Retrospective study of breast cancer in young women: patient and disease characteristics

A Thesis Submitted By

Mariam Emil Francis

M.B.B.Ch.

In Partial Fulfillment of Master Degree

Under The Supervision of

Prof. Dr. Mohamed Mahmoud Mousa

PROFESSOR OF CLINICAL ONCOLOGY

FACULTY OF MEDICINE CAIRO UNIVERSITY

Dr.Soha Mohammed Talima

LECTURER OF CLINICAL ONCOLOGY

FACULTY OF MEDICINE
CAIRO UNIVERSITY

Dr.Shaimaa Farouk Lasheen

LECTURER OF CLINICAL ONCOLOGY

FACULTY OF MEDICINE CAIRO UNIVERSITY

2016

ACKNOWLEDGEMENT

Before all , I should express my thanks and gratitude to **GOD** , the greater doctor , the most merciful healer , the creative of all creatures and the beholder of all knowledge.

I would like to express my sincerest appreciation and gratitude to my professor, **Prof. Dr. Mohammed Mahmoud Mousa**, professor of clinical oncology, Faculty of medicine, Cairo university, for his valuable supervision, generous help in each step, and precious criticism and suggestions for this work. It was a pleasure and privilege to work under his supervision and constructive guidance.

I am also deeply grateful and indebted to **Dr.Soha Mohammed Talima**, Lecturer of clinical oncology, Faculty of medicine, Cairo university, for her sincere effort, fruitful suggestions, meticulous advice and continuous encouragement.

And my deep thanks to **Dr. Shaimaa Farouk Lasheen**, lecturer of clinical oncology, Faculty of medicine, Cairo university, for her cooperation and kind support.

I am most deeply thankful to those whom I burdened a lot, keep pushing me forward and supporting me throughout my life My Father, My Mother and My family since without their encouragement, I would have not been able to accomplish this work.

Table of contents

List of abbreviations	ii
List of tables.	V
List of figures.	vi
Abstract	viii
Introduction and aim of work	1
Review of literature	3
Chapter 1 Breast Cancer at Young age	3
Chapter 2 Management	12
Chapter 3 Unique Challenges	28
Chapter 4 Pregnancy Associated Breast Cancer	40
Patients and methods	
Results	56
Discussion	92
References	105
Summary and recommendations	128
Arabic summary	129

List of abbreviations

AMH Antimüllerian Hormone

AR Androgen Receptor

BCT Breast Conservation Therapy

BMI Body Mass Index

CBE Clinical Breast Examination

CNS Central Nervous System

CIA Chemotherapy-Induced Amenorrhea

CRA Chemotherapy Related Amenorrhea

CT Computed Tomography

DFS Disease Free Survival

EBCTCG Early Breast Cancer Trialists' Collaborative Group

EGFR Epidermal Growth Factor Receptor

 $\mathbf{E}\mathbf{R}\alpha$ Estrogen Receptor α

ERβ Estrogen Receptor β

ET Endocrinal Therapy

FSH Follicle-Stimulating Hormone

G-CSF Granulocyte Colony-Stimulating Factor

GnRH Gonadotropin-Releasing Hormone

Gy Grey

HER2 Human Epidermal Growth Factor 2

HR hormone receptor

IHC Immunohistochemistry

IQ Intelligence Quotient

IVF In-Vitro Fertilization

MAPK Mitogen-Activated Protein Kinase

MR Magnetic Resonance

mRNA Messenger Ribonucleic Acid

mTOR Mammalian Target Of Rapamycin

OS Ovarian Suppression

PALB2 Partner And Localizer of BRCA2

PBSO Prophylactic Bilateral Salpingo-Oophorectomy

pCR Pathological Complete Remission

PDL 1 Program Death Ligand 1

PMRT Postmastectomy Radiotherapy

PR Progesteron Receptor

PABC Pregnancy-Associated Breast Cancer

PTEN Phosphatase and Tensin Homologue

RANKL Receptor Activator of Nuclear Factor Kappa B

Ligand

RCOG Royal College of Obstetricians and

Gynaecologists

RT Radiotherapy

SBE Self-Breast Examination

SEER Surveillance, Epidemiology, and End Result **SLNB** Sentinel LN biopsy **TP53** Tumor Protein 53 WBRT Whole Breast Radiation Therapy iv

List of tables

- **Table 1**: Breast cancer features in younger patients
- **Table 2:** contraindications to breast conservative surgery
- Table 3: Risk stratification for adjuvant chemotherapy in breast cancer
- **Table 4:** Rate of chemotherapy related amenorrhea associated with standard chemotherapy regimens
- **Table 5:** Potential fertility preservation options
- Table 6: Results, Occurrence of relapse and correlation with variables
- **Table 7:** Results, Relapse site and correlation with other variables
- **Table 8:** Results, DFS according to age, pregnancy at presentation, stage and biological subtype
- Table 9: Results, Personal and disease characteristics according to age
- Table 10: Results, Treatment according to age
- **Table 11**: Results, Personal and disease characteristics according to pregnancy at presentation
- Table 12: Results, Treatment according to pregnancy at presentation

List of figures

Figure 1: Meta-analysis anthracycline based vs CMF.

Figure 2: SOFT trial curves Tamoxifen alone vs exemestane +OS

<u>Figure 3:</u> Results, Family history-total patients.

Figure 4: Results, Side of malignancy-total patients.

Figure 5: Results, Distant metastasis-total patients.

Figure6: Results, Stage at presentation-total patients.

Figure 7: Results, Pathological types-total patients.

Figure 8: Results, Node positivity -total patients

Figure 9: Results, Grade-total patients

Figure 10: Results, Biological subtype-total patients

Figure 11: Results, Treatment setting.

<u>Figure 12:</u> Results, First line chemotherapy type.

Figure 13: Results, Second line chemotherapy type.

Figure 14: Results, Use of bisphosphonates.

Figure 15: Results, Radiotherapy aim

Figure 16: Results, First line hormonal treatment aim

Figure 17: Results, 1st line hormonal treatment drug

Figure 18: Results, DFS of 132 patients

Figure 19: Results, DFS according to age group (<35 vs.35-39)

Figure 20: Results, DFS according to pregnancy at presentation

Figure 21: Results, DFS according to stage

Figure 22: Results, DFS according to biological subtype

Figure 23: Results, Stage at presentation in patients less than 35 vs patients 35-39

Figure 24: Results, Biological subtype in patients less than 35 vs patients 35-39

Figure 25: Results, Onset of presenting symptom PABC vs no pregnancy

<u>Figure 26</u>: Results, Occurrence of distant metastasis. PABC vs no pregnancy

Figure 27: Results, Surgery type No pregnancy vs PABC

Figure 28: Results, First line chemotherapy aim. No pregnancy vs PABC

Abstract

Background:

Although uncommon, breast cancer in young women is worthy of special attention due to the unique and complex issues that are raised. More aggressive biology and late stages at presentation present specific challenges associated with the care of younger breast cancer patients. Other unique challenges which include fertility preservation, management of inherited breast cancer syndromes, maintenance of bone health, secondary prevention, and attention to psychosocial issues require further attention from health professionals.

Patients & Methodology:

This is a retrospective study conducted at Kasr-Al-Ainy oncology center "NEMROCK" in the period from March 2015 to September 2016. The medical records of female patients diagnosed with breast cancer under the age of 40 years in the period from January 2005 to December 2014 were retrospectively reviewed and reported upon.

Results:

There was no statistically significant difference in disease characteristics and treatment outcomes between patients aged less than 35 and patients aged 35-39.

Pregnancy associated breast cancer patients presented with stage 4 disease more than non-pregnancy associated. Time from onset of presenting symptom to diagnosis was significantly longer in PABC patients.

Conclusion:

Young women diagnosed with breast cancer tend to have more aggressive biology and consequently poorer prognosis. PABC patients tend to present late and consequently at later stages.

Key words:

Breast Cancer - Young- Kasr Al Ainy-below 40

Introduction and Aim of Work

Approximately 7% of women with breast cancer are diagnosed before the age of 40 years, and this disease accounts for more than 40% of all cancer in women in this age group. Survival rates are worse when compared to those in older women, and multivariate analysis has shown younger age to be an independent predictor of adverse outcome. Chemotherapy, endocrine, and local therapies have the potential to significantly impact both the physiologic health—including future fertility, premature menopause, and bone health—and the psychological health of young women as they face a diagnosis of breast cancer.

Study Objectives:

- -To retrospectively evaluate the clinical and pathological data as well as the outcome of patients diagnosed with breast cancer at an age younger than fourty.
- -To retrospectively compare the clinic-pathological data and the outcome of patients diagnosed at an age younger than 35 to those diagnosed at an age of 35-39 years (in an effort to define which is a more relevant age cut-off for breast cancer diagnosed at a young age in our region).

-To retrospectively report on those patients diagnosed with pregnancy-
associated breast cancer (defined as breast cancer diagnosed during
pregnancy and till one year after labour).(193)
2

Review of literature

CHAPTER 1

BREAST CANCER AT YOUNG AGE

Introduction

Early-onset breast cancer is relatively rare; however, it represents the commonest cause of cancer in women under age the of 40 (1). In the US, approximately 33,000 women under the age of 45 years are diagnosed with breast cancer every year, and it is the leading cause of cancer-related deaths in this age group (2). Compared to older women with breast cancer, younger women tend to have a more aggressive biology and a poorer prognosis (Table 1). Younger women with breast cancer also face unique challenges such as premature ovarian failure, psychosocial issues with ongoing careers, and raising young families, as well as extended survivorship periods and its attendant complications. It is therefore imperative to recognize the unique issues that younger women face and plan management in a multidisciplinary fashion to optimize clinical outcomes.

Breast cancer screening

Screening for breast cancer should begin at age 40 for average-risk women (3). This includes annual mammography and clinical breast examination (CBE). Breast self-examination (BSE) is an additional option. For average-risk women under age 40, screening consists of CBE every 3 years with optional BSE; routine use of imaging is not recommended.