Prevalence and severity of anaemia in persons with haemophilia and von Willebrand disease at Charlotte Maxeke Johannesburg Academic Hospital, South Africa

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Background. Haemophilia and von Willebrand disease (VWD) are inherited bleeding diatheses characterised by spontaneous or traumatic bleeding resulting in varying degrees of anaemia. Early diagnosis, treatment and prevention of anaemia are crucial to improving physical and mental health and enhancing health-related quality of life. The global prevalence of anaemia and its associated risk factors is well established; however, there is a paucity of data on those with inherited bleeding disorders (IBD).

Objectives. To describe the prevalence and severity of anaemia in haemophilia and VWD in a quaternary care facility.

Methods. Adult patients with haemophilia or VWD of any subtype were identified through hospital record reviews. After excluding those without anaemia, defined as haemoglobin (HB) <13 g/dL for males and <12 g/dL for females, data from patients with anaemia were anonymised, captured, collated and analysed. Quantitative data were summarised with standard statistical tools, and qualitative data were described. The IBD cohort demographics, anaemia severity and prevalence data were compared with those of the controls, who were age- and sex-matched adult patients admitted to the haematology ward.

Results. Of 1 100 patients with IBD screened, 77 met the eligibility criteria. These comprised 68 (88.3%) haemophilia patients and 9 (11.7%) patients with VWD. The majority of IBD patients were males, comprising 90.9% (*n*=70), while females comprised 9.1% (*n*=7). Of the 886 screened controls, 77 age- and sex-matched patients were selected for comparison. The prevalence of anaemia in the study cohort was 38.96% (*n*=30). Most patients with anaemia (96.7%, *n*=29) were male, with only a single female, while in the control group, 85.7% (*n*=66) were male and 14.3% (*n*=11) were female. The prevalence of severe anaemia, defined as HB <8 g/dL, was 7% in the IBD group, compared with 22.8% in the control group. In the IBD group, 40% (*n*=12) of patients had borderline anaemia, compared with the control population with a predominance of life-threatening anaemia (31.2%, *n*=24). Mild anaemia (HB <11 g/dL) was noted in 37% of the IBD study cohort v. 13% in the control population. Life-threatening anaemia was seen in 13% of the IBD cohort v. 31.2% in the control population. The prevalence of moderate anaemia was 3% in the IBD cohort v. 28.6% in controls. In the IBD cohort, 43% of the anaemic patients had iron deficiency anaemia, and 6.5% of patients in the control group had iron deficiency anaemia.

Conclusion. This study indicates the burden of anaemia in the IBD population. Health professionals must be proactive in screening and treating anaemia in these patients. Further research is required to explore additional contributing factors. Optimisation of therapeutic strategies tailored to the unique needs of these patients is vital.

Keywords: anaemia, haemophilia, inherited bleeding disorders, von Willebrand disease

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The global prevalence of anaemia remains high, with a third of the world population, >2.5 billion people, having this diagnosis.[1] Its presence is rarely isolated, and often indicates an underlying inherited or acquired disorder.[2] Further investigation is usually required. The most common cause of anaemia worldwide is iron deficiency, affecting >1.2 billion individuals globally.[3] Well-recognised populations susceptible to anaemia are infants, children aged <2 years, pregnant and breastfeeding individuals and the elderly.[4] There is a tendency to overlook those with inherited bleeding disorders (IBDs). There is, therefore, a paucity of data on the prevalence of anaemia in this specific group.

IBDs encompass a spectrum of conditions that affect coagulation, clotting factors, platelets, or vessel wall abnormalities. They have varying clinical manifestations that depend largely on the underlying cause.[5] The most common IBDs are VWD and haemophilia. Patients living with haemophilia, particularly those with a severe bleeding phenotype, frequently present with persistent joint and muscle bleeds. This chronic bleeding poses an increased risk of developing anaemia, which may also include iron deficiency. Studies demonstrating this are, however, limited. As in patients with haemophilia, patients living with VWD commonly face chronic bleeding, which is often severely compounded by heavy menstrual bleeding in females, and thus also carry an increased risk of iron deficiency anaemia. Our understanding of anaemia, particularly iron deficiency anaemia, in patients with VWD is better than that in patients with haemophilia.

The sequelae and complications of anaemia in people with IBDs are many, and include musculoskeletal, neurological and other organ dysfunctions. Quality of life is negatively affected by both anaemia and IBD. It is, therefore, crucial to recognise the risk factors of anaemia and to prevent its development through adequate management. The goal is to limit the effect of impaired health-related quality of life in individuals with bleeding disorders.[6]

A structured literature search was conducted using various database search platforms. It included combinations of keywords and

MeSH terms to refine the results. In light of the paucity of available literature on this issue, this article aims to explore the prevalence of anaemia in individuals with haemophilia or VWD at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), South Africa (SA), to enhance the current data and overall awareness.

Objectives

To evaluate the prevalence and severity of anaemia in patients with haemophilia and VWD at a quaternary public healthcare centre/hospital in Johannesburg, SA.

Methods

Study design and population

This is a single-centre retrospective case-control study performed at CMJAH, a quaternary healthcare facility in Johannesburg, SA. Data were collected from January 2016 to December 2019.

Data collection and file reviews were conducted for all adult outpatients followed up at CMJAH between 2016 and 2019. Data were recorded on a data collection sheet prior to analysis.

Study setting

CMJAH is a quaternary hospital in Parktown, Johannesburg. It serves patients from across Gauteng Province and neighbouring provinces, the bulk of whom are from the low- to middle-income class, offering both inpatient and outpatient services ranging from tertiary to highly specialised. The haemophilia care centre cares for 1 100 patients, both paediatric and adult, who are seen and reviewed by the paediatric and adult departments, respectively. It is additionally staffed with a multidisciplinary team including specialised nursing staff skilled in the care of haemophilia and other rare chronic bleeding disorders.

Study population

Of the 1 100 patients attending the haemophilia care centre at Area 295 at CMJAH, 77 were eligible for record assessment using the eligibility criteria.

Inclusion criteria

The study included patients aged ≥18 years with documented IBD confirmation. Specifically, it encompassed individuals with haemophilia showing a factor level <50% and those with VWD exhibiting both antigen and activity levels below the normal range, with a laboratory threshold of 50% set for both. Compliance with treatment was additionally required, relating particularly to haemophilia patients on prophylactic factor regimens. This was assessed using their bleeding charts, which record the total factor given at each follow-up/clinic visit (which can predict how long a prescription should last). Lastly, the presence of comprehensive clinical records was required. Control patients included adult patients who were admitted to the haematology ward and documented to have anaemia, with a formal record of a full blood count (FBC).

Exclusion criteria

Patients without documented/traceable diagnostic records, paediatric patients (<18 years of old) and patients who were non-compliant with treatment were excluded from the study. Patients with established causes of bleeding other than an IBD were also excluded from the review. For control patients, those with no FBC record were not reviewed. Haemophilia patients admitted to the ward were also excluded from the control population.

Statistical analysis

Quantitative data were summarised into tables and figures and presented graphically. Summary statistics were described using means, medians with interquartile ranges (IQRs) and counts with percentages. Statistical analysis was performed using Excel (Microsoft, USA). $P<0.05$ was considered statistically significant.

Ethical considerations

This study was reviewed and approved by the University of the Witwatersrand Human Research Ethics Committee (ref. no. M210818) and the CMJAH CEO and research committee (ref. no. GP_202107_045).

Results

Patient demographics

Of all the reviewed files, 77 adult patients were eligible.

The majority of the study patients were expectedly male, accounting for 90.9% (*n*=70), while female patients comprised 9.1% (*n*=7), one of whom was identified as a haemophilia carrier. The ages ranged from 20 to 72 years old, with a median (IQR) age of 40 (17) years (Table 1).

Disease distribution

Haemophilia patients accounted for the majority of the study population, comprising 88.3% (*n*=68), while patients living with VWD accounted for 11.7% (*n*=9) of all patients. Among the haemophilia patients, haemophilia A was most prevalent, in 56 patients (72.7%). Eleven (14.3%) patients had haemophilia B, and a single patient was identified as a haemophilia carrier (1.3%). More than half (55.9% (*n*=38)) of all the haemophilia patients were noted to have severe disease, that is, a factor level of <1%. Patients with moderate disease accounted for 23.5% (*n*=15), while patients with mild disease comprised 13.2% (*n*=9) of all haemophilia patients. Disease severity/diagnostic factor levels in four haemophilia patients (7.4%) could not be determined. Regarding presence of inhibitors, 11 (16.2%) patients were identified to have inhibitors, all of whom were patients with haemophilia A. Only a single patient with inhibitors had moderate disease, while the remaining patients (90.9%) all had severe disease.

Patients with VWD accounted for 11.7% (*n*=9) of all study patients, the majority of whom were female (*n*=6), with an expected minority of male patients (*n*=3).

The most common type of VWD type noted was type 1, in four patients (44.4%). There were two patients each with type 2 and type 3, accounting for 22.2%. In a single patient, VWD type was undocumented (Table 2).

Prevalence of anaemia

Of the total 77 enrolled patients, 30 (38.98%) were noted to have anaemia as per the World Health Organization (WHO) classification, that is, a haemoglobin <120 g/L (Table 3). The majority of these patients had a grade 0/borderline anaemia (*n*=12), followed by 11 (14.3%) patients with a grade 1/mild anaemia. A single patient had grade 2/moderate anaemia, 2 (6.7%) patients had grade 3/severe anaemia and 4 (5.2%) had grade 4/life-threatening anaemia. A total of 96.7% (*n*=29) of all patients with anaemia were patients with haemophilia, while only one had VWD. The cause of anaemia in these patients was consistently noted to be blood loss.

When comparing the study cohort with the control patients, it was noted that the majority of control patients admitted to the haematology ward with anaemia had life-threatening/grade 4 anaemia (31.2%; *n*=24), followed by grade 2/moderate anaemia (28.6%; *n*=22). Patients with grade 3/mild anaemia accounted for

Table 1. Demographic characteristics of study and control populations

Characteristic	Study population (*n*=77)	Control population (*n*=77)
Age, years		
Range	20 - 72	18 - 87
Mean	41.1	42.4
Median (IQR)	40 (17)	37 (24)
Sex, *n* (%)		
Male	70 (90.9)	67 (87.0)
Female	7 (9.1)	10 (13.0)

IQR = interquartile range.

Table 2. Summary of study population characteristics (*N*=77)

Characteristic	*n* (%)*
All patients	
Haemophilia	68 (88.3)
VWD	9 (11.7)
Total	77
Haemophilia type	
Haemophilia A	56 (72.7)
Haemophilia B	11 (14.3)
Haemophilia carrier	1 (1.3)
Haemophilia severity	
Severe (<1%)	38 (55.9)
Moderate	15 (23.5)
Mild	9 (13.2)
Unknown	4 (7.4)
VWD sex distribution, *n*	
Female	6
Male	3
VWD type	
1	4 (44.4)
2	2 (22.2)
3	2 (22.2)
Undocumented	1 (11.1)

VWD = von Willebrand disease.
*Unless otherwise indicated.

Table 3. WHO grades of anaemia

Severity of anaemia, grade	WHO HB value
0	>110 g/L
I (mild)	95 - 109 g/L
II (moderate)	80 - 94 g/L
III (severe)	65 - 79 g/L
IV (life-threatening)	<65 g/L

WHO = World Health Organization; HB = haemoglobin.

22.1% (*n*=17), and 12.9% (*n*=10) had grade 1/mild anaemia. In contrast to the study patients, a minority (5.2%) had borderline/grade 0 anaemia accounting for 5.2% (*n*=4) (Fig. 1).

Just under half (43.4% (*n*=13)) of the patients in the study group with anaemia were noted to have an iron deficiency. Of additional note, there was a population of patients who were assessed and found to have an iron deficiency, but did not manifest with anaemia. These patients accounted for 5.2% (*n*=4) of the study cohort. These patients therefore had a non-anaemic iron deficiency. Only 6.5% (*n*=5) of the control patients had a documented iron deficiency.

Discussion

This retrospective case-control study provides insight into the prevalence of anaemia in 77 people living with haemophilia or VWD who attend the CMJAH haemophilia comprehensive care centre, compared with a control group admitted to the haematology ward. In addition, our study demonstrates the disease distribution of these coagulation disorders in our centre, a quaternary public healthcare facility. Given the paucity of available data proving the prevalence of anaemia in persons living with haemophilia or VWD, this study aims to narrow that gap.

Consistent with existing literature,[7] our study demonstrated a male predominance among patients with haemophilia, with haemophilia A representing the most prevalent subtype. Severe forms of haemophilia, characterised by factor levels <1%, were observed in a substantial proportion of patients (55.9%), correlating with a higher likelihood of developing inhibitors. This subset of patients is at heightened risk for spontaneous bleeding episodes and subsequent complications, emphasising the critical need for regular monitoring and comprehensive management strategies. Moderate and mild forms of haemophilia accounted for 23.5% (*n*=15) and 13.2% (*n*=9) of the cohort, respectively, highlighting the spectrum of disease severity observed in clinical practice.[8,9] These patients are known to generally present with milder bleeding phenotypes, triggered by major surgery or trauma.

VWD affected a smaller proportion of our study population (11.7%). This bleeding disorder, characterised by deficiency or dysfunction of von Willebrand factor (VWF), exhibited a notable sex disparity, with most affected individuals being female (66.7%), in keeping with the available literature.[10] Although VWD is the most common bleeding disorder,[11] patients who have been diagnosed with VWD often do not seek medical care regularly because their symptoms are usually mild. They typically only present to healthcare facilities after undergoing surgical procedures, post trauma or when experiencing severe and unusual mucocutaneous bleeding.

Among the patients with VWD, type 1, characterised by a quantitative deficiency in VWF, was the most prevalent subtype (44.4%, *n*=4), consistent with what is demonstrated in the literature.[12] Types 2 and 3 VWD, though less common, represented significant subsets of the VWD cohort, each comprising 22.2% (*n*=2) of the patients with documented subtype classification.

Anaemia, defined by the WHO as a haemoglobin level <120 g/dL in females and <130 g/dL in males, was identified in 38.96% of the study cohort. Patients with anaemia were predominantly male, as expected, given that the IBD cohort largely comprised patients with haemophilia, which predominantly affects males. Life-threatening (grade 4) and moderate (grade 2) anaemia categories were more prevalent in the control group than the study cohort, which demonstrated milder grades of anaemia, that is, 40% (*n*=12) grade 0/borderline anaemia followed by 36.6% (*n*=11) with grade 1/mild anaemia. Life-threatening (grade 4) and moderate (grade 2) anaemia were more prevalent in the control group than in the study cohort, which predominantly demonstrated milder anaemia, with 40% (*n*=12) classified as grade 0 (borderline) and 36.6% (*n*=11) as grade 1 (mild). Despite this, a notable burden of anaemia remains among patients with IBD, likely attributable to chronic bleeding and associated comorbidities, including anaemia of inflammation. This distinction may also reflect differences in underlying pathophysiology

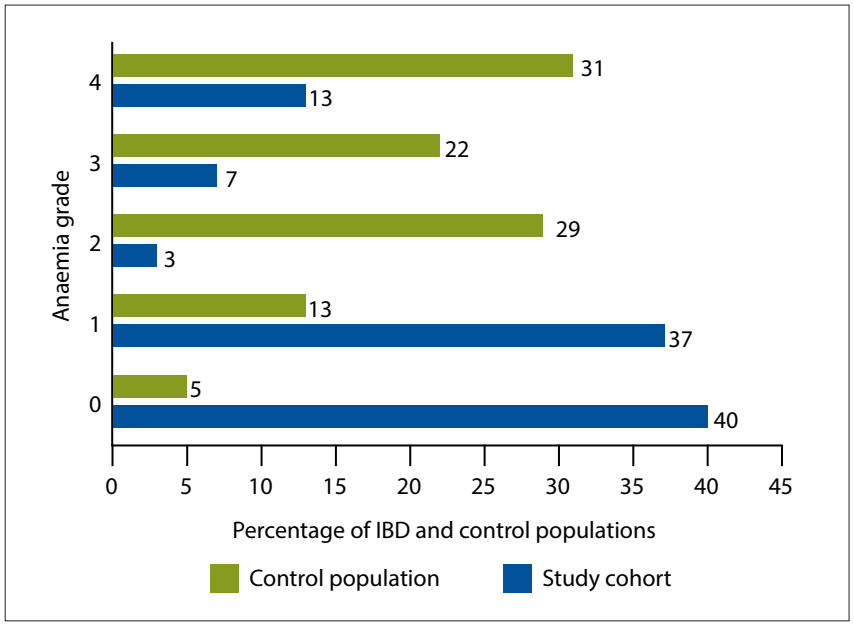

Fig. 1. Severity of anaemia in study cohort v. control population. (IBD = inherited bleeding disorder.)

and management strategies, as the study cohort undergoes regular clinical follow-up and proactive management, allowing earlier detection and intervention and thereby limiting progression to severe anaemia. In contrast, control patients may present later in the disease course, often when symptoms are severe enough to require admission..

The literature highlights a higher prevalence of anaemia, particularly in women and children, highlighting them as a population at risk and impacted to a greater degree than men.[13] Our study emphasises men, primarily those with haemophilia, as an additional population at risk of developing anaemia.

According to the WHO, the accepted cut-off level for serum ferritin below which iron stores are depleted, thus defining an iron deficiency, is <15 ug/L. However, further studies suggest that increasing the cut off to 30 µg/L increases the sensitivity to 92% while maintaining a specificity of 98%,[14,15] and as such, this is the cut-off used in our study. Iron deficiency was identified in a significant proportion of anaemic patients with haemophilia and VWD, compared with the control group (43.4% v. 6.5%), emphasising the high prevalence of anaemia in persons with haemophilia and VWD, as well as highlighting the role of chronic blood loss as a primary contributing factor in anaemia. Interestingly, a subset of patients exhibited iron deficiency without anaemia (5.2%), suggesting a crucial need for ongoing monitoring and detection for anaemia in these vulnerable patients, allowing for early intervention.

Study limitations

Several limitations should be acknowledged, including the retrospective nature of data collection and the potential selection bias inherent in single-centre studies. The limited number of patients in our study cohort is an additional limitation. However, this highlights the scarcity of these disorders. Future research could benefit from prospective cohort designs and inclusion of a broader demographic and clinical variables to elucidate multifactorial contributors to anaemia in patients with IBDs.

An additional limitation to consider includes selection bias in the control group, selected from the years 2018 and 2019, rather than 2016 and 2017, as with the study cohort population. Comparison with available literature, although scarce, helped alleviate this bias.

Conclusion

In conclusion, our findings emphasise the high prevalence of anaemia among patients with haemophilia and VWD, particularly those with severe disease. Early detection and management of anaemia, including iron deficiency, are critical to improving this population's clinical outcomes and quality of life. Further research is warranted to explore additional contributing factors and to optimise therapeutic strategies tailored to the unique needs of patients with IBDs.

Data availability. The data used in this study are available from the authors on request.

Declaration. This research was completed as a requirement for completion of RM's MMed (Haematological Pathology) degree at the University of the Witwatersrand.

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Author contributions. JM conceived the study topic, supervised the conduct of the study and data collection, analysed the data, wrote the article and approved the final version. RM wrote the study protocol, collected data, analysed the data, wrote the article and approved the final version.

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1. Prevalence, years lived with disability, and trends in anaemia burden by severity and cause, 1990 - 2021: Findings from the Global Burden of Disease Study 2021. Lancet Haematol 2023;10(9):e713-734.
2. World Health Organization. The global prevalence of anaemia in 2011. Geneva: WHO, 2011. https://www.who.int/publications/i/item/9789241564960 (accessed 9 August 2024).
3. Camaschella C. Iron deficiency. Blood 2019;133(1):30-39. https://doi.org/10.1182/blood.2022018610
4. Chaparro CM, Suchdev PS. Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. Ann N Y Acad Sci 2019;1450(1):15-31. https://doi.org/10.1111/nyas.14092
5. Alli N, Vaughan J, Louw S, Schapkaitz E, Mahlangu J. Inherited bleeding disorders. S Afr Med J 2018;108(1):9-15. https://doi.org/10.7196/samj.2018.v108i1.13020
6. Rae C, Furlong W, Horsman J, et al. Bleeding disorders, menorrhagia and iron deficiency: Impacts on health-related quality of life. Haemophilia 2013;19(3):385-391. https://doi.org/10.1111/hae.12014
7. Lusher JM. Hemophilia: From plasma to recombinant factors. Hematology.org, 2008. https://www.hematology.org/about/history/50-years/hemophilia (accessed 12 August 2024).
8. Coffin D, Gouider E, Konkie B, et al. The World Federation of Hemophilia World Bleeding Disorders Registry: Insights from the first 10,000 patients. Res Pract Thromb Haemost 2023;7(8):102264. https://doi.org/10.1016/j.rpth.2023.102264
9. Singh A, Rawat S, Kushwaha R, Jain M, Verma SP, Singh US. Clinicopathological parameters of haemophilia patients at a tertiary care centre in Northern India. Cureus 2023;15(7):e41670. https://doi.org/10.7759/cureuus.41670
10. Weyand AC, Flood VH. Von Willebrand disease: Current status of diagnosis and management. Hematol Oncol Clin North Am 2021;35(6):1085-1101. https://doi.org/10.1016/j.hoc.2021.07.004
11. James PD, Connell NT, Ameer B, et al. ASH ISTH NHF WFH 2021 guidelines on the diagnosis of von Willebrand disease. Blood Adv 2021;5(1):280-300. https://doi.org/10.1182/bloodadvances.2020003265
12. Bharati KP, Prashanth UR. Von Willebrand disease: An overview. Indian J Pharm Sci 2011;73(1):7-16. https://doi.org/10.4103/0250-474x.89751
13. Gardner W, Razo C, McHugh T, et al. Prevalence, years lived with disability, and trends in anaemia burden by severity and cause, 1990 - 2021: Findings from the Global Burden of Disease Study 2021. Lancet Haematol 2023;10(9):e713-e734. https://doi.org/10.1016/s2352-3026(23)00160-6
14. Miller JL. Iron deficiency anemia: A common and curable disease. Cold Spring Harbor Perspect Med 2013;3(7): a011866. https://doi.org/10.1101/cshperspect.a011866
15. Dignass A, Farrag K, Stein J. Limitations of serum ferritin in diagnosing iron deficiency in inflammatory conditions. Int J Chronic Dis 2018;2018:9394060. https://doi.org/10.1155/2018/9394060

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