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Burden of Haemophilia A in South Korea: A Serial Cross-Sectional Study From 2008 to 2021

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Abstract

Background: Overall use of factor VIII (FVIII) and prophylactic use have increased in South Korea over the past decade. However, there are no nationwide outcome data demonstrating its impact. This study aimed to identify patients with haemophilia A (PwHA) and observe trends in joint-related outcomes and life-threatening haemorrhages using national claims data.

Methods: This serial cross-sectional study analysed claims data from the Health Insurance and Review Assessment in South Korea. PwHA treated with FVIII at least twice between 2007 and 2022 were identified. We observed joint procedures, life-threatening haemorrhages and comorbidities between 2008 and 2021.

Results: The number of identified PwHAs was 1193 in 2008 and 1517 in 2021. The proportion of older adult patients has increased over the past 14 years. The joint procedure rates per 1000 patients were 61.2 (95% CI 48.0–76.9) in 2008 and 17.1 (11.2–25.1) in 2021. The rate was highest in patients with a severe phenotype. Annually, less than 2% of patients experienced life-threatening haemorrhages, with approximately 90% of the cases attributed to central nervous system and gastrointestinal bleeding. The prevalence of hypertension and diabetes increased over the years (6% in 2008 and 15% in 2021, and 6% in 2008 and 9% in 2021, respectively).

Conclusion: This study revealed previously unreported long-term trends in haemophilia-related outcomes and comorbidities in Korean PwHA. Although the number of older adult patients has increased, joint-related complications have decreased over time. The trends, observed over 14 years, provide valuable insights for enhancing the treatment of PwHA.

1 | Introduction

Haemophilia A (HA) is a lifelong bleeding disorder characterized by improper blood clotting resulting from an inherited deficiency of factor VIII (FVIII) [1, 2]. The severity of HA is determined by the extent of FVIII deficiency, and classified as severe (FVIII activity < 1% of normal or clotting factor level < 1 IU/dL), moderate (FVIII activity 1%–5% or 1–5 IU/dL), or mild (FVIII activity 5%≤ 40% or 5–40 IU/dL) [2, 3]. Individuals with severe HA may encounter spontaneous bleeding, particularly in the joints

Abbreviations: CNS, central nervous system; FVIII, factor VIII; HA, haemophilia A; HIRA, health insurance review and assessment; IU, International Units; PwHA, patients with haemophilia A; SD, standard deviation.

and other areas such as soft tissues, the gastrointestinal tract and central nervous system (CNS) [2, 3]. The care of HA aims to prevent fatal bleeding and reduce the effects of bleeding on the joints and muscles [1, 2, 4]. Over the past few decades, life expectancy and quality of life for individuals with haemophilia have notably improved [1, 5, 6], owing to advances in treatment and comprehensive care [1, 7]. Specifically, primary prophylaxis helps maintain joint function in children with haemophilia compared to using on-demand treatment [8]. However, it has led to substantial increases in the cost of managing haemophilia [9, 10].

Data on the nationwide burden of HA in South Korea are limited despite its importance in optimizing treatment effectiveness within the healthcare system. Moreover, most of the current understanding of complications and comorbidities comes from Western countries [11, 12]. Therefore, a comprehensive analysis of the disease burden, particularly regarding joint and bleeding complications, among patients with HA (PwHA) who are receiving FVIII treatment is warranted. This study aimed to observe trends in joint procedures, haemophilic arthropathy, life-threatening haemorrhage, comorbidities and the use of FVIII in PwHA using national claims data covering the entire Korean population between 2008 and 2021.

2 | Methods

2.1 | Data Sources

Under the universal coverage healthcare system in South Korea, the Health Insurance Review and Assessment (HIRA) collects comprehensive and rich information pertaining to healthcare services such as treatments, pharmaceuticals, procedures and diagnoses for almost 50 million beneficiaries during the process of reimbursing healthcare providers in South Korea. It contains the claims data of the entire nation. We used HIRA claims data to identify PwHA and examine the trajectory of outcomes [13].

2.2 | Study Design

This was a serial cross-sectional analysis of claims data from HIRA. Typically, cross-sectional designs are used for population-based surveys and to assess the prevalence of diseases in clinic-based samples [14]. We identified PwHA from the data between 1, January 2007, and 31, July 2022, which comprises the index period. The index date was defined as the first date of a claim with a diagnosis code for HA during the index period. Patients were observed from the index date to the latest year (between the year in which the diagnosis was confirmed and 2021). All patients included in the target population of interest were analysed by year (2008–2021). The Ethics Committee of Kyung Hee University Hospital at Gangdong (KHNMC 2023-02-011) approved the analysis of claims data represented in this study.

2.3 | Study Population

The study population comprised PwHA who were treated with FVIII in South Korea. First, we identified patients having a diagnosis of HA (disease code of hereditary factor VIII deficiency: D66) or a specific reimbursement code for haemophilia

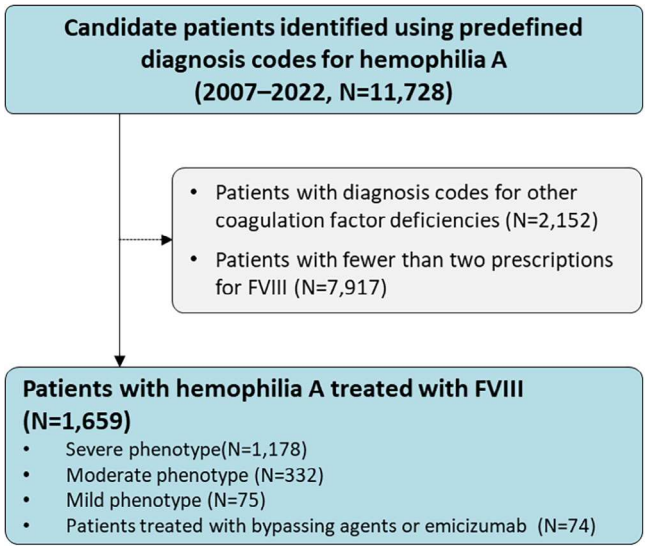


FIGURE 1 | Conceptual flow diagram of the patient selection process.

(V009). Among the identified patients, those conforming to the following criteria were excluded: (1) those prescribed with FVIII concentrates less than twice during the study period and (2) patients having a diagnosis of other clotting factor deficiency (D67-Hereditary factor IX deficiency; D680-Von Willebrand's disease; D681-Hereditary factor XI deficiency; D682-Hereditary deficiency of other clotting factors). In addition to a previous study [15], which researched Korean PwHA with the same data, we considered the use of FVIII throughout the study period as a criterion for more precise patient selection [16] as the claims data is inherently inconclusive regarding diagnostic information. The conceptual patient selection process is presented in Figure 1.

After identification, the patients were classified into four groups according to the frequency of FVIII prescriptions and the use of bypassing agents or emicizumab. First, patients who received at least three doses of bypassing agents or emicizumab were identified. In South Korea, until April 2023, emicizumab was reimbursed only for patients with inhibitors. Therefore, all patients who received emicizumab during our study period are likely to have had an inhibitor. The remaining patients were categorized into three groups according to the severity of their phenotype: severe (patients with an average interval of $\leq$ 45 days between FVIII prescriptions), moderate (patients who had neither a severe nor a mild phenotype), and mild (patients with an average interval of $\geq$ 12 months between FVIII prescriptions). To the best of our knowledge, there is no evidence for classifying disease severity using claims data. Therefore, three healthcare professionals (haemophilia specialists) developed an algorithm-based approach using operational definitions to identify PwHA with severe phenotypes in our claims data. This approach leverages the varying FVIII prescription requirements of individuals with different HA severities.

2.4 | Outcomes

Joint procedures and long-term treatment–requiring haemophilic arthropathy were determined as joint-related complications.

The codes for the joint procedures are presented in eTable 1. Replacement arthroplasty, revision of replacement arthroplasty, resection arthroplasty and arthrodesis were classified into major joint procedures. The rest of the procedures were classified into non-major joint procedures. The joint procedure rate was calculated by dividing the number of joint procedures each year by the number of patients in the given year, and it was presented annually as units per 1000 patients. The number of patients who underwent major/non-major joint procedures according to age group was also estimated. Patients with long-term treatment–requiring haemophilic arthropathy were defined as those having claims with a diagnosis of arthritis or arthropathy (eTable 2) and using analgesics for 60 consecutive days or more within the same year. This approach was adopted to distinguish patients with haemophilic arthropathy from those experiencing bleeding episodes because analgesics are frequently prescribed for acute pain control associated with bleeding, often for shorter durations. The number of long-term treatment–requiring haemophilic arthropathy represents the total number of patients with haemophilic arthropathy in each year.

To determine the burden of bleeding, the number of patients who experienced life-threatening haemorrhages was captured. These haemorrhagic events were primarily defined based on the presence of a procedure code for transfusion (whole blood or red blood cells) in the claims related to bleeding (eTable 3). Patients admitted with a primary or secondary diagnosis of CNS haemorrhage were also categorized, irrespective of whether a transfusion was performed.

Given the nature of claims data, it is inherently difficult to determine whether a clinical event truly occurred based on diagnostic codes alone. Therefore, operational definitions were used to approximate clinically meaningful outcomes as accurately as possible, given constraints of the data. In this study, long-term treatment–requiring haemophilic arthropathy and life-threatening haemorrhages were defined operationally using diagnosis, prescription and procedure codes. These definitions were developed in consultation with three clinical experts who manage PwHA at hospitals in South Korea to ensure clinical relevance. The experts confirmed that the repeated use of pain medications is consistent with common clinical practice for identifying significant haemophilic arthropathy.

Comorbidities were defined using the diagnostic codes (eTable 4) for hypertension, diabetes, heart disease, cerebrovascular disease, malignancy and liver disease. The proportion of patients with each disease was estimated annually.

2.5 | Data Analysis

Continuous variables were summarized using the mean and standard deviation (SD). Categorical variables were summarized using frequencies and percentages. As the study objectives were descriptive in nature, missing data were not imputed. All data analyses were performed using SAS EG version 7.1 or higher. All analyses were performed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines [17].

To evaluate temporal trends in the age distribution of PwHA, we calculated the cumulative proportion of individuals in each age group for every year. The results were presented as a cumulative age distribution plot to clearly illustrate shifts in the overall demographic structure of the study population over time. The number and age distribution of the general population in South Korea, as shown in Figure 2, were obtained from the Korean Statistical Information Service [18] and used for comparison with the age distribution of PwHA.

To estimate the prevalence of comorbidities in the general population, the number of patients with claims for those diagnoses was obtained from the Health Insurance Review and Assessment Service big data open portal [19]. To ensure consistency with national reporting standards, diagnosis codes used in this study were aligned with those defined by HIRA (eTable 4). For liver disease, as the HIRA does not provide the aggregated number of patients with liver disease, we estimated the overall prevalence by summing the number of patients across relevant diagnosis codes (eTable 4).

3 | Results

Among the 11,728 patients with claims data and a diagnosis of HA, 1659 patients without a diagnosis of other clotting factor deficiencies were prescribed FVIII concentrates at least twice (Figure 1). In this subgroup, the number of patients with severe, moderate, and mild phenotypes was 1178 (71.0%), 332 (20.0%) and 75 (4.5%), respectively. Seventy-four patients (4.5%) were treated with bypassing agents or emicizumab. Of the total patients, 1633 (98.43%) were men.

3.1 | Prevalence of HA

The initial patient count was 1193 in 2008, which increased to 1517 in 2021. This figure has consistently increased annually (Figure 2). The prevalence of HA varied from 2.41 to 2.94 per 100,000 people (eTable 5). For the subgroups, the number of patients with severe phenotypes remained relatively stable, whereas those with moderate or mild phenotypes; moreover, those using bypassing agents/emicizumab exhibited a more notable increase over time (eTable 5). Notably, the proportion of patients aged 41 or older significantly increased (> 60 years, 2% in 2008 to 7% in 2021; 41–60 years, 15% to 28% over the same period), whereas patients in the ≤ 10 age group decreased from 17% to 11%.

3.2 | Joint-Related Outcomes

For 14 years (2008-2021), the overall joint procedure rate was 33.1 (95% CI: 30.6–35.7) per 1000 patient-years. This total rate was composed of 14.9 (13.2–16.7) major procedures and 18.2 (16.4-20.2) non-major procedures per 1000 patient-years (eTable 6). The 2008–2021 rate for patients with a severe phenotype was 38.8 (35.6–42.2) per 1000 patients, with 18.0 (15.8–20.3) major procedures and 20.8 (18.5–23.3) non-major procedures. During the same period, the rates for patients with moderate phenotype were 17.1 (13.2–21.7) per 1000 patients, with 5.8 (3.6–8.7) major

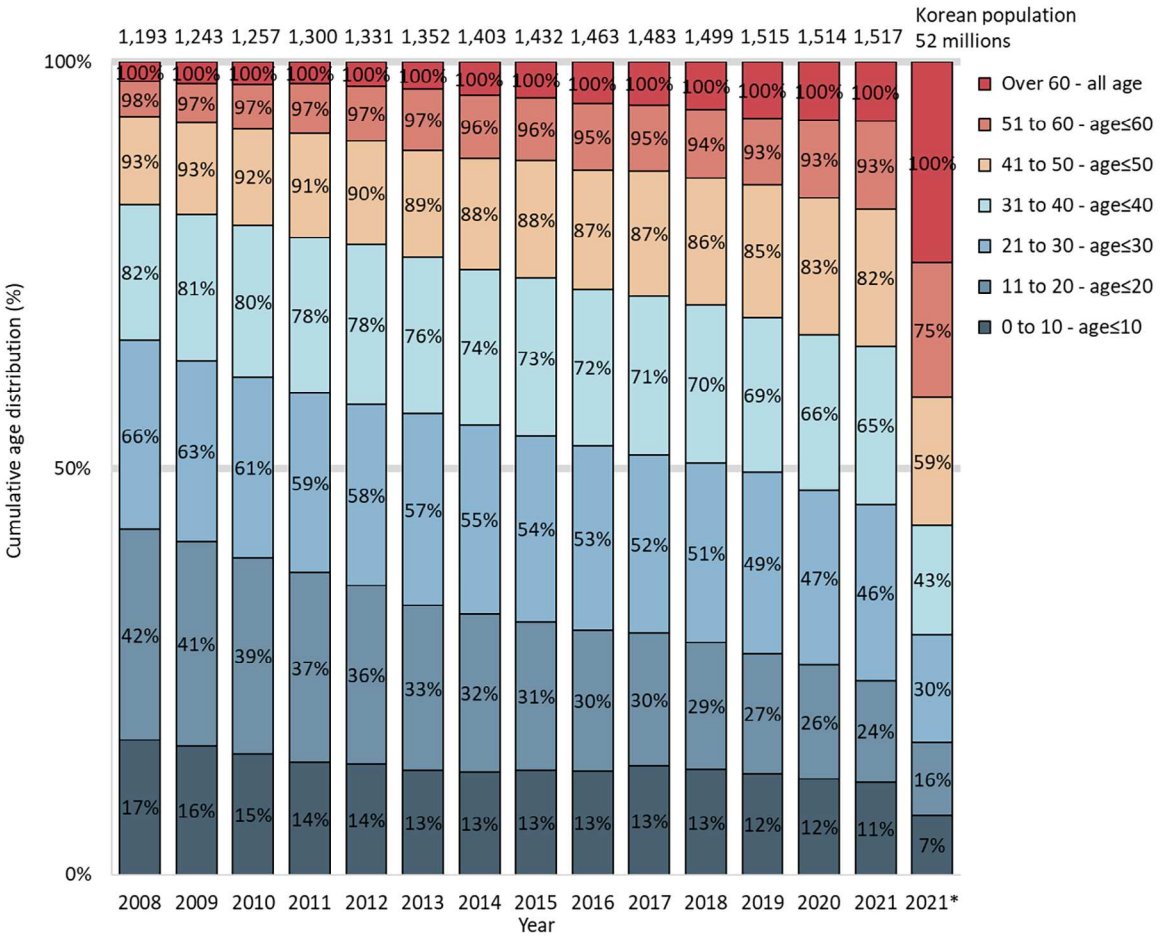


FIGURE 2 | Annual age distribution of patients with haemophilia A (2008–2021), The numbers at the top of each bar represent the total number of patients with haemophilia A for that year. *The rightmost bar represents the age distribution of the total Korean population in 2021, based on data from the Korean Statistical Information Service (https://kosis.kr, accessed on 22, September 2024).

procedures, while patients with mild phenotype had the lowest rates overall.

In total patients, the yearly procedure rates per 1000 patients peaked around 2008 (Figure 3). Patients with a severe phenotype consistently had higher overall procedure rates compared to the total population and generally mirrored the declined overall trend (eFigure 1). Patients using bypassing agents/emicizumab showed similar procedure rates to patients with severe phenotypes, but with extreme fluctuations between years (eFigure 1).

eFigure 2 presents the proportion of patients with joint procedures across different age groups by year. The median age group was the 30s in 2008 but was likely the 40s since 2016. The 0–20 age group had the lowest percentage of joint procedures throughout the period. No patients under 10 years old have had joint procedures since 2014. Within each age group, more patients in their 40s and 50s underwent joint procedures than those in their 20s and 30s (eTable 7).

In 2008, 13 patients (1.1%) were diagnosed with long-term treatment–requiring haemophilic arthropathy, whereas in 2021, this number increased to 165 patients (10.9%). That in older patients was relatively higher than those in younger patients (Table 1). In 2021, patients in the 51–60 years age group (21.5%) constituted the highest proportion of patients diagnosed with haemophilic arthropathy, followed by the > 60 years and 41–50 years age groups (18.9% and 16.7%, respectively). No cases were reported in the group of age under 10.

3.3 | Life-Threatening Haemorrhage

The proportion of PwHA who experienced life-threatening haemorrhage varied from 0.9% in 2020 to 2.3% in 2014 (Table 2). In 2021, CNS and gastrointestinal haemorrhages each accounted for 0.7%. CNS haemorrhage rates remained relatively stable, ranging from 0.6% to 0.9%, whereas gastrointestinal haemorrhage rates revealed more variability, ranging from 0.4% to 1.3%.

3.4 | Use of FVIII Concentrate

Most patients received FVIII treatment in an outpatient setting throughout the study period (96.6%–100% across whole years). eFigure 3 presents the proportion of patients using FVIII concentrates according to the type of concentrate administered. Octacog alfa, a recombinant FVIII with a standard half-life, was used most frequently from 2011 onwards. In contrast, the use of plasma-derived FVIII steadily declined throughout the study period and

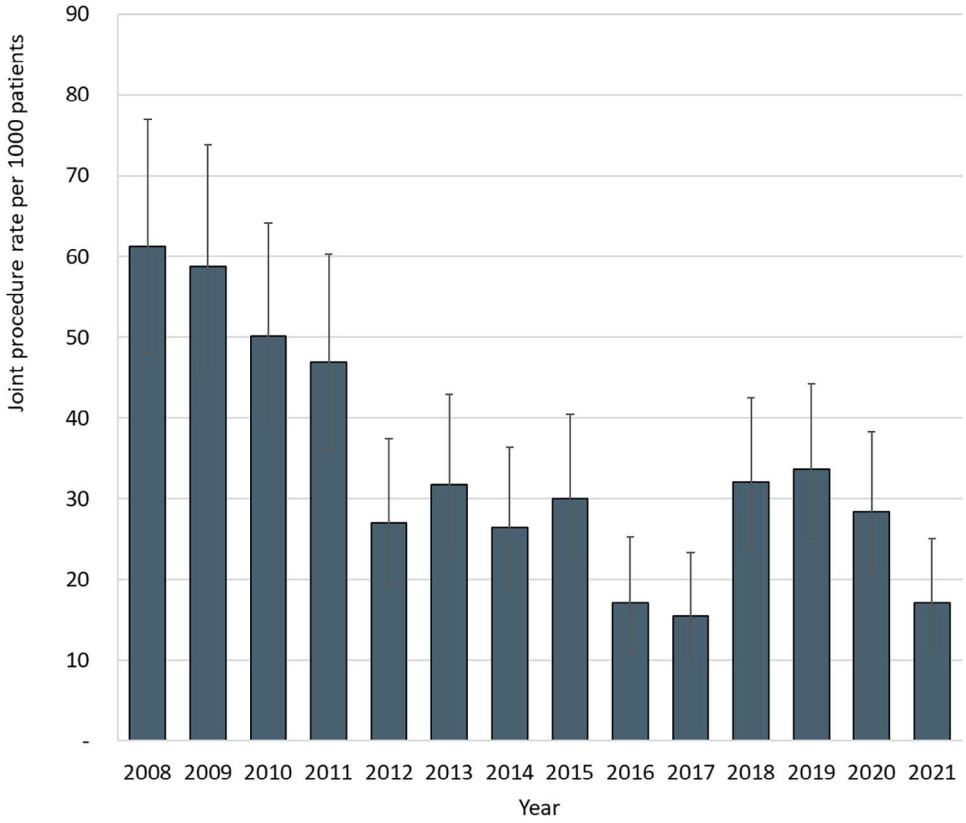


FIGURE 3 | Annual joint procedure rates per 1000 patients with haemophilia A (2008–2021). Error bars represent 95% confidence intervals.

became less prevalent over time (from 57.95% in 2008 to 19.71% in 2021). Since 2018, the number of patients using recombinant FVIIIs with an extended half-life has rapidly increased with a decrease in the use of recombinant FVIIIs with a standard half-life.

3.5 | Comorbidity

With the increasing trend in older patients, the proportion of patients with comorbidities steadily increased throughout the study period (Figure 4). Specifically, the proportion of patients with liver disease remained relatively high; however, despite fluctuations, an overall upward trend was observed, peaking at 24% in 2021. Hypertension has exhibited a steady and significant increase over time, from 6% in 2008 to 15% in 2021. Diabetes has been variable, with an overall increasing trend despite few fluctuations, rising from 6% in 2008 to 9% in 2021. The proportion of patients with cerebrovascular disease, heart disease, or any type of cancer remained low and stable, ranging from 2% to 3%.

4 | Discussion

This study offers an overview of PwHAs in South Korea, encompassing data on the annual number of patients, prevalence of joint procedures across various age groups, incidence of haemorrhagic episodes, and comorbidities. The findings indicate a steady increase in the total number of PwHAs, particularly among older patients. Moreover, the study underscores a shift in treatment patterns, marked by a reduction in the use of plasma-derived FVIIIs and a rise in the application of recombinant FVIII.

Although this study did not analyse survival, a gradual shift in the age distribution—specifically, an increase in the median age over time—may indirectly reflect improved survival in the HA population. Notably, the number of patients aged > 40 years has increased in recent years, which is comparable with previously reported data in South Korea [20, 21]. The median age of haemophilia patients was 18.9 years in 1999 [22] and 26.5 years in 2022 [23]. In recent years, there has been a notable improvement in life expectancy for people with haemophilia, primarily owing to advancements in treatment and comprehensive care [5, 7]. Although we did not investigate the survival rates directly, our results can be interpreted as an improved survival, which is similar to those reported in other countries [5, 7].

In addition, we observed comorbidities and noted that the incidence of hypertension and diabetes increased over the past decades. Although age-stratified analyses were not performed, this trend may be partly explained by the ageing haemophilia population. As advances in treatment have improved life expectancy, more patients are surviving into older age, where comorbidities such as hypertension, liver disease and chronic kidney disease become increasingly prevalent [24].

Interestingly, the prevalence of liver disease, hypertension, cerebrovascular disease and diabetes in PwHA was higher than that in the general Korean population (as shown in eTable 4), even though the median age of PwHA was lower (as shown in Figure 2). This finding is consistent with the fact that PwHA

TABLE 1 | Number of patients diagnosed with long-term treatment–requiring haemophilic arthropathy.

Year	Total	Age group, *N* (%)						
		0–10	11–20	21–30	31–40	41–50	51–60	≥ 61
2008	13 (1.1)	—	—	4 (1.4)	1 (0.5)	5 (3.9)	2 (3.8)	1 (3.4)
2009	19 (1.5)	—	1 (0.3)	4 (1.4)	2 (0.9)	6 (4.3)	2 (3.4)	4 (11.8)
2010	21 (1.7)	—	—	3 (1.1)	5 (2.1)	4 (2.7)	3 (4.4)	6 (17.1)
2011	31 (2.4)	—	1 (0.3)	4 (1.4)	4 (1.6)	10 (6.0)	6 (7.7)	6 (16.7)
2012	47 (3.5)	—	2 (0.7)	7 (2.4)	12 (4.6)	11 (6.5)	9 (10.0)	6 (15.0)
2013	55 (4.1)	—	3 (1.1)	10 (3.1)	8 (3.1)	15 (8.4)	12 (11.7)	7 (15.6)
2014	79 (5.6)	1 (0.6)	—	12 (3.7)	18 (6.7)	26 (13.5)	13 (12.0)	9 (15.5)
2015	74 (5.2)	—	1 (0.4)	15 (4.6)	20 (7.2)	19 (9.1)	12 (10.8)	7 (11.1)
2016	81 (5.5)	—	—	14 (4.2)	19 (6.8)	24 (11.2)	12 (10.1)	12 (15.8)
2017	80 (5.4)	—	2 (0.8)	15 (4.6)	12 (4.1)	23 (10.0)	15 (12.5)	13 (16.5)
2018	114 (7.6)	—	1 (0.4)	22 (6.6)	31 (10.7)	31 (13.2)	13 (10.3)	16 (18.2)
2019	126 (8.3)	—	3 (1.3)	18 (5.3)	26 (9.0)	39 (15.7)	20 (16.1)	20 (19.0)
2020	147 (9.7)	—	2 (0.9)	17 (5.2)	37 (12.8)	48 (18.8)	25 (17.1)	18 (16.7)
2021	165 (10.9)	—	1 (0.5)	24 (7.3)	41 (13.9)	43 (16.7)	35 (21.5)	21 (18.9)

Note: % = the number of patients with long-term treatment–requiring haemophilic arthropathy/the number of patients with haemophilia A in each year across age groups.

TABLE 2 | Number of patients with life-threatening haemorrhage by year.

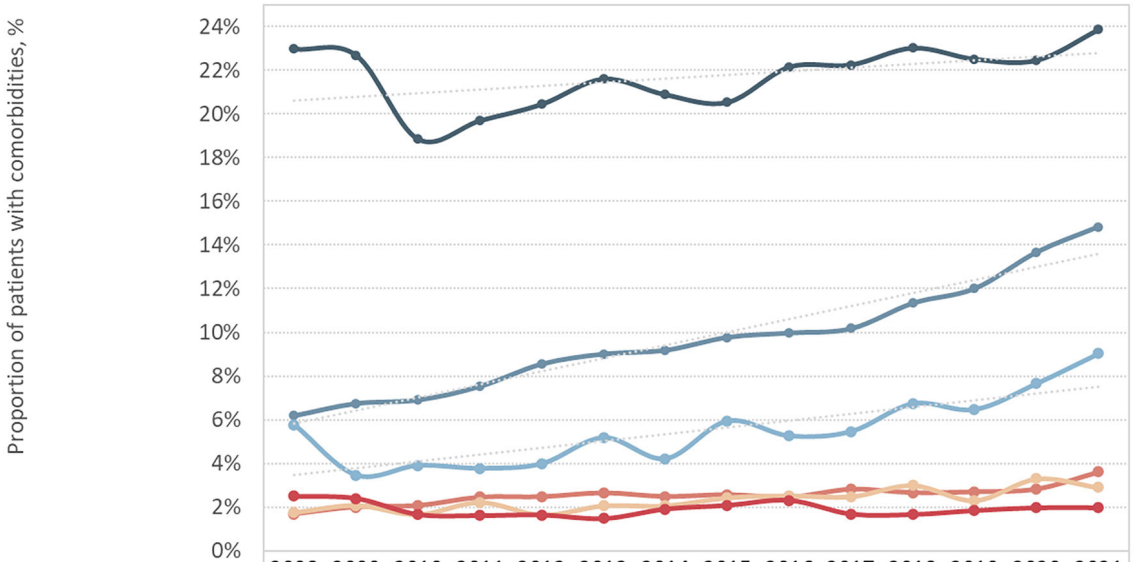
Year	Any, *N* (%)	Central nervous system, *N* (%)	Gastro-intestinal, *N* (%)
2008	21 (1.8)	11 (0.9)	10 (0.8)
2009	20 (1.6)	7 (0.6)	12 (1.0)
2010	21 (1.7)	7 (0.6)	12 (1.0)
2011	16 (1.2)	10 (0.8)	5 (0.4)
2012	13 (1.0)	4 (0.3)	6 (0.5)
2013	22 (1.6)	8 (0.6)	11 (0.8)
2014	32 (2.3)	10 (0.7)	18 (1.3)
2015	21 (1.5)	11 (0.8)	9 (0.6)
2016	28 (1.9)	13 (0.9)	12 (0.8)
2017	27 (1.8)	12 (0.8)	13 (0.9)
2018	19 (1.3)	9 (0.6)	7 (0.5)
2019	15 (1.0)	2 (0.1)	10 (0.7)
2020	14 (0.9)	6 (0.4)	7 (0.5)
2021	21 (1.4)	10 (0.7)	10 (0.7)

Note: % = the number of patients with severe haemorrhagic episodes/the number of patients with haemophilia A in each year.

are prone to traditional cardiovascular disease, hypertension and diabetes [2, 25, 26]. In contrast, a study from the United States has reported lower rates of hypertension, stroke and cardiovascular disease among PwHA compared to the general population, although the prevalence of diabetes was higher [11]. Moreover, one study found that the 5-year incidence of cardiovascular disease in PwHA was lower than the predicted risk based on models for the general population [27]. Although this study used nationally representative data, further investigations, particularly those incorporating age-stratified and longitudinal analyses, are warranted to better understand the evolving comorbidity burden in this population.

Our results consistently revealed a decreasing trend for joint procedures throughout the study duration, indicating that the patients were well-managed. A study [28] analysing the US haemophilia registry assessed trends in prophylactic use and their impact on arthropathy among individuals with severe HA. Joint bleeding decreased over time, whereas prophylactic use increased from 31% to 59%. Another study [29] investigating the long-term effects of primary prophylaxis with FVIII concentrates on the joint health of patients with severe HA demonstrated that the key factor in the long-term preservation of joint health was the early initiation of primary prophylaxis, particularly at a younger age. In this study, the efficacy of FVIII as a prophylactic could not be conclusively determined owing to the limited clinical information available from claims data. As of 2022, 68.7% of PwHA in South Korea [23] were receiving prophylaxis, and the average IU of FVIII concentrate used per patient had doubled over the decades (84,100 in 2008; 163,505 in 2021) [20, 30]. The use of prophylaxis has been observed to increase in South Korea following its inclusion in clinical guidelines [15, 31]. Therefore, the decrease in joint-related procedure outcomes in this study can be interpreted as a result of prophylaxis.

Repeated haemarthrosis can lead to a severe complication known as haemophilic arthropathy [32]. During the study period, haemophilic arthropathy increased, whereas the incidence of



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Liver disease	23%	23%	19%	20%	20%	22%	21%	21%	22%	22%	23%	23%	22%	24%
Hypertension	6%	7%	7%	8%	9%	9%	9%	10%	10%	10%	11%	12%	14%	15%
Diabetes	6%	3%	4%	4%	4%	5%	4%	6%	5%	5%	7%	6%	8%	9%
Cerebrovascular disease	2%	2%	2%	2%	2%	3%	2%	3%	2%	3%	3%	3%	3%	4%
Heart disease	2%	2%	2%	2%	2%	2%	2%	2%	3%	2%	3%	2%	3%	3%
Any cancer	3%	2%	2%	2%	2%	1%	2%	2%	2%	2%	2%	2%	2%	2%

FIGURE 4 | Annual trends in the proportion of patients with comorbidities among individuals with haemophilia A (2008–2021).

joint procedures decreased. Considering the number of procedures performed, the results should be interpreted with caution. In 2008, 57 patients underwent joint procedures, but only 13 were reported to have used analgesics for more than 60 days with the codes of diagnosis. In 2021, the procedures were administered to 24 patients, and 165 were treated for haemophilic arthropathy. Patients with long-term treatment–requiring haemophilic arthropathy were notably lower in 2008. This disparity may reflect changes in physicians' approaches to managing haemophilic arthropathy. The rise in diagnosed cases of haemophilic arthropathy in this study could be attributed to enhanced physician awareness, patient age, and an increase in claims related to arthritis, arthrosis, and other joint disorders, rather than a true increase in the disease prevalence.

This study has several limitations, primarily due to the nature of claims data. The HIRA database is designed for administrative and reimbursement purposes, which restricts its ability to capture detailed clinical information. To improve specificity, we identified PwHA based on the administration of FVIII concentrates rather than diagnostic codes alone, although it was not possible to distinguish between prophylactic and on-demand FVIII use, nor could disease severity be directly assessed. Instead, the severity phenotype was defined operationally in consultation with three clinical experts who manage PwHA at hospitals in South Korea. When validating this classification, the distribution of severity in our dataset was consistent with the Korean Hemophilia Annual Report [21] (severe: 74%, moderate: 21%, mild: 5%; excluding patients treated with bypassing agents or emicizumab: severe 72%, moderate 16%, mild 11%). Clinically meaningful outcomes such as haemophilic arthropathy and life-threatening haemorrhages were also identified using operational definitions based on diagnosis, prescriptions and procedure codes. While this approach may lead to misclassification or underestimation, particularly among patients with mild symptoms, three clinical experts reviewed and validated the definitions and outcome patterns, confirming their consistency with real-world clinical practice.

The operational definition of haemophilic arthropathy may not fully capture all clinically relevant cases, particularly in younger patients with significant joint damage who may not require regular pain medications. Therefore, in this study, we specifically defined arthropathy as haemophilic arthropathy requiring long-term treatment to reflect more clinically apparent cases. Nevertheless, the absence of clinical details such as laboratory results and imaging findings did not limit our ability to assess long-term trends in FVIII utilization and related treatment outcomes at the population level, which was the primary objective of this study.

In this study, we utilized nationwide claims data representative of the Korean population to analyse trends in FVIII treatment outcomes among PwHA. Since Korea's national health insurance system covers the entire population, the HIRA database offers comprehensive information on healthcare utilization across the country. Consequently, our findings reflect the real-world experiences of all PwHA treated with FVIII in South Korea. This population-based approach enhances the generalizability of our results and provides meaningful insights into nationwide treatment patterns, outcomes and the evolving disease burden over time.

5 | Conclusion

This study provides valuable insights into trends in Korean PwHA over the past 14 years. Over the past decade, joint-related complications of PwHA have been managed with improved awareness. However, the increasing proportion of older PwHA suggests a need for attention to geriatric diseases as life expectancy continues to increase.

Author Contributions

Y.-S.P. and A.J. conceptualized the study. S.-H.K., J.H.N., A.J., and Y.-S.P. designed the study. A.-R.J., S.M., and J.H.N. curated and analysed the data. All authors participated in the interpretation of the results. S.-H.K., S.M., and J.N. drafted the manuscript. All the authors participated in the review and editing of the manuscript. All the authors have read and approved the final version of the manuscript.

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Ethics Statement

The Ethics Committee of Kyung Hee University Hospital at Gangdong (KHNMC 2023-02-011) approved the analysis of claims data represented in this study.

Consent

Informed consent was not required because the study used anonymised and de-identified claims data.

Conflicts of Interest

Young-Shil Park reported receiving research support from participating as the principal investigator for BioMarin Pharmaceutical Inc., CSL Behring, Novo Nordisk, Sanofi, Takeda, Pfizer, and Chugai. Aeran Jung is a full-time employee of Takeda Korea Co., Ltd. No other disclosures are reported.

Data Availability Statement

This study used nationwide claims data from the Health Insurance Review and Assessment Service (HIRA research data M20230302002). The data may be shared by HIRA with permission.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.