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Correlation of blood glucose and prostatic-related parameters in patients with prostate enlargement

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Abstract

Enlarged prostate, either in benign prostatic hyperplasia or prostate cancer is the predominant urological disease affecting older men. Metabolic syndrome including high blood glucose was considered to take part in the development of prostate enlargement, although their association is still unclear. This study aims to investigate the correlation between blood glucose with prostatic-related parameters. A cross-sectional study was conducted involving 91 men with prostate enlargement from Urology Polyclinic, Tabanan Hospital, Bali Province, Indonesia. Prostatic-related parameters collected include patient's international prostate symptoms score using the questionnaire, prostate-specific antigen and random blood glucose analysis from serum blood sample, and prostate volume determined with transabdominal ultrasonography. Patient's mean age was 65.4 ± 10 years, mean prostate volume 52.7 ± 26 ml, mean prostate-specific antigen (PSA) 9.2 ± 17 ng/ml, mean international prostatic symptoms score (IPSS) 14.31 ± 7.1, mean random blood glucose 121.1 ± 40.5 mg/dl. This study found weak positive correlation between random blood glucose and prostate volume ($r=0.269$; $p=0.01$). PSA and prostate volume showed moderate positive correlation ($r=0.365$; $p<0.001$). No correlation between random blood glucose with PSA or IPSS was found in this study. This study found random blood glucose has positive correlation with prostate volume. We recommend enhancing blood glucose control to prevent the progress of prostate enlargement.

Keywords: blood glucose, prostate, prostate-specific antigen, urology

1. Introduction

Enlarged prostate is the most common cause of lower urinary tract symptoms in elderly men. As life expectancy increases, the elderly population is increasing and so does the incidence of prostate enlargement. Research in Asia showed the prevalence of benign prostatic hyperplasia (BPH) increases after the age of 40 years, with a prevalence of 8-60% at the age of 90 years (1). Prostate enlargement causes various morbidity and high financial burden, thus making prevention efforts mandatory. Risk factors thought to affect prostate enlargement are divided into non-modifiable factors and modifiable factors. Non-modifiable factors include age, race, and genetics, while modifiable factors include sex steroid hormones, metabolic syndrome, obesity, diabetes, physical activity, diet, and inflammation (2). Investigating the association of those risk factors with prostate enlargement, particularly the modifiable one, can be beneficial to prevent and treat prostate enlargement.

Besides the increase in the prevalence of prostate enlargement, diabetes mellitus prevalence was also increasing (3). By 2030, the global prevalence of type 2 diabetes mellitus is expected to increase up to 7079 cases per 100,000 people, demonstrating an ongoing rise in all regions (4). Type 2 diabetes mellitus was commonly seen in developed countries, but there are alarming tendencies in lower-income nations. The prevalence of diabetes in hospital-based studies may be underestimated because blood glucose measurements were never carried out by many people until there is a symptom. A lot of diabetic patients also do not comply with treatment, resulting in consistently high blood glucose (5).

Evidence showed that hyperglycemia is considered to take part in the development of prostate enlargement (6). Although, the association between the two is still unclear. Understanding the potential relationship of hyperglycemia with prostate enlargement could improve men's quality of life significantly. This study aims to investigate the correlation between random blood glucose with prostatic-related parameters including

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prostate volume, international prostate symptoms score (IPSS), and prostate-specific antigen (PSA).

2. Materials and Method

This study was a cross-sectional study conducted at the Urology Polyclinic of Tabanan Hospital, Bali Province, Indonesia from January-March 2022. This study methodology has been approved by the Institutional Review Board of Tabanan Hospital with the ethical clearance letter number 800/3102/KEPEG/RSUD. Informed consent has been obtained from all patients. We included all patients with prostate enlargement (prostate volume >20 ml) which was determined by transabdominal ultrasonography. Patients with repeated admission, incomplete data, and who refused to participate were excluded from this study. Research participant selection was done using total sampling methods. The independent variable in this study was random blood glucose (RBG), while the dependent variables were prostate volume, IPSS, and PSA. The patients were asked to fill out and submit the IPSS questionnaire, with the total score being the sum of the scores in each question. Serum blood samples were used to measure PSA and RBG on a clinical chemistry analyzer (Thermo Scientific Indiko Plus, Finland). Prostate volume was measured by transabdominal ultrasonography (GE® LOGIQ P9, South Korea) and calculated from transverse images by using the prostate ellipsoid formula (0.524 × height × width × length).

Data analysis was performed by using IBM Statistical Package Software for Social Science® version 23.0. The normality of numerical data distribution was measured using the Kolmogorov-Smirnov test. The correlation between random blood glucose and prostate-related parameters was analyzed using the Pearson correlation test for normally distributed data. Otherwise, the Spearman correlation test will be used. Further analysis was carried out using multiple linear regression analysis to investigate the association between prostate volume and other parameters. A two-tailed $p<0.05$ was considered a statistically significant association.

3. Results

There were a total of 114 men with prostate enlargement visiting the Urology Polyclinic at Tabanan Hospital from January-March 2022. 23 patients were excluded due to refusal to participate. There were a total of 91 patients who fulfilled the inclusion criteria. Baseline characteristics of the patients were shown in Table 1.

Table 1. Baseline characteristics

Variables (n=91)	Mean	SD	Range
Age (years)	65.41	10.074	48-91
Random Blood Glucose (mg/dL)	121.14	40.469	79-303
IPSS	14.31	7.136	1-28
PSA (ng/mL)	9.20	17.01	0-123
Prostate Volume (mL)	52.69	26.09	20.4-148

IPSS: International Prostate Symptoms Score, PSA: Prostate-Specific Antigen

Kolmogorov-Smirnov test revealed that the data was not normally distributed, therefore correlation analysis was carried out using Spearman Test. A significant correlation between RBG and prostate volume was found, but there was no correlation between RBG with IPSS and PSA (Table 2).

Table 2. Correlation test between variables

Variables	Correlation	p
RBG and IPSS	0.137	0.197
RBG and PSA	0.063	0.551
RBG and Prostate Volume	0.269	0.010

RBG: random blood glucose

Random blood glucose was found to be associated with prostate volume only, therefore only prostate volume was investigated in the multivariate analysis. Multiple linear regression revealed that there was a significant correlation between random blood glucose and prostate volume. There was also a significant correlation between PSA and prostate volume (Table 3).

Table 3. Multivariate analysis of possible risk factors affecting prostate volume

Variables	Correlation	95% CI	p
Age	0.056	-0.378 - 0.670	0.582
Random Blood Glucose	0.279	0.053 - 0.307	0.006
IPSS	0.062	-0.500 - 0.954	0.537
PSA	0.239	0.053 - 0.680	0.022

IPSS: International Prostate Symptoms Score, PSA: Prostate-Specific Antigen

4. Discussion

This study revealed that random blood glucose has a positive correlation with prostate volume. This finding was consistent with previous studies which found that there was an association between hyperglycemia and prostate size and that abnormal glucose was correlated with prostate enlargement. In patients younger than 70 years, compared with the normal glucose group, the adjusted odds ratio for prostate volume enlargement in the prediabetic group and the diabetic group was 2.27 (95% CI 1.29 - 4.00) and 4.74 (95% CI 2.18 - 10.30) respectively (6). Prostate volume was found to be higher in patients with HbA1c levels ≥6.5% (45.69±3.97 vs. 36.64±3.30) (7). Another study by Qu et al. showed that BPH patients with fasting glucose ≥7 mmol or oral glucose tolerance test >110 mg/dl had increased prostate volume (41.18 vs 51.52 $cm^{3,}$ p=0.005) (8). Opposite findings were reported in the study by Zhang et al. that found no correlation between fasting blood glucose and HbA1c with prostate volume, except fasting insulin (r=0.421). In the study by Yim et al., increased prostate volume is associated with fasting blood glucose (9).

While the precise mechanism was still unclear, there are several proposed mechanisms on how blood glucose could impact prostate enlargement. First, hyperglycemia was found to induce an inflammatory state in vitro and in vivo (10). A study showed an increase in c-reactive protein and increased reactive oxygen species in hyperglycemic patients compare to control (11). Inflammatory cells are frequently found in BPH and are also present in prostate cancer. Findings of T lymphocytes, B lymphocytes, and macrophages were reported, which are associated with prostate size in prostatectomy specimens. Second, hyperglycemia was found to be related to

raised sympathetic nerve activity, which increased the smooth muscle tone of the prostate and subsequent blockage of the bladder outlet and cause obstructive symptoms. Third, related to the increase of sex hormones in prostate cells. Hyperglycemia leads to hyperinsulinemia which is related to a lower level of sex hormone-binding globulin and leads to the increased quantity of sex hormone entering prostatic cells, thus influencing the growth of the prostate in size (10). Another proposed mechanism is that hyperinsulinemia (as a result of hyperglycemia) might induce prostate growth through the insulin-like growth factor (IGF) pathway that stimulates cell proliferation. Additionally, elevated insulin levels (as in diabetic patients) increase catecholamine levels in plasma and tissue, which may have a trophic effect causing an enlarged prostate by lowering the progression of apoptosis (12).

This study revealed that there was no correlation between blood glucose and IPSS. Chen et al. revealed that IPSS were higher in patients with HbA1c levels ≥6.5% (16.30±3.31 vs. 9.87±1.0) (7). Another study by Ferreira et al. stated that patient with type 2 diabetes mellitus has significantly higher IPSS (13). This discrepancy might be due to the difference in blood glucose parameters being used. This study also revealed that there was no correlation between blood glucose and PSA, although a previous study found PSA was higher in diabetic compared to the non-diabetic group (3.23 vs 1.94, p=0.013) (8). A study by Duarsa et al. in the Balinese population also found that increased PSA and age were correlated with prostate volume progression (14). Meanwhile, age was not correlated with prostate volume in this study.

The blood glucose parameter was chosen over the history of diabetes mellitus because of several conditions met in our patient. First, we were lacking the diagnostic standard to diagnose diabetes mellitus such as fasting blood glucose, because most of the patients were not fasting during the examination. Second, a lot of patients who admitted to not having a history of diabetes mellitus, never actually check their blood glucose levels which turned out to be high. Third, patients with a history of diabetes mellitus may have low blood glucose due to diabetic medication and still have high blood glucose due to non-adherence to medication.

This study has several limitations. First, this study design is cross-sectional and thus was unable to reveal causal associations between blood glucose and the prostatic parameters measured. Second, this study was a single institutional study and all patients have not undergone transurethral resection of the prostate (TURP) procedure, therefore in this study, we were unable to identify the cause of the prostate enlargement and differentiate between BPH and prostate cancer by biopsy. Although, prostate cancer was found to be associated with a higher prostate volume than BPH (15). Third, several variables that might be a significant factor for prostate volume such as previous medication was also not investigated and might be confounding factors. 5-a reductase inhibitor was known to be associated with prostate volume reduction (16), metformin was also found to inhibit prostate growth in an animal study (17), while insulin is associated with prostate cell growth (18). Oral hyperglycemic drugs were also not investigated and may have affected the levels of blood glucose measured.

This study showed that random blood glucose has a positive correlation with prostate volume. This study has demonstrated the necessity for blood glucose control to prevent the progress of prostate enlargement. We recommended further studies conducted with a better methodological approach, a larger sample size, and including more variables in a multivariate analysis, to better understand the association between blood glucose and prostate volume.

Ethical statement

This study methodology has been approved by the Institutional Review Board of Tabanan Hospital with the ethical clearance letter number 800/3102/KEPEG/RSUD.

Conflict of interest

The authors declare there is no conflict of interest.

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Authors' contributions

Concept: I.B.G.T.Y.Y., A.A.S.M.P., Design: I.B.G.T.Y.Y., A.A.S.M.P., P.M.W.T., Data Collection or Processing: I.B.G.T.Y.Y., I.B.T.Y., A.A.N.O.D., K.C.M., Analysis or Interpretation: I.B.G.T.Y.Y., A.A.S.M.P., P.M.W.T., Literature Search: I.B.G.T.Y.Y., A.A.S.M.P., P.M.W.T., Writing: I.B.G.T.Y.Y., A.A.S.M.P.

References

1. Lim K Bin. Epidemiology of clinical benign prostatic hyperplasia. Asian J Urol. 2017 Jul;4(3):148–51.
2. Patel ND, Parsons JK. Epidemiology and etiology of benign prostatic hyperplasia and bladder outlet obstruction. Indian J Urol. 2014 Apr;30(2):170–6.
3. Kharroubi AT, Darwish HM. Diabetes mellitus: The epidemic of the century. World J Diabetes. 2015 Jun;6(6):850–67.
4. Khan MAB, Hashim MJ, King JK, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of Type 2 Diabetes - Global Burden of Disease and Forecasted Trends. J Epidemiol Glob Health. 2020 Mar;10(1):107–11.
5. Liu C, Yuan Y-C, Guo M-N, Xin Z, Chen G-J, Bentley AR, et al. Incidence of Type 1 Diabetes May Be Underestimated in the Chinese Population: Evidence From 21.7 Million People Between 2007 and 2017. Diabetes Care. 2021 Nov;44(11):2503–9.
6. Wu Y, Ding Y, Cao QF, Qian SB, Wang C, Duan HQ, et al. The relationship between glucose homeostasis status and prostate size in aging Chinese males with benign prostatic hyperplasia. World J Urol. 2020 Nov;38(11):2923–31.
7. Chen Z, Miao L, Gao X, Wang G, Xu Y. Effect of obesity and

hyperglycemia on benign prostatic hyperplasia in elderly patients with newly diagnosed type 2 diabetes. Int J Clin Exp Med. 2015;8(7):11289–94.

8. Qu X, Huang Z, Meng X, Zhang X, Dong L, Zhao X. Prostate volume correlates with diabetes in elderly benign prostatic hyperplasia patients. Int Urol Nephrol. 2014 Mar;46(3):499–504.

9. Yim SJ, Cho YS, Joo KJ. Relationship between metabolic syndrome and prostate volume in Korean men under 50 years of age. Korean J Urol. 2011 Jun;52(6):390–5.

10. Breyer BN, Sarma A V. Hyperglycemia and insulin resistance and the risk of BPH/LUTS: an update of recent literature. Curr Urol Rep. 2014 Dec;15(12):462.

11. Kahal H, Halama A, Aburima A, Bhagwat AM, Butler AE, Graumann J, et al. Effect of induced hypoglycemia on inflammation and oxidative stress in type 2 diabetes and control subjects. Sci Rep. 2020;10(1):4750.

12. Nugroho EA, Kurniawan R. Association between Hyperglycemia and Prostate Volume in Patients with Benign Prostate Enlargement: A Hospital Case-Control Study. J Biomed Transl Res [Internet]. 2017 Dec 31;3(2):46. Available from: https://ejournal2.undip.ac.id/index.php/jbtr/article/view/1971

13. Ferreira FT, Daltoé L, Succi G, Cunha F, Ferreira JM, Lorenzetti F, et al. Relation between glycemic levels and low tract urinary symptoms in elderly. Off J Int Soc Study Aging Male. 2015 Mar;18(1):34–7.

14. Duarsa GWK, Dau DO, Pramana IBP, Tirtayasa PMW, Yudiana IW, Santosa KB, et al. Risk Factors for Prostate Volume Progression After Prostate-Transurethral Resection. Res Reports Urol [Internet]. 2020 May [cited 2022 Oct 1];Volume 12:175–8. Available from: /pmc/articles/PMC7211307/

15. Al-Khalil S, Ibilibor C, Cammack JT, de Riese W. Association of prostate volume with incidence and aggressiveness of prostate cancer. Res reports Urol. 2016;8:201–5.

16. Kim EH, Brockman JA, Andriole GL. The use of 5-alpha reductase inhibitors in the treatment of benign prostatic hyperplasia. Asian J Urol. 2018 Jan;5(1):28–32.

17. Xu C, Xu Y, Shen Z, Zhou H, Xiao J, Huang T. Effects of metformin on prostatic tissue of rats with metabolic syndrome and benign prostatic hyperplasia. Int Urol Nephrol. 2018 Apr;50(4):611–7.

18. Wang Z, Olumi AF. Diabetes, growth hormone-insulin-like growth factor pathways and association to benign prostatic hyperplasia. Differentiation. 2011;82(4–5):261–71.