Prostatic Diseases : The Role of the Prostate - Specific Antigen in Clinical Assessment

Thesis Submitted
by

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M.B.B.ch.

for the Partial Fullfilment of the Master Degree
in Clinical and Chemical Pathology

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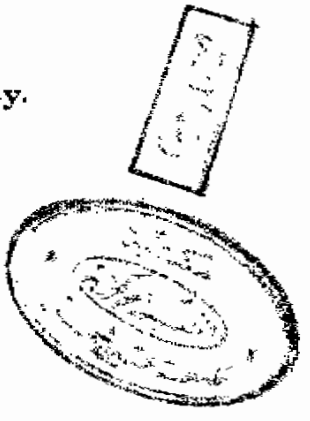

Clinical Pathology Department
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1991

بسم الله الرحمن الرحيم

وقل اعملوا فسيرى الله عملكم

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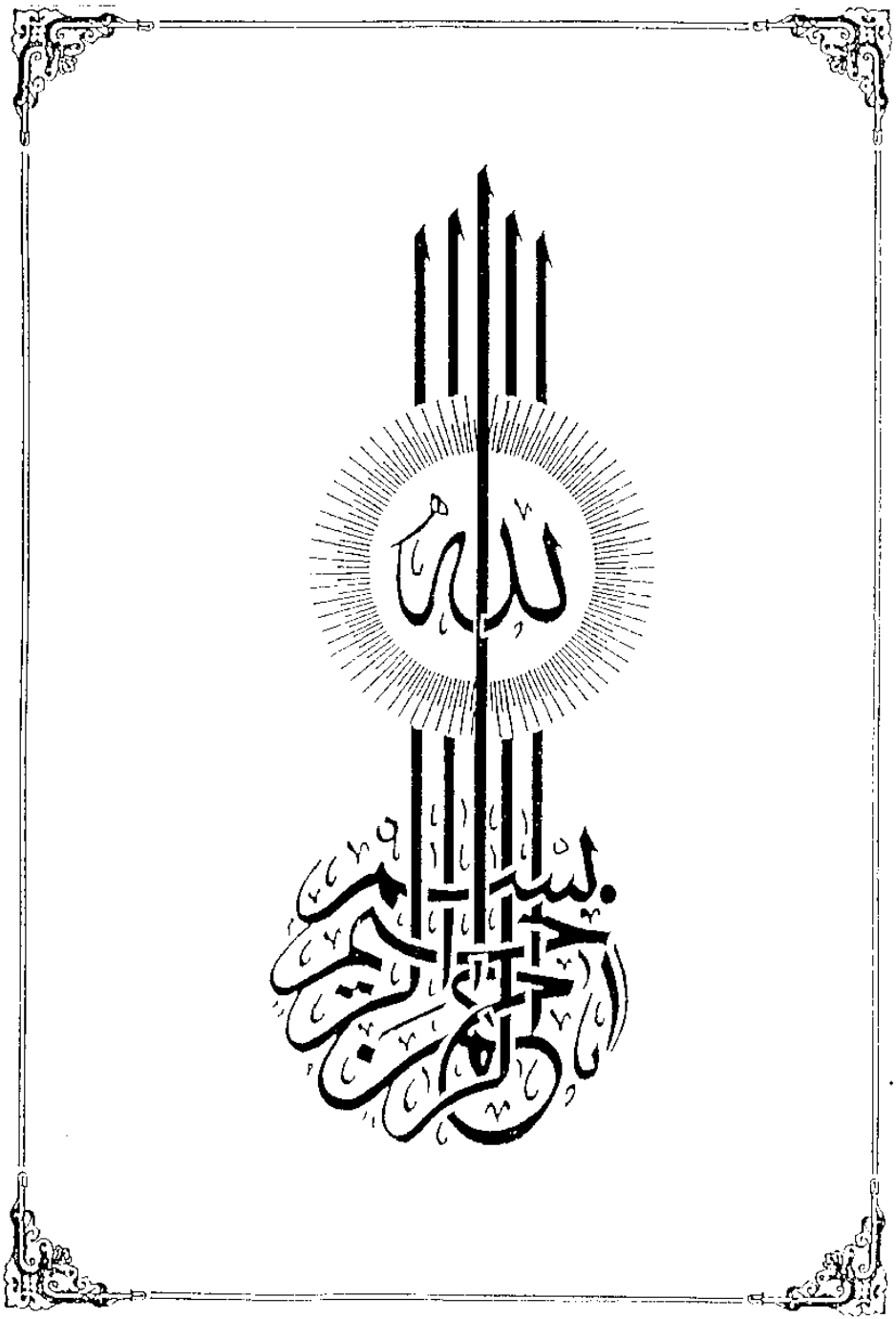

ACKNOWLEDGMENT

It is my pleasure to express my sincere gratitude to Dr. Gehane Kamal–El Din Hassan Aly, Assistant Professor of Clinical Pathology, Ain Shams University, for her ceaseless efforts and insightful supervision which made this research possible.

I would like to thank Dr. Reda Abd–El Tawab Khalil, Assistant Professor of General Surgery, Ain Shams University, for the keen interest he has offered throughout his supervision of the present work.

I am grateful to Dr. Nadia Ali Abd–El Sattar, Lecturer of Clinical Pathology, Ain Shams University, her valuable suggestions and stimulating ideas.

I owe a great debt to Professor Dr. Sawsan Hosni Hamza, Professor of Clinical Pathology and Head of Clinical Chemistry Unit, Ain Shams University, for her constant encouragement and advice during the writing of this thesis.

I wish to thank the staff of the Clinical Pathology Department, Faculty of Medicine, Ain Shams University, for their indispensable help.

ABBREVIATIONS

AJC :	American Joint Committe
ANOVA :	Analysis of Variance
AUS :	American Urology Society
BPH :	Benign Prostatic Hyperplasia
CEA :	Carcinoembrionic Antigen
CIEP :	Counterimmunoelectrophoresis
CK-BB :	Creatine Kinase - BB
CT :	Computed Tomography
CV :	Coefficient of Variation
DOF :	Degrees of Freedom
I^{125} :	Iodine-125
Ir^{192} :	Iradium-192
LDH :	Lactic Dehydrogenase
NPCP :	National Prostatic Cancer Project
PAP :	Prostatic acid phosphatase
PGI_2 :	Prostacyclin
PI :	Isoelectric Point
PSA :	Prostate-Specific Antigen
RIA :	Radioimmunoassay
RNase :	Serum Ribonuclease

ROC : Receiver-Operator Characteristics

SAP : Serum Acid Phosphatase

SD : Standard deviation

SEM : Standard error of the Mean

SST : Gel Barrier Serum Separator Tubes

TAP : Total Acid Phosphatase

UROC : Uro-Oncology Research Group

US : Ultrasonography

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INTRODUCTION

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Prostate Specific Antigen (PSA) was first identified and purified in 1979,(Wang et al.,1979). It is released into the serum only from prostatic tissue or from its metastases, (Sinha et al., 1987). Prostatic acid phosphatase (PAP), if elevated, is indicative of prostate cancer which has spread beyond the confines of the gland. While PSA levels reflect the volume of prostate tissue present in the body, (benign or malignant) and thus may be elevated in the presence of benign prostate hyperplasia as well as in carcinoma, (Cooner et al., 1987). However , PSA has a much greater percentage of elevation in all stages of prostate cancer as compared to PAP, especially in early stages, (Stamey et al., 1987).

Aim of the Work

The aim of our study is to evaluate the clinical performance of the PSA in the diagnosis of prostatic diseases. We investigate the correlation of PSA and PAP in such diseases in an aim to find out if PSA contributes better in the diagnosis and prognosis of prostatic cancer. Total acid Phosphatase (TAP) is also included in our study.

REVIEW OF LITERATURE

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Cancer Prostate

The annual incidence of prostatic cancer in the United States is approximately 50 per 100,000 white man and 95 per 100,000 black man. Moreover, some reports indicate that the incidence of prostatic cancer is rising, (Winkelstien & Ernster, 1979).

Many hormones and chemical substances control the proliferation and behaviour of the prostatic cell e.g.: Testicles, Adrenal cortex, pituitary and hypothalamus, (Byar et al., 1972-Catalona et al., 1974).

There are no environmental factors which cause this disease such as living in rural or urban areas. Moreover research has not proved any relation between smoking and cancer prostate, (Hammond, 1975). The authors of a Japanese study found no relation between residence in Hiroshima and Nagasaki areas at the time of atomic bomb explosion and the

subsequent development of cancer prostate, (Bean et al., 1973). But a familial association has been reported, (Krain, 1973).

Zinc which is related to chronic prostatitis, is known to be concentrated in prostate. Cadmium which acts as Zinc antagonist has been suspected to be a causative agent in prostatic carcinoma but there is no statistically significant risk proving this until now. Studies of Catholic priests in Los-Angeles have shown no deficit in prostate cancer mortality cases when compared with the population as a whole, (Ross et al., 1983). Noble demonstrated that the prostate is androgen sensitive when he injected testosterone subcutaneously in rats and developed cancer prostate, (Noble, 1977).

Anatomical Considerations

The prostate is a solid organ surrounding the Urethra between the base of the bladder and the urogenital diaphragm. It has a walnut shape, somewhat pyramidal. It is situated just distal to the bladder neck and its apex is resting against the urogenital diaphragm. Its consistency is

similar to that of the tip of the nose. Characteristically carcinoma is having a firmer consistency. The normal weight of the prostate gland is approximately 20 grams,(Catalona, 1984).

Classically the prostate has been described as consisting of five lobes: anterior, posterior, median and two lateral lobes. The posterior lobe is the part of the gland felt by the examining rectal finger. More recent study by McNeal in 1981 defined four anatomical areas:

I. Peripheral zone, constituting 70% of the glandular prostate. Almost all carcinomas of the prostate arise in this gland.

II. The central zone is constituting 25% of the glandular prostate. The central zone is markedly different histologically from peripheral zone.

III. The periprostatic region is the Urethral segment proximal to the verumontanum. This is the exclusive site of benign prostatic hyperplasia.

IV. The anterior fibromuscular stroma is the anterior surface of the gland.

The prostatic acini are lined with columnar epithelium with two cell layers. The peripheral ducts are lined with

glandular epithelium which then change into transitional epithelium at the central prostatic duct and Urethra, (McNeal et al., 1981).

Natural History of Prostatic Cancer and Route of Spread

More than 95% of prostatic carcinomas arise in the glandular epithelium of the peripheral glands of the prostate, (McNeal, 1965), in contrast to benign prostatic hyperplasia, which originates from the central or periurethral portions of the gland. These observations led McNeal in 1969 to conclude that evidence from volume distribution data suggests that there are not two types of prostatic carcinoma with different biological potential, but a single species having slow growth rate with a logarithmic growth curve. The development of carcinoma in the gland follows predictable patterns, including early involvement of the capsule and perinural spaces. The later course of tumor growth is characterised by a loss of differentiation and the ability to penetrate the capsule and periurethral stroma.

Stage "A" lesion is assumed to be the source of all prostatic cancer but it never becomes clinically manifest.

It is usually found in autopsy studies, (Whitmore, 1973).

The tumor may form one or more nodules in one or more lobes. 77% of pathologic specimens of radical prostatectomy multiple tumor foci were found throughout the gland, because of the peripheral location of the lesions. The tumor then extends into and through the capsule of the gland and invades the periprostatic tissues. It may extend into the seminal vesiecls and later involves bladder neck or rectum. Tumor invasion of perineural spaces, lymphatics and blood vessels explains the lymphatic and distant metastases, (Jewett, 1980).

The lymph nodes metastases depends on the tumor extent and on the degree of differentiation. First they found correlation between the rise of the tumor and the probability of lymphatic metastases, (Flocks et al., 1959). In a recent study, they demonstrate the relationship between the clinical stage and the degree of differentiation with the frequency of the nodal metastases, (middleton, 1987). The first lymph nodes to be affected are the periprostatic and the obturator lymph node, then the tumor extends to the external iliac and the hypogastric group and later to common iliac and preaortic nodes. About 7% of patients get