

## Dedication

To my father

To my mother

To my brothers and sisters

To my wife and sons

To my kind colleagues

I dedicate this work

## Acknowledgement

Firstly, I would like to thank Allah for giving me knowledge and sport to complete this work.

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## ملخص الاطروحة

اجريت هذه الدراسة الوصفية المستشفوية طويلة المدى في مستشفيات الخرطوم، بن سينا وسوبا في الفترة من يوليو 2006م وحتى يوليو 2008م. هدفت الدراسة لتقويم صلاحية واسمات الاورام BCL<sub>2</sub>, Her<sub>2</sub>, P53, CEA, PSA والثايتوكيراتين ذو الوزن الجزيئي العالي في التعرف والتشخيص التفريقي لاورام البروستاتا.

تم جمع 100 خزعة نسيجية و 100 عينة من دم الوريد عشوائيا من مرضى يعانون من اورام البروستاتا . تم صيغ الخزع النسيجية بطريقتين، طريقة الهيماتوكسلين والايوسين للتشخيص بواسطة امراض الانسجة وطريقة تقنية الانسجة المناعية باستخدام طريقة الافيدين والبايوتين للكشف عن واسمات الاورام . كذلك تم تقدير واسمتي PSA و CEA الدمويتان في عينات الدم باستخدام طريقة التقدير المناعى الاشعاعى (RIA). تم تحليل النتائج باستخدام البرنامج الاحصائي المحوسب المعروف ببرنامج SPSS.

من مجموع 100 مريض يعانون من اورام البروستاتا وعند تشخيص عيناتهم بواسطة امراض الانسجة كانت النتائج كالآتي: 25 حالة ورم البروستاتا الحميد ، 42 حالة سرطان البروستاتا الجيد التفريق و 33 حالة سرطان البروستاتا الضعيف التفريق.

وجدت الدراسة ان مستوى PSA في الدم كان ايجابيا في 34 حالة من مجموع المرضى. واعتمادا على طريقة التشخيص بواسطة امراض الانسجة كمرجعية ذهبية وجد ان الخصوصية النوعية ، درجة الحساسية ، القيمة التنبؤية الموجبة والقيمة التنبؤية السالبة لهذه الواسمة كانت ( 80% )، (45%)، (85%) و(30%) على التوالي. وكان PSA النسيجي ايجابيا في 96 حالة من مجموع العينات، وكان توزيعها كالآتي: 32 حالة اورام البروستاتا الحميد، 41 حالة سرطان البروستاتا الجيد التفريق و 32 حالة سرطان البروستاتا الضعيف التفريق واعتمادا على طريقة التشخيص بواسطة امراض الانسجة كمرجعية ذهبية وجد ان الخصوصية النوعية

ودرجة الحساسية والقيمة التنبؤية الموجبة والقيمة التنبؤية السالبة لهذه الواسمة كانت (8%) ، (98%) ، (76%) و (50%) على التوالي.

وجدت الدراسة ان مستوى CAE في الدم كان ايجابيا في 19 حالة

من مجموع المرضى وكان توزيعهم كالآتي: 3 حالات اورام البروستاتا الحميد ، 8 حالات سرطان البروستاتا ضعيف التفريق و 8 حالات سرطان البروستاتا جيد التفريق، مع خصوصية نوعية، درجة حساسية ، قيمة تنبؤية موجبة و قيمة تنبؤية سالبة لهذه الواسمة كانت (88%) ، (25%) ، (84%) و (27%) على التوالي. وكان CEA النسيجي ايجابيا في 28 من مجموع المرضى وكان توزيعهم كالآتي: 16 حالة ورم بروتاتا حميد ، 11 حالة سرطان بروتاتا جيد التفريق وحالة واحدة فقط سرطان بروتاتا ضعيف التفريق مع خصوصية نوعية ، درجة حساسية ، قيمة تنبؤية موجبة وقيمة تنبؤية سالبة لهذه الواسمة كانت (16%) ، (64%) ، (20%) و (27%) على التوالي.

اما الواسمة P53 فقد اعطت نتيجة ايجابية في 49 حالة من مجموع

المرضى وكان توزيعهم كالآتي 17 حالة ورم بروتاتا حميد ، 29 حالة سرطان بروتاتا ضعيف التفريق و 3 حالات سرطان بروتاتا جيد التفريق مع وجود علاقة ذات دلالة احصائية بين وجود هذه الواسمة وحدة السرطان مع خصوصية نوعية ، درجة حساسية ، قيمة تنبؤية موجبة وقيمة تنبؤية سالبة كالآتي: (88%) ، (61%) ، (93%) و (43%) على التوالي.

اما الواسمة ثايتوكيراتين ذات الوزن الجزيئي العالي فقد اعطت

نتيجة ايجابية في 32 حالة من مجموع المرضى وكان توزيعهم كالآتي 20 حالة ورم بروتاتا حميد، 9 حالات سرطان بروتاتا جيد التفريق و 3 حالات سرطان بروتاتا ضعيف التفريق مع وجود علاقة ذات دلالة احصائية بين هذه الواسمة ونوع السرطان مع خصوصية نوعية ، درجة حساسية ، قيمة تنبؤية موجبة وقيمة تنبؤية سالبة كالآتي (84%) ، (80%) ، (63%) و (93%) على التوالي.

وجدت الدراسة ان العلاقة بين سرطان البروستاتا وافراز  
الواسمتين Her2 و Bcl2 في الانسجة ليست ذات دلالة احصائية.  
كما وجدت الدراسة ان العلاقة بين مستوى واسمتي الاورام PSA و  
CEA في الدم وايجابية افرازها في الانسجة ليست ذات دلالة احصائية.  
وجدت الدراسة ايضا انه من مجموع 100 مريض يعاني من اورام  
البروستاتا ان 62 حالة من مجموع المرضى منهم كانوا من مدخني التبغ  
وكان توزيعهم كالاتي: 6 حالات ورم بروتاتا حميد و 56 حالة سرطان  
البروستاتا مع وجود علاقة ذات دلالة احصائية بين التدخين وسرطان  
البروستاتا.

وجدت الدراسة ايضا انه لا توجد علاقة ذات دلالة احصائية بين  
سرطان البروستاتا مع التاريخ العائلي للسرطان , عدد الزوجات وتعاطي  
الكحول.

خلصت الدراسة الى ان طريقة التشخيص بواسطة امراض الانسجة  
مازالت هي الافضل في تشخيص سرطان البروستاتا وان مستوى  
واسمتي CEA و PSA في الدم غير فعال في التشخيص  
المبكر لسرطان البروستاتا وان تحديد واسمات الاورام Bcl<sub>2</sub>, Her<sub>2</sub> و  
PSA في الانسجة غير فعال في التشخيص التفريقي لاورام البروستاتا و  
ان تحديد واسمات الاورام P53, CEA, والثايتوكيراتين ذات الوزن الجزيئي  
العالي في الانسجة لها فاعلية في التشخيص التفريقي لاورام البروستاتا.

## Abstract

This is a hospital base longitudinal descriptive study aimed to evaluate the validity of PSA, CEA, Her<sub>2</sub>, BcL<sub>2</sub>, P53 and HMW cytokeratin tumor markers in the identification and differential diagnosis of prostate tumors. The study was conducted in Khartoum, Soba, and Ibsina hospitals during the period from July 2006 to July 2008. One hundred biopsies and venous blood samples were randomly collected from patients presenting with prostate tumors. Tissue sections were stained using two methods, histochemical method using haematoxylin and Eosin technique for histopathological diagnosis, and immunohistochemical method using avidin biotin technique immunohistochemical for tumor markers detection. Blood samples were used for estimation of circulating PSA and CEA tumor markers using Radio Immuno Assay (RIA) technique. The obtained Data were analyzed using SPSS computer program.

Out of the 100 patients with prostatic lesions, histopathological diagnosis revealed benign prostatic hyperplasia in 25 patients, well differentiated adenocarcinoma in 42 patients and poorly differentiated adenocarcinoma in 33 patients. Positive PSA levels were found to be in 34 patients. Depending on the histopathology as gold standard the specificity, sensitivity, positive predictive value and negative predictive value of serum PSA were found as (80%), (45%), (85%), and (30%) respectively.

Tissue PSA was positive in 96 patients distributed as follows 23 patients were diagnosed as BPH, 41 patients were diagnosed as well differentiated adenocarcinoma and 32 patients were diagnosed as poorly differentiated adenocarcinoma. Depending on the histopathology as golden standard the specificity, sensitivity, positive predicative value and

negative predictive value of tissue PSA were found as follow (8%) (98%), (76%) and (50%) respectively.

Nineteen patients were found to be positive with CEA levels, which distributed as follows three patients were diagnosed as BPH, eight patients were diagnosed as well differentiated adenocarcinoma and eight patients were diagnosed as poorly differentiated adenocarcinoma, with specificity, sensitivity, positive predictive value and negative predictive value as follow (88%), (25%), (84%) and (27%) respectively. The tissue expressions of CEA were found to be positive in 28 patients. Out of 28 patients with positive CEA expression, 16 patients were diagnosed as BPH, 11 patients were diagnosed as well differentiated adenocarcinoma and only one patient was diagnosed as poorly differentiated adenocarcinoma, with specificity, sensitivity, positive predictive value and negative predictive value as follow (16%), (64%), (20%) and (27%) respectively.

P53 was detected in 49 patients, distributed as follow 17 patients were diagnosed as BPH, 29 patients were diagnosed as poorly differentiated adenocarcinoma and three patients were diagnosed as well differentiated adenocarcinoma, with significant correlation between P53 expression and prostate cancer the P value  $<0.01$ , with specificity, sensitivity, positive predictive value and negative predictive value as follow (88%), (61%), (93%) and (43%) respectively.

HMW cytokeratin was detected in 32 patients, distributed as follow: 20 patients were diagnosed as BPH, nine patients were diagnosed as well differentiated adenocarcinoma and three patients were diagnosed as poorly differentiated adenocarcinoma, with significant correlation between HMW cytokeratin expression and prostate cancer the P value  $<0.01$ . The specificity, sensitivity, positive predictive value and negative

predictive value of HMW cytokeratin were found as follow (84%), (80%), (63%) and (93%) respectively.

The relation between serum levels and tissues expression of PSA and CEA markers were statistically insignificant, the P value  $> 0.01$ .

The study showed that there is no significant relation between prostate cancer and tissues expression of Her<sub>2</sub> and bcl<sub>2</sub> tumor markers.

Out of 100 patients with prostate lesion 62 patients were tobacco users, distributed as follow six patients were diagnosed as BPH and 56 patients were diagnosed as prostatic adenocarcinoma, with significant correlation between tobacco using and prostate cancer the P value  $>0.01$ .

The study found that there was no significant relation between prostate cancer and family history, number of wives and alcohol consumption.

As a conclusion of this study, histopathology still represents the golden standard for specific diagnosis of prostate lesions. PSA and CEA serum levels are insignificant for early defection of prostate cancer. PSA, BcL<sub>2</sub>, and Her<sub>2</sub> tumor markers are invalid in the differential diagnosis of prostate lesions. P53, CEA and HMW cytokeratin tumor markers can be useful in the differential diagnosis of prostate lesions.



## List of abbreviations

<b>ABP</b>	Acute Bacterial Prostatitis
<b>BCL</b>	B. Cell Lymphocyte
<b>BPH</b>	Benign Prostatic Hyperplasia
<b>BRCA</b>	Breast Cancer Gene
<b>CA<sub>125</sub></b>	Carbohydrate 125
<b>CEA</b>	Carcino Embryonic Antigen
<b>DRE</b>	Digital Rectal Examination
<b>FNA</b>	Fine Needle Aspiration
<b>GnP</b>	Granulomatous Prostatitis
<b>H&amp;E</b>	Haematoxylin and Eosin
<b>HCG</b>	Human Chorionic Gonatotropin
<b>HIV</b>	Human Immunodeficiency Virus
<b>HMW</b>	High Molecular Weight
<b>HER</b>	Human Epidermal Growth Factor
<b>I<sub>125</sub></b>	Iodine 125
<b>IGF</b>	Insulin – Like Growth Factor
<b>PBS</b>	Phosphate Buffer Saline
<b>PIN</b>	Prostatic Intra Epithelial Neoplasia
<b>PNH</b>	Prostatic Nodular Hyperplasia
<b>PSA</b>	Prostate Specific Antigen
<b>RIA</b>	Radio Immuno Assay
<b>TRUS</b>	Trans Rectal Ultrasound

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