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Transfusion Safety: Lessons Learned In Ibero-America And Considerations For Their Global Applicability

Sécurité transfusionnelle: Leçons Apprises en Amérique Latine et Considérations Relatives à Leur Applicabilité Mondiale

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ABSTRACT

The safety of blood used for transfusions has historically been the main focus of the international health community. In the Americas, during the first decade of the 21st Century, the attention switched to the patients who need transfusions and to the individuals who donate blood, that is, to transfusion safety. Timely and universal access to blood components implied adequate availability to sufficient blood components by patients who require transfusions in every hospital of every country. Clinical conditions and local non-medical factors influence decisions to admit and transfuse ill individuals. Locally-developed pertinent transfusion guidelines contribute to better estimate blood needs. Replacement blood donation hinders access to blood stocked in the hospitals blood banks and results in excessive component expiry and financial losses. Focusing on patient transfusion needs and on patient outcomes permits implementing national blood collection, processing and distribution, in consonance with the national health system. Analyses of general health conditions, by using the national Human Health Indexes, and the operational characteristics of blood services, by using the blood center density index, permit identification of locally pertinent interventions to improve transfusion safety. For this article, the analytical approaches used in Ibero-America were applied to blood data from South-East Asian and African countries. Data collection and validation were identified as priorities for Asian countries. Estimating blood component requirements at the local level and adjusting blood collection, processing and distribution systems are important in Africa.

RÉSUMÉ

La sécurité du sang utilisé pour les transfusions a toujours été la principale préoccupation de la communauté internationale de la santé. Dans les Amériques, au cours de la première décennie du 21^e siècle, l'attention s'est portée sur les patients qui ont besoin de transfusions et sur les donateurs de sang, c'est-à-dire sur la sécurité transfusionnelle. L'accès universel et opportun aux composants sanguins impliquait une disponibilité suffisante en suffisamment de composants sanguins pour les patients nécessitant une transfusion dans chaque hôpital de chaque pays. Les conditions cliniques et les facteurs non médicaux locaux influencent les décisions d'admettre et de transfuser des personnes malades. Les directives pertinentes en matière de transfusion développées localement contribuent à une meilleure estimation des besoins en sang. Le don de sang de remplacement empêche l'accès au sang stocké dans les banques de sang des hôpitaux et entraîne une péremption excessive des composants et des pertes financières. Se concentrer sur les besoins des patients en matière de transfusion et sur leurs résultats permet de mettre en place une collecte, un traitement et une distribution du sang au niveau national, conformément au système de santé national. Les analyses de l'état de santé général, en utilisant les index nationaux de la santé humaine, et les caractéristiques opérationnelles des services de transfusion sanguine, en utilisant l'indice de densité du centre du sang, permettent d'identifier des interventions localement pertinentes pour améliorer la sécurité transfusionnelle. Pour cet article, les approches analytiques utilisées dans la région ibéro-américaine ont été appliquées aux données sur le sang de pays d'Asie du Sud-Est et d'Afrique. La collecte et la validation des données ont été identifiées comme une priorité pour les pays asiatiques. L'estimation des besoins en composants sanguins au niveau local et l'ajustement des systèmes de collecte, de traitement et de distribution du sang sont importants en Afrique.

INTRODUCTION

The international health community has historically focused on reducing the infectious potential of blood for transfusions, that is, on blood safety. The first World Health Assembly (WHA) resolution on blood services, adopted in 1975, sought to curtail commercial blood collection and plasmapheresis in developing countries. The concerns of the WHA were the possible negative consequences of such activities for donors' health and for the safety of the resulting products.^{1,2} The 1975 resolution urged countries to instead promote blood services based on voluntary blood donation (VBD) and to protect the health of both blood donors and recipients. It was not until 1987 that the WHA discussed blood safety issues again, as part of the global strategy for AIDS prevention and control,³ approach that persisted within the World Health Organization (WHO) for two decades.⁴⁻⁶ The strategy for AIDS control laid the groundwork for the Global Safe Blood Initiative and provided the framework for initial actions to strengthen blood services by the WHO African Region^{7,8} and the Pan American Health Organization⁹ (PAHO). During the first decade of the 21st century, the WHA established a global plan for universal access to safe blood¹⁰ with five components: a) development of nationally coordinated blood transfusion services, b) exclusive collection of blood from VBD, c) quality-assured laboratory testing, d) reduction of inappropriate transfusions, and e) implementation of quality blood collection and distribution systems.

In the Americas, by contrast, the First Pan American Conference on Blood Safety, held in 2003, developed an innovative plan to improve transfusion safety in the Region by 2010¹¹ through: a) proper collection and preparation of sufficient blood components, b) timely access to blood components for patients, c) highest level of safety for blood products, d) appropriate transfusion practices, and e) efficient use of national resources. The strategies were: a) planning and management of the national blood network system, based on local needs b) promotion of VBD, through user-friendly blood collection services, c) quality assurance based on locally pertinent standards, and d) appropriate use of blood and blood components based on hospital-adapted transfusion guidelines. This article reviews lessons learned from the implementation of the Regional Plan for Transfusion Safety in Ibero-American countries and provides insights on how those lessons may be applicable in other regions of the world. The article takes as points of departure the following key concepts:

Global blood safety is not a measure of the risk of transmission of infectious agents through transfusion, but actually the goal of attaining the safest possible blood for every patient in every country

blood from voluntary altruistic donors only, to carry out universal, pertinent and precise laboratory blood testing, and to protect blood components from contamination during their preparation and storage. Local surveillance of transfusion-transmissible infections (TTI), training of blood service staff, national oversight by health authorities and collaboration among stake holders are considered basic in the quest for global blood safety.¹²

VBD is that which is made with the purpose of contributing to the national sufficiency and general timely access to blood, without the intention of benefiting a specific patient. Voluntary donors do not profit by collecting either money or other material benefits.¹³

Replacement blood donation (RBD) is that which is made on behalf of a specific patient in response to a hospital requirement and prior to that patient being admitted, treated or discharged by the hospital. The patients or their family members are responsible for recruiting replacement donors.¹⁴

Transfusion safety is the expression of the pursuit of global blood safety in a given population while ensuring the protection of both the individuals who donate blood and those who receive it, and also making efficient use of local resources. Maximum transfusion safety can be achieved when ethical principles, locally pertinent clinical guidelines, and quality assurance measures are applied.¹⁵

COUNTRY DATA

The 2016 WHO Global Status Report on Blood Safety and Availability¹⁶ was used as the source of all country data for 2013. This publication contains information collected from 178 countries as part of the Global Data Base on Blood Safety. The national data are presented in 12 annexes which detail for each nation the numbers of blood centers, of whole blood donations from VBD, RBD and paid donors, and of apheresis donations, methods and coverage of TTI screening, prevalence of TTI markers, numbers of blood components prepared and transfused, and indicators of policy, governance and quality assurance. The IBCO data from the PAHO report on the Supply of Blood for Transfusion in Latin American and Caribbean Countries 2012-2013¹⁷, published in 2015, are part of the Global Database and are usually included in the WHO Global Reports. Post-2013 national information for IBCO was obtained from a 2017 report on blood supply for the Americas¹⁸, while that for specific blood services was provided by IBCO national health authorities, as indicated in each corresponding table.¹⁹⁻²¹

LESSONS

National Requirements For Blood Components Are Determined Locally And Cannot Be Estimated Using Generic Global Indicators

Accurate estimates of patient needs are essential if blood services are to provide sufficient components for all who need transfusions²² and to achieve the goal of universal access to blood.²³ Indicators that have been proposed for estimating yearly requirements at the national level include (a) 1-5% of the population,²³⁻²⁵ (b) the number of hospital beds multiplied by 5-15²⁶ and (c) 0.40 units/patient admitted to hospitals.²⁷ Recently, the Lancet Commission on Global Surgery recommended that countries collect at least 15 units/1 000 population in order to provide adequate surgical care.²⁸

In 2013, IBCO had 600 304 000 inhabitants and 1 211 353 hospital beds. Based on an annual collection rate equal to 3% of the population—considered sufficient by WHO to cover all needs—the estimated requirement was 18 009 120 units, equivalent to 226% of the actual documented collection of 8 337 141 units. The latter figure is 98% of the estimate that would be obtained by multiplying the number of hospital beds by seven, or 8 479 471. The similarity between these two numbers suggests that estimates based on hospital beds might be sufficiently accurate to guide annual collection. Examining the individual country donation rates proves this conclusion incorrect: national collection rates based on units/hospital bed were 4.44-13.92 (median=9.61), and only three countries collected 7 units/bed/year; those with collection rates below 7/bed discarded 10-33% of their red blood cells (RBC), suggesting that hospital beds do not provide a valid criterion to either estimating needs or assessing sufficiency of blood for transfusion in IBCO.

Table 1 lists IBCO according to their Human Health Index (HHI, range 0.727-0.992, median 0.843), which is a composite of life expectancy at birth²⁹ and provides more meaningful context for health issues than national income. Blood collection rates are expressed as units/10 000 inhabitants. According to this indicator (range 66.52-365.52, median 129.35), Cuba collected 5.5 times more blood than Peru, three countries had rates above 200, and four had rates below 100. Units collected/physician ranged from 5.20 to 22.42 (median 7.45). The numbers of blood units collected/hospital bed were independent of HHI ($r_s=-0.294$, $p=0.221193$), numbers of units/physician were inversely correlated with HHI ($r_s=-0.594$, $p=0.009411$) and collections per 10 000 inhabitants were directly correlated with HHI ($r_s=0.4609$, $p=0.04751$). The proportions of RBC discarded (range 4.10-33.25, median 14.66) did not correlate with units collected/population ($r_s=-0.2179$,

$p=0.3866$), indicating that RBC disposal was not due to excessive collection by those countries with more blood available. Six countries, including two with collection rates below 100/10,000 population, discarded more than 20% of their RBC. The national rates of RBC used/10 000 population (range 52.26-350.53, median 110.41) not only correlated more strongly with HHI ($r_s=0.4917$, $p=0.03238$) than the corresponding collection rates but also demonstrated that only two countries utilized more than 200 units/10 000 inhabitants and eight used less than 100.

In order to estimate blood needs, it is important to understand how blood is used in clinical settings. In Guatemala, two national high-complexity reference hospitals in the capital city transfused 40 and 72 units/1 000 admissions, respectively; eight regional reference hospitals transfused 8-51; 16 provincial hospitals used 7-40; and two district hospitals transfused 13 and 16 units/1 000 patients.¹⁵ Overall, in Guatemala's 33 national hospitals, 45% of all patients were cared for at the emergency wards. Wide variations, up to five-fold, were seen in the annual use of RBC among hospitals of the same level of complexity when admissions and emergencies combined were used as the denominator.¹⁵

Observations in Nicaragua³⁰ showed significant monthly variations in hospital admissions, in the proportion of those who receive RBC, and in the numbers of RBC units administered. In addition to the patients' clinical condition, doctors' decisions to admit and/or transfuse patients were also influenced by factors such as distance, travel time and expenses involved in reaching the hospital, and the potential of losing patients to follow-up, indicating that the application of pertinent locally developed transfusion guidelines facilitates more reliable estimation of blood needs.

The Development Of Blood Services Depends On The General Development Of The National Health System

In the Region of the Americas, the national availability of blood for transfusions, expressed as units/10 000 population, is inversely correlated with national maternal mortality ratios (MMR).³¹ National rates of RBC use/10 000 population correlate directly with HHI ($r_s=0.4917$, $p=0.032384$), and higher utilization of RBC is associated with lower MMR and infant mortality rates¹⁵ (IMR). There is a direct correlation between MMR and IMR ($r_s=0.8064$, $p=0.000093$). National rates of blood collection per physician are directly correlated with both national MMR (range: 16.0-229.0, median 61.6; $r_s=0.5996$, $p=0.008479$) and IMR (range: 4.2-24.8; median 14.6; $r_s=0.6118$, $p=0.011874$), suggesting that the higher collection rates reflect shortages of physicians in deficient health care facilities rather than augmented blood collection. This would explain why transfusion rates in IBCO tend to be lower in those

Table 1. Blood collection and use in Ibero-American countries, 2013

Country	HHI	Annual blood collection				Rate of RBC discard (%)	Rate of RBC use/10 000
		Number	Rate/10,000	Rate/bed	Rate/physician		
Costa Rica	0.992	68 209	138.13	12.56	5.50	21.55	108.36
Chile	0.992	229 911	129.35	5.88	7.11	9.95	116.48
Cuba	0.912	411 545	365.52	7.17	5.22	4.10	350.53
Panama	0.885	53 529	136.34	5.93	8.58	14.97	115.93
Mexico	0.885	1 364 395	110.21	7.35	5.20	14.88	93.81
Uruguay	0.880	99 151	290.00	11.60	6.17	9.08	263.73
Ecuador	0.869	229 018	143.20	9.61	9.02	9.38	129.04
Argentina	0.866	966 059	231.10	4.72	6.08	33.25	154.26
Nicaragua	0.844	72 658	118.74	13.92	14.13	4.23	113.72
Peru	0.843	204 871	66.52	4.44	6.55	21.43	52.26
Venezuela	0.841	340 345	110.32	12.26		10.33	98.92
Colombia	0.831	740 173	151.27	10.08	9.00	14.66	129.05
Brazil	0.830	2 969 204	146.97	6.39	9.69	24.87	110.41
Honduras	0.828	69 082	83.62	11.94	9.95	16.92	69.49
Dominican Republic	0.822	110 780	105.21	6.58	6.88	8.89	95.86
El Salvador	0.809	98 088	153.65	13.97	6.68	10.70	137.24
Paraguay	0.804	86 056	126.20	9.70	7.79	28.14	90.68
Guatemala	0.802	121 921	78.87	12.81	10.38	25.29	58.92
Bolivia	0.727	102 146	94.16	8.56	22.42	12.72	82.12

Notes: Adapted with permission from Cruz JR. Satisfacción de los requerimientos de hemocomponentes [Satisfaction of the requirements for blood components]. In: Cortes-Buevas A, Cabezas-Belalcázar AC, García-Castro Gutiérrez M, Urcelay-Uranga S, editors. Promoción de la donación voluntaria de sangre en Iberoamérica. *Calí, GCIAMT*. 2017:61-70.¹⁵ Data obtained from these studies.^{16,17}

█ : Not available. HHI/Collection rate per 10,000 correlation: $r_s=0.4609$, $p=0.04751$. HHI/collection rate per physician correlation: $r_s=-0.5940$, $p=0.009411$. HHI/RBC use rate correlation: $r_s=0.4917$, $p=0.003238$.

Abbreviations: HHI, Human Health Index; RBC, red blood cells.

countries with less access to renal and liver transplants and with lower numbers of diagnosed cases of hemophilia.¹⁵ In Guatemala, intra-hospital maternal deaths associated with bleeding commonly occur during weekends and national holidays, and in high-risk remote areas (Table 2). During working days, deaths are more likely to occur between 11 pm and 5 am. In Bolivia, mothers with delivery complications did not have access to blood units stored in the hospitals because they were deposited for specific patients as a requisite for elective surgery (aka, replacement donation).³² This phenomenon results not only in poor patient management but also inefficient use of dedicatedly stocked blood. In two consecutive years, 131 mothers died due to peripartum hemorrhage in 32 Guatemalan hospitals where 6 401 RBC units, or 49 units per deceased woman, were discarded during the same period.^{19,20} Focusing on patient transfusion needs and patient outcomes is necessary for implementing adequate national blood collection, processing and distribution processes.

More Blood Banks Do Not Result In Better Availability Or Access To Blood Components

In 2015, there were 2 254 blood processing centers in IBCO.¹⁸ Fifteen countries had fewer than 100 such centers while the four nations with federal-type government -Argentina, Venezuela, Brazil and Mexico-had 259, 339, 530 and 572 centers, respectively (Table 3), a result of the blood services being set up and managed by each autonomous state/province. The mean number of blood units processed annually per center in each country varied from 884 to 37 477 (median 4,478, Table 3). Given that smaller centers are more prone to producing inaccurate laboratory testing results^{33,34} and to being financially inefficient,³⁵ assessing the availability of blood and the operational efficacy of such processing systems is important. Using the number of blood processing centers/100 000 inhabitants as an indicator, it becomes clear that countries with blood center density indexes (BCDI) higher than the median process fewer units per center, have lower proportions of VBD, defer

Table 2. Maternal deaths due to hemorrhage in public hospitals of Guatemala, 2015-2016

Type of hospital	Number of hospitals with deaths	Number of deaths	Deaths on weekends and holidays		Number of RBC units discarded
			Number	Proportion	
National reference	2	20	4	20%	2 482
Regional	8	52	25	48%	1 769
Provincial	9	41	18	44%	1 935
District, Contingency, Health Center	13	18	12	67%	215
Total	32	131	59	45%	6 401

Note: Data obtained from these studies.^{19,20}

Abbreviation: RBC, red blood cells

more prospective donors, have higher prevalence of TTI markers, prepare fewer components per unit, and discard more RBC due to expiry as compared to countries with indexes lower than the median (**Table 3**, $\text{Chi}^2=14.93$, $p<0.0001$). The BCDI show no correlation with national rates of RBC use ($r_s=0.0754$, $p=0.760329$), indicating that more blood processing centers do not result in increased availability of or access to blood components.

In Guatemala, just five of the existing 60 blood centers processed 42% of all the units collected in the country (**Table 4**).²⁰ In Honduras, the three blood centers managed by the Red Cross accounted for 50% of national blood collection in 2018. Processes and operational results differed among the three Honduran centers (**Table 5**), a finding that led to closure of the smallest center in 2019.²¹

These data, and the impact of reducing the processing centers from 37 to two in Nicaragua,¹⁴ demonstrate that planning and implementing national blood systems with the suitable number of centers can result in optimum availability of blood components and efficient use of national resources, including blood.

Regular Voluntary Donation Is A Major Contributor To Transfusion Safety

During 2015, there were 4.9 million VBD and 6.7 million RBD in IBCO.¹⁸ The respective deferral rates were 15.5% and 24.4%, amounting to 2.4 million individuals. Limited-scope observations point to low hemoglobin and risk behaviors for infectious disease transmission as major causes of deferral in both VBD and RBD. Unjustified deferral reasons include lipemic plasma, inappropriate veins, recent food intake, menstruation and over-stocked blood type.^{35,36} Despite these common factors, VBD were deferred in lower proportions (range: 4.63-23.57; median: 17.98) than RBD (Range: 7.97-33.01; Median 23.29). Lower deferral rates translate into more blood available and more efficient use of the resources to register and screen donors. With the pre-donation interview lasting 15 minutes, the 2 380 501 deferrals represent 316.5 full-time employees. The 57% excess associated with RBD compared

to VBD equals 124 full-time jobs. Once allowed to donate, VBD, especially those who have donated before, are less likely to have adverse reactions to donation³⁷⁻⁴⁰ and markers for TTI.^{41,42} The attributable monetary loss of 323 013 TTI-reactive donations in 2015 is US\$40.85 million.

Blood components derived from units that are not deposited for specific patients are available to any person in need of a transfusion. RBD not only limits access to available blood but also deters VBD, as the public is inclined to save their blood for family members or friends who may call on them as RBD.¹¹ Eliminating the requirement for blood replacement is the most important intervention to achieve universal VBD, as has been shown in Nicaragua and Buenos Aires.^{12,14}

In 2008, PAHO recommended that blood systems managers educate regular blood donors and to have them donate twice a year⁴³. The purpose of the education process should be to provide the individuals with the capacity and competences to decide to become blood donors, to protect their health, to understand why their blood donations are important for society, and to donate blood repeatedly.³ Limiting regular donations to two annually allows groups of females and males to donate together, reduces the risk of draining hemoglobin to unacceptable levels in repeat donors, and facilitates programming extramural collections. Additionally, should unforeseen circumstances suddenly deplete the RBC stock, there would be enough eligible regular donors to replenish it. The initiative "Pledge2 save lives" was created with those considerations in mind.⁴³

National Blood Systems Based On Consolidated, Stand-Alone Blood Processing Centers Which Focus On Serving Blood Donors And Satisfying Patient Needs Are More Effective And Contribute To Public Health

Considering that blood components for transfusion are essential medicines and prepared locally using biological materials obtained from multiple individuals, PAHO proposed that consolidated

Table 3. Operational indicators of blood centers, Ibero-American countries, 2015

Country	Blood processing centers		Donors			Viral TTI markers	Separation index	RBC expiry
	Number	Density/100,000	Per center	Voluntary	Deferred			
Nicaragua	2	0.0320	37 477	100	9.0	0.61	2.12	2.18
Paraguay	6	0.0853	14 353	10.2	7.7	0.93	2.50	15.48
Chile	17	0.0948	14 091	28.5	22.3	0.06 ^a	2.62	7.18
Ecuador	22	0.1365	11 222	68.3	15.7	0.85	2.40	6.21
Bolivia	18	0.1633	6 007	40.9	29.4	0.85	2.43	9.00
Colombia	83	0.1675	9 588	91.1	18.0	0.70	2.35	7.50
Honduras	19	0.1899	4 478	18.6	15.7	0.65	1.83	9.78
El Salvador	13	0.2013	7 145	17.0	25.0	0.35	2.72	7.74
Brazil	530	0.2602	5 848	61.3	19.3	0.77	2.30	17.1
Peru	89	0.2856	2 302	4.6	29.7	1.17	2.32	13.03
Guatemala	60	0.3691	2 104	5.4	25.9	1.16	1.82	12.16
Cuba	46	0.4089	9 064	100	4.6	1.78	1.53	10.96
Mexico	572	0.4567	3 794	3.8	28.5	0.87	2.27	9.02
Panama	22	0.5517	2 560	7.0	23.0	0.73	2.09	14.75
Argentina	259	0.6143	3 965	45.7	14.2	1.06	2.20	7.30
Costa Rica	32	0.6397	2 367	60.4	22.5	0.45	2.83	14.35
Dominican Republic	71	0.6665	1 106	11.2	23.0	1.27	0.57	15.37
Venezuela	339	1.0833	884	5.8	19.6	0.98	2.36	12.07
Uruguay	54	1.5743	1 679	51.4	23.4	0.53	1.90	20.56

Notes: ^a Confirmed testing results.¹⁶ "Poor outcomes" in relation to the median values are shaded.²⁹

Abbreviations: TTI, Transfusion-transmitted infections; RBC, red blood cells

Table 4. Blood processing in Guatemala, 2016

Institution	Larger centers		Smaller centers		Institutional mean number of units
	Number	Total units	Number	Total units	
Ministry of Health	2	30 089 (34%)	31	57 353 (66%)	2 650
Social Security	2	17 560 (67%)	3	8 552 (33%)	5 224
Private sector	1	7 636 (41%)	21	10 970 (58%)	846
All	5	55 285 (42%)	55	76 875 (58%)	
Annual mean		11 057		1 398	2 203

Note: Date obtained from this study.²⁰

Table 5. Blood collection and processing, Honduran Red Cross National Program, 2018

Blood center	Donors		Units		Separation Index	RBC expiry
	Voluntary	Deferred	Collected	TTI markers		
CENASA	6 446 (34%)	2 436 (11%)	18 837	441 (2.34%)	2.34	338 (1.84%)
CERESA	4 969 (23%)	3 622 (15%)	21 175	861 (4.07%)	2.40	66 (0.32%)
CESAAT	0	1 255 (22%)	4 489	229 (5.1%)	1.79	0
All	11 415 (26%)	7 313 (14%)	44 501	1 531 (3.44%)	2.31	404 (0.94%)

Note: Data obtained from this study.²¹

processing facilities be responsible for distributing sufficient blood components to predetermined hospitals.⁴² Fewer processing centers are easier to oversee and make it easier to standardize operating procedures, implement quality assurance, hire specialized personnel, purchase and maintain equipment, procure consumables, acquire automated technology, manage donor and product information, reduce inequity in access to blood, and interact with public health and plasma fractionation institutions.³³⁻³⁵

The lessons described above are likely applicable in other parts of the world.

In 2013, 53 low- and lower-middle-income countries (LLMC) — 41 AFCO, 8 SECO and 4 IBCO— collected only 24% of the global blood supply and discarded the highest proportion of RBC among all income groups.¹⁶ These nations often fail to provide adequate, equitable, consistent, safe and timely blood supplies to their populations.^{44,45} Lack of government oversight, inadequate resources and fragmented national systems are some of the factors identified as responsible for poor access to safe blood,^{46,47} which in turn leads to poor patient outcomes.^{48,49} Recognizing regional heterogeneities,⁵⁰ identifying gaps within each country, focusing attention at the local levels, and using successful experiences as models⁵¹⁻⁵⁴ have been suggested as the basis for improving transfusion safety in LLMC. **Table 6** summarizes the major health indicators for the three geographically distinct groups of countries. HHI ($p \leq 0.0023$) is highest in IBCO, while both MMR and IMR are highest ($p < 0.0001$) in AFCO. All values for SECO are intermediate. The general main causes of death are infectious in AFCO,

a mix of infectious and non-infectious in SECO, and non-infectious, including violence and road accidents, in IBCO. Understanding that the level of development of blood services depends on the general development of the health systems, it is not surprising that blood collection rates are lowest in AFCO, intermediate in SECO and highest in IBCO ($p = 0.0668$); the prevalence of viral TTI markers among donors follows the reverse pattern ($p \leq 0.0588$, **Table 6**).

Table 7 shows HHI, main causes of death, MMR, IMR, proportion of births attended by skilled personnel, blood collection rates, and the estimated RBC transfusion rates in SECO. Maldives, Thailand, and Sri Lanka have the highest HHI and are also countries with upper-middle income. The Democratic Republic of Korea and Nepal, with low income, fall in the middle of the table. HHI is inversely correlated with both MMR ($p = 0.008516$) and IMR ($p = 0.000145$), confirming that HHI is a more valid reference for health issues than national income. IMR is inversely correlated with skilled attendance at birth ($p = 0.000544$), and IMR and MMR are positively correlated ($p = 0.000672$), indicating that the level of health care determines both MMR and IMR and affects neonatal preterm mortality. “Poor outcomes” by all measures, including blood collection rates, are more likely to occur in countries with lower HHI. These rates seem to be lower than expected in at least five countries and in agreement with the assessment that SECO have an 11% deficit of blood based on the distribution of the global population.¹⁸ Reliable RBC transfusion rates could not be estimated for all countries.

Table 6. Major health indicators of Ibero-American, African and South-East Asian countries, 2013

Countries	Main causes of death	Indicator						
		Measure	HHI	Maternal mortality ratio	Infant mortality rate	Blood collection/10 000	Viral TTI makers (%)	RBC use/10 000
African	LRI, malaria, HIV, diarrhea	Median	0.597	492	48.5	50.64	7.800	49.79
		Range	0.393 0.848	42 1 360	12 96	2.44 391.66	0.35 22.62	3.18 369.36
South-East Asian	IHD, stroke, neonatal conditions, LRI	Median	0.769	166	30	90.79	0.980	86.17
		Range	0.695 0.891	21 291	9 47	18.82 184.99	0.32 6.82	16.89 180.05
Ibero-American	IHD, violence, stroke, road accidents	Median	0.843	66.6	14.6	129.35	0.835	110.40
		Range	0.727 0.992	16 229	4.2 24.8	66.52 365.52	0.34 1.82	52.26 350.53

Abbreviations: HHI, Human Health Index; TTI, transfusion-transmissible infections; RBC, red blood cells; LRI, lower respiratory infections; IHD, ischemic heart disease

Table 8 shows HHI, main causes of death, MMR, IMR, proportion of births attended by skilled personnel, blood collection rates, and the estimated RBC transfusion rates in AFCO. Cape Verde, Mauritius, and Seychelles, with HHI above 0.800, have low-medium, upper-medium and high income, respectively, and, together with upper-middle-income Algeria, show the lowest MMR and IMR of all 48 AFCO. There is no correlation between HHI and blood collection rates. The rate of RBC use correlates directly with HHI ($p=0.03108$) and inversely with both MMR ($p=0.00031$) and IMR ($p=0.00067$), supporting the idea that estimating national needs

and assessing sufficiency of blood by using blood transfusion rates is more appropriate than using collection rates. Reliable data on RBC use were available for only 29 AFCO. Skilled attendance at birth correlates inversely with IMR ($p=0.000735$), and IMR and MMR are directly correlated ($p<0.000001$). In general, “poor outcomes” on all measures are more likely to occur in the 24 countries with lower HHI ($p=0.0001$), corroborating that HHI segregates countries in a manner that facilitates understanding the relationships between national health services and local transfusion safety.

Table 7. Human Health Index, mortality, and patient care, South-East Asian countries, 2013

Country	HHI	Mortality			Patient care		
		Main causes	Maternal mortality ratio	Infant mortality rate	Skilled- attended births	Blood collection rate/10 000	RBC transfusion rate/10 000
Maldives	0.891	IHD, Congenital	70	9	100	146.75	141.41
Thailand	0.837	IHD, Stroke	21	10	99	90.79	61.77
Sri Lanka	0.835	IHD, Self-harm	32	9	100	184.99	180.05
Indonesia	0.782	Stroke, IHD	140	25	93	108.03	
Bangladesh	0.779	Stroke, IHD	201	33	50	37.68	
Dem Rep Korea	0.769	Stroke, IHD	87	18	100	40.72	39.70
Nepal	0.745	LRI, IHD	291	33	58	71.87	
Bhutan	0.743	NN preterm, IHD	166	30	89	115.89	110.57
Timor Leste	0.731	LRI, NN preterm	248	47	57	18.82	16.89
India	0.714	IHD, NN preterm	189	39	81	77.81	
Myanmar	0.695	Stroke, LRI	189	44	60	51.81	

Notes: “Poor outcomes” in relation to the median values are shaded. [redacted] : Not available. HHI/Maternal mortality ratio correlation: $r_s=-0.697$, $p=0.017032$. HHI/Infant mortality rate correlation: $r_s=-0.8859$, $p=0.000283$. Maternal mortality ratio/Infant mortality rate correlation: $r_s=0.8604$, $p=0.000672$. Infant mortality rate/skilled-attended births correlation: $r_s=-0.8664$, $p=0.000544$. HHI/collection rate correlation: $r_s=0.5364$, $p=0.04423$.

Abbreviations: HHI, Human health index; RBC, red blood cells; IHD: ischemic heart disease; NN, neonatal; LRI, lower respiratory infections.

Table 8. Human Health Index, mortality, and patient care, African countries, 2013

Country	HHI	Mortality			Patient care		
		Main causes	Maternal mortality ratio	Infant mortality rate	Skilled attended births	Blood collection rate/10 000	RBC transfusion rate/10 000
Cape Verde	0.848	LRI, Stroke	42	19	92.3	61.65	58.82
Mauritius	0.825	IHD, Diabetes	53	13	99.8	391.66	369.36
Seychelles	0.818	IHD, LRI	57	12	99.0	176.92	152.20
Algeria	0.785	IHD, NN preterm	144	22		125.43	109.69
Sao Tome & Principe	0.713	LRI, NN sepsis	156	29	92.5	48.11	41.72
Benin	0.695	Malaria, LRI	405	69	77.2	75.36	
Madagascar	0.688	LRI, Diarrhea	353	37	44.3	9.78	
Namibia	0.684	HIV, LRI	265	37	88.2	118.74	112.02
Botswana	0.683	HIV, TB	129	35	99.9	93.20	80.79
Rwanda	0.678	LRI, HIV	290	35	90.7	37.96	
Ethiopia	0.671	LRI, Diarrhea	353	48		8.14	
Gabon	0.669	HIV, Malaria	291	39		99.19	74.49
Senegal	0.668	Diarrhea, LRI	315			46.62	
Eritrea	0.659	Diarrhea, LRI	501	36	34.1	16.61	14.74
Sudan	0.647	NN preterm, congenital	311	48		50.20	
Kenya	0.642	HIV, Diarrhea	510	37		34.49	
United Republic of Tanzania	0.639	HIV, LRI	398	44	48.9	31.33	25.48
Mauritania	0.639	LRI, NN sepsis	602	58	65.1	26.79	24.20
Ghana	0.633	Malaria, LRI	319	43		58.45	49.79
Comoros	0.629	LRI, Diarrhea	335	58	82.2	33.33	29.77
Liberia	0.624	LRI, Malaria	225	63	61.1	60.60	
Zimbabwe	0.613	HIV, Diarrhea	443	45	80.0	36.96	35.65
Uganda	0.603	HIV, LRI	343	43		52.26	
Congo	0.597	HIV, Malaria	442	39	94.4	103.62	93.89
Gambia	0.597	LRI, NN sepsis	706	45	57.2	52.46	51.09
Niger	0.591	Malaria, Diarrhea	553	56	29.3	39.68	34.87
Zambia	0.586	HIV, LRI	224	48	64.2	72.59	61.99
South Africa	0.568	HIV, Violence	138	34	94.3	173.80	169.05
Togo	0.562	Malaria, HIV	368			57.40	
Burkina Faso	0.559	Malaria, LRI	371	58		57.27	43.13
Guinea	0.556	Malaria, LRI	679	64	45.3	35.34	28.81
Malawi	0.543	HIV, Malaria	634	46		34.52	18.30
South Sudan	0.543	Diarrhea, LRI	789	63	17.2	2.44	3.18
Mali	0.539	Malaria, Diarrhea	587	73	57.1	27.08	18.59
Somalia	0.539	Diarrhea, LRI	712	89		20.96	
Cameroon	0.539	HIV, Malaria	596	62	64.7	20.50	17.68
Guinea Bissau	0.528	LRI, Diarrhea	549	64	45.0	27.26	23.22
Burundi	0.525	LRI, Diarrhea	712	51		56.28	51.24
Nigeria	0.500	Malaria, Diarrhea	814	73		7.09	
Angola	0.491	LRI, Malaria	477	64	46.7	57.32	
Chad	0.480	Diarrhea, LRI	856	80	24.3	51.05	40.63
Cote D'Ivoire	0.473	Malaria, HIV	645	71		59.039	
Mozambique	0.465	HIV, Malaria	725	61	54.3	43.73	
Central African Republic	0.464	Malaria, HIV	882	96		35.30	
Democratic Rep of the Congo	0.461	Malaria, LRI	693	78	80.1	59.042	50.01
Lesotho	0.453	HIV, Diarrhea	487	72	77.9	37.24	
Eswatini	0.446	HIV, LRI	389	49	88.3	106.20	93.43
Sierra Leone	0.393	Malaria, LRI	1,360	96	59.7	61.13	58.10

Notes: "Poor outcomes" in relation to the median values are shaded. : Not available. HHI/collection rate per population, Correlation: $r_s=0.2252$, $p=0.1232$. MMR/IMR correlation: $r_s=0.8036$, $p<0.00001$. RBC use/MMR correlation: $r_s=-0.6044$, $p=0.00031$. RBC use/IMR correlation: $r_s=0.577$, $p=0.00067$. IM/Skilled-attended births correlation: $r_s=-0.5655$, $p=0.000735$. Skilled-attended births/RBC use correlation: $r_s=0.7723$, $p=0.000001$. Abbreviations: HHI, Human Health Index; RBC, Red blood cells; IHD, ischemic heart disease; NN, Neonatal; LRI: lower respiratory infections.

Table 9. Operational indicators of blood centers, South-East Asian countries, 2013

Country	Blood centers		Blood collection		Voluntary donation	Viral TTI markers	Whole blood separation
	Number	Density	N units	per center			
Indonesia	375 (321) ^a	0.1448	2 722 758	8 482	84.72	2.110	60.4
India	2 760 (2 545)	0.1990	9 949 012	3 909	85.00	1.600	60.0
Bangladesh	327	0.2075	593 774	1 816	29.64	0.976	18.7
Thailand	170	0.2495	618 675	3 639	100	0.480	96.4
Nepal	100 (86)	0.3573	201 122	2 339	87.79	0.570	25.6
Sri Lanka	90	0.4272	380 808	4 231	100	0.324	100
Maldives	2	0.5038	5 826	2 913	29.54	0.920	100
Timor Leste	6	0.5068	2 227	372	33.15	6.820	74.7
Myanmar	334 (145)	0.6491	266 540	1 838	76.86	3.210	79.5
Dem Rep Korea	188 (12)	0.7524	101 742	8 479	100	0.920	70.0
Bhutan	27	3.5340	8 854	328	63.12	1.180	50.8

Notes: ^aNumbers of blood centers which provided information “Poor outcomes” in relation to the median values are shaded.

Abbreviation: TTI, transfusion-transmissible infections.

Table 9 shows operational indicators of blood centers in SECO, with a caveat: only 6 of the 11 countries included all their centers in their reports. The BCDI shown were calculated using the number of centers that exist in the country, while the mean blood collection by center was estimated based on the number of centers included in the WHO report.¹⁷ Taking into consideration that lower BCDI regularly result in more units processed by each center, in the case of SECO a better approximation to operational efficiency may be achieved by examining the number of units collected per center in the six countries with complete data. Sri Lanka and Thailand, with the largest number of units collected per center, have 100% VBD, have the lowest prevalence of TTI markers, and separate over 95% of their units into components. Maldives, with only two centers, processes all its units into components and shows the third lowest prevalence of TTI markers despite having only 29.54% VBD. Bangladesh, Timor Leste, and Bhutan reported the highest TTI prevalence rates and the lowest separation of blood into components. Total RBC discard was estimated at 31.2% and, as a consequence, 68% of RBC collected were actually transfused. Implementing universal VBD in SECO would result in improved availability and safety of blood. Nevertheless, in order to better understand the status of transfusion safety in SECO, the first priority should be the systematic local collection, validation, and analysis of data from blood centers and hospitals. Regulation and inclusion understand the status of transfusion safety in SECO, the first priority should be the systematic local collection, validation, and analysis of data from blood centers and hospitals. Regulation and

inclusion of unbanked directed blood transfusion⁴⁷ and unlicensed blood brokers⁴⁹ requires special attention by health authorities, since they may manage up to 25% of the blood transfused in SECO.⁸⁵¹

Table 10 shows operational indicators of the blood centers in AFCO. The BCDI fluctuate between 0.0134 and 1.2072 (median 0.1173). The number of blood units processed/center annually varies from 489 in the Democratic Republic of Congo to 86,172 in South Africa. There are 7 AFCO with VBD below 20%; 17 of them collect more than 90% of their units from VBD, with 9 having universal VBD. Prevalence rates of viral TTI markers vary from 0.35 in South Africa to 22.62 in Mali. Seychelles, Mauritius, Namibia, and Algeria report viral TTI prevalence under 1.00; 16 countries find more than 10% of their donations reactive for viral TTI. Twenty-two countries prepare components from less than 50% of the units collected. Eighteen of 29 AFCO with data discard more than 10% of the RBC they prepare. It was estimated that 11.6% of the collected RBC were discarded and, as a consequence, 88% of the RBC collected during 2013 were transfused. Operational “poor outcomes” are more likely among the 24 AFCO with BCDI above the median ($p=0.0001$). Eritrea, Namibia, Eswatini, Mauritius, Sao Tome and Principe, and Seychelles have only one blood center. Countries with two centers may want to keep them both as part of a contingency plan and because of the size of territory and transportation facilities. Independent of the BCDI, understanding where, when, and how many blood components are

Table 10. Operational indicators of blood centers, African countries, 2013

Country	Blood centers		Blood collection		Voluntary donation	Viral TTI markers	Whole blood separation	Rate of RBC discard (%)
	Number	Density	N units	per center				
Tanzania	7	0.0134	163 645	23 378	84.59	6.22	23	18.67
South Sudan	2	0.0173	2 812	1 406	2.31	19.91	0	
Eritrea	1	0.0191	8 692	8 692	92.48	3.18	92.6	11.26
South Africa	11	0.0202	947 890	86 172	99.96	0.35	99.7	2.73
Malawi	4	0.0234	48 579	12 145	30.09	7.80	6.9	46.49
Nigeria	43	0.0244	125 101	2 909	42.98	8.50		
Ethiopia	25	0.0257	79 274	3 171	67.72	5.50	30.8	
Niger	5	0.0261	75 977	15 195	33.91	12.28	1.6	12.12
Togo	2	0.0277	41 488	20 774	95.35	5.35	66.4	
Zimbabwe	5	0.0324	56 958	11 392	100	1.33	95.8	31.54
Uganda	14	0.0360	202 935	14 495	100	3.64	60	
Namibia	1	0.0422	28 143	28 143	100	0.89	99.8	5.66
Sierra Leone	30	0.0423	43 273	1 442	10.00	15.27	0	4.95
Rwanda	5	0.0441	43 074	8 615	100	3.30	100	
Central African Republic	2	0.0443	11 423	5 712	98.92	17.10		
Sudan	20	0.0529	189 432	9 472	17.11	7.45		
Mali	9	0.0530	45 932	5 104	30.60	22.62	55.9	31.35
Zambia	9	0.0576	113 386	12 598	100	10.50	10.6	14.60
Burundi	7	0.0708	55 666	7 952	99.97	10.52	39.8	8.95
Eswatini	1	0.0786	13 498	13 498	100	4.63		12.02
Mauritius	1	0.0794	49 349	49,349	84.36	0.40	49.9	5.69
Cote D'Ivoire	23	0.1021	133 023	5 784	100	7.75	94.5	
Gabon	2	0.1067	18 598	9 299	68.30	6.41	97.3	24.90
Kenya	54	0.1173	158 742	2 940	100	2.32	60.7	
Senegal	21	0.1444	67 815	3 229	94.23	10.09	51.8	
Lesotho	4	0.1864	7 988	1 997	96.62	4.95	43.4	
Madagascar	47	0.1992	23 075	491	18.60	4.89	35.8	
Somalia	31	0.2294	28 330	914	35.00	4.09	0	
Burkina Faso	43	0.2445	100 716	2 342	67.55	16.74	91.4	24.69
Cameroon	55	0.2473	46 483	845	8.14	11.52	0	13.76
Botswana	6	0.2767	20 207	3 368	100	1.96	100	13.31
Guinea Bissau	5	0.2898	4 703	941	28.79	18.94	0	14.82
Mauritania	13	0.3199	10 886	837	25.21	16.86	100	9.67
Guinea	38	0.3219	41 718	1 098	11.10	11.40	0.8	18.48
Mozambique	153	0.3676	119 003	778	43.87	9.54	100	
Ghana	103	0.3820	160 295	1 556	33.00	11.50	16.6	14.82
Benin	40	0.3889	77 510	1 938	95.49	14.18		
Chad	56	0.4127	69 265	1 237	6.22	15.15	1.9	20.46
Algeria	200	0.5113	490 633	2 453	31.28	0.54	92.4	15.55
Angola	139	0.5163	154 300	1 110	14.75	7.23	10.5	
Sao Tome & Principe	1	0.5236	919	919	65.29	12.96	75.0	13.28
Congo	29	0.5954	50 472	1 740	38.54	10.38	53.8	9.39
Gambia	12	0.6260	10 057	838	21.50		0	
Comoros	5	0.6588	2 530	506	11.46	5.14	0	10.68
Liberia	40	0.9112	26 602	665	26.31		0	
Seychelles	1	1.0990	1 610	1 610	50.93	0.00*	1.1	13.97
Cape Verde	6	1.1407	3 243	540	85.17	1.81	98.9	4.59
Democratic Rep of Congo	890	1.2072	435 275	489	35.70	6.24	75.0	15.30

Notes: "Poor outcomes" in relation to the median values are shaded. : Not available. Prevalence of "poor outcomes" higher in countries with blood center density > 0.13085; $Chi^2 = 14.42, p = 0.0001$

Abbreviations: TTI, transfusion-transmissible infections; RBC, red blood cells.

needed is essential to plan adequate blood collection, preparation and delivery to hospitals before patients' medical conditions indicate transfusions. A national plan to avoid excessive discard of RBC will result in considerable financial savings.

FINAL REMARKS

Important lessons were learned from efforts to improve transfusion safety in IBCO during the last 25 years. Initial work focused on prevention of TTI. The systematic communication among national blood programs to assure valid data on TTI facilitated the establishment of a quality-controlled blood processing information system and solid collaboration among stakeholders. Delayed, deficient or lack of provision, however, called for securing timely access to blood by patients. The negative consequences of RBD as a requirement for patient treatment at hospitals became obvious. The pursuit of universal VBD was hindered by unawareness of time- and space-driven requirements for blood components at hospitals, and the preference among the public to save their blood for a relative potentially in need of RBD. Review of transfusion practices showed poor record keeping and variable patient management. It was understood that only hospital-based clinical guidelines provide a valid framework for estimating future patterns of blood needs. Blood donors were recognized as vital for achieving blood sufficiency and timely access to transfusions; therefore, nurturing donors became a central strategy. Recognizing that blood transfusion services are part of the national health system is indispensable for self-sufficiency and timely access to blood. The application of lessons learned in IBCO may allow countries of other parts of the world to improve their blood safety in the near future.

ABBREVIATIONS

AFCO: African countries. BCDI: Blood center density index. HHI: Human Health. Index. IBCO: Ibero-American countries. IMR: Infant mortality rate. LLMC: Low- and lower-middle income countries. MMR: Maternal mortality ratio. PAHO: Pan American Health Organization. RBC: Red blood cells. RBD: Replacement blood donation. SECO: South-East Asian countries. TTI: Transfusion transmissible infections. VBD: Voluntary blood donation. WHA: World Health Assembly. WHO: World Health Organization.

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DATA AVAILABILITY

Pan American Health Organization. Supply of blood for transfusion in Latin American and Caribbean countries 2012 and 2013. http://iris.paho.org/xmlui/bitstream/handle/123456789/28420/9789275118672_eng.pdf?sequence=1&isAllowed=y.

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The author was Regional Advisor on Laboratory and Blood Services (1994-2011) and Senior Advisor on Health Technologies for Quality of Care (2009-2011), Pan American Health Organization, Regional Office for the Americas, World Health Organization. He was also a member of AABB Global Standards Committee (2015-2017). He is an honorary member of Grupo Cooperativo Ibero-Americano de Medicina Transfusional (GCIAMT, 2013-present), a member of Education Committee of the African Society for Transfusion Medicine (2017-present). The author reports no other conflicts of interest in this work.

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