THE DIAGNOSTIC AND PROGNOSTIC POTENTIALS OF CA 15.3 AS A TUMOUR MARKER IN PATIENTS WITH BREAST CANCER

Thesis

Submitted for the Partial Fulfilment of M.D. degree in General surgery



Abd El-Ghany Mahmoud Elshamy

6 16.99449 M.B., B.Ch. M.S

Supervisors

Prof. Dr. Abd El Meguid El-Shinnawy

Prof. of General Surgery Faculty of Medicine Ain Shams University

Prof. Dr. Ali Khalifa

Prof. of Biochemisty Faculty of Medicine

Ain Shams University

Dr. Thanaa Helal

Assistant Prof. of Pathology Faculty of Medicine Ain Shams University

Dr. Ahmed Mohamed Lotfi

Lecturer of General Surgery Faculty of Medicine Ain Shams University

Faculty of Medicine Ain Shams University

ACKNOWLEDGEMENT

First and foremost thanks are to **ALLAH** " The most beneficent, the merciful".

Second, I would like to express my deepest thanks and gratitude to Prof. *Dr. Abd El-Meguid Elshinnawy*, professor of surgery, Faculty of Medicine, Ain Shams University, for his guidance, his instructive advice and continuous support. Moreover, I sincerely appreciate his valuable time, effort and understanding. No words can express my feelings and respect for him.

I am very much priviledged and honoured to have prof. *Dr. All Kalita*, professor of Biochemistry and head of Diagnostic Oncology unit, Faculty of medicine, Ain Shams University, Supervise This work. I am grateful to him for his kind supervision, continuous guidence and valuable advices.

Appreciative thanks to *Dr. Thanaa Helai* Assistant professor of pathology, Ain Shams university, for her valuable help and advice during the production of this work.

I am deeply indebted to *Dr. Ahmed Lotti* Lecturer of surgery, Ain Shams University for his valuable advices, scientific guidance, his fruitful discussion and for the continuous assistance during this work.

I wish to express my sincere thanks to *Dr. Moustafa El Rasad*, Assistant professor of Biochemistry for his helpful advice and revision of this work.



Finally, I appreciate the effort done by many members of section (6) surgery at ELDEMERDASH Hospital and members of Diagnostic Oncology Unit, Faculty of medicine, Ain Shams University in leading profitable discussion and collecting references of this work.

Abd El-Ghany Elshamy

1992

To my mother's soul

CONTENTS

	Page	
□ Introduction & Aim of the work	1	
☐ Review of the Literature		
* Aetiologic and risk factors of breast cancer	4	
* Diagnosis of breast cancer	15	
* Pathology of breast cancer	41	
* Tumour Markers	95	
Classification of tumour markers in breast cancer	106	
Carcinoembryonic Antigen (CEA)	117	
Cancer Antigen 15.3 (CA15.3)	127	
Other new turnour markers in breast cancer	150	
☐ Materials & Methods	156	
□ Results	165	
☐ Discussion	207	
□ Conclusion	220	
□ Summary	221	
□ References	223	
☐ Arabic Summary		

ABBREVIATIONS

AFP: Alpha Fetoprotein.

APR : Acute phase reactants.

BH CG : Beta Human Chorionic Gonadotropin.

B.S : Bone Scanning

CA 15.3: Cancer Antigen 15.3.

Cath D: Cathepsin D.

CEA : Carcinoembryonic Antigen.

CIS : Carcinoma In Situ.

CR : Complete response.

CT/M : Computed Tomography Mammography.

EIA : Enzyme Immunoassay.

EMA : Epithelial Membrane Antigen.

FNAB : Fine needle Aspiration Biobsy.

IDC : Infiltrating ductal Carcinoma.

ILC : Infiltrating Lobular Carcinoma.

IRMA : Immuno radiometric Assay.

LCIS : Lobular Carcinoma In Situ.

MCA : Mucinous Carcinoma Antigen.

MRI : Magnetic Resolance Imaging.

MSA : Mammary Serum Antigen.

n : Number.

NED: No evidence of disease.

ng/ml : Nanogram per milliliter.

NHcl : Normal hydrochloric acid.

nm : Nano meter.

NOS : Not otherwise specified.

P : Probability.

PAP : Prostatic acid phosphatase.

POA : Pancreatic oncofetal antigen.

PSA: Prostatic specific antigen.

RIA: Radio immunoassay.

S.D : Standard deviation.

SD : Stable disease.

TPA : Tissue polypeptide antigen.

U/ml : Unit per milliliter.

W.H.O: World health organization.

> : more than.

< : less than.

μl Microliter.

LIST OF TABLES

			Page
Table	(1)	The clinical data of breast cancer group.	167
Table	(2)	The pathological data of breast cancer group.	168
Table	(3)	Clinical & pathological data of benign breast disease	
		group.	169
Table	(4)	Clinical data for the control group.	170
Table	(5)	Biochemical Results of the Breast Cancer Group.	171
Table	(6)	Biochemical Results of the Control Group.	172
Table	(7)	Biochemical Results of the Benign Breast Group.	172
Table	(8)	CEA serum values in control, benign and Malignant	
		groups.	174
Table	(9)	The Sensitivity and specificity at different cut off values	
		for CEA.	175
Table	(10)	Correlation between preoperative CEA serum value and	
		clinical stage of Breast cancer.	178
Table	(11)	Preoperative CEA serum level in relation to Axillary ly-	
		mph node infiltration.	179
Table	(12)	Correlation between the Preoperative CEA serum level	
		and Histologic grade.	180
Table	(13)	Preoperative CEA serum level in relation to vascular in-	
		vasion in breast cancer group.	181
Table	(14)	Preoperative CEA serum level in relation to Metastasis	
		Detected on follow up.	182
Table	(15)	Comparison between the preoperative and post	
		operative (three months) CEA serum levels in breast	
		cancer group.	184

			Page
Table	(16)	Post operative (three months) CEA serum values in	
		relation to Metastasis Detected on follow up.	185
Table	(17)	Comparison between preoperative and postoperative	
		CEA serum values in cases that did not develop meta-	
		stasis on follow up.	186
Table	(18)	Comparison between preoperative and postoperative	
		CEA serum values in cases that developed metastasis	
		on follow up.	187
Table	(19)	CA 15-3 serum values in Control, Benign and Malignant	
		Groups.	189
Table	(20)	The sensitivity and specificity of CA 15.3 at different cut-	
		off values.	190
Table	(21)	Preoperative CA 15-3 serum values in different stages of	
		Breast cancer.	193
Table	(22)	Preoperative CA15-3 serum level in relation to Axillary	
		lymph node infiltration.	194
Table	(23)	Preoperative CA 15-3 serum level in relation to	
		Histologic grade.	195
Table	(24)	Preoperative CA15-3 serum level in relation to vascular	
		invasion.	196
Table	(25)	Preoperative CA15-3 serum level in relation to	
		Metastasis Detected on follow up of breast cancer group.	197
Table	(26)	Comparison between preoperative and postoperative	
		(One and three months) CA15.3 serum values in breast	
		cancer.	200
Table	(27)	Post operative (one month) CA15-3 serum level in rela-	
		tion to Metastasis Detected on follow up.	201

			Page
Table	(28)	Post operative (three months) CA 15-3 serum value in	
		relation to Metastasis Detected on follow up of breast	
		cancer group.	202
Table	(29)	Comparison between preoperative and postoperative	
		CA15.3 serum values in cases that did not develop met-	
		astasis.	203
Table	(30)	Comparison between preoperative and postoperative	
		CA15.3 serum values in cases that developed metasta-	
		sis.	204
Table	(31)	Correlation coefficient between preoperative CA15.3	
		and CEA serum levels in breast cancer group.	206
Table	(32)	Correlation coefficient between post operative (after	
		three months) CA 15.3 and CEA serum levels in breast	
		cancer group.	206

LIST OF FIGURES

			Page
Fig.	(1)	Preoperative CEA mean serum values in different groups.	174
Fig.	(2)	CEA serum values in control, Benign and breast cancer patients.	176
Fig.	(3)	Preoperative CEA mean serum value in different stages of breast cancer.	178
Fig.	(4)	Preoperative CEA mean serum level in relation to Axillary lymph nodes infiltration.	179
Fig.	(5)	Preoperative CEA mean serum level in relation to different Histologic grades.	180
Fig.	(6)	Preoperative CEA mean serum level in correlation with vascular invasion.	181
Fig.	(7)	Preoperative CEA mean serum level in correlation with metastasis detected on follow up.	182
Fig.	(8)	Comparison between preoperative and post operative (after three months) CEA mean serum values in breast	
Fig.	(9)	cancer group. Postoperative (3 Ms) CEA mean serum values in	184
		correlation with metastasis detected on follow up postoperatively.	185
Fig.	(10)	Comparison between preoperative and postoperative (after three months) CEA mean serum levels in cases	
Fig.	(11)	that did not develop metastasis on follow up.	186
· ·g·	(,,,	(three months) CEA mean serum values in cases that	107
Fig.	(12)	'	187
Fig.	(13)	groups. CA 15.3 serum values in control, Benign and breast can-	189
		cer patients.	191

			Page
Fig.	(14)	Preoperative CA 15.3 mean serum values in different	
		stages of breast cancer.	193
Fig.	(15)	Preoperative CA 15.3 mean serum level in relation to	
		Axillary L.N infiltration.	194
Fig.	(16)	Preoperative CA 15.3 mean serum levels in different	
		Histologic grades.	195
Fig.	(17)	Preoperative CA 15.3 mean serum levels in correlation	
		with vascular invasion.	196
Fig.	(18)	Preoperative CA 15.3 mean serum levels in correlation	
		with postoperative metastasis detected on follow up.	197
Fig.	(19)	Comparison between preoperative and post operative	
		(one and three months) CA 15.3 mean serum values in	
		breast cancer group.	200
Fig.	(20)	Postoperative (1 M) CA15.3 mean serum level in	
		relation to metastasis detected on follow up of breast	
		cancer group.	201
Fig.	(21)	Postoperative (3 Ms) CA 15.3 mean serum value in	
		relation to metastasis detected on follow up	
		postoperatively.	202
Fig.	(22)	Comparison between preoperative and post operative	
		(one and three months) CA 15.3 mean serum levels in	
		cases that did not develop metastasis on follow up.	203
Fig.	(23)	Comparison between preoperative and post operative (1	
		and 3 Ms) CA 15.3 mean serum values in cases that	
		developed metastasis on follow up.	204

INTRODUCTION AND AIM OF THE WORK

INTRODUCTION

Breast cancer is one of the commonest cancers which affect females and continued to be the leading cause of death from cancer in women (Contesso & Tawfik, 1984).

In the united states breast cancer is extremely common disease. About 120,000 cases are diagnosed annually. Fewer than 10% of patients will present with advanced disease and about 40% of patients will develop metastatic disease despite advances in early diagnosis, local treatment, and adjuvant therapy. A ten years report (1970 - 1981) from the national cancer institute in Cairo showed that breast cancer is the most frequent malignancy among females presenting to the institute, accounting for 34.7% of all female cancer cases and 14% of all cases of cancer registered (Contesso & Tawfik, 1984).

Breast cancer still stands as a handicap in front of surgeons who aim at cure. Diversity of biological behaviour and lines of management, reflect the unique behaviour of this type of malignancy. The only remaining hope is the full study of other aspects of this disease that may help to alter the unsatisfactory results achieved up till now. Thanks to the many biological, biomolecular and endocrinological implications, breast cancer appears to be one of the most promising fields of investigation, from which most of scientists expect fundamental discoveries to be made, that can be then applied to other oncological areas (Contesso & Tawfik, 1984).

Although we all feel frustrated by the bitter knowledge that the real causes of breast cancer are still unknown and that very little can be done