


# Diagnosis of VWD in Clinically Suspected Patients: A single centre study


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# Introduction

- Von willibrand disease is one of the most common inherited bleeding disorder.
- Incidence worldwide is 5 in 100,000 births.
- Expected number of patients in Pakistan according to the population of 160 million is 8000.
- There is no central registry. The data obtained from HPWS 268 registered patients.

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- VWD is characterized by varying degree of increased bleeding tendency in the patients, it occurs due to the qualitative or quantitative deficiency of vWF antigen.
  - Caused by inherited mutation in the vWF gene on chromosome 12.
  - It is transmitted both in autosomal dominant and recessive fashion.

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- vWF is synthesized in endothelial cells and Megakaryocytes.
  - It mediates adhesion of plts to sites of vascular injury via interaction with plt GP1b and subendothelial matrix.
  - VWF Ag acts as carrier protein for FVIII.

# Classification of VWD

- Type I – Mild quantitative
- Type 2 – Qualitative deficiency of vWF
  - 2A - With decreased HMW multimers
  - 2B - Increased affinity for plt GP 1b
  - 2M - Decreased plt-dependent function
  - 2N - Decreased affinity for FVIII
- Type 3 - Virtually complete deficiency of vWF

# Clinical presentation

- Mucocutaneous bleed
  - bruises
  - gum bleed
  - Epistaxis
  - Menorrhagia
- Surgical bleed
- Joint bleed very rare



# Tests required for Diagnosis

- vWF Antigen
- FVIII Level
- vWF:Rco
- Multimer analysis
- vwF:CB
- VWF:FVIII binding
- Genetic mutation



# Objective of study

- In Pakistan majority of the patients are still not diagnosed. The reason being lack of awareness and lack of reliable diagnostic tests facilities.
- Diagnosis of vWD is not simple. There is not a single test which can alone diagnose and subtype vWD. Group of tests are required for confirmation.
- The objective of the study is to diagnose and subtype vWD ,in clinically suspected patients presenting with unexplained muco-cutaneous bleed ,with limited number of tests.



# Material and Method

- Setting: Pathology deptt. PAEC general hospital Islamabad
- Duration: Two years, 1<sup>st</sup> jan 2008 to 31<sup>st</sup> Dec 2009
- Sample size: 130 patients
- Inclusion criteria: All patients with clinical suspicion of VWD
- Exclusion criteria: Already diagnosed cases or patients with family history of a diagnosed case of VWD.
- Study design: cross sectional
- Sampling Technique: Non probability consecutive sampling.



# Data collection procedure

- Samples referred from both in-door and out- door patients
- Informed consent was taken from all patients
- History Performa filled in isolation
- Sample collected in vaccutainers containing sodium citrate
- Sample centrifuged to obtain platelet poor plasma.
- Plasma stored at -40 centigrade freezer

# Sample collected in two tubes



# Double centrifuge



# Labeled and stored at -40



# Taken out when batch run





# Lab Tests performed


- CBC
- PT,aPTT – kit used is Actin FS.
- vWF:Ag – by Immunoturbidometric method.
- FVIII - by Coagulometric method.
- All tests were performed on a fully automated coagulation analyzer CA- 550 by Sysmex using Dade Behring kits and reagents.

# Results

Table - 1	
TOTAL NO.OF PTS	130
MALE	44 (33.8%)
FEMALE	86 (66.15%)
Age – 1 - 15 years	50 (38.4%)
16 - 30 years	49 (37.6%)
31 - 45 years	25 (19.2%)
46 - 65 years	06 (4.6%)

# Result contd...

Table – 2	Clinical features	Percentage of patients
	Menorrhagia	58%
	Epistaxis	38%
	Gum bleeding	35%
	Prolong bleed after cut and bruises	25%
	Surgical bleed	10%

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- VWD was detected in 62 patients
  - Low vWF:Ag was detected in - 59 patients  
Normal range - 60% to 150%
  - Low FVIII level detected in - 57 patients  
Normal range - 50% to 150%
  - PT was prolonged in one patient
  - APTT was prolonged in 56 patients
  - All patients had normal platelet count

# Detail of pts with low vWFAg

VWFAg levels	No. of patients	FV III levels range & mean
< 1 %	41 (71.9%)	< 1 - 10.8 (4.0%)
1 - 20%	03 (5.2%)	15 - 38 (29.6%)
21 - 40%	03 (5.2%)	8.1 - 19 (14.7%)
41 - 59%	12 (21.0%)	5.8 - 95 (49.98%)

# Type 3 VWD

- Type 3 VWD was detected in 41 patients (71.9%)
- vWF was less than one percent in all cases
- Mean FVIII level was 4.8%
- They all had parents close relative .
- Clinically presented with severe mucocutaneous bleed off and on.
- The incidence of Type 3 vWD is 1 in 1 million. Twenty percent of all vWD cases have type 3 disease.

# Type 1 vWD

- In type 1 vWD the FVIII is low in proportion to vWF:Ag.
- six patients had FVIII level low in proportion to vWF:Ag and show clinical severity accordingly.
- They seem to fall in the subtype 1vWD.

## Type 1 vWD

Sr No.	vWF:Ag %	FVIII %
1	49	39
2	53	49
3	28	36
4	54	42
5	57	44
6	48	33



## Type 2 vWD

- patients having very low FVIII level as compared to vWF:Ag seems to have qualitative defect which can be confirmed by VWF:Rco
- There were three patients having low FVIII but normal VWF:Ag. These patients were differentiated from Hemophilia by;
  1. Clinical pattern of bleeding
  2. Poor response to recombinant FVIII and good response to FVIII concentrates containing VWF.
- They seem to fall in the subtype 2N.

# Probable Type 2

Sr No.	VWF:Ag %	FVIII %
1	22	8.1
2	38	19
3	40	17
4	41	20
5	54	8.8
6	59	32

# Probable Type 2N

No.	VWF:Ag %	FVIII %
1	60	9.1
2	79	10.2
3	67	1.5



# Conclusion

- VWD is a common disorder in our society but is under diagnosed.
- Diagnosis and subtyping of VWD is not simple it requires detail history and number of tests ,many of which are expensive and needs expertise to interpret.
- Detail clinical history of bleeding, and tests like aPPT,vWF:Ag and FVIII levels can help us to diagnose substantial number of VWD patients.
- There is a need to have referral labs which are at least able to perform VWF:Ag , FVIII levels and vWF:Rco



Thanks