

Variations in Von Willebrand Factor Concentration Associated with Hemorrhagic Pathological Pregnancies at the Yaoundé Central Hospital, Cameroon

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Abstract

Introduction: Von Willebrand factor (VWF) levels rise physiologically during normal pregnancy. Failure of this rise may underlie hemorrhagic pathological pregnancies, as maternal-fetal cellular distress is thought to drive abnormal VWF production. This study aimed to describe VWF level variation among women with hemorrhagic pathological pregnancies at the Yaoundé Central Hospital (YCH). **Methods:** An analytical cross-sectional study was conducted in the Clinical Biology Laboratory and the Department of Obstetrics and Gynecology of YCH between February and May 2025. A 5 mL venous blood sample without anticoagulant was collected from each eligible patient on admission and centrifuged; VWF antigen (VWF:Ag) was measured in serum by sandwich ELISA (Biofine reagent). Data were analyzed with SPSS version 26.0, using the chi-square test for proportions and the independent-samples t-test for comparison of means. **Results:** Among 834 pregnant women received during the study period, 91 (10.9%) presented with a hemorrhagic pathological pregnancy; 80 consented and were sampled. The overall mean VWF:Ag concentration was $163.60\% \pm 25.80\%$ (1.64 ± 0.26 IU/mL). VWF:Ag concentration was higher, but not significantly so, in women with blood group O

(167.44% $\pm$ 21.34%) than in non-O women (157.82% $\pm$ 30.79%; mean difference 9.62 percentage points, 95% CI -2.94 to 22.18 ; $p = 0.13$), and higher, again not significantly, in the presence of fetal complications (169.76% $\pm$ 24.44%) than in their absence (159.83% $\pm$ 26.69%; mean difference 9.93 percentage points, 95% CI -1.45 to 21.31 ; $p = 0.09$). VWF levels varied with disease severity across pathology subgroups; this reached statistical significance only for ruptured ectopic pregnancy (hemodynamic instability vs. stability; $p = 0.004$) and was of borderline significance for retroplacental hematoma (Sher grade 3 vs. grade 2; $p = 0.048$), while differences by severity of pre-eclampsia, hemorrhagic placenta previa, and postpartum hemorrhage were not statistically significant. **Conclusion:** Most between-group differences in VWF:Ag concentration, including the higher levels seen in blood-group-O women, were not statistically significant; a significant difference was observed only for hemodynamic instability in ruptured ectopic pregnancy, with a borderline difference by Sher grade in retroplacental hematoma. These exploratory findings suggest VWF concentration may track maternal-fetal distress in hemorrhagic pathological pregnancy, but given the small subgroup sizes this remains hypothesis-generating and warrants confirmation in larger, adequately powered, multicenter studies.

Keywords

Pathological Pregnancy, Von Willebrand Factor, Feto-Maternal Distress, Yaoundé Central Hospital

1. Background

Pregnancy is a physiological state associated with substantial hematological changes that can underlie several disorders. From the first trimester onward, Von Willebrand factor (VWF) concentration rises, reaching up to three times baseline by term. Failure of this physiological rise (VWF stagnation) has been proposed as a contributor to the hemorrhagic complications of pregnancy: pre-eclampsia, ruptured ectopic pregnancy, retroplacental hematoma, hemorrhagic placenta previa, and postpartum hemorrhage.

Half of maternal deaths worldwide occur in sub-Saharan Africa [1]. In France, Saucedo *et al.* (2010) reported 70 to 75 maternal deaths per year between 2001 and 2006, an estimated rate of 8 to 12 per 100,000 live births [2]. A study conducted at the Yaoundé University Teaching Hospital found an alarming maternal mortality ratio of 287.5 per 100,000 live births, with unsafe abortion (25%) and postpartum hemorrhage (22.9%) as the leading causes, followed by ectopic pregnancy, hypertensive disorders, and placenta previa [1]. Data on maternal mortality risk factors nonetheless remain scarce in Cameroon. Hemorrhagic pathological pregnancy represents a high-risk situation for both mother and fetus, underscoring the importance of identifying biomarkers of this maternal-fetal distress.

2. Methods

2.1. Study Design and Setting

This was an analytical cross-sectional study, conducted in the Department of Obstetrics and Gynecology of the Yaoundé Central Hospital (YCH), a national referral center, a setting that increases the local prevalence of hemorrhagic pathological pregnancies relative to primary-care facilities. Recruitment and data collection took place between February and May 2025.

2.2. Participants

All pregnant women presenting with a hemorrhagic pathological pregnancy and received in the department during the study period were eligible. Inclusion criteria were a confirmed hemorrhagic pathology of pregnancy and informed, voluntary consent to participate. Women who declined participation were excluded.

2.3. Variables

The dependent variables were the type of hemorrhagic pathology of pregnancy (the leading cause of maternal mortality worldwide according to the World Health Organization, accounting for approximately 27% of deaths [3]) and VWF:Ag concentration. The independent variable was ABO blood group, a stable genetic determinant of baseline plasma VWF concentration; individuals with blood group O are known to have physiologically lower baseline VWF levels than non-O individuals. The primary comparison of interest, specified a priori, was the difference in mean VWF:Ag concentration between blood-group-O and non-O women in the overall sample (Table 1). Comparisons stratified by pathology type, by presence of fetal complications, and by disease-severity subgroup (Tables 2-4) were secondary, exploratory analyses intended to generate hypotheses for confirmatory testing in larger studies; they were not adjusted for multiple comparisons, and their p-values should be interpreted accordingly.

2.4. Data Sources/Measurement

Data were collected using a structured questionnaire, supplemented by medical records and laboratory results. A 5 mL venous blood sample without anticoagulant was drawn aseptically from the antecubital vein of each patient on arrival, then centrifuged at 3500 rpm for 5 minutes; serum was aliquoted into sterile cryotubes and stored at -20°C until analysis. VWF:Ag was measured by sandwich ELISA (Biofine reagent), a kit validated by the manufacturer for use with serum. The concentration of each sample was read from a calibration curve constructed according to the manufacturer's instructions. The reference range for VWF:Ag was taken as 50% - 150% (0.5 - 1.5 IU/mL).

2.5. Bias

Recruitment was consecutive and based on convenience, which may have introduced selection bias, and the single-center referral setting may limit generalizabil-

ity to non-referral facilities. Eleven eligible women declined participation because of needle phobia; if this refusal was associated with pathology or severity, non-response bias cannot be excluded. Subgroup sample sizes were small for some pathologies (e.g., postpartum hemorrhage, $n = 4$), which limits the precision of subgroup estimates. A gestational age (mean $\pm$ SD or median [IQR]) at sampling for each diagnostic group, and the interval between symptom onset/admission and blood sampling relative to delivery; also state, for each group, the proportion who had already received a blood transfusion, intravenous fluid resuscitation, or other treatment (e.g. magnesium sulfate, uterotonics) before the sample was drawn, since these factors can independently affect VWF:Ag concentration and their imbalance across groups would be a potential confounder.

2.6. Study Size

No prior sample size calculation was performed. During the study period, 834 pregnant women were received in the department; 743 did not meet the inclusion criteria and were excluded, leaving 91 women with a hemorrhagic pathological pregnancy. Of these, 11 declined consent because of needle phobia, yielding a final analytic sample of 80 participants.

2.7. Quantitative Variables

VWF:Ag concentration was analyzed as a continuous variable (% , converted to IU/mL). ABO blood group was dichotomized as O versus non-O (A, B, AB). Within each pathology, disease severity was further categorized using standard clinical classifications (the Sher classification for retro-placental hematoma; grade for hemorrhagic placenta previa; severe versus mild for pre-eclampsia and postpartum hemorrhage; and hemodynamic stability for ruptured ectopic pregnancy). The diagnostic and severity criteria actually applied in this study, e.g.: pre-eclampsia diagnosed as new-onset hypertension $\geq 140/90$ mmHg after 20 weeks' gestation with proteinuria or another severe feature, graded severe when blood pressure $\geq 160/110$ mmHg or a severe feature (thrombocytopenia, hepatic or renal impairment, pulmonary oedema, cerebral/visual symptoms) was present; retro-placental hematoma graded by the Sher classification (grade 2: moderate bleeding with evidence of fetal distress in a live fetus; grade 3: severe bleeding with fetal death, subdivided into 3a without and 3b with coagulopathy); hemorrhagic placenta previa graded 1 - 4 by the degree of os coverage (low-lying to complete); postpartum hemorrhage defined per WHO criteria (blood loss ≥ 500 mL after vaginal birth or ≥ 1000 mL after caesarean within 24 hours), classified as severe when blood loss exceeded 1000 mL or hemodynamic instability was present; and ruptured ectopic pregnancy classified as hemodynamically unstable when presenting with systolic blood pressure < 90 mmHg, heart rate > 100 bpm, or clinical signs of hypovolemic shock.

2.8. Statistical Methods

Data were entered in Microsoft Excel and analyzed with SPSS version 26.0. Quan-

titative variables are presented as mean $\pm$ standard deviation. The chi-square test was used to compare proportions, and the independent-samples t-test was used to compare mean VWF:Ag concentrations between groups. A p-value < 0.05 was considered statistically significant.

2.9. Ethical Considerations

This study complied with the fundamental principles of medical research. Administrative authorization (N° 011/25/AR/MINSANTE/SG/DHCY/CM) and ethical clearance (N° 0050/CHRRSHC/2025) were obtained prior to data collection, and written informed consent was obtained from all participants.

Table 1. Mean VWF:Ag concentration by ABO blood group among women with hemorrhagic pathological pregnancy (N = 80).

ABO blood group	VWF:Ag, mean $\pm$ SD (%)	Mean difference (pp)	p-value
Blood group O (n = 48)	167.44 $\pm$ 21.34	9.62 (95% CI -2.94 to 22.18)	0.13
Non-O blood group (A, B, AB) (n = 32)	157.82 $\pm$ 30.79	-	-

VWF:Ag: Von Willebrand factor antigen; SD: standard deviation; pp: percentage points; CI: confidence interval. Independent-samples t-test with Welch's correction for unequal variances; mean differences and p-values recalculated from the reported means, SDs, and sample sizes. This comparison was the pre-specified primary analysis; $p < 0.05$ was considered statistically significant, but this difference did not reach that threshold.

Table 2. VWF:Ag concentration by type of hemorrhagic pathological pregnancy and ABO blood group (N = 80).

Pathology	ABO blood group (n)	VWF:Ag, mean $\pm$ SD (%)	Mean diff. (pp)	p-value
Pre-eclampsia (n = 37)				
	O (n = 22)	160.50 $\pm$ 23.79	7.00 (95% CI -14.00 to 28.00)	0.50
	Non-O (n = 15)	153.50 $\pm$ 34.08		
Ruptured ectopic pregnancy (n = 18)				
	O (n = 13)	169.50 $\pm$ 20.79	9.30 (95% CI -8.90 to 27.50)	0.29
	Non-O (n = 5)	160.20 $\pm$ 13.40		
Retroplacental hematoma (n = 12)				
	O (n = 8)	182.75 $\pm$ 7.47	0.25 (95% CI -11.87 to 12.37)	0.96
	Non-O (n = 4)	182.50 $\pm$ 8.18		
Hemorrhagic placenta previa (n = 9)				
	O (n = 4)	169.25 $\pm$ 25.59	11.85 (95% CI -39.00 to 62.70)	0.60
	Non-O (n = 5)	157.40 $\pm$ 38.39		
Postpartum hemorrhage (n = 4)				
	O (n = 3)	161.66 $\pm$ 6.80	38.66 (n = 3 vs. n = 1; not testable)	n/a†
	Non-O (n = 1)	123.00		

VWF:Ag: Von Willebrand factor antigen; SD: standard deviation; pp: percentage points; CI: confidence interval. †Not computed: single observation in the non-O postpartum-hemorrhage subgroup (n = 1). Independent-samples t-test with Welch's correction for unequal variances, recalculated from the reported means, SDs, and sample sizes. These pathology-stratified comparisons are secondary/exploratory and were not adjusted for multiple comparisons; none reached statistical significance.

Table 3. VWF:Ag concentration by presence of fetal complications among women with hemorrhagic pathological pregnancy (N = 80).

Fetal complications	VWF:Ag, mean $\pm$ SD (%)	Mean difference (pp)	p-value
Present (n = 38)	169.76 $\pm$ 24.44	9.93 (95% CI -1.45 to 21.31)	0.09
Absent (n = 42)	159.83 $\pm$ 26.69		

VWF:Ag: Von Willebrand factor antigen; SD: standard deviation; pp: percentage points; CI: confidence interval. Independent-samples t-test with Welch's correction for unequal variances; mean difference and p-value recalculated from the reported means, SDs, and sample sizes (the original mean difference of 11.62 pp was an arithmetic error; the correct value is 9.93 pp). This comparison did not reach statistical significance.

Table 4. VWF:Ag concentration by disease-severity subgroup within each hemorrhagic pathological pregnancy.

Pathology	Severity subgroup (n)	VWF:Ag, mean ± SD (%)	Mean diff. (pp)	p-value
Pre-eclampsia (n = 36)				
	Severe (n = 34)	150.01 ± 29.89	10.32 (95% CI -55.82 to 35.18)	0.41
	Mild (n = 2)	160.33 ± 11.93		
Ruptured ectopic pregnancy (n = 18)				
	Hemodynamic instability (n = 12)	177.20 ± 9.70	30.87 (95% CI 13.53 to 48.21)	0.004*
	Hemodynamic stability (n = 6)	146.33 ± 16.48		
Retroplacental hematoma (n = 12)				
	Sher grade 3 (n = 7)	186.42 ± 4.96	9.02 (95% CI 0.13 to 17.91)	0.048*
	Sher grade 2 (n = 5)	177.40 ± 7.19		
Hemorrhagic placenta previa (n = 9)				
	Grade 2 - 3 (n = 6)	177.16 ± 11.65	43.49 (95% CI -58.54 to 145.52)	0.22
	Grade 4 (n = 3)	133.67 ± 43.06		
Postpartum hemorrhage (n = 4)				
	Severe (n = 2)	159.00 ± 7.07	14.00 (n = 2 vs. n = 2)	0.64
	Mild (n = 2)	145.00 ± 31.11		

VWF:Ag: Von Willebrand factor antigen; SD: standard deviation; pp: percentage points; CI: confidence interval. Sher grade: classification of retroplacental hematoma severity (grade 3 > grade 2). Independent-samples t-test with Welch's correction for unequal variances, recalculated from the reported means, SDs, and sample sizes; the postpartum-hemorrhage comparison (n = 2 per subgroup) is reported for completeness but is not statistically meaningful given the minimal sample. These severity-stratified comparisons are secondary/exploratory and were not adjusted for multiple comparisons. *p < 0.05, statistically significant.

3. Results

3.1. Sampling

Of 834 pregnant women received in the department during the study period, 743 did not meet the inclusion criteria. Of the 91 women identified with a hemorrhagic pathological pregnancy, 11 declined to participate because of needle phobia, leaving 80 women who consented and were included in the final analysis.

3.2. Descriptive Data

Among the 80 participants, 48 (60.0%) had blood group O and 32 (40.0%) had a

non-O blood group (A, B, AB). By pathology type, 37 women had pre-eclampsia, 18 had a ruptured ectopic pregnancy, 12 had a retroplacental hematoma, nine had hemorrhagic placenta previa, and four had postpartum hemorrhage. One pre-eclampsia patient (1/37) had incomplete severity documentation and was excluded from the severity-stratified analysis (Table 4), a missing-data pattern considered unrelated to VWF concentration and unlikely to bias the reported comparison.

3.3. Outcome Data

The prevalence of hemorrhagic pathological pregnancy among all pregnant women received during the study period was 10.9% (91/834). The overall mean VWF:Ag concentration in the 80 participants was 163.60% $\pm$ 25.80% (1.64 $\pm$ 0.26 IU/mL).

3.4. Main Results

VWF:Ag concentration was higher in women with blood group O (167.44% $\pm$ 21.34%) than in non-O women (157.82% $\pm$ 30.79%; mean difference 9.62 percentage points, 95% CI -2.94 to 22.18), but this difference did not reach statistical significance using an independent-samples t-test with unequal variances (Welch's $t = 1.54$, $df = 50.6$, $p = 0.13$) (Table 1, Figure 1).

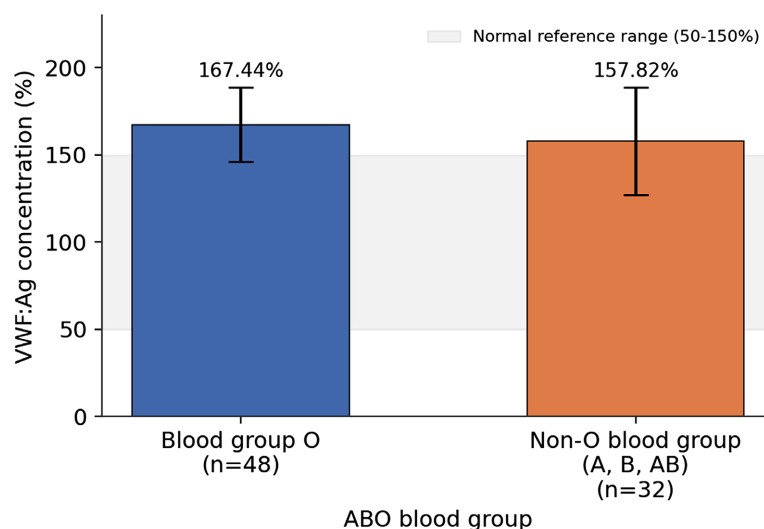


Figure 1. Mean VWF:Ag concentration ($\pm$ SD) by ABO blood group among women with hemorrhagic pathological pregnancy (N = 80). Shaded band: normal reference range (50% - 150%).

By pathology type, mean VWF:Ag concentrations differed by blood group as follows (none reaching statistical significance): pre-eclampsia, 160.50% $\pm$ 23.79% (O) versus 153.50% $\pm$ 34.08% (non-O; 95% CI -14.00 to 28.00; $p = 0.50$); ruptured ectopic pregnancy, 169.50% $\pm$ 20.79% (O) versus 160.20% $\pm$ 13.40% (non-O; 95% CI -8.90 to 27.50; $p = 0.29$); retroplacental hematoma, 182.75% $\pm$ 7.47% (O) versus 182.50% $\pm$ 8.18% (non-O; 95% CI -11.87 to 12.37; $p = 0.96$); hemorrhagic

placenta previa, $169.25\% \pm 25.59\%$ (O) versus $157.40\% \pm 38.39\%$ (non-O; 95% CI -39.00 to 62.70 ; $p = 0.60$); and postpartum hemorrhage, $161.66\% \pm 6.80\%$ (O, $n = 3$) versus 123.00% (non-O, $n = 1$), for which a variance-based test could not be computed given the single non-O observation (**Table 2**).

VWF:Ag concentration was higher in the presence of fetal complications ($169.76\% \pm 24.44\%$) than in their absence ($159.83\% \pm 26.69\%$; mean difference 9.93 percentage points, 95% CI -1.45 to 21.31 ; $p = 0.09$), a difference that did not reach conventional statistical significance (**Table 3**, **Figure 2**).

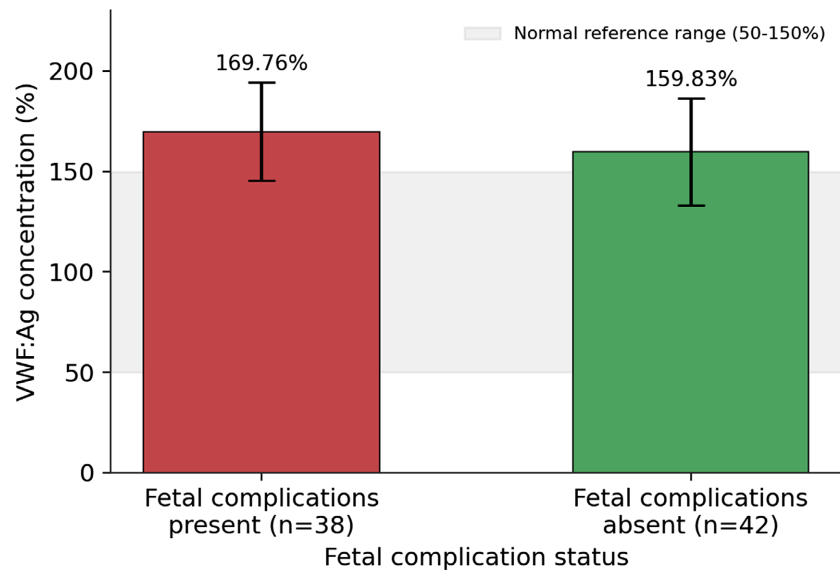


Figure 2. Mean VWF:Ag concentration ($\pm$ SD) by presence of fetal complications among women with hemorrhagic pathological pregnancy ($N = 80$). Shaded band: normal reference range (50% - 150%).

VWF:Ag concentration also varied with disease severity within each pathology category (**Table 4**). In pre-eclampsia, levels were lower in severe disease ($150.01\% \pm 29.89\%$) than in mild disease ($160.33\% \pm 11.93\%$; 95% CI -55.82 to 35.18 ; $p = 0.41$), a comparison in which the mild-disease subgroup was very small ($n = 2$). In ruptured ectopic pregnancy, levels were significantly higher with hemodynamic instability ($177.20\% \pm 9.70\%$) than with hemodynamic stability ($146.33\% \pm 16.48\%$; 95% CI 13.53 to 48.21 ; $p = 0.004$). In retroplacental hematoma, levels were higher in Sher grade 3 ($186.42\% \pm 4.96\%$) than in Sher grade 2 ($177.40\% \pm 7.19\%$; 95% CI 0.13 to 17.91 ; $p = 0.048$), a difference of borderline significance. In hemorrhagic placenta previa, levels were higher in grade 2 - 3 disease ($177.16\% \pm 11.65\%$) than in grade 4 disease ($133.67\% \pm 43.06\%$; 95% CI -58.54 to 145.52 ; $p = 0.22$), which did not reach statistical significance once unequal variances were accounted for. In postpartum hemorrhage, levels were higher in severe cases ($159.00\% \pm 7.07\%$) than in mild cases ($145.00\% \pm 31.11\%$; $p = 0.64$), though with only two observations per subgroup this comparison is not statistically meaningful.

3.5. Other Analyses

No additional subgroup or sensitivity analyses were performed.

4. Discussion

Women with blood group O who had a hemorrhagic pathological pregnancy had a numerically higher, but not statistically significant, mean VWF concentration ($167.44\% \pm 21.34\%$) than non-O women ($157.82\% \pm 30.79\%$; $p = 0.13$). This finding is, at first glance, counterintuitive: plasma VWF concentration is physiologically lowest in blood-group-O individuals, an effect classically attributed to accelerated proteolytic clearance of VWF multimers in this group [4]. In a cohort selected entirely for hemorrhagic pathology, this baseline genetic effect could in principle be superseded by disease-related endothelial activation, which releases VWF from endothelial Weibel-Palade bodies in proportion to the degree of vascular or tissue stress rather than to ABO genotype alone [5]; however, because the between-group difference did not reach statistical significance, this explanation remains speculative rather than confirmed by our data. Our results also contrast with those of Ewodo *et al.* (2014) in Douala, who reported very low VWF levels in non-O pregnant women [6]. This discrepancy could be explained by the fact that the Ewodo *et al.* study concerned uncomplicated pregnancies rather than pathological pregnancies as in the present study, by potentially more severe complications among group O patients here, and by their over-representation in our sample (60%).

Group O patients with pre-eclampsia had a higher mean VWF concentration ($160.50\% \pm 23.79\%$) than non-O patients ($153.50\% \pm 34.08\%$), but this difference was not statistically significant (95% CI -14.00 to 28.00 ; $p = 0.50$). This numerically higher value is consistent with the direction reported by Lecarpentier *et al.* (2016) in France, who described VWF as a marker whose abnormal concentration contributes to the pathogenesis of pre-eclampsia through impaired trophoblastic invasion and secondary endothelial dysfunction [7]. Elevated VWF in this setting is generally thought to reflect early placental hypoperfusion rather than overt hemorrhage, which distinguishes its proposed role in pre-eclampsia from its role as a marker of acute blood loss in the other pathologies studied here.

Group O patients with ruptured ectopic pregnancy had a higher, though not statistically significant, mean VWF level ($169.50\% \pm 20.79\%$) than non-O patients ($160.20\% \pm 13.40\%$; 95% CI -8.90 to 27.50 ; $p = 0.29$), which could reflect stress- and inflammation-related endothelial activation, triggering a transient VWF rise even in group O patients, who normally carry lower baseline levels [8]. This pattern mirrors observations in traumatic and hemorrhagic-shock states more broadly, where VWF behaves as an acute endothelial-activation marker released in proportion to the severity of vascular injury and hypoperfusion, largely independent of baseline ABO-related levels [9].

Patients with retroplacental hematoma, across both blood-group categories, had markedly elevated VWF concentrations, with only a 0.25-percentage-point

difference favoring group O (95% CI -11.87 to 12.37 ; $p = 0.96$), essentially no difference between groups, and the smallest between-group gap of any pathology studied, alongside the highest absolute VWF levels overall. In Senegal, Coly *et al.* (2021) demonstrated a significant association between blood group O and the occurrence of retroplacental hematoma [10]; blood group O may influence endothelial activation and the feto-maternal immune response involved in its pathogenesis. The near-equivalence between blood groups observed here suggests that, once retroplacental bleeding is established, the intensity of local endothelial and platelet activation may override any modulating effect of ABO genotype.

VWF concentrations were numerically, but not statistically significantly, higher in group O women with hemorrhagic placenta previa ($169.25\% \pm 25.59\%$) than in non-O women ($157.40\% \pm 38.39\%$; 95% CI -39.00 to 62.70 ; $p = 0.60$). These findings are in the same direction as those of Nightingale and Cutler (2013) and Steffes *et al.* (2022), who showed that VWF, produced predominantly by vascular endothelium, rises in response to vascular stress or tissue injury, both common in hemorrhagic placenta previa. This numerically higher level in group O patients could represent an adaptive response that improves local hemostasis [11] [12].

VWF concentrations were higher in group O patients ($161.66\% \pm 6.80\%$) among the three women with postpartum hemorrhage who had this blood group, compared with the single non-O patient (123.00%); with only one observation in the non-O subgroup this comparison is descriptive only and no significance test could be computed. The direction is consistent with the work of Khallikane *et al.* in Morocco, who reported elevated VWF levels during the postpartum period [13]. Higher levels in group O women could reflect a compensatory hemostatic response, consistent with VWF's broader role as an endothelium-derived acute-phase reactant that rises whenever blood loss or vascular injury demands enhanced platelet adhesion [5].

Finally, VWF levels varied with the severity of the pathologies studied, a pattern broadly consistent with its proposed role as a marker of maternal-fetal distress, although only two of these severity comparisons reached statistical significance in our sample. The work of Foidart *et al.* (2009) [14] and Ewodo *et al.* (2014) [6] shows elevated VWF in the presence of fetal complications; in our cohort this difference was in the same direction (169.76 vs. 159.83%) but did not reach statistical significance ($p = 0.09$). A comparable relationship between VWF elevation and hemodynamic severity has been described outside obstetrics, in traumatic and hemorrhagic-shock injury, where VWF release tracks the degree of vascular compromise [9]; in the present cohort, this relationship reached statistical significance for ruptured ectopic pregnancy, where VWF was higher with hemodynamic instability than with hemodynamic stability ($p = 0.004$). The Sher classification (1985) similarly links the severity of retroplacental hematoma (Sher grade 3 > grade 2) to greater endothelial disruption and, in our cohort, to higher VWF elevation [15] ($p = 0.048$, of borderline significance); a comparable, non-significant gradient was observed in severe postpartum hemorrhage ($n = 2$ per subgroup).

The decrease in VWF with worsening pre-eclampsia observed in the present study ($150.01\% \pm 29.89\%$ in severe disease versus $160.33\% \pm 11.93\%$ in mild disease; 95% CI -55.82 to 35.18 ; $p = 0.41$, not statistically significant, and based on a mild-disease subgroup of only $n = 2$) departs from most of the published literature. Several studies, including that of Hulstein *et al.* (2006), have shown that VWF antigen levels rise rather than fall as pre-eclampsia progresses toward HELLP syndrome, reflecting acute endothelial activation with release of highly reactive VWF multimers [16]; a recent review similarly reports that VWF:Ag is typically elevated in pre-eclampsia and HELLP syndrome, while its cleaving protease ADAMTS13 tends to be reduced [17]. The lower levels observed here in severe cases may instead reflect increased consumption of VWF within microvascular thrombi once endothelial injury becomes advanced - a mechanism analogous to the consumptive coagulopathy described in severe HELLP syndrome - together with the very small severe-disease subgroup available for comparison ($n = 34$ vs. $n = 2$), which limits the precision of this estimate and warrants confirmation in a larger sample. Ley (2010) similarly reported lower VWF levels in total placenta previa than in grade 2 - 3 disease [18], a difference that in our data (grade 2 - 3 vs. grade 4) was likewise in this direction but did not reach statistical significance once unequal variances were accounted for ($p = 0.22$); a finding that, as in severe pre-eclampsia, may reflect either exhaustion of the endothelial secretory response or excessive consumption of this glycoprotein once bleeding becomes severe and sustained.

5. Conclusion

This study found that mean VWF:Ag concentration was numerically, but not statistically significantly, higher in blood-group-O women and in the presence of fetal complications among women with hemorrhagic pathological pregnancy at the Yaoundé Central Hospital. VWF concentration also varied with disease severity across pathology subgroups; this reached statistical significance only for hemodynamic instability in ruptured ectopic pregnancy ($p = 0.004$), with a borderline association for the severity of retroplacental hematoma (Sher grade 3 vs. grade 2; $p = 0.048$). Differences by severity of pre-eclampsia, hemorrhagic placenta previa, and postpartum hemorrhage were not statistically significant, and several subgroup comparisons were based on very small numbers. These exploratory findings are compatible with, but do not establish, a potential role for VWF as a biomarker of maternal-fetal distress in hemorrhagic pathological pregnancy; confirmation in larger, adequately powered, multicenter studies with pre-specified primary comparisons is warranted.

Data Availability Statement

The data supporting the conclusions of this study are available from the corresponding authors upon reasonable request.

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Author Contributions

Claudia Vanelle Djidjion: study design, data collection and analysis, biological analyses, manuscript drafting; **Symphorien Ewodo:** study supervision, study design, manuscript drafting; **Madye Ngo Dingom:** study supervision, manuscript drafting; **Tracy Grace Njike Alima:** manuscript drafting; **Donald Muwud Tebo:** manuscript drafting, data analysis, manuscript translation; **Charlotte Tchente Nguefack:** manuscript drafting; **Dieudonné Adiogo:** study design, manuscript drafting; All authors have read and approved the final version of the manuscript and agree to be responsible for all aspects of the work, in accordance with study criteria.

Conflicts of Interest

The authors declare no conflicts of interest.

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