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INFANTS WITH MODERATE OR SEVERE HEMOPHILIA IN ASIA: HEALTH-RELATED LIFE QUALITY, IMMEDIATE MEDICAL AND SOCIAL EXPENSES

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Abstract:
Aim: *Infants with moderate or severe hemophilia in Asia: health-related life quality, immediate medical and social expenses.*
Methods: *The Hemophilia Utilization Group Studies Part Vb acquired analysis of changes from ten US hemophilia treatment clinics from May 2020 to April 2021. Individuals having HB answered preliminary questionnaires on sociodemographic, clinical features, and society that treats. Participants indicated bleeding episodes, job absence, and caregiver time quarterly throughout a 2-year period. These figures were used to compute ABR and indirect expenses. Direct expenses were determined utilizing medical chart information dating back one year and pharmacy records dating back two years.*
Results: *119 of the 175 respondents had comprehensive medical records and one or more follow-up surveys. Total average yearly per individual expenses for mild/moderate HB were $87,856 (median $21,170), $197,737 (median$148,892) for extreme HB, and $5,140,250 (median$63,617) for all individuals without inhibitor (P o 0.0001). The mean ABR for patients with severe HB receiving prophylaxis (5.5 7.9 bleeds/y) remained nearly half than that of those managed episodically. Clotting expenditures accounted for 87% of overall prices, while indirect costs accounted for 11%. Prophylaxis use was connected to 2.6-fold higher clotting factor costs (P value 0.02), lower but substantially more missed familial workdays (P o 0.0002) and physician (P o 0.002) or nursing visits (P o 0.0001), less part-time employment and unemployment, and lesser hospitalization costs (P 14 0.18) and ABR (P value 0.0002).*
Conclusion: *The substantial economic burden of HB is mostly due to clotting factor expenses. Nonetheless, prophylaxis therapy has therapeutic advantages and may lower relevant costs.*
Keywords: *severe hemophilia, Asia, Moderate Hemophilia, Infants.*

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INTRODUCTION:

Hemophilia A (a lack of coagulation factor VIII owing to a variation in the F8 gene) and hemophilia B (a lack of coagulation factor IX [FIX] due to a mutation in the F9 gene) are X-linked bleeding diseases [1]. In one study, 6.8% of infants with hemophilia A and 5.4% of individuals with hemophilia B suffered intracranial hemorrhage (ICH) in the first three months of life, with the most happening before five days of birth. ICH, in addition to producing immediate mortality, can have substantial long-term consequences [2-6]. There are currently no effective interventions for preventing ICH in hemophilia infants. But even though the ideal way of birth for hemophilia fetuses is still being debated, less consideration has been devoted to components of postnatal care that could assist to the development, diagnosis, and therapy of newborn ICH [7]. The sole published recommendation that addresses those difficulties is a declaration by the United Kingdom Hemophilia Centers Doctors Organization in 2021, and it is uncertain how effectively this recommendation represents current practice [8]. Studies conducted in Asia in 2019 and Europe in 2018 revealed that there had been no agreement on the usage of factor concentrates and imaging. Those surveys, though, have serious limitations: specific conditions that could necessitate specific therapies were not recognized, and only hematologists were polled [9-12]. Researchers carried out a poll of hematologists and neonatologists/pediatricians who care for infants to characterize present system in particular medical settings and to recognize significant disparities in practice between such communities, since other practitioners might well be designed to meet the needs of infants with hemophiliac [13].

METHODOLOGY:

The first author wrote the survey instrument in English, and it was evaluated by all of the writers. The second and fourth authors both adapted the instrument into French. A sample group of hematologists and neonatologists pilot assessed the instrument for accessibility and simplicity, as well as to determine how long it would take to complete. The poll had 30 dozens of questions. The first question asked responders if they have treated a baby with hemophilia within the previous four years. Seventeen questions on hemophilia care were presented within the framework of three medical situations, which are summarized in Box 1. Those questions focused on vitamin K delivery, the use of accordance with the work and other hemostatic medications, the utilization of testing to confirm hemophilia diagnosis, the use of neuroimaging, and the scheduling of hematology consultation. The last ten questions requested statistical profile on the participants and their organizations (the survey instrument is available on request). To be eligible for the research, hematologists and neonatologists/pediatricians had to be practicing in Asia and have managed a newborn with hemophilia during the previous two years. Only those who satisfied those requirements were encouraged to finish the whole survey. The respondents were drawn from the Association of Hemophilia Clinic Directors of Asia's membership list. Many physicians listed from such listings were discovered to be no longer in practice and were thus eliminated. Two of the researchers of the current study were identified upon those lists but were not included. Persons selected as potential participants got an invitation e-mail in June 2020 outlining the goal of the study and seeking their engagement. This was followed by an electronic mailing of the instrument using Survey Monkey, with a follow-up e-mail sent one week later to those who had not yet answered. The electronic survey has been ended in September 2020, and a printed version of the instruments was distributed, together with a small inducement, to physicians that had not answered to the internet instrument and those who did not have a valid e-mail address. Every survey items' reaction percentages were investigated. All replies were given equal weight. Intergroup variations in answer proportions have been examined for chosen survey questions using Pearson's 2 test or Fisher's exact test, as applicable. Two-sided P0.06 was judged statistically relevant, and no multiple comparison corrections were used.

RESULTS:

The electronic instrument was sent to 531 of the 634 people identified as possibly qualified to participate in the survey, while the paper instrument was sent to 552. Figure 1 depicts the survey's methodology. Number of responses for the electronic instrument were 13.8% (69 responses from 529 prospective respondents) and 19.9% for the paper questionnaire (106 replies from 548 potential respondents). The combined response rate for both instruments was 26.9% (172 responses from 616 prospective respondents). Fifty-nine participants (35% among all respondents; 28 hematologists and 28 neonatologists/pediatricians) had handled a baby with hemophilia in the previous two years and then were qualified to perform the whole survey instrument. Participants who answered the whole survey was in practice for an average of 12 years, and 34% were members of the Asian Association of Hemophilia Clinic Directors. The projected average number of neonates with hemophilia treatment at participants' facilities each

year was one for 33% of respondents, one to two for 48%, and more than one for 25%. Fourteen percent of those surveyed said their institution had a documented plan for managing neonates with hemophilia, and 6% said their institution had guidelines for evaluating infants at significant risk of ICH. Seventeen percent of respondents said they had treated an infant with hemophilia who had had a neonatal ICH in the previous two years. In the two scenarios wherein the mother was a recognized carrier but the diagnosis of hemophilia A hasn't been affirmed antenatally, substantially more hematologists than neonatologists/pediatricians ideal hematology consultation regarding the care of the newborn happen before delivery (25 of 30 [92%] versus 19 of 30 [64%] in scenario 1; P=0.01; 25 of 29 [85%] versus 18 of 28 [58%] in scenario 2; P=0.002). Whenever an initial diagnosis of hemophilia was made, there was even a agreement in favor of prenatal pediatric hematology consultation (27 of 30 [90%] versus 24 of 29 [87%]; P=0.40). In the two instances where the identification had not been confirmed antenatally, participants were asked questions about testing to confirm a hemophilia diagnosis.

Hematologists were more probable than neonatologists/pediatricians to quantify the FVIII level in the cord blood (22 of 30 [73%] versus 13 of 30 [42%]; P=0.018) and less probable to measure the FVIII level in peripheral blood (nine of 30 [32%] versus 18 of 30 [58%]; P=0.036) in the situation involving an infant to bruising following a tough delivery. A significant correlation was detected in the situation of a healthy infant following an easy birth, although the distinction was not statistically significant. Figure 1 shows the findings of a poll asking respondents regarding empirical therapy in the three scenarios. Participants generally opted not to treat a healthy infant following an uncomplicated delivery, but significant proportions in both classes wanted to treat a wounded but apart from that asymptomatic newborn. Therapy was recommended by substantial percentages in the case of a problematic infant, although there was a notable distinction among the groups: hematologists virtually entirely opted to treat with FVIII concentration rather than alternative products. Figure 2 depicts participants' preference for neuroimaging investigations in various contexts.

Image 1:

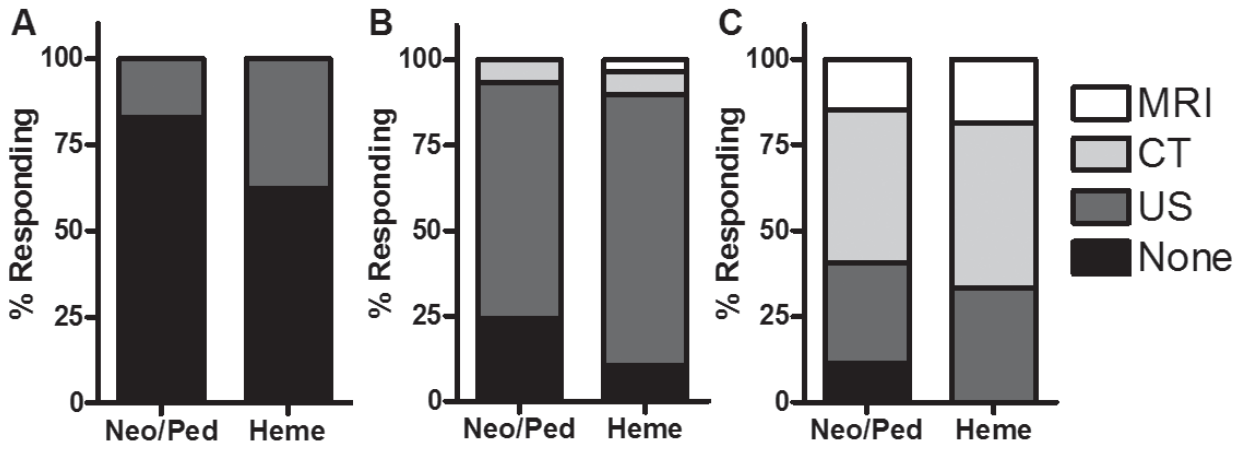

Table 1:

	N (%)
Severe Hemophilia A	112 (12.8%)
Moderate Hemophilia A	695 (73%)
Severe Hemophilia B	32 (6%)
Moderate Hemophilia B	94 (13.2%)
Family History	
Known History	452 (45%)
Unknown	470 (47%)
No info of family history	16 (8%)

Delivery Mode	
Cesarean Delivery	294 (42%)
Vaginal Delivery	635 (58%)
Gestational age	
No info	63 (5.9%)
Born term	78 (8%)
Born preterm	790 (86.1%)

Image 2:

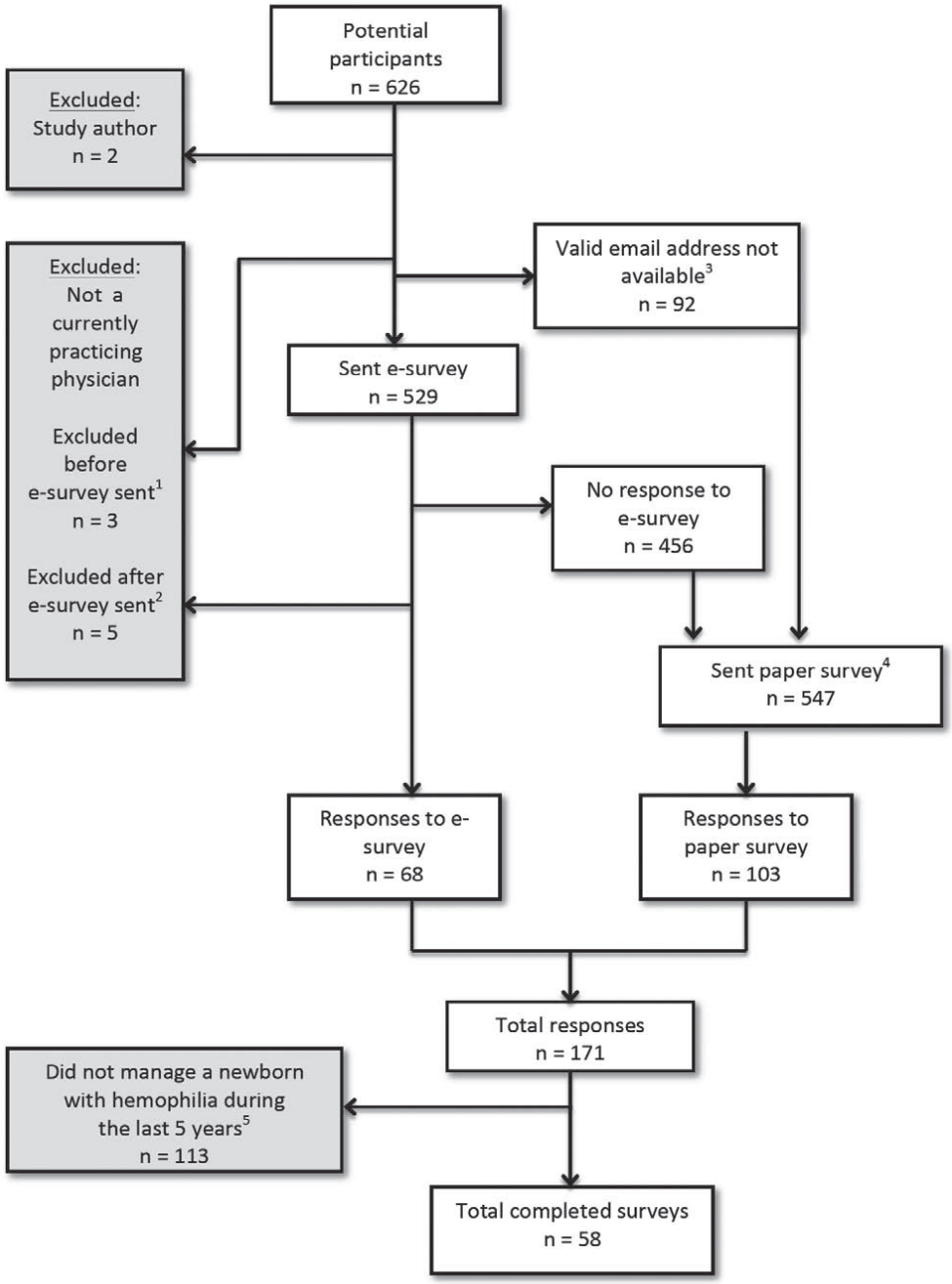

Table 2:

Signs	Sum of ill infants (%)
Serious Distress	73
Breech and malpresentation	65
Previous delivery cesarean	42
Preeclampsia	38
Dystocia	26
Placenta	14
Cephalopelvic	13

DISCUSSION:

The latest research the initial to conduct a comprehensive investigation of doctors' recommended therapy of neonates with hemophilia in certain clinical settings, as well as the first to compare hematologists' and neonatologists'/pediatricians' viewpoints [14]. There had been consistent disparities in reactions in between two groups when it comes of testing to confirm a hemophilia diagnosis, vitamin K administration, and therapy product selection for a problematic infant [15]. These disparities in hemophilia-specific areas could suggest a desire for enhanced communication and education of neonatologists/pediatricians on the management of neonates having hemophilia [16]. This might be accomplished by early pediatric hematology consultation, which was another area where we found a distinction between the two groups. In the two scenarios where a prenatal hemophilia diagnosis had not been made, 87% and 91% of hematologists preferred prenatal pediatric hematology discussion, particularly in comparison to only 58% and 63% of neonatologists and pediatricians (in correlation, the rate of prenatal engagement of Hemophilia Treatment Centers from the Universal Data Collection project in the United States was estimated 63%) [17-21]. In example, virtually all of our participants opted not to treat an asymptomatic infant following an easy birth, whereas around might well treat a newborn having bruises following a tough delivery. There is no systematic data to assist doctors in determining which babies require preventative medication, and more study is needed in this area [22]. Although there were no major differences in requesting neuroimaging tests between hematologists and neonatologists/pediatricians, there was substantial diversity in both these groups. When imaging asymptomatic neonates, cranial ultrasonography was favored. A real screening test should be very sensitive, which ultrasound lacks [23]. Nevertheless, computed tomography exposes patients to radiation, and magnetic resonance imaging frequently necessitates anesthesia; as a result, these techniques have significant limits [24-26]. The necessity for routine imaging, the timing of this imaging, and the proper imaging technology to utilize are all unresolved questions that require further investigation [27]. The choice to acquire neuroimaging of a problematic infant was virtually unanimous in the poll, which corresponded to the UKHCDO's advice. Nevertheless, there wasn't agreement on the best mode of application [28].

CONCLUSION:

The current study found significant disparities in practice among hematologists and neonatologists/pediatricians, as well as substantial heterogeneity between practitioners when it comes to empirical treatment with element concentrate, cranial imaging, and vitamin K administration for babies with hemophilia. This variation is due to a lack of evidence to support recommendations in these areas, and further study is needed. Multidisciplinary education and access to higher education Hematologists, neonatologists, neurologists, and radiologists must formulate Asian standards and guidance.

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