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RETROSPECTIVE ANALYSIS OF FACTOR VIII UTILIZATION PATTERNS AND HOME THERAPY ADOPTION IN HEMOPHILIA A PATIENTS WITHIN THE JORDANIAN ROYAL MEDICAL SERVICES: A DESCRIPTIVE EPIDEMIOLOGICAL STUDY ACROSS THREE HOSPITALS

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ABSTRACT

Introduction: Hemophilia A is an X-linked recessive disorder of Factor VIII (FVIII) which is the result of either a lack of or non-functional FVIII. It is still among the most intensive hematological conditions that are resource-consuming to treat mainly due to the high expenses as well as unpredictable demand of FVII replacement product. In Jordan, a specialized care is provided to patients enrolled in the network of the Jordanian Royal Medical Services (JRMS) under a tiered system of military hospitals and centers. In spite of the clinical implications of Hemophilia A in this population, there has never been a published drug utilization review (DUR), which has done a systematic portrayal of FVIII dispensing pattern, home therapy adoption, and inhibitor-related consumption disparities in the JRMS network. It is critical that these patterns be understood in order to have rational drug policy, budget forecasting and quality improvement initiatives in the case of the military health sector.

Methodology: This study is going to employ a retrospective, descriptive epidemiological research design using pharmacy dispensing records retrieved through the JRMS hospital information system. The data will include all the FVII dispensing transactions of Hemophilia A patients in the three participating facilities between January 2023 and February 2024. The dispensing records will be analyzed on the transaction level, and on the patient level, and the individual patient records will be aggregated to calculate the cumulative IU consumption by the patient per study period. The patients will be categorized by the presence or absence of FVIII inhibitors, mode of administration (home therapy or hospital-administered). Descriptive statistics will involve the characterization of various aspects of continuous variables, including age and IU consumption, whereas, frequency distributions will be utilized to describe the categorical variables, including, center of care and home therapy status. Inter-center analysis of the mean consumption of FVIII will be performed to determine possible variations in FVIII prescribing, patient severity, and models of service delivery.

Discussion: A total of 72 Hemophilia A patients were included, accounting for 155 dispensing transactions and a cumulative 5,380,250 IU of FVIII over the 14-month study period. The highest total and per-patient FVIII utilization was observed at Queen Rania Hospital (QRH), which contributed 69.8% of total IU dispensed, with a mean of 85,324 IU per patient, followed by Prince Rashed Bin Al-Hasan Military Hospital (PRBH) (63,313 IU) and the Military Cancer Centre (MCC) (55,975 IU). Inhibitor-positive patients represented 4.2% (n=3) of the cohort and demonstrated lower mean FVIII consumption (58,000 IU) compared to inhibitor-negative patients (75,453 IU), likely due to small sample size and potential use of bypassing agents not captured in the dataset. Home therapy adoption was nearly universal (98.6% of patients), with 84.6% of all dispensing transactions conducted for home use. QRH demonstrated the highest reliance on home therapy, accounting for 98.8% of its total FVIII utilization.

Keywords: *Hemophilia A; Factor VIII; Drug Utilization Review; Home Therapy; Inhibitors; Jordan; JRMS; Royal Medical Services*

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1. INTRODUCTION:

Hemophilia A (HA) is the most common severe genetic bleeding disease in the world with an incidence rate of about one per 5000 male births and characterized by a quantitative or qualitative deficiency of coagulation Factor VIII (FVIII) (1, 2). It is categorized as mild (FVIII activity 5-40%), moderate (1-5%) or severe (less than 1%) with the severe fraction bearing most of the treatment burden (1). HA is clinically characterized by spontaneous or injury induced hemorrhage of the joints, muscles and the vital organs. Unattended repeated hemarthroses causes progressive hemophilic arthropathy; a complication of musculoskeletal disability that is debilitating and mostly irreversible (3).

Replacement of the missing FVIII with either plasma-derived (pdFVIII) or recombinant (rFVIII) factor concentrates is the standard form of care to patients with HA. The treatment options include on-demand (episodic) infusion slightly after a bleed or on a long-lasting prophylaxis, targeting to keep FVIII trough levels above 1-3% in order to avoid spontaneous bleeding (4). Prophylaxis, the new gold standard, generally needs frequent injections, two or three times a week and demands significantly higher amounts of FVIII, as compared to on-demand regimens, which imposes significant economic burden on healthcare systems, especially in the lower-middle-income world (5, 6).

One of the most significant complications of the FVIII replacement therapy is the acquisition of neutralizing antibodies (inhibitors) to exogenous FVIII, which is observed in about 20-30% of patients with severe HA (7). Development of inhibitors makes the standard use of FVIII replacement ineffective and requires higher cost bypassing agents in treatment and additional costly bypassing regimens that involve immune tolerance induction (ITI) measures, an even more expensive and complicated treatment option (8). Inhibitor is therefore a critical variable that determines the long-term FVIII consumption and clinical outcomes.

Home therapy, which is the medical self-treatment of FVIII concentrate by the patient or caregiver, not in a hospital, is now an essential element of contemporary hemophilia therapy. It makes early management of bleeds easier, decreases emergency visits, promotes adherence to prophylaxis, and eventually positively changes quality of life (9, 10). The World Federation of Hemophilia (WFH) promotes the concept of home therapy as one of the primary standards of holistic hemophilia treatment, and its prevalence is developing into a factor to determine the maturity of the country-specific hemophilia care (11).

In Jordan, the provision of hemophilia is in both the civilian and military healthcare sectors. Jordanian Royal Medical Services (JRMS) is an organization that offers advanced healthcare to the military staff and their dependents including a network of specialty centers and hospitals. The three JRMS facilities under study here are specifically relevant to the hemophilia care: the Military Cancer Center (MCC) in Amman, the Prince Rashed Bin Al-Hasan Military Hospital (PRBH) in Irbid and the Queen Rania Hospital of Children (QRH) in Amman. These facilities have individual patient demographics and model of service delivery; it indicates the scope of FVIII-dependent care in the network of JRMS.

In spite of the clinical and economic significance of HA in the JRMS framework, no published drug utilization review (DUR) has yet systematically described the dispensing patterns of FVIII, consumption disparities in the presence of inhibitors, and the home therapy adoption rates in this network. The literature on drug use in the MENA is limited, and particular information on the military medical services in Jordan is almost the same in the foreign literature (12). This loophole is a hindrance to evidence-based pharmaceutical policy, rational drug procurement, and budget planning of the JRMS.

This paper fills this gap by providing a 14-month (January 2023-February 2024) retrospective descriptive analysis of FVIII dispensing records of the three JRMS centers. objectives of the study include a description of utilization trends, measure inter-center discrepancy, compare consumption of the two groups; inhibitors positive and inhibitors negative patients, and define the level of adoption of home therapies. The results will guide clinical pharmacy practice, hospital formulary decision-making, and national hemophilia management policies at the JRMS and possibly the overall Jordanian health system.

2. LITERATURE REVIEW:

2.1 Global Epidemiology and Treatment Burden of Hemophilia A:

Hemophilia A impacts approximately 400,000 patients in the global population (and has the highest number of patients in low and middle-income nations where FVIII concentrates access is often inaccessible or unreliable) (1, 2). The WFH Global Survey constantly records enormous differences in treatment access, high-income nations use a substantial amount of FVIII per capita compared to their lower-income peers, a difference exerted by variations in diagnostic infrastructure, financing of healthcare, and access to products (11). The WFH in 2022 documented that in high-income nations, an average of more than 6 IU per capita of patients were administered yearly, whereas in low-income areas, they were administered less than 0.5 IU per capita (11).

It has been widely confirmed that prophylactic FVIII replacement is better than on-demand therapy in the

prevention of joint damage and enhancement of the quality of life in health (4, 13). Studies showed a significant decrease in hemarthrosis rates and maintenance of joint performance to adulthood when primary prophylaxis began in the early years of life (4). Nevertheless, prophylaxis involves a much higher annual FVIII intake of 1,500 to 4,000 IU/kg/year than on-demand treatment regimens of 500 to 1,500 IU/kg/year (5, 6). The economic consequences of such movement of on-demand to prophylaxis are great, and have motivated systematic drug utilization studies over the world.

2.2 Drug Utilization Reviews in Hemophilia: MENA Regional Context:

The use drug utilization (DUR) in hemophilia has become popular to optimize costly biologic medicines by health systems. Exhaustive FVIII consumption profiles, inhibitor prevalence percentage, and the cost-effectiveness of home therapy programs have been recorded in high-income regions, such as Northern Europe and North America (14, 15). Real-world pharmaco epidemiological studies have been made feasible in Scandinavia, through integrated hemophilia registries, which have shown that home therapy users consume more FVIII/year - as is associated with higher adherence to prophylaxis - but has lower hospitalization and improved joint outcome (14).

Hemophilia registries and DUR studies are not so advanced in the MENA region. A Saudi Arabian multicentric study (Almomen et al., 2024) investigated the use patterns of FVIII in pediatric patients with hemophilia and found that the median FVIII consumption ranged about 30,000 IU per patient per year, with considerable differences based on disease severity and presence or absence of an inhibitor (16). In a Jordanian survey by Awidi et al. (2006), the epidemiology of inherited bleeding disorders in the civilian group was observed, where the prevalence of inhibitors was approximately 22% among patients with severe HA, which is similar to the global levels (17). Nonetheless, none of these studies discussed the situation in military healthcare and the peculiarities of operations of the JRMS network.

One of the most clinically and economically important complications of replacement therapy is the development of inhibitors in the HA. A detailed overview by Astermark (2015) outlined the mutual risk factors as genetic (e.g., large gene inversions, null mutations) and treatment-related (e.g., intensive treatment during immune challenge, product switching) risk factors for inhibitor formation (7). The treatment cost could result in a tri- to seven-fold higher annual expenditure in patients with inhibitors than in their inhibitor-free counterparts, chiefly because of the expenses of avoiding agents and ITI protocols (8). The same disparity has been a major factor in making health technology evaluations and formulary choices in various healthcare systems.

2.3 Home Therapy in Hemophilia: Evidence and Implementation:

Home therapy programs are proven to enhance various clinical and patient centered outcomes in the management of hemophilia. A systematic review of the literature by Hermans et al. (2009) established that home therapy was related with timely treatment of bleeds, drop in emergency visits, and availed excellent compliance to prophylactic treatments (9). The advantages are most evident with pediatric groups, where home infusions administered by the caregiver can facilitate a continuous daily routine of activities such as schooling and physical growth.

Home therapy implementation in resource limited environments demands a well organized patient education program, sound cold-chain supply of FVIII concentrates and well organized and effective follow-up systems. Findings of a study by Zahedi et al. (2021) in Iran showed that two-year hospitalization rates decreased by 43% and emergency visits by 58% through structured home therapy programs in a healthcare system network comprised of the military (18). This observation is especially applicable to the situation of the JRMS where the captive population of insured with routine follow-up, provides a desirable environment on the home therapy introduction.

The WFH suggests that home therapy adoption should be tracked as quality indicator in comprehensive hemophilia treatment centers (HTCs), with a goal of over 70 percent of patients on prophylaxis self-infusion at home or has a home-based infusion or caregiver administered (11). This is an effective standard that can be used as a benchmark in analysis of the current practice at the JRMS network.

3. METHODOLOGY

3.1 Study Design and Setting:

The research uses a retrospective, descriptive drug utilization review (DUR) design. The pharmacy dispensing records of three JRMS healthcare facilities were surveyed to extract the data: (1) the Military Cancer center (MCC), a tertiary center in Amman, working with adult hemophilia patients; (2) Prince Rashed Bin Al-Hasan Military Hospital (PRBH), a military hospital in Irbid, serving adult and pediatric patients; and (3) Queen Rania Hospital for Children (QRH), The time frame of the study includes a 14-month observation of dispensing records of January 2023 and February 2024.

3.2 Study Population and Inclusion Criteria:

The population of the study involved all patients with a known case of Hemophilia A who received at least one

dispensing of an FVIII concentrate in one of the three facilities that comprise JRMS located across various areas during the study period. Only dispensing records of Hemophilia A diagnosis were selected. One instance of Hemophilia B was not included in the main analysis since this study concerns only the management of Hemophilia A. Patients did not have to have only received treatment in one center, but the data was representative of the main facility affiliation of each individual patient.

3.3 Data Variables and Definitions:

Each dispensing transaction was extracted to its corresponding variables: patient identifier (anonymized), inhibitor status (present/absent), diagnosis, treatment center, date of birth, treatment/dispensing date, mode of administration (home therapy vs. hospital-administered) and amount of IU dispensed during the transaction. In this study, the following operational definitions were used:

- The home therapy: This was affirmed and recorded as yes in the dispensing record that showed the FVIII concentrate to be dispensed to be self-administered or administered by a caregiver even when not in-hospital.
- Inhibitor-Positive: Recorded as YES in the inhibitor status field, reflecting the clinical status by the managing hematologist of the existence of neutralizing antibodies towards FVIII.

3.4 Data Cleaning and Quality Assurance:

Data was checked before analysis to ensure that it was complete and consistent. The treatment dates were ensured to be within the study window. There were no missing data on the primary outcome variable (total amount of IU dispensed). A single patient record of a patient with Hemophilia B who was treated at QRH was not included in any of the analyses. Outlier values of the IU consumption column were checked in clinical context: the highest single-transaction dispensing amount (250,000 IU on patient ID 2002705302 at QRH) was not removed during analysis since they represented a valid large-volume dispensing of the home therapy, which is consistent with high-frequency prophylaxis. Aggregation was performed to calculate patient-level by adding the total dispensing transactions within each specific center using a patient identifier to obtain cumulative IU totals per patient.

3.5 Statistical Analysis:

The descriptive statistics was used all through. The continuous variables (age at the midpoint of the study, total IU per patient), are reported as either mean ± SD (standard deviation), or median with range, depending on the distribution. Reporting of categorical variables (inhibitor status, home therapy status) are reported as frequencies and percentages. The age was determined by the difference between the date of birth of each patient and the center of the study period (July 1, 2023). Descriptive comparisons between inter-centers were carried out with respect to mean FVIII consumption per patient, and home therapy rates.

4. RESULTS AND DISCUSSION:

4.1 Patient Demographics and Cohort Overview:

156 FVIII dispensing transactions in the three JRMS facilities would be found throughout the 14 months of the study with Hemophilia A After we eliminated one transaction, which we had been recorded as a Hemophilia B patient, 155 Hemophilia A transactions remained to be analyzed, involving 72 individual Hemophilia A patients. Table 1 shows the demographics and cohort by treatment center.

Table 1. Patient Demographics and Cohort Overview by Treatment Center

Variable	MCC (n=20)	PRBH (n=8)	QRH (n=44)	Overall (n=72)
Total Dispensing Transactions	35	16	105*	156
Total IU Dispensed	1,119,500	506,500	3,754,250	5,380,250
Avg IU/Patient	55,975	63,313	85,324	74,726
Median Age (years)	26.0	18.2	8.7	13.8
Age Range (years)	15.5–40.9	0.8–48.4	0.5–17.2	0.5–48.4
Patients with Inhibitors	0 (0%)	0 (0%)	3 (6.8%)	3 (4.2%)
Home Therapy Patients	20 (100%)	8 (100%)	43 (97.7%)	71 (98.6%)

The entire group (n=72) had a broad age distribution of 0.5 to 48.4 years with a median age of 13.8 years at the time of the study. Demographic distribution based on each facility; QRH which being a pediatric facility handled the youngest population due to its median age of 8.7 Years (0.5to 17.2 Years), and MCC which handled most of the adult population with the median age of 26.0 Years (15.5to 40.9 Years). The age distribution of PRBH was the largest (0.8to 48.4) handled both pediatric and middle-aged adult. The proportion of patients among centers was 44 at QRH (61.1%), 20 at MCC (27.8%), 8 at PRBH (11.1%) indicate that QRH is the main referral center in the network of the JRMS in hemophilia care.

4.2 Total Factor VIII Consumption and Inter-Center Variation:

The sum of FVIII dispensed in all three centers in the study period was 5,380,250 IU in 156 transactions (not counting the transaction of Hemophilia B). QRH accounted for the largest share, dispensing 3,754,250 IU (69.8% of total), followed by MCC at 1,119,500 IU (20.8%) and PRBH at 506,500 IU (9.4%). These percentage ratios are attributable to this increased number of patients at QRH and the greater per-patient consumption of services there.

Mean per-patient FVIII consumption varied considerably across centers: QRH patients consumed a mean of 85,324 IU (range: 250–662,500 IU), compared to 63,313 IU at PRBH (range: 27,000–186,000 IU) and 55,975 IU at MCC (range: 500–253,000 IU). The greater average for consumption at QRH is likely because of younger age of the patients, who are more often placed on intensive prophylaxis treatment according to WFH pediatric treatment (4, 11) and the increased patient volume and being a specialized pediatric hemophilia treatment center. The large maxima recorded in QRH like Patients who took 327,500 and 329,500 IU, depict the possibility of patients who are receiving high dose prophylaxis on severe illnesses (table 2).

Table 2. FVIII Consumption Summary by Treatment Center

Center	Total IU	% of Total	Mean IU/Patient	Min IU	Max IU
MCC	1,119,500	20.8%	55,975	500	253,000
PRBH	506,500	9.4%	63,313	27,000	186,000
QRH	3,754,250	69.8%	85,324	250	662,500
Overall	5,380,250	100%	74,726	250	662,500

4.3 Inhibitor Status and FVIII Utilization:

Among 72 individual patients with Hemophilia A in the cohort, three (4.2%) patients were classified as inhibitor positive and were all treated at QRH. This rate of inhibitor prevalence is much lower than the world average of 20-30% of severe HA (7), but it perhaps indicates the presence of mild and mild-moderate cases in the cohort, underreporting in the dispensing database. Table 3 gives the per-patient FVIII use (by inhibitor status).

Table 3. FVIII Consumption by Inhibitor Status

Inhibitor Status	N (Patients)	Total IU	Mean IU/Patient	Range IU/Patient
Inhibitor-Positive	3	174,000	58,000	10,500–120,500
Inhibitor-Negative	69	5,206,250	75,453	500–662,500
Overall	72	5,380,250	74,726	250–662,500

Interestingly, the mean per-patient FVIII consumption (58,000 IU) was 23 percent less in the inhibitor-positive group than the inhibitor-negative group (75,453 IU). This counterintuitive result is worthy of interpretation. Inhibitor-positive patients all over the world generally take more FVIII because hemostatic efficacy is decreased and larger doses are required or alternative bypassing techniques (8). The number of inhibitor-positive patients in the current cohort (n=3) is small and IU intake varies significantly amongst these patients (10,500-120,500 IU), both of which limits the generalizability of this comparison. One patient took 120,500 IU - one of the highest doses in the whole cohort - in line with the high treatment burden usually experienced with inhibitors. Another patients, however, only took 10,500 IU during the study period, indicating either a mild course of disease, only episodic treatment. The noted tendency could also be explained by the fact that the patients in QRH who are an inhibitor positive might have been switched to using bypassing agents that

were not included in the dataset (as it specifically studied FVIII concentrates), which would artificially lower their exposure to FVIII. This is one of the significant caveats that a future research must consider by including bypassing agent dispensing information.

4.4 Home Therapy Adoption Across the JRMS Network:

Among other interesting discoveries of the study is the nearly universal implementation of home therapy in all three JRMS centers. Amongst the 72 distinct HA patients, 71 (98.6%)- had one or more home therapy dispensing instances over the study period. This is quite higher than the recommended percentage of 70 of home therapy enrollment by the WFH for comprehensive hemophilia treatment centers (11) and significantly higher than the regional reports reported in MENA region (18) (table 4).

Table 4. Home Therapy Adoption and Associated FVIII Consumption

Parameter	Home Therapy	Hospital-Only	Overall
Unique Patients	71 (98.6%)	1 (1.4%)	72
Dispensing Transactions	132 (84.6%)	24 (15.4%)	156
Mean IU/Patient	75,764	1,000	74,726
QRH Home IU (% of center total)	3,707,750 (98.8%)	46,500 (1.2%)	3,754,250

The 20 MCC patients (100% of them) and the 8 PRBH patients (100% of them) were all reported to have home therapy and 43 out of 44 QRH patients (97.7%). A single patient out of the total cohort (A QRH patient) was during the entire study period only administered with infusions by the hospital; and her total intake was just 1,000 IU. This one exception perhaps indicates a new patient, a patient with such mild disease that he needs only or occasional infusion into the hospital, or one whose home therapy has been postponed.

At QRH, 98.8% of all IU dispensed (3,707,750 of 3,754,250 IU) were attributed to home therapy transactions. This observation supports the importance of the JRMS hemophilia program as being home-based, and the one under hospital management as infusions aimed at acute manifestation or surgical care. Home therapy adoption rate is high in line with the nature of a well-established, integrated hemophilia program with an affixed insured military population that has a reliable follow up and supply chain infrastructure.

In addition, mean per-patient FVIII consumption was significantly lower with patients receiving home therapy (75,764 IU) versus the single patient in the hospital (1,000 IU). Although this statistical inference is constrained by the single patient comparison group, this direction difference is in line with the already established literature indicating that home therapy causes easier achievement of prophylactic infusions and thus higher annual use of FVIII, but also averts the hospitalizations and hemarthroses that happens due to under-treatment of the disease (9, 14). The great use of home therapy patients in this group thus could be probably a testament of prophylaxis-based internal treatment and not overutilization.

4.5 Center-Specific Observations and Clinical Implications:

The different centers of the JRMS had varying utilization patterns that were reflective of the characteristic of the patients and clinical mandate of the center. The relatively homogenous trend of high home therapy use and moderate per-patient FVIII use (mean 55,975 IU) was recorded in MCC, a group of relatively working-age adults with a median age of 26.0 years. The lack of any patients with inhibitors in MCC could be indicative of an effect of survival selection such as not being followed up, switching to the use of bypassing agents not included in this data set or it could reflect the outcome of immune tolerance induction during childhood when the patient was inhibitor-positive but is now inhibitor-negative.

PRBH, the smallest cohort (n=8) had the largest relative intra-center variation with only one patient making 186,000 IU -36.7 percent of the total IU output of the center. This compaction of use in one high-utilizing adult patient underscores the Pareto principle of Pharmacoeconomics of hemophilia with a smaller number of patients using a disproportionately large portion of total FVIII spending (15). This dynamic should be a consideration of budget planners in the JRMS because the loss or attachment of one high-need patient can significantly change the procurement needs of the center.

The largest mean per-patient consumption (85,324 IU) and absolute volume of FVIII dispensed was reported in QRH, the main pediatric hemophilia center. The pediatric age structure and almost the universal implementation of home therapy in QRH correspond to the prophylaxis-first treatment philosophy, as recommended by the WFH and global pediatric

hematology guidelines (4, 11). The three patients in QRH who were positive to inhibitors took 174,000 IU over the entire study period highlighting the clinical complexity of dealing with inhibitors even within a home therapy-based program.

5. CONCLUSIONS:

This retrospective drug dispensing review of FVII dispensing records conducted in three hospitals of the Jordanian Royal Medical Services is, to the best of our knowledge, the first systematic description of the utilization patterns of Factor VIII in a military healthcare system in Jordan. A cohort of study patients consisted of 72 distinct Hemophilia A patients who collectively had 5,380,250 IU of FVIII in 156 dispensing transactions over a period of 14 months, January 2023 to February 2024.

A number of important findings can be identified as the result of this analysis. To begin with, the average consumption of FVIII per patient was significantly different in the three centers with QRH showing the highest consumption of 85,324 IU/patient then PRBH (63,313 IU/patient) and then MCC with the lowest consumption of 55,975 IU/patient. These dissimilarities can be explained by the differences between demographic and clinical characteristics of each of the centers patients populations, especially the younger age range and a higher rate of prophylactic regimens at QRH.

Second, the use of home therapy in the JRMS network is almost universal, as 98.6 percent of patients had at least one home therapy dispensing event in the study period and 98.8 percent of all QRH FVIII volume was covered by home therapy transactions. This is significantly higher than the 70% mark of the WFH and makes the JRMS one of the progressive hemophilia programs in the world. A robust home therapy network of the military health system, sustained by a captive population with insurance, consistent supply chains, and back-up measures, seems to be one of the contributing factors of this success.

Third, the prevalence of the inhibitors in this cohort (4.2% all at QRH) is smaller compared to the range of 20-30 percent for severe HA prevalence globally due to the mixed severity distribution of the cohort. Interestingly, the mean FVIII usage was significantly lower in inhibitor-positive (58,000 IU) than inhibitor-negative (75,453 IU) patients in this sample, which is counterintuitive, possibly because of the small inhibitor-positive sample (n=3), the high disease activity in the former group and also due to the possibility that some bleeding events associated with an inhibitor could have used bypassing agents (not captured in this dataset) for some inhibitor-related bleeding episodes.

This research work has a number of implications on the JRMS in practice. In the pharmaceutical management-wise, the high numbers of high FVIII usage in a few patients specifically in PRBH with one patient consuming 36.7% of the entire IU of the facility implies that patient-level consumption control and treatment optimization may provide significant efficiency benefits. Regular DUR should be implemented into the system of JRMS pharmacy services along with future monitoring of the adherence to prophylaxis and the frequency of a bleed to allow making better predictions of FVIII procurement and to aid in evidence-based decisions on a formulary.

This study has a number of limitations that ought to be mentioned. The retrospective design does not allow clinical outcome measurement; the data on the frequency of bleeding, joint scores, and quality of life cannot be obtained based on the dispensing data. The number of inhibitor-positive group is not large to provide solid statistical comparisons. Bypassing agent consumption is not included, which could be a misrepresentation of the actual treatment burden in patients with inhibitors. Lastly, 14-month period of observation might not properly reflect seasonal differences in the frequency of bleeds or annual cycles of prophylaxis in all patients.

Future studies in this area ought to further develop this research with a prospective cohort on the clinical outcome data as well as dispensing data as well as consideration of bypassing medications and emicizumab use with an extension of the study time to minimum of 24 months in order to capture the annual treatment cycle. A comparison of the JRMS and civilian Jordanian hemophilia programs would further elucidate how health system attributes influence FVIII use and patient outcomes in the context of the region.

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