Vol. 15, No. 2
ORIGINAL PAPER

HEC No. 1428 ISSN No. 1681-5491

BIOCHEMISTRY / ONCOLOGY

MEDICAL CHANNEL
APRIL - JUNE 2009

SERUM LEVELS OF INSULIN, IGF-1 AND PSA IN PROSTATE CANCER PATIENTS IN LOCAL POPULATION

1. **MUHAMMAD ILTAF** (M.Phil)
2. **KHEMOMAL A. KARIRA** (M.Phil)
3. **NUDRAT A. ZUBERI** (M.Phil)
4. **SALEEM UL HAQ**
5. **JAGDESH**
6. **HARESH** M.Phil Student

1. ***Medical Technologist,*** **Department of Biochemistry,** BASIC MEDICAL SCIENCES INSTITUTE, JINNAH POSTGRADUATE MEDICAL CENTRE, KARACHI.
2. ***Head Department of Biochemistry,*** BASIC MEDICAL SCIENCES INSTITUTE, JINNAH POSTGRADUATE MEDICAL CENTRE, KARACHI.
3. ***Associate Professor*** **Department of Biochemistry,** BASIC MEDICAL SCIENCES INSTITUTE, JINNAH POSTGRADUATE MEDICAL CENTRE, KARACHI.
4. ***Assistant Professor,*** HAMDARD COLLEGE OF MEDICINE & DENTISTRY, KARACHI.
5. ***Senior Lecturer,*** MUHAMMAD MEDICAL COLLEGE, MIRPURKHAS
6. **Department of Biochemistry** BASIC MEDICAL SCIENCES INSTITUTE, JINNAH POSTGRADUATE MEDICAL CENTRE, KARACHI.

Correspondence
MR. MUHAMMAD ILTAF, (M.Phil)
Medical Technologist,
Department of Biochemistry, BASIC MEDICAL SCIENCES INSTITUTE, JINNAH POSTGRADUATE MEDICAL CENTRE, KARACHI.
Mob. #: 03003465383
Email: jlr_mps@yahoo.com

BACK GROUND:

Prostate cancer is becoming an important public health care problem and is now the second leading cause of death in men from cancer. There are various biochemical factors which are related to prostate cancer. In this study we have found out the relationship of serum insulin, IGF-1 and PSA with prostate cancer

AIM OF THE STUDY: *To evaluate the serum level of insulin, insulin like growth factor 1 (IGF-1) and prostate specific antigen (PSA) in prostate cancer patients and normal control subjects and to compare/correlate the values of these parameters between control and patient groups.*

STUDY DESIGN: *This case control study was carried out in the Department of Biochemistry, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi in collaboration with Urology and Radiotherapy units of JPMC Karachi*

SUBJECTS AND METHODS: *A total of 70 subjects were included in this study. 35 diagnosed cases of prostate cancer were mostly taken from Urology and Radiotherapy units of JPMC and 35 age matched control subjects were taken from general population for comparison. Most of the study subjects were above 50 years of age. Written consents were taken from the subjects prior to blood collection.*

RESUTS: *Our study showed highly significant increase ($P < 0.005$) in serum insulin, IGF-1 and PSA in patient group when compared to control group.*

CONCLUSION: *Our study suggested an association of increased levels of insulin, IGF-1 and PSA with prostate cancer. PSA is a diagnostic marker for prostate cancer but IGF-1 and insulin are also handy for the diagnosis of prostate cancer. Therefore, it is concluded that along with PSA, IGF-1 and insulin should be routinely done as diagnostic tools for prostate cancer.*

KEY WORDS: Serum insulin, Serum insulin like growth factor-1(IGF-1), Prostate specific antigen (PSA), Prostate cancer.

INTRODUCTION

Prostate cancer is becoming an increasingly important public health care problem & is currently the second leading cause of death in males from cancer.

There are various biochemical factors which are related to prostate cancer, but in this study we have found out the relationship of serum levels of insulin, Insulin like growth factor-I (IGF-I), & Prostate specific antigen (PSA) with prostate cancer. The effects and relationship of these biochemical parameters with carcinoma of prostate have been reported for the first time in this study in Pakistan. This study was aimed to evaluate the serum levels of these biochemical parameters in prostate cancer patients and control subjects and to compare/correlate these parameters between the patient and control group.

Insulin like growth factor-I (IGF-I), Insulin like growth factor-II (IGF-II) and Insulin like growth factor binding proteins (IGFBPs) represent a group of molecules which modulates growth & differentiation process in a broad range of cells and tissues. Insulin like growth factors (IGFs) are polypeptide hormones, have structural resemblance to that of pro-insulin and they generally mediate anabolic cellular effects via endocrine, paracrine and autocrine mechanisms. In normal and transformed prostate epithelial cells, Insulin like growth factors (IGFs) are reported to have mitogenic and anti-apoptotic effects & are thought to be implicated in the development & progression of prostate cancer [(1)].

Studies have revealed that the circulating IGF-I & IGFBP-3 levels may be altered in prostate cancer patients. In these patients the circulating IGF-I level was shown to be often increased [(2)]. High serum IGF-I level seems to represent a risk factor, rather than

a tumor marker for prostate cancer [3].
The relationship between increased insulin level & advanced tumor stage in prostate cancer is biologically quite possible [4]. Since insulin is a growth factor, insulin resistance & compensatory hyperinsulinemia are thought to be the underlying factors in metabolic or insulin resistance syndrome and can be controlled with diet and exercise. Hyperinsulinemia has been shown to have direct effect on the liver, suppressing the production of sex hormone binding globulins and insulin like growth factor binding protein-I & II while stimulating the production of insulin like growth factor-I (IGF-I) [5].

AIM OF STUDY

To evaluate the serum level of Insulin, Insulin like growth factor-I (IGF-I) and Prostate specific antigen (PSA) in patients suffering from prostate cancer, as well as normal control subjects and to compare/correlate these values between the control and patient groups.

PATIENTS AND METHOD

This case-control study was carried out in the Department of Biochemistry, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi in collaboration with Urology & Radiotherapy Department, JPMC, Karachi under the kind supervision of Prof. Khemomal A. Karira. A total of 70 subjects were included in this study, out of which thirty five were diagnosed cases of Prostate cancer and thirty five normal control subjects for comparison. Normal control subjects were taken from general population. Most of the study subjects were above fifty years of age. A written consent was taken before the collection of blood samples.
Serum insulin, insulin like growth factor-I and Prostate specific antigen were biochemical parameters used in this study and they were matched with same age control group.
Serum insulin was determined by Monobind insulin micro plate ELISA Kit, Product Code No. 2425-300, manufactured by Monobind Inc, USA. The serum IGF-I was determined by IGF-I ELISA- using Kit Cat No. EIA - 2947, manufactured by DRG diagnostics GmbH, Germany. The estimation of PSA was done by AxSYM Total PAS assay (ELISA) list number 3C19; 69-2399/R4, manufactured by Abbott Laboratories USA, on AxSYM system.

RESULTS

Table # 1 shows the mean serum insulin, IGF-1 and PSA levels in patient and control group. The mean insulin values in control & patient group were 8.12 ± 0.48 & 12.06 ± 0.80 respectively with statistically significant difference ($p < 0.005$).

The mean value of IGF-I in the control group was 190.60 ± 5.59 and that of patient group was 230.68 ± 4.25; showing statically significant difference ($p < 0.005$).
Similarly the mean PSA values of control & patient group were 0.83 ± 0.10 and 63.35 ± 9.78 respectively showing statistically significant difference with $p < 0.005$. As a whole this table shows that the levels of insulin, IGF-1 and PSA were significantly higher in patient group when compared to control group.
The table # 2 shows the serum insulin, IGF-I and PSA levels in different age groups. The mean insulin values were 13.82 ± 2.07, 12.34 ± 1.06 and 10.63 ± 0.90 in the age group 51 – 60 years, 61-70 years and 71-80 years respectively. All these values were more than normal. When these values were compared with each other, the age group 51-60 years and 61-70 years showed non-significant difference while the age group 71-80 years showed significantly low levels ($p < 0.005$).
Moreover this table also shows the mean IGF-I values 228.57 ± 9.69, 230.00 ± 6.86 and 233.05 ± 4.37 in the age groups 51-60, 61-70 and 71-80 years respectively. Comparing these values with each other showed non-significant difference. The mean PSA values were 88.60 ± 6.00, 53.60 ± 1.41 and 64.32 ± 1.09 in the age groups 51-60, 61-70 and 71-80 years respectively. When compared with each other, these values showed statistically significant difference ($p < 0.005$).
The table # 2 clearly depicts that among the prostate cancer patients serum insulin was negatively correlated and IGF-1 level was somewhat positively correlated with the age, whereas PSA levels had no specific correlation with the age. This table indicates that serum levels of insulin, IGF-1 and PSA might be dependent on stage of the

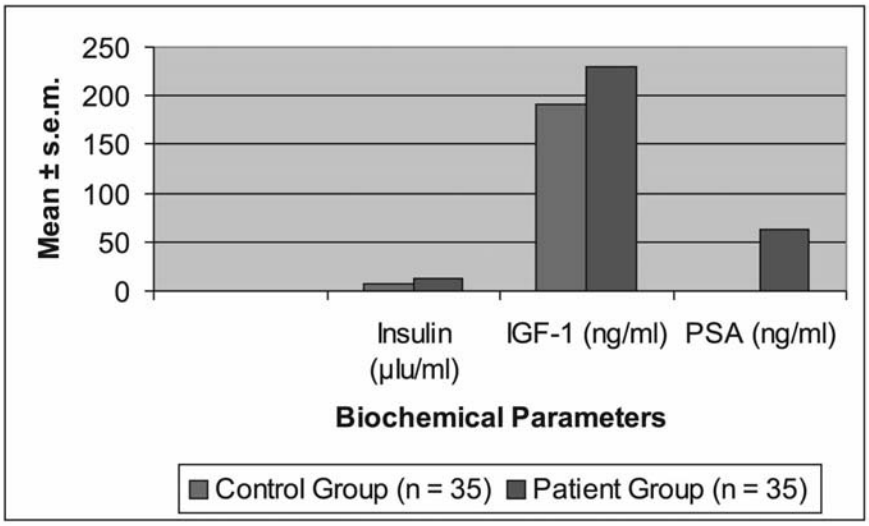
Table 1: Comparison of Biochemical Parameters between Control & Prostatic Carcinoma groups

Values are expressed as mean ± s.e.m.

Parameter	Control Group (n = 35)	Patient Group (n = 35)
Insulin (µIu/ml)	8.12 ± 0.48	12.06 ± 0.80*
IGF-1 (ng/ml)	190.60 ± 5.59	230.68 ± 4.25*
PSA (ng/ml)	0.83 ± 0.10	63.35 ± 9.78

NS = non-significant, *$p < 0.005$ significant when compared to controls.

Figure 1: Comparison of Biochemical Parameters between Control & Prostate Carcinoma groups



cancer irrespective of the age of the subject.

DISCUSSION

The result of our study showed that incidence of carcinoma of prostate is found to be the highest in age group 61-70 years in local population.

Insulin like growth factor-I (IGF-I) is a polypeptide hormone involved in the regulation of cell proliferation, it has potent mitogenic and anti-apoptotic effects on prostate epithelial cells; it is a modification of growth hormone synthesized in liver and is found to be significantly elevated in all patients of prostate carcinoma with p-value less than 0.005. The results of our study matched and justified with other studies in which higher values of IGF-I were found with prostate cancer[6]. Chan also found significantly higher mean IGF-I levels in prostate cancer subjects than controls[2]. Chokkalingam identified that IGF-I, IGF-II and IGFBP are all associated with prostate cancer[7]. Wolk also found significantly high IGF-I levels in prostate cancer subjects when compared to normal controls[8]. Our results of high IGF-I in cancer subjects are in disagreement with the study of Chan [9] who found no association between IGF-I & total prostate cancer risk.

In present study we observed increased insulin as a risk factor, promoting the growth of prostate cancer cells and observed significant elevated levels of insulin in most of the cancer patients. These findings are in agreement with the study of Lehrer [4] who found high level of insulin in prostate cancer subjects. Hsing [10] also found high serum insulin levels with increased risk of prostate cancer while Barry Boyed [11] in a prospective study of non-obese males observed an increased risk of cancer events in those individual with increased insulin resistance (Hyperinsulinemia) reinforcing the growing evidence for an insulin cancer connection.

On the other side we also evaluated fasting blood sugar level and found non-significant difference when compared to normal which helped to exclude diabetic patients; although the serum insulin levels were found significantly raised in our study. Body Mass Index (BMI) used as a one of the biophysical parameter and was found significantly low in prostate cancer subjects, this might be due to cancerous process in such patients causing loss of weight as well as decreasing BMI.

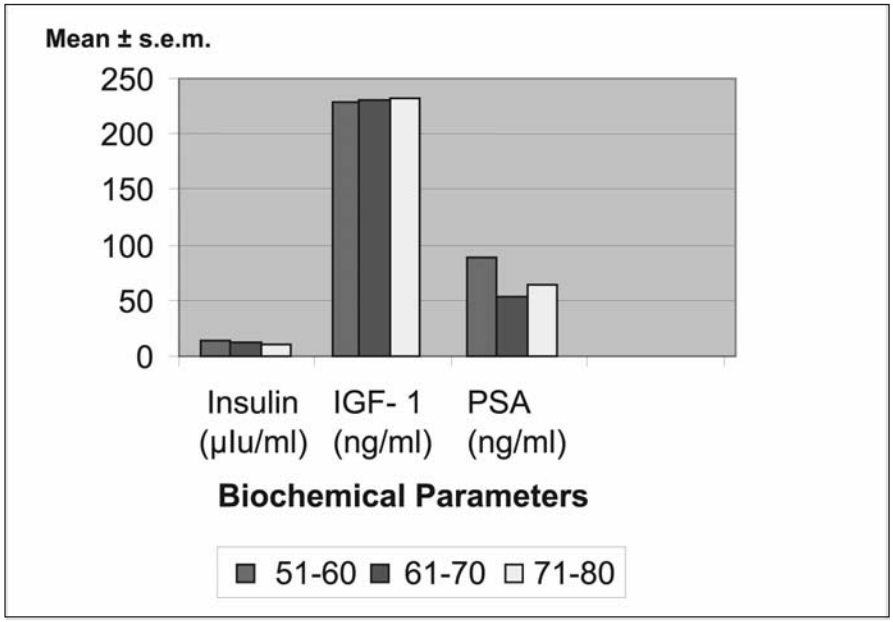
In most of the syndrome-X cases where insulin resistance (Hyperinsulinemia) is associated with increase blood sugar and increased BMI (Obesity) but in our present study hyperinsulinemia was found to be associated with normal blood sugar level and decreased BMI. Therefore hyperinsulinemia may be one of the strong cofactor associated with prostate cancer.

Table 2: Comparison of mean values of Biochemical Parameters in different age groups of Prostate cancer subjects

Age group Years (n)	Insulin (µIu/ml)	IGF-1 (ng/ml)	PSA (ng/ml)
51-60 (n=07)	13.82 ± 2.07	228.57 ± 9.69	88.60 ± 6.00
61-70 (n=19)	12.34 ± 1.06^{NS}	230.00 ± 6.86 ^{NS}	53.60 ± 1.41 *
71-80 (n=09)	10.63 ± 0.90*	233.05 ± 4.37 ^{NS}	64.32 ± 1.09*

NS = non-significant, *p< 0.005 significant when compared to controls

Figure 2: Comparison of mean values of Biochemical Parameters in different age groups of Prostate cancer subjects



CONCLUSION

Research is under way to obtain exact biochemical markers which will help in the diagnosis & immediate treatment of prostate cancer. Recent investigations of our study had suggested an association between increased blood levels of IGF I & Insulin to increase risk of Prostate cancer when values of these parameters were compared to control group. Serum PSA level is a biochemical marker for diagnosis of prostate cancer but our current study suggested that serum IGF1 and insulin levels are also handy along with PSA. This study is being reported for the 1st time in Pakistan, as the sample size is small therefore there is need for further studies on large population of prostate cancer to obtain significant results.

REFERENCES

1. Kurek R, Tunn UW, Eckart O, Aumuller G, Wong J & Rennerberg H. The significance of serum levels of insulin like growth factor-I in patients with prostate cancer. BJU Inter 2000; 85: 125-29.
2. Chan JM, Stampfer MJ, Giovannucci E, Gann PH, Ma J, Wilkinson P, Hennekens CH & Pollak M. Plasma insulin like growth factor-I and prostate cancer risk: a prospective study. Science 1998; 279: 563-66.
3. Nam RK, Trachtenberg J, Jewett MAS, Toi A, Evans A, Emami M, Narod SA & Pollak M. Serum insulin like growth factor-I levels and intraepithelial neoplasia: a clue to the relationship between IGF-I physiology and prostate cancer risk. Cancer epidemiol biomarkers prev 2005; 14(5): 1270-73.
4. Lehrer S, Diamond EJ, Stagger S, Stone NN & Stock RG. Increased serum insulin associated with increased risk of prostate cancer recurrence. The Prostate 2002;

50: 1-3.
5. Barnard RJ, Aronson WJ, Tymchuk CN & Ngo TH. Prostate cancer: another aspect of the insulin resistance syndrome? Obesity reviews 2002; 3(4): 303-08.
6. Shi R, Berkel HJ & Yu H. Insulin like growth factor-I and prostate cancer: a meta-analysis. B J Cancer 2001; 85(7): 991-96.
7. Chokkalingam AP, Pollak M, Fillmore CM, Gao YT, Stanczyk FZ, Deng J, Sesterhenn IA, Mostofi FK, Fears TR, Madigan MP, Ziegler RG, Fraumeni JF & Hsing AW. Insulin like growth factors and prostate cancer: a population based case control study in china. Cancer epidemiol biomarkers prev 2001; 10: 421-27.
8. Wolk A, Mantzoros CS, Anderson SO, Bergstrom R, Signorello LB, Lagiou P, Adami HO & Trichopoulos D. Insulin like growth factor-I and prostate cancer risk: a population based case control study. J Nat Can Inst 1998; 90(12): 911-15.
9. Chan JM, Stampfer MJ, Ma J, Gann P, Gaziano JM, Pollak M & Giovannucci E. Insulin like growth factor-I, IGFBP-3 as predictors of advanced stage prostate. J Nat Can Inst 2002; 94(14): 1099-1105.
10. Hsing Aw, Chua S, Gao YT, Gentzschein E, Cheng L, Deng J, Stanczyk FZ. Prostate cancer risk and serum levels of insulin and leptin: a population based study. J Natl Cancer Institute 2001; 93(10); 783-89.
11. Barry Boyd. Insulin and cancer. Integr Cancer Therap 2003; 2: 315-29.