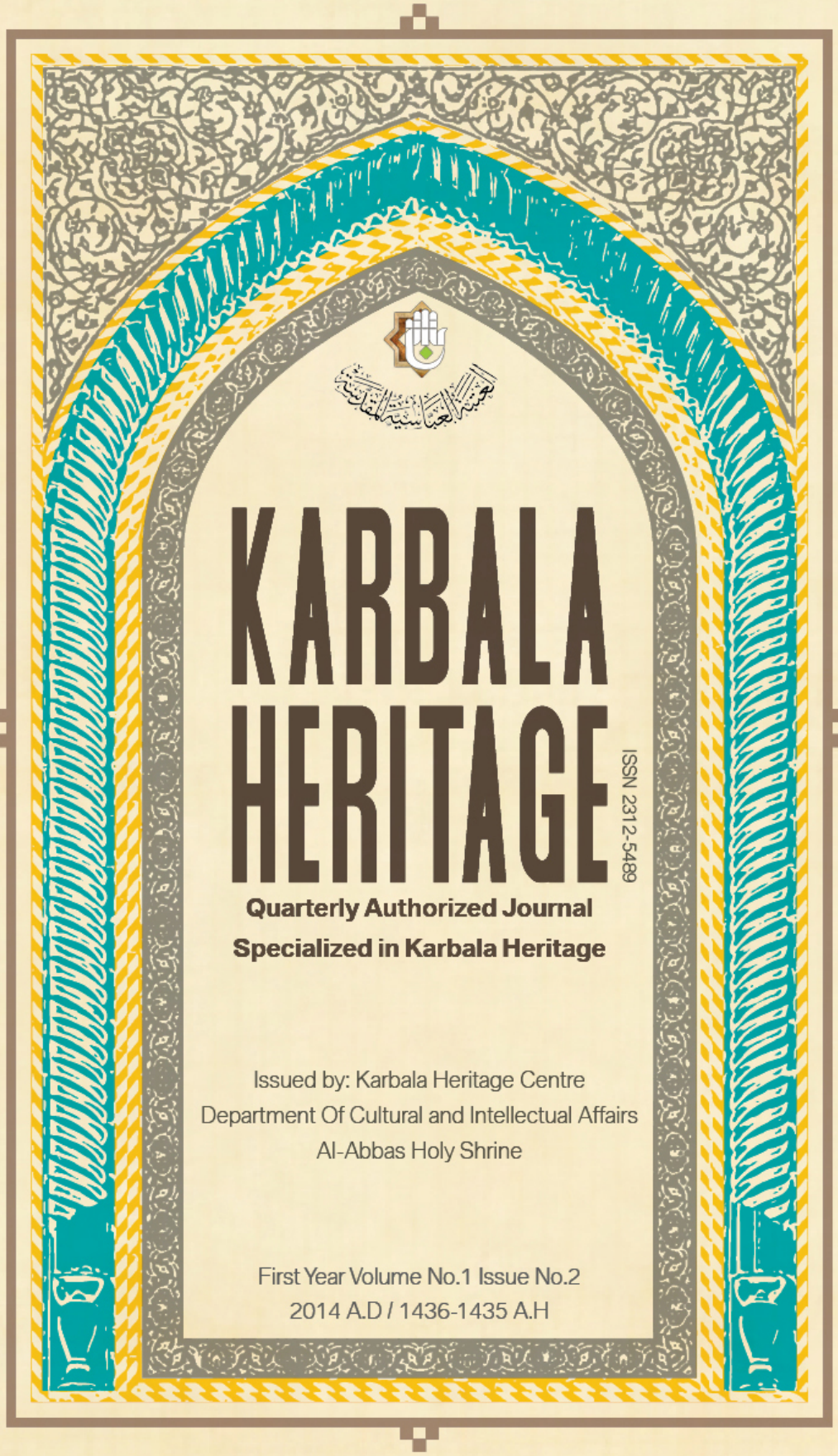

KARBALA HERITAGE

ISSN 2312-5489

Quarterly Authorized Journal

Specialized in Karbala Heritage

Issued by: Karbala Heritage Centre
Department Of Cultural and Intellectual Affairs
Al-Abbas Holy Shrine

First Year Volume No.1 Issue No.2
2014 A.D / 1436-1435 A.H

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Licensed by Ministry of Higher Education
and Scientific Research Republic of Iraq
Reliable For Scient Ific Promotion

First Year Volume No.1 Issue No.2
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Al-Abbas Holy Shrine

Karbala heritage: Quarterly Authorized Journal Specialized in Karbala Heritage /Al-Abbas Holy Shrine. - Karbala: secretary general for Al-Abbas Holy Shrine, 1435-1436 A.H./2014 A.D.

Volume: illustrations; 24 cm.

Quarterly - Second number first year (2014 A.D)

ISSN: 2312-5489

Bibliography.

Text in Arabic; and summaries in English and Arabic

1. Karbla (Iraq)-History - Periodicals. 2. Husayn ibn Ali, -680- Periodicals.

DS79.9.K37 A8 2014 .V1 M2

Classification and Cataloging of Al-Abbas Holy Shrine Library


In the Name of Allah
Most Gracious Most Merciful
But We wanted to be gracious to those abased in the land, and to make them leaders and inheritors
(Al-Qasas-5)

ISSN: 2312-5489

Consignment No. in the House book and Iraqi Documents: 1992-2014.

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Editor–in–chief Speech

In The Name of Allah' All compassionate, All Merciful

Praise be to Allah, Lord of The world and blessings and peace be upon His prophet and His progeny, The ingenuous and virtuous.

All developed countries attach great importance to scientific and experimental research and seriously and intensely try to develop it by providing researchers with all The prerequisites and services to carry out their studies and researches. This has contributed to The development of science in such societies and has been considered a vital source of such development. In order to contribute to spreading out and publishing The heritage and cultural knowledge and also recreating The heritage of Imam Husain's (peace be upon him) city, which is considered a mirror of Ummah and its cultural and educational history and which has had an impact on all types of human

civilization in general and The Islamic one in particular all through human races, Karbala' Heritage centre likes to introduce, for both honest researchers and readers, The First Year. First Vo. First Issue of karbala' Heritage Quarterly Journal of which its efficient board has undertaken The job of publishing The authentic researches denominated scientifically by specialized teachers. As a consequence this provides researchers, both readers and writers, with The an advanced scientific material which is effective in developing and supporting The cultural and scientific process in its two dimemsions The innovative and aesthetic. This what The journal wishes to accomplish through your authentic researches. May Allah, The Most High, help us to extend and spread science and knowledge about which He is satisfied so that this may be rewarded in The Day of Judgement.

The second Step

It is not easy to look at two different worlds with one eye, especially when they belong to two different periods. When adding to this obstacle, the obstacle which is that the observer does not belong to and part of that world observed from a subsequent period, the obstacle will definitely be doubled.

When discussing the from and frame of the design of the journal, mechanism of activating it and the techniques of issue continuation, these two obstacles have been greately considered by the two boards responsible for the journal, I mean the advisory and the editorial boards. But as the first step starts to appear the walker will, no doubt, find that the difficulties in the road will be surmounted, and the feet will be accustomed to that road in spite of the difficulties. The two boards, consequently found that the road started to become easier as their steps started to appear, especially when the

journal has put forward its first step in its appearance.

The second step, I mean the second I ssue of the journey of the journal issuing, comes to prove that the road will be easier and the steps will start again not caring for the obstacle or the obstacles that may encounter as some may encounter as some may think.

The five sections or the journal, I mean the society section, the History section, the literature section, the Art section and the science section included a number of researches of an authorized scientific impression; they were greatly appreciated by specialist experts from different universities who were known by their efficiency and scientism, in addition to the writer of the researches of the journal issue from different Iraqi universities.

This is an appeal and invitation to all academic specialists in Kerbala Heritage inside Iraq and from abroad to send their writer researches according to the conditions of the scientific research to the journal address because continuity of the journal issuing is my Allah help only by what their pens write .

Contents

Studying the Effect of Male Hormones in the Serum Sample of Patients in the Province of Holy Karbala on Benign Prostate Hyperplasia

Researcher

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Abstract

Benign prostatic hyperplasia (BPH), is one of the most common diseases and major cause of morbidity in elderly men which may lead to bladder outflow obstruction and lower urinary tract symptoms (LUTS). Although Androgen hormones play fundamental roles in prostate growth, their clinical significance is not completely clear. In the present study, we assessed whether serum hormones level is a cause of prostate disease.

Patients and Methods:

This study includes (40) patients, with benign prostatic hypertrophy, Sample selected in AL-Hussein Hospital / the province of holy Karbala and (40) control group with age range (41-79) and (42-71) years respectively. The following biochemical investigations have been studied: Testosterone, dihydrotestosterone (DHT), and Prostatic Specific Antigen

(PSA) levels using ELISA method which correlated with the disease. Also body mass index (BMI), the prostate size and configuration by digital rectal examination (DRE) and ultrasound, flow rate, and American Urology Association Symptoms Index (AUASI), of the patients which correlate hormones levels with age.

Results:

The PSA concentrations were significantly higher in patients with BPH thanin control group ($p \leq 0.05$). The testosterone concentrations were significantly lower in patients with BPH thanin control group ($p \leq 0.05$), while the DHT levels did not differ significantly in patients with BPH from control group.

دراسة تأثير الهرمونات الذكرية في مصل عينة من المرضى في محافظة كربلاء المقدسة على تضخم البروستات الحميد

الباحثة
خولة إبراهيم عبد الموسوي
ماجستير علوم كيمياء/ جامعة بغداد/ موظفة في مجلس محافظة كربلاء المقدسة
كربلاء المقدسة/ العراق

الملخّص

تضخم البروستات الحميد (BPH) هو واحد من أكثر الأمراض شيوعا عند الرجال كبار السن مما قد يؤدي إلى تلكأ وانسداد تدفق المثانة ونقصان حجم البول (LUTS). على الرغم من أن الهرمونات الستيرويدية الجنسية تلعب دورا أساسيا في نمو البروستات، وأهميتها السريرية غير واضحة تماما، فقد تم في هذه الدراسة تقييم ما إذا كانت مستويات هرمونات المصل كدالات على مرض البروستات الحميد.

طرق العمل والمرضى:

تشمل هذه الدراسة (٤٠) مريضاً مصابا بتضخم البروستات الحميد كعينة منتقاة في مستشفى الحسين/ محافظة كربلاء المقدسة ، وتمت مقارنتهم بـ (٤٠) رجل اصحاء البنية تراوح معدل العمر مابين (٧٩-٤١) و(٧١-٤٢) سنة على التوالي. تم قياس مستويات التيستوستيرون، ألدايهايدروتيستوستيرون (DHT)، وPSA بأستخدام طريقة (ELISA). وقياس مؤشر كتلة الجسم (BMI)، حجم البروستاتا بجهاز السونار، ومعدل التدفق، AUASI. وكذلك مقارنة التغير بالهرمونات مع تقدم العمر.

النتائج:

توصلت هذه الدراسة الى أن PSA، كانت أعلى ($p<0.05$) في المرضى المصابين بتضخم البروستات الحميد مقارنة بالمجموعة الضابطة. علما ان مستويات هرمون التيستوستيرون أقل بكثير في المرضى المصابين بتضخم البروستات الحميد مقارنة بالمجموعة الضابطة ($p<0.05$)، في حين أن مستويات هرمون الدايهايدرو – تيستوستيرون (DHT) بينما لم تختلف كثيرا في المرضى الذين يعانون من (BPH) من مجموعة المراقبة.

الاستنتاج:

مستويات DHT تبقى طبيعية مع الشيخوخة، على الرغم من انخفاض هرمون التستوستيرون في مصل دم المرضى المصابين بتضخم البروستات الحميد (BPH).

Keywords

Benign Prostatic Hyperplasia (BPH), Testosterone (T), Dihydrotestosterone (DHT), Prostatic Specific Antigen (PSA).

Introduction

Benign prostatic hyperplasia (BPH), is one of the most common disease and major cause of morbidity in elderly men which may lead to bladder outflow obstruction and lower urinary tract symptoms (LUTS)[1]. Although, the pathogenesis of BPH is not well understood, it is probably linked to age-related changes in hormonal and other growth-regulatory factors that affect prostate growth and volume[2].Though some males start to have prostatic hyperplasia after the fourth decade of life, it is not known why some develop it earlier and some males don't develop it at all. However, the overall incidence increases with age[3] and its prevalence reaches about 90% in men in their 80s, of whom only a proportion suffer from urinary symptoms. Although medical and conservative treatments are used in management, but most patients eventually need surgery to get rid of the troublesome symptoms of BPH. Until recently little has been known about

the etiopathology and risk factors for this disease[4]. Studies on the etiopathology and risk factors seem insufficient and are derived mainly from animal rather than human studies[5].

PSA, is aglycoprotien that acts as a serine protease, of 33,000 MW. It contains 7% carbohydrate and is found almost exclusively in the epithelial cells of the prostate[6]. One possible biologic role of PSA is to lyse the clot of the ejaculate, however, it is yet not known why this clotting and lysing mechanisms are important to reproductive physiology[7]. Serum PSA is a powerful predictor of natural history of BPH. PSA values of more than 1.4 ng/ml reflect heightened risk of disease progression in middle aged and elderly men[8].

Androgens in males rise steadily followed by a slow decline in the mid-30s[9]. After the 40s, the levels of androgens either remain constant or there is a slow decline with age. Though androgens, estrogens and their relative concentrations in the peripheral circulation are related to prostatic hyperplasia[10], it is not understood why prostatic hyperplasia develops in that period of life when serum androgens and probably estrogens in the peripheral circulation are relatively lower. However,

many growth factors and their receptors are regulated by androgens. Thus, the action of testosterone and DHT in the prostate is mediated indirectly through autocrine and paracrine pathways. Whether there are any changes in androgens and other sex steroid concentrations in those who develop prostatic hyperplasia is also not clear[11]. It is important to find out whether there is any change in the sex steroid levels in prostatic hyperplasia. In addition, the age related changes in those hormones after 40 years of age need to be examined.

The present study aim to determine whether there is any change in the concentration of Testosterone, DHT in prostatic hyperplasia and also to determine to what extent these hormones change with age.

Materials and Methods:

For this study, 40 BPH patients had been selected and 40 well-matched males without BPH as control group from the inpatient and outpatient of AL-Hussein Hospital located in the city of Karala, Iraq during December 2012 to April 2013. Detailed medical and urological examinations were done on each subject before inclusion. Control samples were drawn from 40 men who had no more than 5 missing American urology association symptoms index (AUASI) values, no less than 11 Qmax, no more than 33cm^3 of volume prostate, no surgical or medical treatment for BPH, and no report of a physician diagnosis of BPH.

Participants completed a previously validated baseline questionnaire that assessed LUTS severity from questions similar to those in the AUASI, and a composite symptom index score was estimated. Participants also voided into a portable urometer to measure peak urinary flow rate. Also

prostate volume and configuration was determined by DRE and ultrasound. The clinical and laboratory characteristics of the patients group and control groups are shown in (Table 1).

Venous blood samples were collected from each subject at the morning (9-12 am), 5 ml of blood were obtained by vein puncture using a 10 ml disposable syringes. The blood sample was left for 15 minutes to clot at room temperature, and then separated by centrifugation at (3000 rpm) for (5 min) then serum was collected. Serum was divided into three aliquots; in an Eppendroff tubes and stored in the freezer (-20) C0 until laboratory analysis. Laboratory assays were done within 3months of collection. Serum samples were assayed for testosterone (T) (Monobind Inc, USA Kit), Dihydrotestosterone (DHT) (DRG Instruments GmbH, Germany Kit), prostatic specific antigen (PSA) (Diagnostic Automation, INC, USA Kit). Each Kit was supplied with instruction for hormone assay by ELISA (USA). Analysis of data was carried out using the available statistical package of SPSS-18 (Statistical Packages for Social Sciences-version 18 “PASW” Statistics).

Results

The present study has found a significant difference in the mean serum concentration of testosterone, DHT, and PSA between BPH patients and control groups (Table 2). Combining the patients group and control group, no significant correlation was found in testosterone, DHT, with age. (Table 3), (Figure 1, 2).

Table (1)

Clinical profile of patients and control groups.

Parameters	Patients group (n=40)	Control group (n=40)
Age (year)	60.85±9.24	51.02±3.42
Volumeof prostate (cm3)	49.55±8.63	25.12±3.27
Prostatic symptom score	16.05±6.26	2.86±1.18
Qmax	7.65±1.59	13.30±1.34

Values as mean±SD

Table (2)

The mean±SD of Serum testosterone, DHT, and prostatic specific antigen levels for BPH patients and control groups.

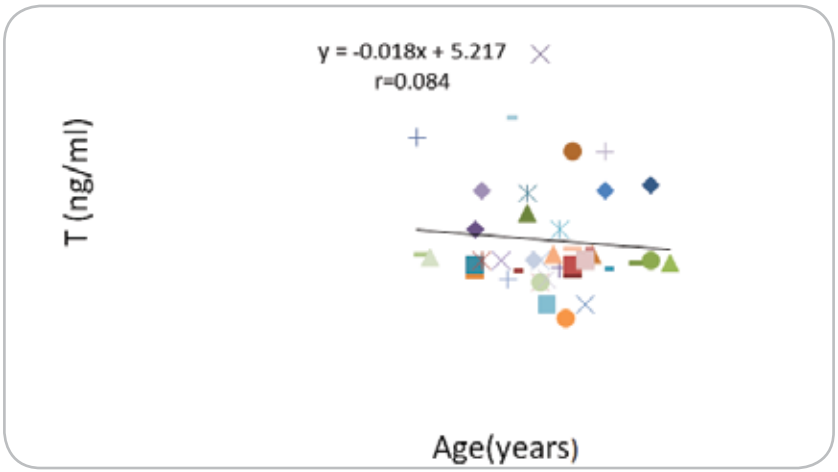
Parameters	Patients group (n=40)	Control group (n=40)	P value
Testosterone (ng/ml)	2.89±1.89	4.12±1.34	0.002*
DHT (pg/ml)	654.20±474.0	624.73±257.95	0.731
PSA (ng/ml)	2.85±1.58	1.02±0.62	0.0001*
T/DHT ratio	0.006±0.005	0.007±0.003	0.176*
BMI (kg/m^2)	28.41±4.77	28.03±4.14	0.706

significant at p<0.05*

Table (3)

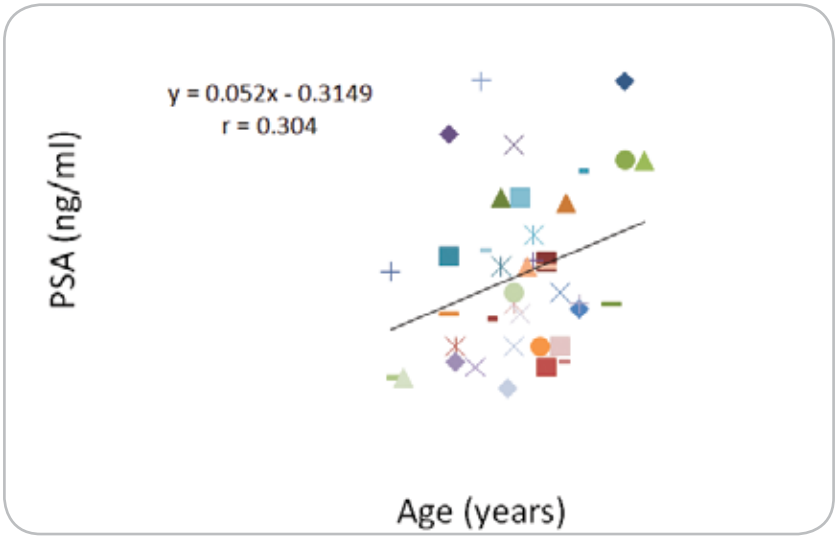
Correlations of testosterone, and DHT with age.

Parameters	Correlation coefficient	P value
T (ng/ml)	-0.084	0.605
DHT (pg/ml)	-0.031	0.808
PSA (ng/ml)	0.304	0.057



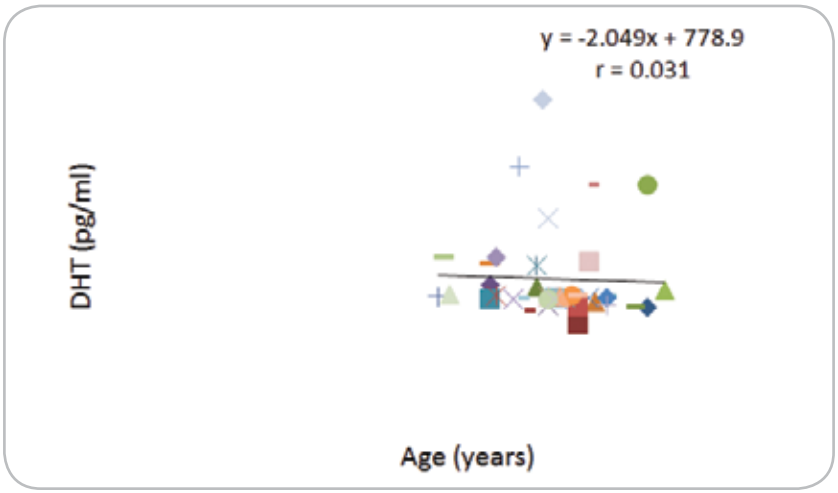
Figure(1)

Correlation between Testosterone (T) levels and age in patients with BPH.



Figure(2)

Correlation between DHT levels and age in patients with BPH.



Figure(6)
Correlation between Prostatic Specific Antigen (PSA) levels and age in patients with BPH.

Discussion

Serum PSA, is primarily a tissue-specific marker. PSA, is a valuable index of BPH disease risk. After prostate cancer is excluded PSA is a reasonable clinical surrogate marker for prostate volume[12]. Men with large prostate glands have high PSA and are at increased risk for BPH disease progression[13].

Therefore, PSA is also a marker for BPH risk disease as shown in current study (table 2).

In the present study there has been found a significant association as shown in (table 2) in serum testosterone level in benign prostatic hyperplasia. These results agree with earlier studies where high serum testosterone levels were associated with lower BPH risk. Kristal et al[14]. reported the same results for androgens concentration as in current study. In fact, most of the recent studies found strong change in serum testosterone concentration in prostatic hyperplasia. Prehn[15] also reported that with low testosterone, the normal

milieu might be varied enough to disrupt the normal growth and maintenance of prostatic tissue, while compensatory hyperplasia arises when the prostate atrophies might lead to cell mutations and consequent selection of androgens-independent aggressive prostate cell growth. Two studies have found that high testosterone was associated with reducing lower urinary tract symptoms[16]. Ansari MAJ et al[17]. reported that there was no significant change in serum levels of testosterone, estradiol, in clinical BPH as compared with age-matched asymptomatic males with a normal-sized prostate. Meigs et al. and Gann et al[18]. found no association between serum sex hormone levels and development of BPH. In the study by Marberger et al where clinical BPH was found to occur in elderly males with different baseline serum testosterone, ranging from low to high normal levels[19].

The principal prostatic androgen is dihydrotestosterone (DHT). Levels of DHT remain normal with aging, despite a decrease in the plasma testosterone, and are not elevated in benign prostatic hyperplasia (BPH)[20].

Current study, as shown in (Table1), found high serum

DHT level, but not significant in prostatic hyperplasia, this agrees with study by Meigs et al. and Gann et al. reported[21], but differs from studies where, raised androgen levels were reported in prostatic hyperplasia[22]. This discrepancy is mainly due to differences in sample selection, laboratory analysis and methods of comparison adopted in those studies as compared to the present study.

Luminal secretory cells require androgens, particularly the intracellular metabolite of testosterone, dihydrotestosterone (DHT), for terminal differentiation and secretory functions. DHT is predominantly generated by the prostatic 5-a reductase, which is present in fibroblasts of the stroma and in basal epithelial cells. In two interesting papers, Roberts et al. reported higher DHT activity in BPH relative to normal prostate gland tissue[23] resulting as a permissive, rather than a transformative, mediator in the development of BPH. Moreover, in studies based on the analysis of cadaver specimens, an increased accumulation of DHT was observed in BPH tissues[24]. Conversely, other authors reported no differences in DHT pattern when fresh specimens of prostate

tissue were used[25].

In other studies, the method of sample selection was such that asymptomatic BPH cases could not be excluded from the control due to the unavailability of modern imaging techniques. For example, selecting cases and control based on the presence or absence of lower urinary tract symptoms (LUTS) and digital rectal examination without measuring prostatic size by imaging technique seems insufficient to exclude or include prostatic hyperplasia. The laboratory methods for hormone assays were also less sensitive than those available now. Because of the fact that the presence or absence of LUTS cannot include or exclude prostatic hyperplasia with certainty, it is possible that there could be a few asymptomatic prostatic hyperplasia cases included within the control group in our study and this might have confounded our results. However, we considered that cases of LUTS with enlarged prostate, excluding prostatic carcinoma, are practically cases of prostatic hyperplasia. With this limitation in mind our comparisons were between symptomatic BPH cases to age matched males without LUTS and a normal-sized prostate.

We found no significant association between T: DHT and the risk of BPH. This differs from studies that have examined the ratio of T: DHT which have found that high levels of testosterone relative to DHT are significantly associated with reduced risks of clinical BPH[26], lower urinary tract symptoms[27], surgical BPH treatment[28] or with smaller prostate size[29].

Most studies support our findings as shown in (Table 3), (Figure 1) of no change in serum T with age[30], while few studies report a slow decline of andrsogens in aging males[31]. In contrast to those studies where an age related decline of androgens were reported[32].

In summary, the serum levels of T in the present study were associated with clinical BPH as compared with age-matched asymptomatic males with a normal size of prostate while there is no association between serum DHT with clinical BPH. In addition, there is no significant age-related change in serum Testosterone,

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