

Research Article

Assessment of Plasma von Willebrand Factor Antigen in Non-metastatic Prostate Cancer Patients: A Cross-sectional Study of the Sudanese Population

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Abstract

Backgrounds: Von Willebrand disease (VWD) is reportedly the most common inherited bleeding disorder and can also arise as an acquired syndrome (AVWS). These disorders arise due to defects and/or deficiency of the plasma protein von Willebrand factor (VWF). High plasma VWF concentrations have been reported in patients with various types of cancer, such as prostatic cancer. Metastasis may be associated with activation of hemostatic processes resulting in increased levels of circulating factor VIII-related antigen (FVIII:RAg) (von Willebrand factor antigen).

Objective: To evaluate the status of VWF antigen in Sudanese patients with prostate cancer attending RICK hospital.

Methods: This is a cross-sectional study carried out in Khartoum state at Khartoum oncology (RICK) hospital, during the period from April to June 2018, 45 samples were collected from patients with non-metastatic CA prostate, their ages ranged from 51 to 82 yr. The VWF level was measured using Enzyme-linked immunosorbent assay (ELISA). Data were analyzed by the statistical package for social science (SPSS).

Results: Serology for VWF antigen was done for 45 cases of prostate cancer. According to the age, 2 (8%) patients with age 51–66 yr had a high concentration of VWF, while 24 (92%) had normal VWF antigen concentration; of those with age 67–82 yr, 4 (21%) had high VWF antigen and 15 (79%) had normal antigen.

Conclusion: The study revealed that more than 80% of Sudanese patients with non-metastatic prostate cancer have a normal concentration of VWF.

Keywords: VWF, prostate cancer, age, ELISA

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1. Introduction

The glycoprotein von Willebrand factor (VWF) mediates the adhesion of platelets to subendothelial surfaces in primary hemostasis in case of vascular injury [1]. Plasma

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VWF levels vary over a very broad range extending from 40 to 240% of the mean value [2]. A major determinant of plasma VWF levels is the ABO blood group, but several clinical conditions, such as myocardial infarction, diabetes mellitus, liver disease, and acute infections, induce increased plasma VWF concentrations [3–8]. There are some studies describing a correlation of VWF with different cancers like prostate cancer, cervical and ovarian cancer, head and neck cancer, larynx cancer, and colorectal cancer (CRC) [9–15]. Experimental models favor the hypothesis that VWF connects tumor cells to platelets and so assists during the pathogenesis of metastases. It is supposed that these VWF-tumor-cell-emboli are hardly detected by the immune system [16–18]. As VWF levels increase with progressive disease [14, 15], it is considered as a potential clinical marker in CRC. Metastasizing may be associated with activation of hemostatic processes resulting in increased levels of circulating von Willebrand factor antigen.

The objective of this study was to evaluate the status of VWF Ag in Sudanese patients with non-metastatic prostate cancer attending RICK.

2. Methods

This is a retrospective cross-sectional study in which a total of 45 (non-metastatic) PC patients were recruited at the RICK hospital, in the period from April to June 2018.

A venous blood sample (3 ml) was taken from each subject into a tube containing 3.8% trisodium citrate, platelet poor plasma was prepared and used for the assessment of VWF level. The VWF level was measured using Enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions (TECHNOZYM, Austria).

2.1. Ethical consideration

Ethical clearance was obtained from the Institutional Review Board at Al Neelain University. Principal investigator obtained written informed consent from all participants prior to their inclusion in the study.

2.2. Data analysis

All obtained results were analyzed using Statistical Package for the Social Sciences (SPSS) version 20.0, with Pearson's chi-square test used to assess intergroup significance and *t*-test used to determine differences in means, other variables frequencies

and odd ratio calculated for comparison and presented in form of figures and tables. *P*-value and odd ratio were used to assess the significance of the results.

3. Results and Discussion

High-plasma VWF concentrations have been reported in patients with several types of cancers, such as prostatic cancer head and neck and laryngeal cancer, probably representing an acute phase reactant. In the present study, we evaluated the status of VWF antigen (VWF:Ag) in 45 patients diagnosed with prostate cancer (non-metastatic). Their mean age was 66.5 yr, 26/45 (58%) patients were 51–66 years old, and 19/45 (42%) were 67–82 Years old. The patient's marital status: 34/54 (76%) of them were married and 11/45 (24%) were unmarried; 12/45 (27%) patients had hypertension and 4/45 (9%) had diabetes mellitus. Serology for VWF antigen was done in 45 cases of prostate cancer. According to the age, 2 (8%) with age 51–66 yr had high concentration of VWF, 24 (92%) with same age had normal VWF antigen, and those with age 67–82 yr, 4 (21%) with high VWF antigen and 15 (79%) with normal antigen. In association with marital status: 5 (15%) of the married patients had high VWF antigen and 29 (85%) were normal. In unmarried men, 1 (9%) was found to have high Ag level and 10 (91%) with normal Ag level. In association with hypertension and diabetes mellites, 2 (17%) of the hyper-tensive patients had high antigen and 10 (83%) had normal antigen concentration. Among the non-hypertensive patients, 4 (12%) had high concentration and the other 29 (88%) had normal Ag concentration. Of the diabetic patients, 4 (100%) had normal antigen concentration and among the non-diabetic patients, 6 (15%) had high concentration and other 35 (85%) had normal value.

4. Conclusion

The study revealed that more than 80% of Sudanese patients with non-metastatic prostate cancer presented with a normal concentration of VWF.

TABLE 1: Demographic and clinical data in the population study.

Variables	Frequency	Percentage (%)
Age		
51–66 Years	26	58
67–82 Years	19	42
Marital status		
Married	34	76
Unmarried	11	24
HT		
Yes	12	27
No	33	73
DM		
Yes	4	9
No	41	91
Total	45	100

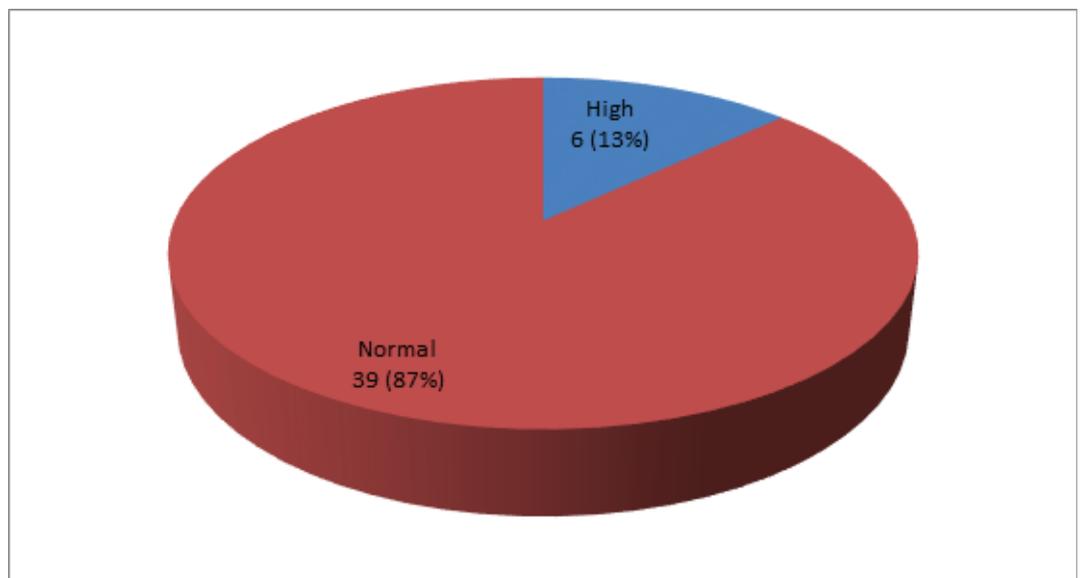


Figure 1: Distribution of Von Willebrand factor antigen in Sudanese Prostate Cancer patients.

References

- [1] Ruggeri, Z. M. (1991). Structure and function of von Willebrand factor: relationship to von Willebrand's disease. *Mayo Clinic Proceedings*, vol. 66, pp. 847–861.
- [2] Sadler, J. E., Mannucci, P. M., Berntorp, E., et al. (2000). Impact, diagnosis and treatment of von Willebrand disease. *Thrombosis and Haemostasis*, vol. 84, pp. 160–174.

TABLE 2: Correlation between variables and study parameters.

Variables	vWF Ag		P-value	OR	CI Lower	CI Upper
	High	Normal				
Age						
51–66 Years	2 (8%)	24 (92%)	0.195	0.313	0.051	1.921
67–82 Years	4 (21%)	15 (79%)				
Marital status						
Married	5 (15%)	29 (85%)	0.541	1.724	0.179	16.591
Unmarried	1 (9%)	10 (91%)				
HT						
Yes	2 (17%)	10 (83%)	0.541	1.450	0.230	9.160
No	4 (12%)	29 (88%)				
DM						
Yes	0 (0.0%)	4 (100%)	0.552	1.171	1.032	1.330
No	6 (15%)	35 (85%)				

- [3] Gallinaro, L., Cattini, M. G., Sztukowska, M., et al. (2008). A shorter von Willebrand factor survival in O blood group subjects explains how ABO determinants influence plasma von Willebrand factor. *Blood*, vol. 111, pp. 3540–3545.
- [4] Shima, M., Fujimura, Y., Nishiyama, T., et al. (1995). ABO blood group genotype and plasma von Willebrand factor in normal individuals. *Vox Sanguinis*, vol. 68, pp. 236–240.
- [5] Lufkin, E. G., Fass, D. N., O'Fallon, W. M., et al. (1979). Increased von Willebrand factor in diabetes mellitus. *Metabolism*, vol. 28, pp. 63–66.
- [6] Giustolisi, R., Musso, R., Cacciola, E., et al. (1984). Abnormal plasma levels of factor VIII/von Willebrand factor complex in myocardial infarction-expression of acute phase reaction or index of vascular endothelium damage? *Thrombosis and Haemostasis*, vol. 51, p. 408.
- [7] Castillo, R., Maragall, S., Rodes, J., et al. (1977). Increased factor VIII complex and defective ristocetin-induced platelet aggregation in liver disease. *Thrombosis Research*, vol. 11, pp. 899–906.
- [8] Sousa, N. C., Anicchino-Bizzacchi, J. M., Locatelli, M. F., et al. (2007). The relationship between ABO groups and subgroups, factor VIII and von Willebrand factor. *Haematologica*, vol. 92, pp. 236–239.
- [9] Ablin, R. J., Bartkus, J. M., and Gonder, M. J. (1988). Immuno-quantitation of factor VIII-related antigen (von Willebrand factor antigen) in prostate cancer. *Cancer Letters*, vol. 40, pp. 283–289.

- [10] Facchini, V., Gadducci, A., Baicchi, U., et al. (1988). Factor VIII:Ag plasma levels in patients with cervical and ovarian carcinoma. *European Journal of Gynaecological Oncology*, vol. 9, pp. 87–93.
- [11] Gadducci, A., Baicchi, U., Marrai, R., et al. (1993). Pretreatment plasma levels of fibrinopeptide-A (FPA), D-dimer (DD), and von Willebrand factor (vWF) in patients with operable cervical cancer: influence of surgical-pathological stage, tumor size, histologic type, and lymph node status. *Gynecologic Oncology*, vol. 49, pp. 354–258.
- [12] Sweeney, J. D., Killion, K. M., Pruet, C. F., et al. (1990). von Willebrand factor in head and neck cancer. *Cancer*, vol. 66, pp. 2387–2389.
- [13] Paczuski, R., Bialkowska, A., Kotschy, M., et al. (1999). Von Willebrand factor in plasma of patients with advanced stages of larynx cancer. *Thrombosis Research*, vol. 95, pp. 197–200.
- [14] Damin, D. C., Rosito, M. A., Gus, P., et al. (2002). Von Willebrand factor in colorectal cancer. *International Journal of Colorectal Disease*, vol. 17, pp. 42–45.
- [15] Wang, W. S., Lin, J. K., Lin, T. C., et al. (2005). Plasma von Willebrand factor level as a prognostic indicator of patients with metastatic colorectal carcinoma. *World J Gastroenterology*, vol. 11, pp. 2166–2170.
- [16] Gasic, G. J., Gasic, T. B., Galanti, N., et al. (1973). Platelet-tumor-cell interactions in mice. The role of platelets in the spread of malignant disease. *International Journal of Cancer*, vol. 11, pp. 704–718.