IMMUNOHEMATOLOGY

Original article

Rh disease in Mexico: evaluating regional and institutional differences in treatment availability and disease management

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Background - Rh disease occurs following maternal alloimmunization, which can develop due to RhD blood group antigen incompatibility between a mother and her fetus. Despite developing robust clinical protocols for effective immunoprophylaxis over the last 50+ years, a significant global burden of Rh disease still exists, particularly in low/middle-income countries such as Mexico.
Materials and methods - This study examined disparities in the allocation of maternal and child health resources, as well as clinical knowledge regarding Rh disease, to gain insight into why Rh disease remains prevalent in Mexico. To this end, an 11-question survey was sent to members of the Federación Mexicana de Colegios de Obstetricia y Ginecología (FEMECOG) to evaluate their knowledge of the availability and implementation of anti-RhD immunoglobulin prophylaxis in their practices and institutions, and about managing Rh disease by monitoring fetal anemia risk and providing intrauterine treatment when necessary. Responses were separated by region, and chi-square two-by-two contingency tests were performed to evaluate regional and institutional differences.
Results - Significant variations in prevention and treatment were found within the Mexican healthcare system, particularly, with regard to providing anti-RhD immunoglobulin to prevent alloimmunization, which is critically important for preventing Rh disease. Specifically, Regions 5, 6, and 7 were most lacking in this regard.
Discussion - This study highlights differences in the Mexican healthcare system in preventing and treating Rh disease. Closing the gap in the availability of anti-RhD immunoglobulin should take priority in future efforts aimed at providing equitable care, because this will lead to the more preferable outcome of preventing Rh disease, rather than forcing patients to seek out more complex measures for treating Rh disease after it develops. These data can be used to create strategies to understand and eliminate these healthcare disparities.

Keywords: *Rh disease, hemolytic disease of the fetus and newborn, alloimmunization, anti-RhD immunoprophylaxis, intrauterine transfusion.*

Arrived: 28 January 2024
Revision accepted: 25 June 2024
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INTRODUCTION

Hemolytic Disease of the Fetus and Newborn (HDFN) results from maternal alloimmunization due to maternal-fetal red blood cell (RBC) blood group antigen

incompatibility. Prenatally, this can induce fetal anemia, hydrops, and miscarriage. Postnatal consequences can include cerebral palsy, deafness, kernicterus, other birth disorders, and mortality[1]. Maternal exposure to blood group alloantigens results from prior transfusion, intravenous drug abuse, or pregnancy; the latter, due to paternally-derived antigens on fetal RBCs[1].

Although antibodies to >50 different RBC blood group antigens can cause HDFN, severe cases are often due to alloimmunization to antigens in the Rh system, RhD in particular. Individuals either have (i.e., are RhD+) or lack (i.e., are RhD-) the RhD RBC transmembrane protein, and RhD+ is more common. HDFN due to anti-RhD antibodies is commonly termed "Rh disease." Because of the advent of anti-RhD immunoglobulin prophylaxis in the 1960's, the incidence of Rh disease decreased dramatically; therefore, the relative prevalence of HDFN involving other blood types increased (e.g., in Kell, Duffy, Kidd, and MNS blood group systems)[1-3]. In addition, although fetal-maternal ABO antigen incompatibility is the most common cause of HDFN, it is less clinically important and uncommonly requires clinical intervention[1,4].

Rh disease is prevented by antenatal and postnatal anti-RhD immunoglobulin injections, which effectively block the primary immune response to RhD, but do not induce tolerance. Although its routine use decreased the incidence of Rh disease to ~0.5% in industrialized countries[3], the prevalence of Rh disease remains high in certain low/middle-income countries due to low availability of anti-RhD immunoglobulin and a lack of education regarding Rh disease[2]. Therefore, ~2.5 million additional doses are needed annually to reduce, and potentially eradicate, the global burden of Rh disease[2].

Anti-RhD immunoglobulin should ideally be used during each at risk pregnancy as follows: 1) at ~28 weeks of gestation, 2) anytime an unexpected RhD exposure occurs, and 3) within 72 hours post-partum[3]. It is also important to note that anti-RhD immunoglobulin prophylaxis is ineffective, and not recommended, for RhD- women who have already been alloimmunized to RhD. Finally, whenever an intrauterine transfusion (IUT) is required, the RBCs should be antigen-matched, as much as possible, to the mother's blood type to prevent, or not enhance, maternal alloimmunization and/or to decrease ongoing hemolysis in the setting of HDFN[1]. In resource-limited settings, such as Mexico, home-based transfusion methods may be useful to bridge gaps in hospital access; however, protocols for such "hospital in the home" practices should ensure safe transfusion therapy[5].

Measuring fetal cerebral middle artery peak systolic velocity (CMA-PSV) can estimate the degree of fetal anemia or hydrops, helping to monitor HDFN[1,3,6]. If, towards the end of the second trimester and onwards, fetal CMA-PSV suggests anemia, IUT can potentially prevent neurological damage[1]. Neonatal hemoglobin and bilirubin levels should also be followed closely to determine if therapy is needed post-partum, because HDFN-induced anemia may occur after delivery due to the prolonged half-life of maternal antibodies in the newborn's circulation[1]. Finally, other etiologies may prolong fetal anemia, and monitoring neonatal RBC level and function is important to ensure the health of the newborn[1].

The Mexican federal *Guía de Práctica Clínica* protocol[6] for healthcare practitioners directs that RhD- women should receive a 300 μg dose of anti-RhD immunoglobulin intramuscularly, first at ~28 weeks gestation (if a maternal Indirect Antiglobulin Test is negative), and then within 72 hours of giving birth to an RhD+ baby; a higher dose may be required post-partum if there is significant fetal-maternal hemorrhage. Antenatal anti-RhD reduces the risk of sensitization from 1.9 to 0.2%. Moreover, in unsensitized women giving birth to an RhD+ baby, post-partum anti-RhD decreases the sensitization risk from 16 to 1.6% for the subsequent preganancy[6]. This protocol also involves ABO and Rh typing of the mother at her first prenatal visit, along with an antibody screen, to determine whether the mother is already alloimmunized[1,3,6]. If applicable, the father can also be tested to determine the risk of the fetus inheriting a paternal RhD antigen and, thus, enhancing the mother's alloimmunization risk[1].

Mexico has a large disparity between the amount of anti-RhD immunoglobulin needed to prevent Rh disease versus the amount available; indeed, one study suggests that 50-80% of the post-partum anti-RhD immunoglobulin injections required are not provided[2]. This may result from a complex combination of public health insurance, employer-provided insurance, private out-of-pocket expenses, and disconnected social security institutions, which can lead to serious disruptions in the continuity of care, particularly because hospitals and health care

records are not fully integrated. However, Mexico has a highly organized, comprehensive organization of obstetricians and gynecologists (i.e., the Federación Mexicana de Colegios de Obstetricia y Ginecología [FEMECOG]), allowing for a pilot study to gain insights regarding why Rh disease prevalence remains high. FEMECOG is divided into 7 regions across Mexico (**Figure 1**), each including a portion of the country's states (except for Region 1, which solely comprises Mexico City). Each region contains professional obstetrician/gynecologist associations (i.e., the "*colegios*"). There are 5,083 individuals (i.e., "*federados*") each associated with one of 74 colegios. Federados may work in private and/or public hospitals, although most work in the former, having trained in the latter. In addition, federados may be obstetricians and/or gynecologists, or may practice in other related areas of health or biotechnology, such as oncology. This network can standardize individual physician practices and promote information exchange, although hospitals vary in clinical practices due to a lack of institutional integration. In particular, because regions vary in income (**Figure 1**), they may vary in access to treatment, education, and other resources for preventing and treating Rh disease. Indeed, a map from the *Consejo Nacional de Evaluación de la Política de Desarrollo Social* (CONEVAL, or the National Council for the Evaluation of Social Development Policy; **Figure 1**) shows significant differences in income across states, which, we hypothesize, affect affordability of care and accessibility of resources and education across different FEMECOG regions. To this end, we performed mass telephone surveys and sent out mass email surveys to directors, presidents, and maternal and fetal health practitioners associated with FEMECOG, and used statistical analysis to identify significant results.

MATERIALS AND METHODS

The study's objective was to identify reasons why the prevention, diagnosis, management, and treatment of Rh disease are not implemented in a consistent way in healthcare institutions throughout Mexico.

Preliminary data collection to design the final study

Directors of the seven FEMECOG regions and presidents of the FEMECOG colegios were contacted for a telephone survey. They were asked seven questions (*Online Supplementary*, **Table SI**). Several of these individuals were available to participate in this phase, which served as a preliminary consultation session about the perception of Rh disease throughout FEMECOG and helped us refine the questionaire.

Interviewing federados

Results from the initial survey of presidents were discussed with the directors and presidents of FEMECOG regions and colegios. The questionnaire was then further developed into eleven final questions, in which the answers were semi-quantified and additional questions were added to extract demographic information (*Online Supplementary*, **Table SII**). Some questions were subdivided into separate parts for efficient data analysis, and interviewees were expected to answer the specific parts of the questions that applied to them.

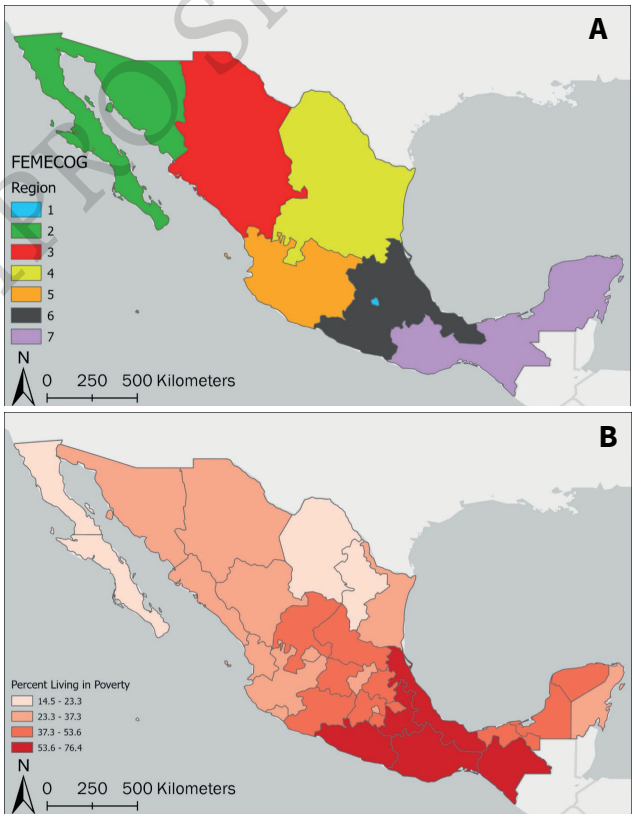

Figure 1 - FEMECOG regions across Mexico and the percent of the population living in poverty
A) FEMECOG regions. Adapted from FEMECOG. Ciudad de Mexico (Mexico City) is in light blue. **B**) Percent living in poverty by state in 2018, stratified using Jenks optimization. Light tan: 14.5-23.3% in poverty; light orange: 23.3-37.3%; orange, 37.3-53.6%; red, 53.6-76.4%. Poverty data were obtained from *Consejo Nacional de Evaluación de la Política de Desarrollo Social*. Maps were made with ArcGIS Pro.

The administrators of the regions and colegios notified their federados one month in advance that the eleven-question survey would be arriving to allow them to prepare their answers. The administrators then sent out the survey via their most efficient method of communication (e.g., WhatsApp or mass email, depending on the region or colegio). The survey was sent out to each of a total of 5,083 federados three times: an initial time, 7 days later, and 21 days later.

Analysis of federados' responses

After receiving the survey responses, the data were separated to identify regional and institutional differences. This allowed the separation of individual questions into different parts, as well as the additional questions identifying demographic information. Duplicated responses (i.e., people who had responded twice) were eliminated from the total.

For questions 5.1 and 5.2, federados were expected to answer the part that pertained to their work environment: if they worked in a public hospital, they answered 5.1; if they worked in a private hospital, they answered 5.2. Those who reported working in both types of healthcare systems answered both parts of question 5. If the respondents answered the incorrect part, their answers were not counted towards the total number of responses for that question. Those who did not answer (i.e., submitted a blank response) were also eliminated from the total. Finally, we did not count those who selected more than one option, as it was impossible to discern which answer was more accurate. Chi-square two-by-two contingency tests were performed using R. To examine differences in available resources in public versus private hospitals, a contingency test was performed on both parts of question 5. To examine practices regarding the use of anti-RhD immunoprophylaxis, a contingency test was performed on questions 6 and 7. Lastly, to examine methods to monitor and treat Rh disease, a contingency test was performed on questions 8 and 9.

RESULTS

Table I displays the response rate organized by question and region. Overall, out of 5,083 federados in FEMECOG, approximately 27% answered the survey, totaling 1,387 responses. The highest response rate was in Region 7, with 40%. Region 5 had the lowest response rate, with 20%. Question 1 of the survey asked federados to report the hospital setting (i.e., private *vs* public) in which they work; federados answered "public," "private," or "both."

For question 5.1, total expected responses were calculated by adding the number of federados who answered "both" and the number of federados who answered "public" for question 1. Region 3 had the highest response rate of 96%, while Region 6 had the lowest response rate of 75%.

For question 5.2, total expected responses were calculated by adding the number of federados who answered "both" and the number of federados who answered "private" for question 1. Region 6 had the highest response rate of

Table I - *Response rate organized by question and region*

Region	Total federados	Total answered	% answered	Question 1			Question 5.1			Question 5.2			Question 6		Question7		Question 8		Question 9	
				Both	Public	Private	Total expected*	Total answered	%	Total expected**	Total answered	%	Total answered	%	Total answered	%	Total answered	%	Total answered	%
1	874	211	24	92	16	102	108	88	81	194	193	99	211	100	211	100	211	100	211	100
2	444	98	22	41	10	47	51	44	86	88	85	97	98	100	98	100	98	100	98	100
3	493	137	28	54	14	69	68	65	96	123	120	98	137	100	137	100	137	100	137	100
4	975	313	32	138	33	142	171	144	84	280	275	98	313	100	313	100	313	100	313	100
5	985	195	20	75	19	101	94	81	86	176	173	98	195	100	195	100	195	100	195	100
6	876	257	29	99	26	132	125	94	75	231	230	99.6	257	100	257	100	257	100	257	100
7	436	176	40	64	30	82	94	89	95	146	142	97	176	100	176	100	176	100	176	100

*Total expected responses for question 5.1 were calculated by adding the number of responses to "both" and "public" to question 1.
**Total expected responses for question 5.2 were calculated by adding the number of responses to "both" and "private" to question 1.

99.6%, while Regions 2 and 7 had the lowest response rate of 97%.

Across all regions, questions 6, 7, 8, and 9 had a 100% response rate out of all the federados who answered the survey.

Availability of anti-RhD immunoglobulin

Question 5.1 and 5.2 evaluated the availability of anti-RhD immunoglobulin within public and private hospitals, respectively. For those who responded "always, 100%" and "never, 0%" to question 5.1 or 5.2, a chi-squared test for contingency was performed for each region to assess if there were statistically significant differences between the availability of anti-RhD immunoglobulin in public versus private settings.

Figure 2, **Panel A** displays the proportion of federados working in public institutions who answered "always (100%)," "usually (80-90%)," "almost never (5-10%)," and "never (0%)," for each region. These results indicate that Regions 5, 6, and 7 had a higher percentage of federados who never have access to anti-RhD immunoglobulin for immunoprophylaxis. Additionally, in no region, except for Region 4, did more than 50% of federados always have access to anti-RhD immunoglobulin, with the highest being 54% in Region 4.

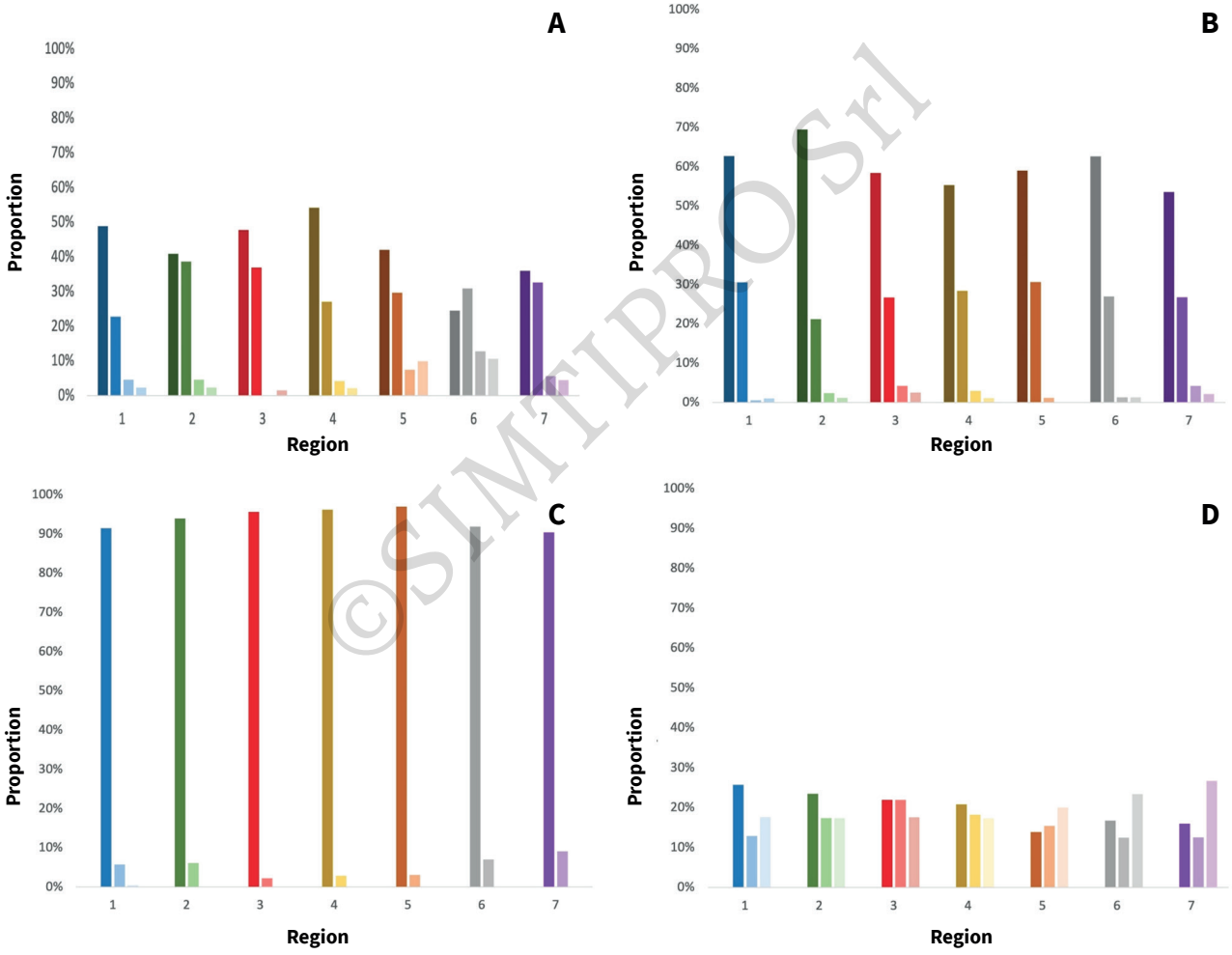

Figure 2 - Access to and utilization of anti-RhD immunoglobulin to prevent RhD alloimmunization

A) Public hospitals have limited access to anti-RhD immunoglobulin to prevent RhD alloimmunization. **B**) Private hospitals have significantly more access to anti-RhD immunoglobulin to prevent RhD alloimmunization. **C**) Anti-RhD immunoglobulin is almost always provided post-partum. **D**) Anti-RhD is underutilized during the antenatal period.

From left to right: darkest shaded bars indicate "always"; next darkest indicate "usually"; second to right indicate "almost never"; and lightest shaded bars indicate "never." Percentages were calculated with "no responses" omitted from the total. One (1) individual in Region 1 reports never applying anti-RhD post-partum; all other regions report 0% for never applying anti-RhD post-partum.

Similarly, **Figure 2**, **Panel B** displays the proportion of federados working in private institutions who had access to anti-RhD immunoglobulin. In regions 1, 2, 5, 6, and 7, there were significant increases in the proportions of federados in private settings who reported always having access to anti-RhD immunoglobulin, as compared to those in public settings (question 5.1). Similarly, in regions 5, 6, and 7, there were statistically significant decreases in the proportions of federados in private settings who reported never having access to anti-RhD immunoglobulin, as compared to those in public settings (question 5.1). The results for statistical contingency tests for questions 5.1 and 5.2 are in **Table II A** and **Table II B**, respectively.

Table II - *Chi-squared tests for contingency*

A) Question 5	Chi-squared value	p-value
Region 1	**4.21**	**0.040**
Region 2	**8.64**	**0.0033**
Region 3	1.52	0.22
Region 4	0.0127	0.91
Region 5	**5.73**	**0.017**
Region 6	**37.4**	**<<0.01**
Region 7	**6.09**	**0.014**
B) Question 5	**Chi-squared value**	**p-value**
Region 1	0.072	0.79
Region 2	$3.12*10^{-30}$	1.0
Region 3	$4.06*10^{-30}$	1.0
Region 4	0.14	0.70
Region 5	**14.56**	**<<0.01**
Region 6	**12.769**	**<0.01**
Region 7	0.40	0.53
C) Questions 6 and 7	**Chi-squared value**	**p-value**
Region 1	**184**	**<<0.01**
Region 2	**97.3**	**<<0.01**
Region 3	**150.61**	**<<0.01**
Region 4	**363**	**<<0.01**
Region 5	**269**	**<<0.01**
Region 6	**289**	**<<0.01**
Region 7	**193**	**<<0.01**

A) Federados who answered "always, 100%" to questions 5.1 and 5.2. **B**) Federados who answered "never, 0%" to questions 5.1 and 5.2. **C**) Federados who answered "always" to questions 6 and 7. A significance level of α=0.05 and one degree of freedom were used. Regions whose p-values imply statistical significance are highlighted in bold.

Preventing Rh disease

Questions 6 and 7 relate to practices regarding preventing Rh disease in Mexico; question 6 asks how often they use anti-RhD immunoglobulin post-partum, and question 7 asks how often they use it during pregnancy. **Figure 2**, **Panel C** shows that an overwhelming proportion of federados always use anti-RhD immunoglobulin post-partum, with the lowest being 90% in Region 7. A small proportion reports usually, but not always, use anti-RhD immunoglobulin post-partum, with the highest being 9% in Region 7. Lastly, across all regions, 0% report never using anti-RhD immunoglobulin post-partum except for Region 1, who reports 1 individual. Using chi-square tests for contingency, there were significantly more federados, across all regions, who used anti-RhD immunoglobulin post-partum 100% of the time, as compared to those who also used antenatal anti-RhD immunoglobulin 100% of the time (**Table II C**).

Figure 2, Panel D shows that a much lower proportion of federados always use antenatal anti-RhD immunoglobulin, with the highest being only 26% in Region 1. Similar proportions of federados report usually, but not always, using antenatal anti-RhD immunoglobulin. Lastly, across all regions, some federados report never using antenatal anti-RhD, with the highest being 27% in Region 7.

Managing and monitoring Rh disease

Questions 8 and 9 relate to managing and monitoring Rh disease; question 8 asks whether federados can refer patients to measure CMA-PSV to determine the degree of anemia; question 9 asks whether federados can refer patients for IUT to help prevent neurological damage.

Figure 3 shows the proportion of federados who have no one to whom they can refer patients for performing CMA-PSV measurements, with the highest being 11% in Region 6. It also shows the proportion of federados who have no one to whom they can refer patients for IUT, with the highest being 71% in Region 1. Significantly more federados reported having no one who can perform IUT for their patients. Using chi-square tests for contingency, there were significantly more federados, across all regions, who had no referrals for IUT, as compared with those who had no referrals for CMA-PSV (**Table III**).

Blood Transfus. 2025; 23(2): 109-117 doi: 10.2450/BloodTransfus.750

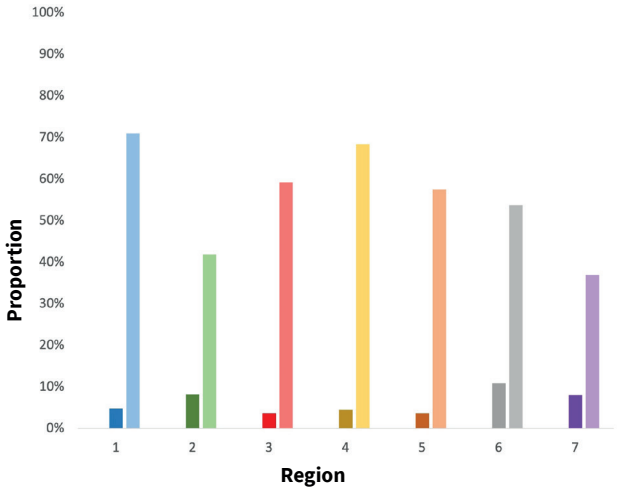

Figure 3 - Federados have significantly more referrals for CMA-PSV than IUT
From left to right: darkest shaded bars represent proportion of federados who report "no referrals" for CMA-PSV (question 8), and lighter shaded bars represent proportion of federados who report "no referrals" to IUT (question 9).

Table III - *Chi-squared test for contingency for federados who answered "no referrals"*

Questions 8 and 9	Chi-squared value	p-value
Region 1	**18.1**	**<<0.01**
Region 2	**42.8**	**<<0.01**
Region 3	**48.3**	**<<0.01**
Region 4	**58.8**	**<<0.01**
Region 5	**70.8**	**<<0.01**
Region 6	**73.0**	**<<0.01**
Region 7	**109**	**<<0.01**

A significance level of α=0.05 and one degree of freedom were used. Regions whose p-values imply statistical significance are highlighted in bold.

DISCUSSION

The results obtained show clear gaps in the Mexican healthcare system regarding preventing and managing Rh disease. Identifying these gaps will allow the design of pilot protocols aimed at closing them and, thereby, decrease the incidence and severity of Rh disease by providing equitable care across the country for pregnant RhD- women who are at risk for sensitization to RhD, or who are already sensitized.

Regions 5, 6, and 7 have significantly more federados working in private hospitals who report that they always have access to methods to prevent and treat Rh disease. In contrast, in Regions 5 and 6, there are significantly more federados working in public institutions who report never having access to prevention or treatment methods. This is consistent with the map in **Figure 1** showing that these regions contain some of the poorest states in Mexico. A possible lack of resources combined with low-income populations make these regions important targets for enhancing the use of anti-RhD immunoglobulin for immunoprophylaxis. Although there are clear practice guidelines in Mexico for preventing RhD sensitization and managing Rh disease, we assume that this lack of access is due to resource constraints in the public sector; nonetheless, this will need to be confirmed in future studies. In addition, our study did not address the extent to which midwives, or even village health workers, are engaged in obstetric care in the context of preventing and treating Rh disease, or the nature of their clinical practices; this should be addressed in the future.

Across all regions, there are significantly more federados who report using anti-RhD immunoglobulin post-partum, as compared to the number who report using antenatal anti-RhD immunoglobulin, even though its use during pregnancy is very important for preventing sensitization. This could be due to several reasons, including: 1) a general lack of access to anti-RhD immunoglobin, or insufficient amounts to use in both settings; 2) no blood group testing performed early in pregnancy to obtain the maternal Rh blood type and determine the risk of disease development; 3) insufficient understanding that anti-RhD immunoglobin should be used antenatally; 4) patient reluctance when offered treatment during pregnancy; and 5) insufficient numbers of RhD- patients in the local population to maintain appropriate supplies of the drug. Given the proven efficacy of providing antenatal anti-RhD immunoglobin and the availability of clear practice guidelines in Mexico, this suggests that education regarding proper clinical practices for preventing Rh disease should be an important consideration in addressing this disparity regardless of how many RhD- patients are present[2,6]. Again, the possibility of improving prevention will need to be addressed in future studies.

Lastly, across all regions, there is a significant number of federados who report having no one to whom they can refer their patients for IUT, as compared to referring them for CMA-PSV. This could indicate a lack of awareness of

available IUT centers in their area or a lack of knowledge about IUT and its role in treating Rh disease.

Several limitations of this study should be acknowledged. For example, although 1,387 of 5,083 federados (i.e., 27%) responded to our survey, this does not guarantee that it is a statistically-representative sample of all of the obstetricians caring for women at risk for Rh disease; for example, an individual's practice approach may have biased their desire to respond. In addition, there was little to no monitoring of the respondents to ensure that survey questions were answered accurately. Nonetheless, the survey was provided in Spanish to enhance accuracy. Furthermore, semi-quantified questions, including questions 5-9, required estimating an approximate range. In addition, responses may not correspond to actions, in that availability of anti-RhD immunoglobulin may not mean that it is used effectively, knowledge of treatment regimens may not mean they are practiced consistently, the ability to refer patients for CMA-PSV and IUT may not necessarily mean that all relevant referrals are provided, and, finally, patients may not necessarily be able take advantage of referrals, even if they are provided.

There also may be inherent biases present in this study. For example, the semi-quantified answer options were limited in their ranges (i.e., 100%, 80-90%, etc.), prompting answers to be chosen based on rough estimates. In addition, to avoid embarrassment, responses may have been given to cast the respondent in a more positive light, as they were not anonymous to the investigators. Additionally, although the response rate was 27%, these respondents may not be a statistically representative sample of obstetricians and gynecologists who most directly consult with patients regarding Rh disease risk and management. Moreover, some physicians may have been too busy to respond, possibly biasing the results. Finally, respondents may have incorrectly recalled the frequency of certain practices and referrals. Thus, future studies could enhance the accuracy and rigor of their results by, for example, using random sampling methods, anonymizing survey responses, improving survey questions, and working to ensure a higher response rate.

Although the results obtained were compared with poverty indicators in these regions, other factors may lead to variable regional medical practices, including ethnic, sociological, ethical, and religious characteristics of these patient populations. In addition, no corrections were made between average income per region and the corresponding levels of anti-RhD immunoglobulin availability, the use of various treatment regimens, or the availability of referrals for CMA-PSV and/or IUT. These issues could be evaluated in future studies.

Because there continue to be differences in healthcare provided to different groups in Mexico, by identifying these differences, one can create protocols that accurately target healthcare disparities and effectively promote the equitable distribution and appropriate utilization of anti-RhD immunoglobulin prophylaxis throughout Mexico, with the ultimate goal of decreasing, or even eradicating, Rh disease. To this end, we plan to use this study's results to identify strategic areas to develop and improve standardized practices in Mexican hospitals to prevent and treat Rh disease.

CONCLUSIONS

This study highlights differences in the Mexican healthcare system in preventing and treating Rh disease. These differences in treatment availability, clinical practices, and patient management are present in all FEMECOG regions, with regions 5, 6, and 7 of greatest concern. Moreover, closing the gap in anti-RhD immunoglobin availability should take priority in future efforts aimed at providing equitable care, because this will lead to the preferred outcome of *preventing* Rh disease, rather than using more complex measures for *treating* Rh disease after it develops.

Evidence from this study can be used to create pilot protocols that strategically target areas of concern in Mexico. For example, future implementation research studies could compare two regions with differing levels of health equity (e.g., Regions 2 and 6) and evaluate the change in the burden of Rh disease in each region after making anti-RhD immunoglobulin immunoprophylaxis more widely available, along with introducing targeted education programs to familiarize FEMECOG federados with the practices necessary to prevent, monitor, and treat Rh disease.

FUNDING

Funding (to JD) was provided by the Anne E. Borghesani Memorial Prize in collaboration with the Department of International Relations at Tufts University and the

Borghesani Family. We thank them for their generous support.

ETHICAL CONSIDERATION

Ethical approval for survey-based studies is not required by Mexico. We presented the project to the board of directors of FEMECOG, who approved moving the study forward. The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki.

AUTHORS' CONTRIBUTIONS

José Antonio Ayala Méndez created the survey questions and circulated the survey to FEMECOG federados. Jessica Ding organized the data and performed the statistical analysis in R. Celina Montemayor-Garcia provided guidance and research consultation. Brie A. Stotler provided guidance and research consultation, particularly regarding the statistical analysis. Steven L. Spitalnik provided guidance and research consultation.

CONFLICTS OF INTEREST

As a potential conflict of interest, all Authors are members of the not-for-profit Worldwide Initiative for Rh Disease Eradication (WIRhE). Nonetheless, no funding was provided by this entity.

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