الآيـــــة

بسم الله الرحمن الرحيم

قال تعالى:

(قالوا سبحانك لا علم لنا الا ما علمتنا أنك أنت العليم الحكيم)

صدق الله العظيم

DEDICATION

To my parents and brothers for their lifelong love and encouragement

……

To my friends and all people that I love, who supported me, believed in me and stood beside my academic aspiration.

ACKNOWLEDGEMENT

At the beginning I thank the God for helping me in doing and completing this work.

I am grateful to my Supervisor Professor Dr. Amel Omer Bakhiet Department of Pathology, College of Veterinary Medicine Sudan, University of Science and Technology who helped me with her time, patience and knowledge.

I am grateful to Dr. Moneira Abd allah Mansour, Department of Histopathology and Cytology, College of Medical Laboratory Science, Sudan University of Science and Technology

Special thanks and acknowledgment to: Nada Salih Salih and to my colleagues.

Yosra Edris Abdallah Karar

ABSTRACT

This is a descriptive retrospective study carried out in Radiation and Isotope Center-Khartoum, Sudan, during the period of February 2012 to July 2012.

The study aimed to detect the association of Epstein- Barr virus expression and ER, PR, and HER2 receptors among Sudanese females with Breast Cancer. The age of the studied group ranged from 20 to 80 years.

Fifty formalin fixed paraffin wax embedded tissue blocks were selected from women patients with breast cancer these consisted of 43 with invasive ductal carcinoma, 1 with invasive papillary carcinoma, 2 with mucinous carcinoma, 2 with ductal carcinoma in situ and 2 with medullary carcinoma. Tissue sections were stained using immunohistochemistry methods for detection of EBV marker. SPSS computer program was used to analyze the obtained data and results.

The results showed that the majority of breast cancer patients have invasive ductal carcinoma (86%) ranging from 31-40 years of age. The majority of cases were high grade (56%).

64% showed positive expression for ER, 49% for PR, 54% for Her-2 and 34% for EBV among breast cancer types.

As well as 28% were positive for EBV among the age group ranging from 31-50, 34% of tumor grade, 18% of ER , 14% of PR and 22% were positive for both EBV and Her-2 while 12% were EBV positive Her-2 Negative.

On the basis of these findings the study concluded that; the expression of EBV were statistically significant among Sudanese women with breast cancer (P value = 0.04) and age (P value=0.02).

No association between the ER, PR, HER2 markers and EBV expression as results indicated.

ملخص الاطروحه

هذه دراسة وصفيه استعادية أجريت في مركز الاشعه والطب النووى، الخرطوم، السودان، خلال الفترة من فبراير 2012 الى يوليو 2012.

هدفت الدراسة إلى الكشف عن العلاقة بين فيروس ابشتاين بار ومستقبلات ER, PR and HER-2 لدى الإناث السودانيات المصابات بسرطان الثدي و اللآتي تتراوح أعمارهن بين 20 إلى 80 عاماً. وقد تم اختيار خمسين عينة مقطع نسيجي من أنسجة الثدي المصابة بالسرطان و المحفوظة في الفورمالين و مثبتة يشمغ البارفين و تحتوي هذه العينات علي 43 عينة من سرطان الأقنية الغازية invasive ductal carcinoma، 1 من سرطان حليمي الغازية، invasive papillary carcinoma ، 2 من سرطان موسينية mucinous carcinoma، 2 من سرطان الأقنية في الموقع ductal carcinoma in situ ، 2 من سرطان النخاع medullary carcinoma .

تم صبغ المقاطع النسيجية باستخدام طريقة الكيمياء النسيجية المناعية للكشف عن علامة الفيروس

وأظهر النتيجه أن الغالبية العظمى من المصابات بسرطان الثدي لديهن سرطان الأقنية الغازية (86٪) و تتراوح أعمارهن ما بين 31-40 سنة من العمر. وكانت غالبية الحالات من الدرجة العالية (56٪).

64% اظهرت ايجابيه لهرمون الاستروجين ، 49% لهرمون البروجسترون، 22% لهير 2 و 34% لفيروس ابشتاين بار بين أنواع سرطان الثدي.

وكذلك كانت 28٪ ايجابيه لفيروس ابشتاين بارا بين الفئات العمرية التي تتراوح 31 بين-50،34% من درجة الورم ،18% لهرمون الاستروجين، 14% لهرمون البروجسترون ،22% كانت ايجابيه لفيروس الابشتاين بار و الهير- 2 ، في حين كانت 12% ايجابيه لفيروس ابشتاين و سلبيه للهير-2 .

على أساس هذه النتائج ، خلصت الدراسة إلى أن الارتباط بين سرطان الثدي عند الإناث السودانيات وفيروس ابشتاين بار ذو دلالة احصائية. والى وجود ارتباط ذو دلالة احصائية بين العمر ووجود الفيروس ' وعدم وجود ارتباط بين المستقبلات والفيروس.

List of Contents

Subject	Page No.
الآية	i
Dedication	ii
Acknowledgement	iii
Abstract	iv
ملخص الاطروحه	v
List of Contents	vi
List of Tables	viii
List of Figures	ix
INTRODUCTION	
Introduction	1
Objectives	2
CHAPTER ONE	
Literature Review	3
1.1. Breast: Anatomy and Histology	3
1.2. Breast benign condition and Inflammation	5
1.3. Signs and symptoms of breast changes	6
1.4. Screening methods	6
1.5. Breast cancer	6
1.5.1. Type of breast cancer	7
1.6. Epstein –Barr virus (EBV)	10
1.6.1. Molecular biology of EBV	10
1.6.2. Strain of EBV	11
1.6.2.1. EBV latent proteins	11
1.6.2.2. Latent membrane protein (LMP)	12
1.6.2.3. EBERs	12

1.6.2. Pathology of EBV	**12**
1.6.3. Immunity of EBV	**13**
1.6.4. Immortalization of Normal Breast Epithelial Cell by EBV	**14**
1.6.5. Epidemiological Cofactors in EBV-Associated Malignancy	**14**
1.6.6. EBV and Breast cancer	**15**
1.7. Immunohistochemistry	**19**
1.7.1 General aspect of Immunohistochemistry	**21**
1.7.2. Antigen Retrieval	**21**
1.7.3. Antibody and Detection system	**22**
CHAPTER TWO	
3. Materials and Methods	**23**
3.1. Study Design	**23**
3.2. Study Area	**23**
3.3. Study population and Sample size	**23**
3.4. Data collection	**23**
3.5. Histopathology	**23**
3.5.1 Sample preparation	**23**
3.5.2. Hematoxylin and Eosin stain	**24**
3.5.3. Immunohistochemical staining	**24**
3.6. Statistical analysis	**25**
CHAPTER THREE	
Results	**26**
CHAPTER FOUR	
Discussion	**46**
Conclusion and Recommendations	**48**
REFERENCES	**49**

List of Tables

Table no.	Title	Page
1	**Diagnosis of EBV in different type of breast cancer in fifty women**	40
2	**Diagnosis of EBV in different age group in fifty women with breast cancer**	41
3	**The description of study population by tumor grade**	42
4	**Expression of EBV among ER cancer marker in fifty women**	43
5	**Expression of EBV among PR cancer marker in fifty women**	44
6	**Expression of EBV among HER-2 cancer marker in fifty women**	45

List of Figures

Figure no.	Title	Page
1	**Distribution of study population with breast cancer by age/ years**	29
2	**Classification of study population by the diagnosed breast cancer**	29
3	**The description of study population with breast cancer by tumor grade**	30
4	**The expression of ER cancer marker among the fifty positive breast cancer study samples**	31
5	**The expression of PR cancer marker among fifty positive breast cancer study samples**	32
6	**The expression of HER2 cancer marker among fifty positive breast cancer study samples**	33
7	**The expression EBV cancer marker among fifty positive breast cancer study samples**	34
8	**Invasive ductal carcenoma in slide stained by H&E (x40)**	35
9	**Positive control for EBV expression (LMP-1) in NPC (x40)**	36
10	**Positive expressions of EBV (LMP-1) in breast cancer, the expression appear as brown nuclear color**	37
11	**Positive expressions of EBV (LMP-1) in breast cancer**	38
12	**Invasive ductal carcenoma in slide stained by H&E by (x 40)**	39