26.6 pg) and (30.8 g/dl) respectively and in post chemotherapy the mean values of Hb, RBCs, PCV, , MCV, MCH, MCHC were (8.1g/dl), ($3.2x10^{12}$/l), (27.3%), (72.3 fl), (25.9 pg) and (30.0 g/dl) respectively.

-Also the mean values in non haematological cancer for Hb, PCV, RBCs, MCV, MCH, MCHC, in pre chemothearapy were (11.8 g/dl), (35.7%), ($4.1x10^{12}$/l), (84.7 fl), (27.7 pg) and (31.8 g/dl) respectively and in post chemotherapy the mean values of Hb, PCV, RBCs, MCV, MCH, MCHC were (10.0 g/dl), (31.9%), ($3.5x10^{12}$/l), (84.6 fl), (26.3 pg) and (30.7 g/dl) respectively. Table (4-2)

Table (4.2): Comparison between pre and post chemotherapy in *Hb*, *RBCs* and *RBCs* indices of haematological cancer (H.CA) and non haematological cancer (NH.CA):

H.CA						NH.CA			
Group		N	Mean	SD	P.value	N	Mean	SD	P.value
Hb g/dl	Pre	10	9.9	1.82	0.000	40	11.8	1.52	0.000
	Post	10	8.1	2.40		40	10.0	1.80	
RBCs	Pre	10	3.6	0.79	0.344	04	4.1	0.63	0.000
	Post	10	3.2	0.78		40	3.5	0.61	
PCV	Pre	10	31.2	4.97	0.045	40	35.7	4.95	0.000
	post	10	27.3	5.21		40	31.9	5.56	
MCV	Pre	10	86.9	9.09	0.000	40	84.7	6.29	0.982
	post	10	72.3	5.21		40	84.6	13.50	
MCH	Pre	10	26.6	3.02	0.090	40	27.7	2.17	0.000
	post	10	25.9	3.89		40	26.3	2.22	
MCHC	Pre	10	30.8	2.26	0.027	40	31.8	1.61	0.020
	post	10	30.0	2.23		40	30.7	2.01	

4.3 Laboratory Data of haematological cancer (H.CA) and non haematological cancer (NH.CA) for TWBCs and Platelet pre and post chemotherapy

-The mean in haematological cancer for TWBCs, platelet count in pre chemotherapy were (159.0 x 10^9 /l) and (205.7 x 10^9 /l) respectively and the mean of TWBCs, platelet count in post chemotherapy were (8.0 x 10^9 /l) and (108.0 x 10^9 /l) respectively.

-Also the mean of TWBCs, platelet count in pre chemotherapy were (30.20 x 10^9 /l) and (323.0 x 10^9 /l) respectively and the mean of TWBCs, platelet count in post chemotherapy were (13.900 x 10^9 /l) and (180.0 x 10^9 /l) respectively. table (4-3).

Table (4.3): Comparison between pre and post chemotherapy in WBCs count and platelet of haematological cancer (H.CA) and non haematological cancer (NH.CA):

H.CA						NH.CA			
Group		N	Mean	SD	P.value	N	Mean	SD	P.value
TWBCs	pre	10	159.0	2,71	0.107	40	30.20	4.7	0.014
	post	10	8.0	6.8		40	13.900	2.1	
Platelet	pre	10	205.7	72.99	0.040	40	323.6	159.73	0.000
	post	10	108.4	6.26		40	180.0	114.59	

Chapter five

Discussion

Conclusion

Recommendation

5.1 Discussion

Cancer is group of diseases involving abnormal cell growth with the potiential to invade or spread to other part of the body [81]

The results of this study obtained showed that strong significant decreased in the in Hb RBCs, MCV, MCH, MCHC, of non haematological cancer after post chemotherapy (P value 0.00) and insignificant decreased in pcv (p.value > 0.05). Also showed a significant decreased in Hb, PCV, MCV, MCHC of hematological cancer post chemotherapy (p.value < 0.05) and no significant decrease in RBCs and MCH (p.value > 0.05) .

Results of this study was agreement with study done by Walter Cj, Bell L To, Parsons S R, Jmd that showed the prevalence of anaemia in patients undergoing long-course neoadjuvant radiotherapy [78].

The results of these study also donated that insignificant decrease in TWBCs of hematological cancer post chemotherapy (p.value> 0.05) and significant decrease of TWBCs in non hematological cancer post chemotheray (p.value<0.05).

These results of this study was agreement with study done by Chul Won Choi,Hwa Jung Sung,Kyong Hwa Park et that showed the early lymphopenia as a risk factor for chemotherapy-induced febrile neutropenia their abstract conclusion the febrile neutropenia (*FN)* is a frequent complication of cancer chemotherapy, which causes death in 4–21% of patients and worsens the quality of life of patients group.[77]

Also these result was agreement with study done by Crawford J ,Dale DC, Lyman GH showed that the cytotoxic chemoyherapy suppresses the heamatopoietic system and the neutropenic complications associated with myelosuppressive chemotherapy are asignificant cause of morbidity and mortality possibly compromised treatment outcomes.[80]

The result of these study prevailed that a significant decreased in platelet count of hematological and non haematological cancer post chemotherapy (p.value< 0.05),

these result was agreement with the study done by Goldberg GL1, Gibbon DG, Smith HO. et al, revealed that Thrombocytopenia occurred in 182 (36.3%) patients with gynecologic cancer treated with chemotherapy [76]

5.2 Conclusion

- Hb, PCV, red cells indices were lower in post chemotherapy when compared by pre chemotherapy result.
- TWBCs and platelet were also lower in post chemotherapy when compared by pre chemotherapy result.
- The chemotherapy was induced anemia, neutropenia and thrompocytopenia.

5.3 Recommendations

1-Haematological and biochemical tests should be checked regularly in cancer disease patients.

3-There is a need to improve the patients' with risk factors of chemotherapy and awareness of chemotherapy complications, This could be achieved by improving patients' counseling by primary care physicians, or through campaigns and media to aware general populations.

4-More investigations should be done for cancer disease patients.

References

1. Breasted JH. The Edwin Smith Surgical Papyrus. Chicago: University of Chicago Press,(2005),vol.1,(pp.451-452).

2. Ebbell B. The Papyrus Ebers. Copenhagen: Levin and Munksgaard,(1937),vol.2,(pp.12-14).

3. Boyle P, and Levin B. World cancer report ,(2008),vol.3,(pp.45-47).

4. Pippa G Corrie PhD FRCP is Consultant Medical Oncologist at Addenbrooke's Hospital and the University of Cambridge,(2007),vol.2,(pp.90-93).

5. Clayton J A, Rodgers S, Blakey J, Avery A and Hall P. "Thiazide diuretic prescription and electrolyte abnormalities in primary care" Br J Clin Pharmacol. January (2006),vol 61,(pp. 87–95).

6. http://www.national heart lung and blood institute diseases and conditions index.nih.gov/health//dci/diseases/bdt-expect.html

7. Hung MJ, Cherng WJ. Comparison of white blood cell counts in acute myocardial infarction patients with significant versus insignificant coronary artery disease. Am J Cardiol (2003),vol. 91,(pp. 39–42).

8. Hanahan D, Cherng WJ. Hallmarks of cancer,(2001),vol.1,(pp.56-60).

9. Couzin-Frankel J. Breakthrough of the year. Cancer immunotherapy. Science, (2013) ,vol.2,(pp. 342-344).

10. Hanahan D, Weinberg R. The Hallmarks of Cancer Cell,.(2000),vol.100,(pp57-70).

11. Hahn W, Weinberg R. Modeling the Molecular Circuitary of Cancer. Nature Reviews Cancer. (2002),vol,2,(pp. 331-341).

12. Chen Z, Sun L. Nonproteolytic Functions of Ubiquitin in Cell Signaling. Molecular Cell.(2009), vol.3,(pp.275-286).

13. Lemmon M, Schessinger J. Cell Signaling by Receptor Tyrosine Kinases. Cell. (2010),vol. 141,(pp.1117-1134).

14. Amaravadi R, Thompson C. The Roles of Therapy-Induced Autophagy and Necrosis in Cancer Treatment. Clin Cancer Res.(2007).vol,13,(pp.7271-7279).

15. Baehrecke E. Autophagy: dual roles in life and death?. Nature Reviews Molecular Cell Biology. (2005),vol. 6(pp.505-510).

16. Carthew R, Sontheimer E. Origins and Mechanisms of miRNAs and siRNAs. Cell. (2009),vol. 136,(pp.642-655).

17. Esquela-Kerscher A, Slack F. Oncomirs- microRNAs with a role in cancer. Nature Reviews Cancer.(2006),vol.6(pp.259-269).

18. Muntean A, Hess J. Epigenetic Dysregulation in Cancer. American Journal of Pathology.(2009),vol 175(pp.1353-1361).

19. Imam J, Buddavarapu K, Lee-Chang J, et al. MicroRNA-185 suppresses tumor growth and progression by targeting the Six1 oncogene in human cancers. Oncogene. (2010),vol. 29(pp.4971-4979).

20. Copeland N, Jenkins N. Harnessing the transposons for cancer gene discovery. Nature Reviews Cancer. (2010),vol.9,(pp. 696-706).

21. O'Donnell K, Burns K. Mobilizing diversity: transposable element insertions in genetic variation and disease. Mobile DNA. (2010),vol.21,(pp.45-49).

22. Gatenby R, Gillies R. Why do cancers have high aerobic glycolysis. Nature Reviews Cancer.(2004).vol.4(pp.891-899).

23. Levine A, Puzio-Kuter A. The Control of the Metabolic Switch in Cancers by Oncogenes and Tumor Suppressor Genes. Science. (2010), vol.330,(pp.1340-1344).

24. Bild A, Potti A, Nevins J. Linking oncogenic pathways with therapeutic opportunities. Nature Reviews Cance ,(2004),vol.6,(pp.223-227).

25. Barabasi A-L, Oltvali Z. Network Biology: Understanding The Cells Functional Organization. Nature Reviews Genetics. (2004),vol. 5,(pp.101-113).

26. union for international cancer Babbu Singh,(2001).

27. Osiecki H Cancer: A Nutritional, Biochemical Approach, Bioconcepts Publishing, (2002)
28. Howes R M. “Dangers of antioxidants in cancer patients: a review,” Philica, Article ID 153, (2009).
29. Ma T , Das S. Pereira , et al., “Efficacy of dietary antioxidants combined with a chemotherapeutic agent on human colon cancer,” (2009), vol. 29,
(pp. 2421–2426).
30. Sagar J, Chaib B, Sales K,. Winslet M, and Seifalian A.“Role of stem cells in cancer therapy and cancer stem cells: a review,” Cancer Cell International, (2007), vol. 7, (pp. 9-19) .
31.. Wu X.Z, “A new classification system of anticancer drugs—based on cell biological mechanisms,” Medical Hypotheses, (2006), vol. 66, (pp. 883–887).
32. Lamson D.W and X Brignall S. “Antioxidants in cancer therapy; their actions and interactions with oncologic therapies,” Alternative Medicine Review , (2006), vol. 4, (pp. 304–329).
33. Cairns R, Papandreou I and Denko N.“Overcoming physiologic barriers to cancer treatment by molecularly targeting the tumor microenvironment,” Molecular Cancer Research, (2006), vol. 4, (pp. 61–70).
34. Myhr G. “MR guided cancer treatment system for an elevated therapeutic index—a macroscopic approach,” Medical Hypotheses, (2008), vol. 70, (pp. 665–670).
35.Ghosh K, Thodeti C.K, Dudley A.C, Mammoto A, Klagsbrun M, and Ingber .E, “Tumor-derived endothelial cells exhibit aberrant Rho-mediated mechanosensing and abnormal angiogenesis in vitro,” Proceedings of the National Academy of Sciences of the United States of America, (2008), vol. 105, (pp. 11305–11310).

36. Fishman P, Bar-Yehuda, Synowitz S .M et al. “Adenosine receptors and cancer,” Handbook of Experimental Pharmacology, (2008), vol. 193, (pp. 399–441).

37. Bansal T, Jaggi M, Khar R.K, and Talegaonkar S.“Emerging significance of flavonoids as P-glycoprotein inhibitors in cancer chemotherapy,” Journal of Pharmacy and Pharmaceutical Sciences, (2009), vol. 12, (pp. 46–78).

38. Lu D.Y, Ch X.Len and Ding .J, “Individualized cancer chemotherapy integrating drug sensitivity tests, pathological profile analysis and computational coordination—an effective strategy to improve clinical treatment,” Medical Hypotheses, (2006), vol. 66, (pp. 45–51).

39. Liska D.J. “The detoxification enzyme systems,” Alternative Medicine Review, (1998), vol. 3, (pp. 187–198).

40. Wu .C.P, C. Hsieh H, and Wu Y.S, “The emergence of drug transporter-mediated multidrug resistance to cancer chemotherapy,” Molecular Pharmaceutics, (2011), vol. 8,(pp. 199–200).

41. Berruti A, Brizzi M.P, Generali D et al. “Presurgical systemic treatment of nonmetastatic breast cancer: facts and open questions,” Oncologist, (2008), vol. 13, (pp. 1137–1148).

42. Steeg P.S and Theodorescu D. “Metastasis: a therapeutic target for cancer,” Nature Clinical Practice Oncology, (2008), vol. 5, (pp. 206–219).

43. Ding W.Q, Liu .B, Vaught .J.L, Palmiter R.D and Lind .S.E, “Clioquinol and docosahexaenoic acid act synergistically to kill tumor cells,” Molecular Cancer Therapeutics, , (2006), vol. 5, (. 1864–1872).

44. Ahmad A, Banerjee S, Wang Z , Kong .D, Majumdar A.P.N and F. H. Sarkar, “Aging and inflammation: etiological culprits of cancer,” Current Aging Science, (2009), vol. 2, (pp. 174–186).

45. Mongrain V and Cermakian N. “Clock genes in health and diseases,” Journal of Applied Biomedicine, (2009), vol. 7, (pp. 15–33).
46. Haus E. “Chronobiology in oncology,” International Journal of Radiation Oncology, Biology, Physics, (2009), vol. 73, (pp. 3–5).
47. Gorbacheva V.Y, Kondratov R.V, Zhang R et al. “Circadian sensitivity to the chemotherapeutic agent cyclophosphamide depends on the functional status of the CLOCK/BMAL1 transactivation complex,” Proceedings of the National Academy of Sciences of the United States of America, (2005), vol. 102, (pp. 3407–3412).
48. Sajan J ,Cinu T.A, Chacko A.J, Litty J and Jaseeda T. “Chronotherapeutics and chronotherapeutic drug delivery systems,” Tropical Journal of Pharmaceutical Research, (2009), vol. 8, (pp. 467–475).
49. Sahar S and Sassone-Corsi P. “Metabolism and cancer: the circadian clock connection,” Nature Reviews Cancer, (2009), vol. 9, (pp. 886–896).
50. Antoch M.P, Kondratov R.V, and Takahashi J.S. “Circadian clock genes as modulators of sensitivity to genotoxic stress,” Cell Cycle, (2005), vol. 4,(pp. 901–907).
51. Zhou H, Zou .P, Chen Z.C, and You. Y. “A novel vicious cycle cascade in tumor chemotherapy,” Medical Hypotheses, (2007), vol. 69, (pp. 1230–1233).
52. Kovacic P. “Unifying mechanism for anticancer agents involving electron transfer and oxidative stress: clinical implications,” Medical Hypotheses, (2007), vol. 69, (pp. 510–516).
53. Loprinzi C.L, Barton D.L, Jatoi A et al. “Symptom control trials: a 20-year experience,” Journal of Supportive Oncology, (2007), vol. 5,(pp. 119–128).
54. Philips B.U. The Case for Cancer Nutritional Support, The Cancer Nutrition Network of Texas, (1999),vol.6(pp.786-787).
55. Al-Tonbary Y, Al-Haggar M, El-Ashry R, El-Dakroory S, Azzam .H and Fouda A “Vitamin E and N-acetylcysteine as antioxidant adjuvant therapy in

children with acute lymphoblastic leukemia," Advances in Hematology, (2009), vol.3,(pp.56-65) Article ID 689639.

56. Kim J.J and Tannock I.F. "Repopulation of cancer cells during therapy: an important cause of treatment failure," Nature Reviews Cancer, (2005), vol. 5, (pp. 516–525) .

57. Semenza G.L. "Defining the role of hypoxia-inducible factor 1 in cancer biology and therapeutics," Oncogene, (2010), vol. 29,(pp. 625–634).

58. Balducci L and Ershler W.B, "Cancer and ageing: a nexus at several levels," Nature Reviews Cancer, (2005), vol. 5, (pp. 655–662).

59. Jopling J , Henry e, Weidmeier S.e & Christensen D. Reference ranges for hematocrit and blood hemoglobin concentration during the neonatal period: Data from a multihospital health care system.Pediatrics, (2009),vol.123, (pp.333–337).

60. Walters M. C. & Abelson H. T. Interpretation of the complete blood count. Pediatric Clinics of North America, (1996),vol. 43,(pp. 1–16).

61. Blackburn S. T. Hematologic and hemostatic systems. In S. T. Blackburn (ed.),Maternal, fetal and neonatal physiology: A clinical perspective, (2007), vol 4, (pp. 227–266)..

62. Brugnara C & Platt O. S. The neonatal erythrocyte and its disorders. In D. g. Nathan & S. H.Orkin (eds.), Nathan and Oski's hematology of infancy and childhood, (1998), vol. 1,(pp. 19–52).

63. Widness J.A. Treatment and prevention of neonatal anemia.NeoReviews, (2008),vol 9,(pp.526–533).

64. Tappero e. Clinical and laboratory evaluation of neonatal infection. In D. F.Askin (ed.), Infection in the neonate: A comprehensive guide to assessment, management, and nursing care, (2004),vol.5, (pp. 129–141).

65. Christensen R. D, Jopling J, Henry e & Wiedmeier S. e. The erythrocyte indices of neonates, defined using data from over 12.000 patients in a multihospital health care system. Journal of Perinatology, (2008),vol. 4,(pp. 24 –28).

66. Dinauer M. C. The phagocytic system and disorders of granulopoiesis and granulocyte function. In D. g. Nathan & S. H. Orkin (eds.), Nathan and Oski's hematology of infancy and childhood, (1998), vol.1, (pp. 890–967).

67. Boxer L. A.. Neutrophil abnormalities. Pediatrics in Review, (2003),vol. 24, (pp.52– 61).

68. Boxer L. A., & Blackwood, R. A. Leukocyte disorders: Quantitative and qualitative disorders of the neutrophil, part I Pediatrics in Review, (1996), vol.17,(pp.19–28).

69. kapur R., Yoder M. C & Polin, R. A. Developmental immunology. In R. J. Martin, A. A. Fanaroff, & M. C. Walsh (eds.), Fanaroff and Martin's neonatal-perinatal medicine: Diseases of thenewborn and fetus, (2006), vol. 2,(pp. 761–882).

70. Polak J. D, Lott J. W & kenner C. Overview of the fetal/neonatal immune system., (1994),vol.2,(pp. 11–20).

71. Manroe B. L, Weinberg A.g & Rosenfeld, C. R. The neonatal blood count in health and disease, Part I: Reference values for neutrophilic cells. The Journal of Pediatrics, (1979),vol.6, (pp 89–98).

72. Maheshwari A. & Christensen R. D. Neutropenia in the neonatal intensive care unit, (2004),vol.5,(pp. 431–443).

73. Buchanan g. R. Thrombocytopenia during childhood, (2005) ,vol. 26,(pp 401–409).

74. Handin R. I. Blood platelets and the vessel wall. In D. gNathan & S. H. Orkin (eds.), Nathan and Oski's hematology of infancy and childhood, (1998), vol. 2,(pp. 1511–1530).

75. Wong W & glader, B. Approach to the newborn who has thrombocytopenia. NeoReviews, (2004),vol. 5, (pp.444–450).

76- Goldberg GL, Gibbon DG, Smith HO, DeVictoria C, Runowicz CD, Burns ER, Clinical impact of chemotherapy-induced thrombocytopenia in patients with gynecologic cancer. (Nov 1994). vol 12, (pp.2317-2320).

77- Chul Won Choi Hwa Jung Sung Kyong Hwa Park et al, Early lymphopenia as a risk factor for chemotherapy-induced febrile neutropenia, (August 2003) , vol 73, Issue4 ,(pp. 263-266)

78 - Walter Cj ,Bell L To, Parsons S R, Wheeler J md , Prevalence and significance of anemia in patients receiving long-course neoadjuvant chemoradiotherapy for rectal carcinoma Atricle in Colorectal Disease ,(May 2012) Vol. 4,(pp.324-327).

79- Jerome E. Groopman Loretta M. Itri, Chemotherapy-Induced Anemia in Adults: Incidence and TreatmentJNCI Journal of the National Cancer Institute, (6 October 1999),vol 91, Issue 19, (pp 1616–1634).

80-Crawford J ,Dale DC, Lyman GH. Chemoherapy induced neutropenia ,risk consequences ,and new directions for its management ,(Jan 2004) , vol 2,(PP.15-37).

81-John wiley and sons,Rachel airly cancer chemotherapy,(2009),vol.1,(pp.53-54).

Appendix

Appendix I

Questionnaire

Assessment of Complete Blood Count Among Patients Receiving Chemotherapy at Tumor Therapy and Cancer Research Center in Shendi Town

-Name…….……No( )

-Sex

Male ( ) Female ( )

-Age

20-50 yrs ( )

51-80 yrs ( )

More than 80yrs ( )

-Type of cancer

H.CA ( )

NH.CA ( )

-CBC Result:

-TWBCs……..…… × 10^9/L

-HB……. g/dl

-RBCs……. 10^{12}/L

-PCV…….…..%

-MCV……..……fl

-MCH…….…….……..pg

-MCHC……..……..…… g/dl

-Platelet……..10^9/L

Appendix II

إقـــرار بالموافقـــة

الاسم :----------

العمر :---------- العنوان :----------

أوافق بمحض إرادتي بالمشاركة في البحث العلمي المتعلق بدراسة تقييم فحص الدم الكامل لدي المرضي الذين يخضعون للعلاج الكيميائي في مركز علاج وأبحاث السرطان بمدينة شندي.

الباحثة/أمل عبد الله عبد الرحمن عوض الله

بعد أن شرح لي بأنه لا يترتب عليه أي أذى جسدي أو نفسي واعلم أن المشاركة في هذا البحث لن تؤثر بأي حال من الأحوال في الرعاية الطبية التي أتلقاها كما أنه يحق لي بدون إبداء أسباب الانسحاب من هذا البحث في أي مرحلة من مراحله.

البحث بإشراف:

د: حمزة احمد حسن محمدالتوم

التوقيع : ---------- التاريخ :----------