International Journal of General Medicine and Pharmacy (IJGMP)
ISSN (P): 2319-3999; ISSN (E): 2319-4006
Vol. 7, Issue 1, Dec - Jan 2018; 21 - 28

International Academy of Science, Engineering and Technology
Connecting Researchers; Nurturing Innovations

DIET, OBESITY AND PROSTATE CANCER, IN A POPULATION OF NORTHERN INDIA

SUPRIYA RANA[1], INDIRA R. SAMAL[2] & RAVJIT KAUR SABHARWAL[3]

[1]Tutor, Department of Biochemistry, Punjab Institute of Medical Sciences, Jalandhar, Punjab, India

[2,3]Professor, Department of Biochemistry, Punjab Institute of Medical Sciences, Jalandhar, Punjab, India

ABSTRACT

Background

The prevalence of carcinoma of prostate is increasing in Asian countries, especially in men consuming non-vegetarian diet and those who are obese.

Materials and Methods

About fifty patients aged between 48-89 years who had attended the Surgery department of Rajindra Hospital, Patiala, India and who were histopathologically positive for carcinoma of prostate, were chosen for the study and evaluated by using a questionnaire and estimating the prostate specific antigen and acid phosphatase levels.

Results

Of the 38% (19) vegetarians, carcinoma of prostate was seen in 8.0% (4) obese subjects. However, 62% (31) of the non-vegetarian subjects, 30% (15) were obese and had carcinoma of prostate. Mean±SD values of serum PSA were 19.80±5.70 ng/ml and 65.40±38.80 ng/ml, in vegetarians and non-vegetarians, respectively.

Conclusions

The prevalence of prostate carcinoma was more in non-vegetarian obese subjects, compared to vegetarians. This data will be useful to the clinicians, to educate and create awareness in the general population about the dietary modifications and lifestyle management in men, so as to prevent the disease.

KEYWORDS: Non-Vegetarian Diet, Obesity, Prostatic Cancer, Vegetarian Diet

INTRODUCTION

Background

According to the American Cancer Society, prostate cancer accounts for about 27% of all incident cancer cases among men and is the second most common (noncutaneous) cancer among men (1). Prostate cancer incidence is increasing in India too, ranking fifth in incidence and fourth in mortality for men in Mumbai. Incidence of prostate carcinoma (PCa) in Chennai is 3.9 men per hundred thousand and 7.2 men per hundred thousand of population in Mumbai (2).

Common risk factors of prostate cancer include positive family history (3), history of diabetes mellitus (4), height, weight and obesity (5), smoking habit, physical activity (6), body mass index (BMI) (7), and vasectomy (8). However, in India, there are limited studies on the actual role of these risk factors on PCa.

Western lifestyle and diet are closely associated with PCa incidence and mortality, worldwide (9). Evaluation of diets in countries with low and high incidences of prostate cancer suggests that, one of the strongest dietary risk factors for the development of CaP is consumption of non vegetarian diet (10). A standard western diet is high in calories,

animal protein, refined carbohydrates, saturated fats and low in fresh fruits, vegetables, and whole grains, leading to lower intake of essential minerals and antioxidants, causing a six fold higher PCa prevalence in Western countries (11). A Western diet is not only linked with the obesity, but can also alter parameters like hormones, known to promote PCa (12). It was also observed that, a vegetarian diet with regular physical activity helped to reduce the progression of PCa (13).

Obesity has become too common, affecting one-third of all adults in the United States and 13% of adults worldwide. Recent epidemiologic studies have found that, obesity is related to increased risk of prostate specific antigen levels (PSA) and prostate cancer mortality (14, 15). Obesity (BMI >30 mg/kg² and 35 mg/kg²) is also associated with higher grade tumors and higher rates of disease recurrence, as compared to non obese men (16, 17). Further, the risk of dying from high grade PCa was 20% - 30% higher, for obese men with raised PSA levels (18).

Higher levels of insulin, IGF-1 and lower levels of androgens and adiponectin in obese men increase the risk of PCa. Both obesity and weight gain in adulthood is linked with a higher risk of advanced prostate cancer and its recurrence (19). Obesity (at the time of diagnosis or treatment) was found to be associated with an increased risk of prostate cancer-specific mortality in many prospective studies. However, significant heterogeneity was observed between the studies, suggesting that obesity and prostate cancer relation vary with patient characteristics, treatment, factors such as timing of BMI measurement. Thus, a better understanding of the weight gain, obesity and PCa is needed (20).

PSA, produced by prostate epithelial cells is an androgen regulated serine protease (21). From its discovery in 1979 to clinical application in 1980s and 1990s, PSA has evolved into an invaluable tool for the detection, staging and monitoring of men diagnosed with PCa. Although, PSA is widely accepted as a PCa tumor marker, it is organ specific but not disease specific (22). Both the American Urologic Association and American Cancer Society recommend yearly assay of serum PSA levels in men ≥ 50 years (23).

Acid phosphatase (ACP) is present in many organs, with highest concentration in the prostate gland (1,000 times greater concentration), and its elevation in serum is a useful marker for PCa, usually in an advanced clinical stage (24). Acid phosphatase plays a prime role in the metabolism of the prostate, as its level increases in serum along with carcinomatous changes in the prostate. Its determination is a useful tool not only for the diagnosis of patients with PCa, but also for the parameter of therapeutic response to the treatment (25). The diagnostic usefulness of serum ACP levels is of little significance in early cases of PCa (26). Thus, many attempts have been made to improve the diagnostic value of serum acid phosphatase.

The present study was carried out to assess the association of diet, obesity, serum levels of PSA and ACP in subjects with prostate carcinoma.

MATERIALS AND METHODS

The present study was conducted on 50 patients of prostatic carcinoma reporting to the department of Surgery, Rajindra Hospital, Patiala. After due permission from Research Ethical Committee of Government Medical College, Patiala, a written consent form was taken from each subject and a questionnaire was designed to collect the data. Inclusion criteria for study group included proven cases of prostate carcinoma by history, clinical and histopathological (FNAC) investigations. Patients below 40 yrs with acute and chronic prostatitis and cases of prostectomy were excluded from the study.

Five ml of venous blood was collected in a plain vacutainers, through venipuncture. The serum was stored in tubes at -20°C for analysis of PSA while total serum acid phosphatase (ACP) was analyzed immediately. Serum PSA levels were determined by enzyme linked immunoassay method (27). Total serum ACP levels were measured by kinetic method using α naphthol phosphate (28) on semi-auto analyzer. The normal reference ranges for PSA was 0-4 ng/ml and ACP was 0-4 IU/L.

STATISTICAL ANALYSIS

The data was statistically described in terms of mean (±SD), frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using Student t test for independent samples if normally distributed. For comparing categorical data, Chi square test was performed. A probability value (*p* value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, and USA) and SPSS (Statistical Package for the Social Science; SPSS Inc. Chicago, IL, USA) version 21.

RESULTS

Of the 38% (19) vegetarians, carcinoma of prostate was seen in 8% (4) obese subjects. However, 62% (31) of the non-vegetarian subjects, 30% (15) were obese and had carcinoma of prostate. Mean PSA levels were 19.80±5.70 ng/ml and 65.40±38.80 ng/ml in vegetarians and non-vegetarians obese, respectively. The difference between the two means was highly significant ($p<0.05$)

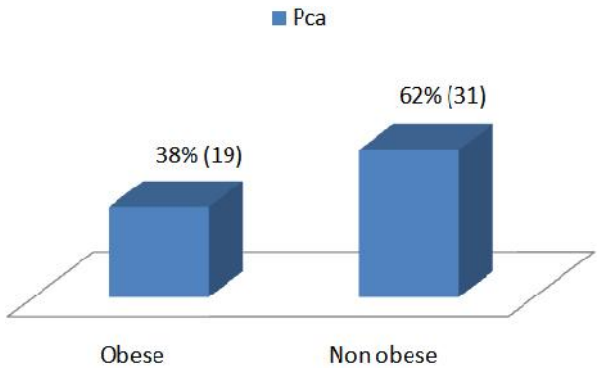

Figure 1: Categorization of PCa Subjects – Obese & Non Obese

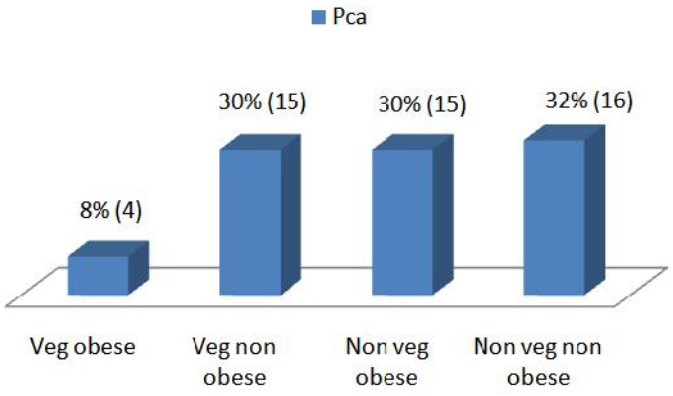

Figure 2: Categorization of PCa Subjects – Veg Obese, Veg Non-Obese, Non-Veg Obese, Non-Veg Non-Obese

Table 1: Categorization of PCa Subjects, Percentage (%), Mean Levels of PSA and ACP

PCa Subjects Category	No. of Subjects	Percentage (%)	(Mean±SD) PSA (ng/ml)	(Mean±SD) ACP (IU/L)
Veg obese	4	8%	19.80±5.70	5.40±1.04
Veg non obese	15	30%	11.30±7.20	3.70±1.60
Non veg obese	15	30%	65.40±38.80	11.30±7.09
Non veg non obese	16	32%	14.40±7.30	4.60±1.90

DISCUSSIONS

Prostate cancer is the most commonly diagnosed malignancy in men and second leading cause of cancer deaths in Western countries (29). In India, there is lack of epidemiological data on the exact prevalence of this disease due to improper screening and under recorded incidence of PCa. PCa is difficult to treat, which makes its early detection a priority. Thus, there is an urgent need for appropriate diagnostic and prognostic markers to detect PCa and to differentiate it from other pathologies of prostate gland (30). The present study was undertaken to assess the relationship of diet, BMI and PSA and ACP levels in prostatic carcinoma.

The mean ± SD value of age for the study group was 69.18±7.90 yrs. According to body mass index, PCa subjects were divided into obese (BMI>30 kg/$m^{2)}$ and non-obese (BMI<30 kg/m^2). The mean±SD value of BMI was 29.64±7.05 kg/m^2. Mean ± SD values of PSA and ACP levels were 29.25±32.31 ng/ml and 6.40±5.20 IU/L, respectively for the study group.

In our study comprising of fifty PCa subjects, 38% (19) of subjects were vegetarians, out of which 8.0% (4) were obese and 30% (15) were non obese. Our study demonstrates a protective association of vegetarian diet, with risk of PCa compared with non-vegetarian subjects (62%).

Similar results were shown by Iranian case-control study, in which subjects on a western dietary pattern had an elevated risk of PCa than those on a healthy diet (31). PCa and its association, with various vegetarian dietary patterns have rarely been discussed. Less intake of animal protein reduces serum insulin-like growth factor 1 (32), a known potent growth factor for prostate epithelium and prostate adenocarcinoma cells. A vegetarian diet, rich in antioxidants, contains less amount of C-reactive protein and is associated with reduced inflammation (33, 34, 35). In conclusion, the subjects on a vegetarian diet have a lower incidence of PCa, than those on a non-vegetarian diet.

In the non-vegetarian subjects who comprised 62% (31) of our study, obesity was prevalent in 30% (15). Prostatic carcinoma was found in 32% (16) of non-vegetarian non obese subjects.

Obesity is associated with increased risk of PCa death. Similar study evaluated that, obese men had higher–tumor grades, greater involvement of the prostate with cancer, and larger tumors than non obese men (36, 37). Many prospective studies reported identical positive associations between BMI, prostate cancer-specific mortality and biochemical recurrence (38). Obesity and weight gain may influence prostate cancer risk through various metabolic, hormonal, and inflammatory pathways and thus, obese men have higher insulin levels with increased the risk of prostate cancer progression (39). Obesity is also associated with altered levels of adipokines, responsible for tumor development (40). In addition, obese men have decreased levels of circulating testosterone, (41) which enhances the growth of poorly differentiated, aggressive prostate tumors (42). Thus, the relation of obesity and PCa is complex, and further research is needed to explore its biologic influence on various stages of prostate carcinogenesis.

The levels of serum PSA and ACP were found to be 19.80±5.70 ng/ml and 5.40±1.04 IU/L in vegetarian obese individuals and 65.40±38.80 ng/ml and 11.30±7.09 IU/L in non-vegetarian obese. Our observations revealed that PSA and ACP levels were significantly high in non-vegetarian obese cases than vegetarians ($p< 0.05$). Increased level of BMI is associated with higher PSA values when compared with normal weight patients and obese patients (BMI≥35 kg/m^2) had higher risk of high grade PCa than patients with BMI < 25 kg/m^2. Combined analysis revealed that obese patients had significantly higher rates of PSA recurrence than non obese patients. (43). Further, obese men tend to have a higher PSA nadir thus, higher BMI more is PSA nadir. This supports the idea that obesity is biologically associated with fast growing tumors and more aggressive PCa. (44). The incidence of the PCa is much lower in Asia, as compared to Western countries however, in the past few years the incidence rate has increased suddenly in most Asian nations faster than the Western world (45). A change in environmental factors, diet and the adoption of western lifestyle are contributing a lot to pathogenesis of PCa (46).

CONCLUSIONS

This study was carried out as a pilot study and will assist the clinicians to educate and create awareness in the general population about dietary and lifestyle modifications to prevent morbidity and mortality.

REFERENCES

1. Siegel R, Ma J, Zou Z, Jemal A. Cancer Statistics, 2014. CA Cancer J Clin. 2014; 64:9–29.
2. Yeole BB. Trends in the prostate cancer incidence in India. AsianPac J Cancer Prev. 2008; 9:141–144.
3. Cerhan JR, Parker AS, Putnam SD Chiu BC, Lynch Cf, Cohen MB, et al. Family history and prostate cancer risk in a population based cohort of lowa men. Cancer Epidemiol Biomarkers Prev. 1999; 8:53-60. (pubMed: 9950240).
4. Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Willett WC, Diabetes mellitus and risk of prostate cancer (United States) Cancer causes control.1998; 9:3-9(pubMed:9486458).
5. Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Willett WC, Height, body weight, and risk of prostate cancer. Cancer Epidemiol Biomarkers Prev. 1997; 6:557-63 (pubMed: 9264267).
6. Cerhan JR, Torner JC, Lynch CF, Rubenstein LM, Lemke JH, Cohen Mb, et al. Association of smoking, body mass and physical activity with risk of prostate cancer in the lowa 65 + Rural healthy Study(united states) Cancer Causes Control. 1997; 8:229-38 (pubMed: 9134247).
7. Adilo S. Bahathiq, Pediatric Obesity and Vitamin D Deficiency: A Concept and Understanding, International Journal of General Medicine and Pharmacy (IJGMP), Volume 4, Issue 4, June-July 2015, pp. 1-16
8. Alyson LJ, White E, Kristal AR. Anthropometrics and prostate cancer risk. Am J Epidemiol.2007; 165:1271-9 (pubMed: 17395597).
9. Platz EA, Yeole BB, Cho E, Jussawalla DJ, Giovannucci E, Ascherio A. Vasectomy and Prostate Cancer: A case- control study in India. Int J Epidemiol. 1997; 26:933-8. (pubMed: 9363512).
10. Hsing AW, Tsao L, Devesa SS. International trends and patterns of prostate cancer incidence and mortality. Int J Cancer. 2000b; 85:60–67.

11. Grant WB. A multicountry ecologic study of risk and risk reduction factors for prostate cancer mortality. Eur Urol. 2004; 45:271–279.

12. Baby Shobana N et al., Comparison of Maternal and Fetal Outcome among Obese and Normal Mothers in View of Developing Maternal Obesity Management Strategy, TJPRC:International Journal of Obstetric, Gynecologic & Neonatal Nursing (TJPRC: IJDGNN), Volume 1, Issue 1, January-June 2017, pp. 9-12

13. Center MM, Jemal A, Lortet-Tieulent J, Ward E, Ferlay J, Brawley O, Bray F. International variation in prostate cancer incidence and mortality rates. Eur Urol 2012; 61:1079–92.

14. Kolonel LN, Hankin JH, Lee J, Chu SY, Nomura AM, Hinds MW.Nutrient intakes in relation to cancer incidence in Hawaii. Br J Cancer. 1981; 44:332–9.

15. Ornish D, Weidner G, Fair WR, Marlin R, Pettengill EB, Raisin CJ, Dunn-Emke S, Crutchfield L, Jacobs FN, Barnard RJ, et al. Intensive lifestyle changes may affect the progression of prostate cancer. J Urol 2005; 174:1065–69.

16. Freedland SJ, Grubb KA, Yiu SK, Humphreys EB, Nielsen ME, Mangold LA et al. Obesity and risk of biochemical progression following radical prostatectomy at a tertiary care referral center. J Urol 2005; 174: 919–922.

17. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med 2003; 348: 1625–1638.

18. Kanchana Bobby S et al., Impact of Obesity on Cognitive Function, TJPRC: International Journal of Pharmacology and Physiology (TJPRC: IJPP), Volume 1, Issue 2, July-December 2015, pp. 15-20

19. Amling CL, Riffenburgh RH, Sun L, Moul JW, Lance RS, Kusuda L, Sexton WJ, Soderdahl DW, Donahue TF, Foley JP, Chung AK, McLeod DG. Pathologic variables and recurrence rates as related to obesity and race in men with prostate cancer undergoing radical prostatectomy. J Clin Oncol. 2004; 22:439–445

20. Bassett WW, Cooperberg MR, Sadetsky N, Silva S, DuChane J, Pasta DJ, Chan JM, Anast JW, Carroll PR, Kane CJ. Impact of obesity on prostate cancer recurrence after radical prostatectomy: data from CaPSURE. Urology. 2005; 66:1060–1065.

21. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med. 2003; 348:1625–1638.

22. Nitin Sippy et al., A Study of Prevalence of Obesity in Adolescents of a Select Primary Urban Health Centre of Navi Mumbai, International Journal of Medicine and Pharmaceutical Sciences (IJMPS), Volume 5, Issue 6, November-December 2015, pp. 39-42

23. Keum N, Greenwood DC, Lee DH, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015; 107(3).

24. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res *(*Phila). 2011; 4(4):486-501.

25. Balk SP, Bubley GJ, Ko YY. Biology of prostate specific antigen. Journal of clinical oncology 2003;21 (2): 383-91

26. Gretzer MB, Partin AW. Prostate cancer and tumor, markers. Campbell-Walsch urology. Wein, Kavoussi, Novick Partin, Peters, edn. Saunders Elsevier: 2007; 2896-97.

27. Sirovich BE, Schwartz LM, Woloshin S. Screening men for prostate and colorectal cancer in the US. Soes practice reflects the evidence. JAMA 2003; 289:1414.

28. G. N. Dwivedi et al., A Study of Childhood and Adolescent Obesity with Special Reference to Effect of a Combined Intervention Therapy, International Journal of Medicine and Pharmaceutical Sciences (IJMPS), Volume 6, Issue 3, May-June 2016, pp. 21-28

29. Stirton S and Batjer JD. Acid Phosphatase and Other Biochemical Markers for Prostatic Carcinoma: Current Status. Laboratory Medicine. 1982; 13(8):506-10

30. Braun, JS, Habig, H and Griisemann, D. Die diagnostische Bedeutung der sauren Phosphatasen im Serum beim Prostatacarcinom. Urologe A.1974; 13*:* 236-241.

31. Letham, H.S. Acid phosphatase: any value in prostatic carcinoma? Va med. Mon. 1971:98*;* 47 49.

32. Stowell LI, Sharman IF, Hamel K, An enzyme linked immunosorbent assay (ELISA) for prostate –specific antigen. Forensic Science Intern 1991; 50:125-38.

33. Hillman GZ. Klin Chem Klin. Biochem 1971; 9:273.

34. Christudoss P, Selvakumar R, Fleming J.J and Gopalakrishnan G "Zinc status of patients with benign prostatic hyperplasia and prostate carcinoma," Indian Journal of Urology, 201 vol. 27, no. 1, pp. 14–18

35. Sarwar S, Adil MAM, Nyamath P and Ishaq M. Biomarkers of Prostatic Cancer: An Attempt to Categorize Patients into Prostatic Carcinoma, Benign Prostatic Hyperplasia, or Prostatitis Based on Serum Prostate Specific Antigen, Prostatic Acid Phosphatase, Calcium, and Phosphorus. Prostate Cancer 2017 Article ID 5687212, 1-7.

36. Lin DW, Neuhouser ML, Schenk JM, et al. Low-fat, low-glycemic load diet and gene expression inhuman prostate epithelium:a feasibility study of using cDNA microarrays to assess the response to dietary intervention in target tissues. Cancer Epidemiol Biomarkers Prev. 2007; 16:2150–4.

37. Shirai T, SanoM, Tamano S, et al. The prostate: a target for carcinogenicity of 2-amino-1-methyl-6-phenylimidazo [4, 5-b] pyridine (PhIP) derived from cooked foods. Cancer Res. 1997; 57:195–8.

38. Zheng W, Lee SA. Well-done meat intake, heterocyclic amine exposure, and cancer risk. Nutr Cancer. 2009; 61: 437–46.

39. Shilpi Singh et al., Hypoglycemic Profile of Gymnemic Acid and Glycyrrhizic Acid on High Fructose Diet Related Obesity Induced Diabetes, International Journal of Medicine and Pharmaceutical Sciences (IJMPS), Volume 6, Issue 3, May-June 2016, pp. 61-84

40. Aronson WJ, Kobayashi N, Barnard RJ, et al. Phase II prospective randomized trial of low-fat diet with fish oil supplementation in men undergoing radical prostatectomy. Cancer Prev Res. 2011; 4: 2062–71.

41. Spencer L, Mann C, Metcalfe M, et al. The effect of omega-3FAs on tumor angiogenesis and their therapeutic potential. Eur J Cancer. 2009; 45:2077–86.

42. Freedland SJ Banez1 LL, Sun, NJ Fitzsimons2 and JW Moul. Obese men have higher-grade and larger tumors: an analysis of the duke prostate center database. Prostate Cancer and Prostatic Diseases. 2009; 12: 259–263

43. Loeb S, Yu X, Nadler RB, Roehl KA, Han M, Hawkins SA et al. Does body mass index affect preoperative prostate specific antigen velocity or pathological outcomes after radical prostatectomy? J Urol. 2007; 177: 102–106.

44. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res *(*Phila). 2011; 4(4):486-501.

45. Giovannucci E, Michaud D. The role of obesity and related metabolic disturbances in cancers of the colon, prostate, and pancreas. Gastroenterology. 2007; 132 (6):2208-2225.

46. Roberts DL, Dive C, Renehan AG. Biological mechanisms linking obesity and cancer risk: new perspectives. Annu Rev Med. 2010; 61:301-316.

47. Kelly DM, Jones TH. Testosterone and obesity. Obes Rev. 2015; 16 (7):581-606.

48. Platz EA, Leitzmann MF, Rifai N, et al. Sex steroid hormones and the androgen receptor gene CAG repeat and subsequent risk of prostate cancer in the prostate-specific antigen era. Cancer Epidemiol Biomarkers Prev. 2005; 14 (5):1262-1269.

49. Zhao R, Cheng G, Wang B, Qin C, Liu Y, Pan Y, Wang J, Hua L, Zhu W and Wang Z BMI and serum lipid parameters predict increasing risk and aggressive prostate cancer in Chinese people. Oncotarget. 2017; 8(39):66051-60.

50. Ho T, Gerber L, Aronson WJ, Terris MK , Presti JC, Kane CJ, Amling CL, and Freedland SJ. Obesity, Prostate-Specific Antigen Nadir and Biochemical Recurrence. After Radical Prostatectomy: Biology or Technique? Eur Urol. 2012; 62(5): 910–916.

51. Center MM, Jemal A, Lortet-Tieulent J, Ward E, Ferlay J, Brawley O, Bray F. International variation in prostate cancer incidence and mortality rates. Eur Urol. 2012; 61:1079-92.

52. Pu YS, Chiang HS, Lin CC, Huang CY, Huang KH, Chen J. Changing trends of prostate cancer in Asia. Aging Male. 2004; 7:120-32.