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IMIP – INSTITUTO DE MEDICINA INTEGRAL PROF. FERNANDO FIGUEIRA

Triagem Pré-Natal de Doença Falciforme em um Hospital no Nordeste do Brasil: resultados de 24 meses após a implantação na rotina do pré-natal.

Relatório final do PIC-FPS - período 2018-2019

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Artigo Original

Triagem Pré-Natal de Doença Falciforme em um hospital no Nordeste do Brasil: resultados de 24 meses após a implantação na rotina do pré-natal.

Prenatal screening for Sickle Cell Disease at a hospital in Northeast Brazil: Results after 24 months from implantation in the routine of prenatal care.

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Resumo

OBJETIVO: avaliar a prevalência de positividade do exame de eletroforese de hemoglobina após a implantação do exame na rotina do pré-natal. **MÉTODOS:** estudo de corte transversal, para analisar os exames de eletroforese de hemoglobina realizados entre abril/2017 e abril/2019 em gestantes durante o pré-natal no Instituto de Medicina Integral Prof. Fernando Figueira, Recife, Brasil. Os dados foram coletados dos prontuários das gestantes cujo exame de eletroforese de Hemoglobina (Hb) foram positivos. Foi realizada a análise das frequências relativa e absoluta das variáveis sociodemográficas, ginecológicas e obstétricas e a proporção de exames de eletroforese de Hb positivo para os diferentes genótipos da DF. **RESULTADOS**: a maioria das gestantes apresentou idade entre 20 e 34 anos (66,4%) e era proveniente da cidade do Recife e sua região metropolitana (66%). Pouco mais da metade (54,5%) das gestantes era acompanhada no pré-natal de alto risco e 59,8% referiram gestação anterior. A média da idade gestacional na primeira consulta de pré-natal foi de 19,9 (±7,4) semanas. A eletroforese de Hb foi normal em 1.621 (95,5%) gestantes, 53 (3,0%) apresentaram traço falciforme (TF) e 9 (0,5%) tinham DF, entre essas últimas, duas (2) eram HbSS. A média da concentração de Hb na primeira consulta do pré-natal das gestantes com resultado normal do exame de eletroforese de Hb foi 11,7 (±1,07) g/dL e das com DF 10,2 (±2,50) g/dL. **CONCLUSÃO**: a baixa positividade da eletroforese da Hb para DF durante o pré-natal sugere que a realização deste exame de forma universal no pré-natal deveria seguir critérios mais específicos e sua inclusão na rotina pré-natal deveria ser reavaliada.

Palavras–chave: Doença Falciforme; Anemia Falciforme; Doença da Hemoglobina S; Pré-Natal

Abstract

OBJECTIVE: To evaluate the prevalence of positivity of hemoglobin electrophoresis after the inclusion in the prenatal routine. METHODS: We conduct a cross-sectional study to analyze hemoglobin electrophoresis performed between April / 2017 and April / 2019 in pregnant women during prenatal care at the Institute of Integral Medicine. Fernando Figueira, Recife, Brazil. The data was collected from medical records of pregnant women whose hemoglobin (Hb) electrophoresis was positive. The analysis of the relative and absolute frequency of the sociodemographic, gynecological and obstetric variables and the proportion of positive Hb electrophoresis exams for the different DF genotypes were performed. RESULTS: Most of the pregnant women were aged between 20 and 34 years old (66.4%) and came from the city of Recife and its metropolitan region (66%). Just over half (54.5%) of pregnant women were attended at high risk prenatal care and 59.8% reported previous pregnancy. The mean gestational age at the first prenatal visit was 19.9 (± 7.4) weeks. The Hb electrophoresis was normal in 1,621 (95.5%) pregnant women, 53 (3.0%) were sickle cell trait (SCT) and 9 (0.5%), SCD. Among these latter, two (2) were HbSS. The mean Hb concentration at the first prenatal visit, the pregnant women with normal Hb electrophoresis was 11.7 (± 1.07) g/dL and those with SCD, 10.2 (± 2.50). g/dL. CONCLUSION: The low positivity of Hb electrophoresis for SCD during prenatal rotine suggests that universal prenatal examination should follow more specific criteria for SCD and its inclusion in the prenatal routine should be reevaluated.

Keywords: Sickle Cell Disease; Sickle cell anemia; Hemoglobin S disease; Prenatal

INTRODUÇÃO

A Doença Falciforme (DF) é uma doença hematológica causada por mutação genética no gene da cadeia beta da hemoglobina (Hb), que acarreta a substituição do ácido glutâmico pela valina, na posição seis dessa proteína, o que origina a HbS. Esta Hb possui características físicas que propiciam o fenômeno da falcização das hemácias, dando a estas células o formato de foice, característico da DF. A falcização leva à ocorrência de: crises álgicas, eventos tromboembólicos e hemólise.[1] Devido a estas características clínicas, a morbimortalidade dos portadores da DF é elevada.[2]

A DF é composta por vários genótipos: quando a HbS está em homozigose a outra HbS (HbSS-Anemia Falciforme) ou em heterozigose a outras hemoglobinas anômalas (como as hemoglobinas C, D e E) e outras hemoglobinopatias (alfa-talassemia e beta-talassemia). A HbSS é a forma mais prevalente e mais grave da DF. A associação da HbS com a HbA (normal) é chamada de traço falciforme (TF), sendo assintomática, mas podendo passar o gene para os descendentes[3].

A doença tem sido reconhecida pela Organização Mundial da Saúde (OMS) como um grave problema de saúde pública mundial, com grande impacto na morbimortalidade da população afetada[4]. É predominante entre negros e afrodescendentes e, no Brasil, a incidência é de 1 para cada 1.000 nascidos vivos com DF e 1 para cada 35 com o TF[5]. A distribuição da DF é heterogênea no Brasil, sendo a região Nordeste a que apresenta maior prevalência (10%), ao passo que, no Sul e no Sudeste, esta taxa é de 2% a 3%. Pernambuco ocupa o 3º lugar no país em número de casos/ano, sendo 1 para cada 1.400 de DF e 1 para cada 23 do TF[3].

Devido à gravidade da DF e a alta prevalência no Brasil, a triagem de DF foi incluída no Programa Nacional de Triagem Neonatal (PNTN), no "teste do pezinho", em 2001, através da Portaria nº 822/2001[6]. O diagnóstico precoce é obtido na primeira semana de vida, por meio do exame de "eletroforese da hemoglobina", com metodologia específica através da detecção da HbS associada às suas frações. Com a detecção precoce, medidas de acompanhamento podem ser instituídas nos primeiros anos de vida, tais como: profilaxia antibiótica com penicilina, imunização contra bactéria encapsulada, assistência multidisciplinar e uso de hidroxiuréia, que são de grande importância na redução da morbimortalidade da DF[7].

Visando identificar os casos de DF em mulheres que não passaram pela triagem neonatal, o Ministério da Saúde (MS) do Brasil incluiu a eletroforese de Hb como exame básico de rotina no pré-natal para todas as gestantes em 2011[8]. Posteriormente,

em 2013, o MS emitiu a Nota Técnica de Detecção de Doença Falciforme no Pré-Natal para reiterar a realização do exame como rotina[7].

Este diagnóstico por meio da triagem durante o pré-natal visa oferecer completa assistência pré-natal às pessoas com DF, bem como minimizar o risco de morbimortalidade nesse grupo de gestantes, permitindo o encaminhamento para um serviço especializado em gestação de alto risco[5]. Deste modo, o objetivo do estudo foi avaliar a prevalência de positividade do exame de eletroforese de hemoglobina durante o acompanhamento pré-natal em gestantes atendidas em um hospital escola, situado em Recife, após sua implantação na rotina do pré-natal.

MÉTODO

Foi realizado um estudo de corte transversal no Centro de Atenção à Mulher do Instituto de Medicina Integral Prof. Fernando Figueira (IMIP), localizado em Recife, Pernambuco, hospital de referência na região e que oferece à população atendimento de pré-natal de baixo e alto risco.

A coleta dos dados foi realizada entre setembro de 2018 e maio de 2019, por meio da identificação no sistema eletrônico do laboratório de análises clínicas, de todos os exames de eletroforese de Hb que foram realizados em gestantes entre os meses de abril de 2017 a abril de 2019. Após esta seleção, os prontuários foram resgatados e aqueles cujo exame tenha sido solicitado durante a consulta pré-natal no serviço foram incluídos no estudo, o que totalizou 1.854 exames. Houve 63 pacientes que haviam realizado dois exames de eletroforese de Hb, sendo então considerado para o estudo apenas um dos exames, resultando em 1.791 exames para análise.

Foram coletados dos prontuários dados sociodemográficos, obstétricos e laboratoriais das gestantes em um formulário e, em seguida, construído um banco de dados no programa Excel. A análise dos dados foi realizada através do programa Stata versão 12. Foram realizadas análises das frequências relativa e absoluta das variáveis sociodemográficas, obstétricas e do resultado da concentração de Hb e da eletroforese da Hb. A associação entre a cor/raça e resultado das eletroforeses de Hb foi avaliada pelo teste quiquadrado de Pearson. A comparação das médias das concentrações de Hb entre as gestantes com exame de eletroforese normal e os diferentes resultados alterados foi realizada através dos testes ANOVA e o teste de comparação múltiplas de Sidak. Foi considerado nível de significância de 5% para todos os testes. O estudo foi iniciado após aprovação pelo Comitê de Ética em Pesquisa do IMIP (CAAE: 78301317.5.0000.5201).

RESULTADOS

Foram encontrados registros de 1.854 exames de eletroforeses de Hb realizados durante o pré-natal, entretanto, em 63 gestantes, o exame havia sido solicitado duas vezes, resultando em exames de 1.791 gestantes.

A média de idade das gestantes foi de 27,2 (± 6,9) anos. A maioria era negra/parda (68,8%), procedente de Recife e de sua Região Metropolitana (66,2%) e possuíam companheiro (68,8%). (Tabela 1).

Em relação às características obstétricas, 54,5% das gestantes estavam sendo acompanhadas em pré-natal de alto risco. A maioria das pacientes já havia engravidado anteriormente (59,8%). A média da idade gestacional na 1ª consulta do pré-natal foi de 19,9 (±7,4) semanas, considerando a data da última menstruação registrada no prontuário. (Tabela 2)

O exame de eletroforese de Hb foi considerado normal em 1.710 (95,5%) gestantes e o TF foi encontrado em 53 (3,0%). Em relação ao resultado compatível com DF, foram encontradas 9 (0,5%) gestantes, sendo que duas eram do genótipo HbSS, uma era HbSC e outras seis possuíam outros genótipos da DF ou outras hemoglobinopatias (Gráfico 1).

Considerando o subgrupo das 1.232 gestantes pardas ou negras, 50 (4,2%) tinham a presença da HbS no exame de eletroforese (7 com DF e 43 com TF). Já no subgrupo das 457 gestantes de outras raças, 12 (2,6%) possuíam HbS no exame. Ao realizar o teste de associação entre cor da pele e resultado da eletroforese, não houve diferença entre os grupos (p=0,107). (Tabelas 3 e 4).

A média da concentração de Hb de todas as mulheres avaliadas foi 11,7 (±1,2) g/dL. Quando avaliado por grupo de resultado da eletroforese, nas gestantes que apresentaram resultado da eletroforese normal, a média da concentração da Hb foi 11,7 (±1,1) g/dL, naquelas com TF foi 11,7 (±1,5) g/dL, e nas gestantes com eletroforese compatível com DF, a média da Hb foi 10,2 (±2,5) g/dL. Houve diferença estatística entre as médias destas Hb (p=0,011) (Tabela 5).

DISCUSSÃO

Neste estudo, a maioria das gestantes era jovem, de cor negra/parda, procedente do Recife ou RMR, possuía companheiro e tinha história prévia de gestação. Pouco mais da metade fazia pré-natal de alto risco. Considerando toda a amostra, as gestantes iniciaram o pré-natal no 2º trimestre e possuíam média de concentração de Hb dentro

dos valores considerados normais para gestante. A maioria tinha eletroforese de Hb normal e apenas nove gestantes tinham DF.

Os achados sociodemográficos encontrados neste estudo são semelhantes aos encontrados na Pesquisa Nacional por Amostra de Domicílios (PNAD-2006), em que a maioria das gestantes da região nordeste tinha idade entre 20 e 34 anos, possuía história de gestação anterior, vivia com companheiro e se autodeclarava de cor/raça negra ou parda[9]. Este fato corrobora a ideia de que a população estudada é representativa da população da região nordeste.

Neste estudo, a primeira consulta de pré-natal foi realizada principalmente no segundo trimestre da gestação (média de Idade Gestacional foi 19,9 [±7,4] semanas), diferente do achado do PNDS, onde aproximadamente 80% das pacientes começaram o pré-natal no primeiro trimestre[9]. Tal diferença pode ser justificada pelo fato de que o presente estudo foi realizado em hospital terciário, para onde as pacientes são referenciadas das unidades básicas de saúde, e o tempo decorrido neste processo.

A média da concentração de Hb (11,7 g/dL) encontrada neste grupo de gestante foi compatível com um estudo realizado com dados das cinco regiões do Brasil, cujo resultado da concentração de Hb durante o 2º trimestre da gestação foi em torno de 11,8 g/dL, considerando as pacientes que não recebem suplementação de ferro.[10] Desta forma, as gestantes não apresentavam níveis compatíveis com anemia, levando-se em consideração o valor de referência da OMS.[11] Vale salientar que, no nosso serviço, a suplementação de ferro só é realizada caso a paciente apresente Hb menor do que 11g/dL.

O resultado do exame de eletroforese foi normal na quase totalidade das pacientes, enquanto em cerca de 3% foi compatível com TF. Apenas 9 (0,5%) resultados foram compatíveis com DF. Estes resultados se assemelham com os de um estudo realizado no nordeste do Brasil em recém-nascidos[12], entre 1996 e 1997, que mostrou que 94,1% dos pacientes possuíam padrão eletroforético normal, 5% eram compatíveis com TF e 0,15% possuíam DF.

A maioria das gestantes com TF ou DF eram negras/pardas, porém, não houve diferença estatística quando comparadas a outras raças. Essa divergência entre os resultados do presente estudo com o que já está bem estabelecido na literatura, em que há uma forte associação da DF com a raça negra, [4,13] deve-se, provavelmente, ao fato de que, no Brasil, a raça/cor é autodeclarada, o que pode resultar em falhas na classificação.

A média do valor da concentração de hemoglobina nas pacientes com DF foi mais baixa e compatível com o valor da hemoglobina de pacientes com DF em outros

estudos,[14] (entre 8 e 10 g/dL), o que evidencia a presença da anemia hemolítica característica da doença.

Entre as limitações do estudo, salienta-se o fato de ter sido um estudo de análise de prontuário, o que pode acarretar falta de alguns dados. Além disso, as análises ficam restritas aos dados registrados. Neste estudo, teve-se acesso à informação de que, das quatro pacientes com as formas mais graves da DF, duas já tinham o diagnóstico prévio da doença; já das outras duas não foi possível obter esta informação.

CONCLUSÃO

Neste estudo, a frequência de positividade da DF nos dois primeiros anos de implantação do exame de eletroforese da Hb na rotina do pré-natal foi baixa.

Diante disso, sugere-se que a realização do exame de eletroforese da Hb de forma universal, como rotina de pré-natal, deve seguir critérios melhor definidos e sua inclusão na rotina no pré-natal deve ser reavaliada.

Conflito de interesse:
Os autores declaram não haver conflito de interesse.

REFERÊNCIAS

1. Galiza Neto GC De, Pitombeira MDS. *Aspectos moleculares da anemia falciforme*. J Bras Patol e Med Lab. 2003;39(1):51-56.

2. Martins PRJ, Moraes-Souza H, Silveira TB. *Morbimortalidade em doença falciforme*. Rev Bras Hematol Hemoter. 2010;32(5):378-383.

3. Anvisa. *Manual de Diagnótico E Tratamento de Doenças Falciformes*. Vol 1.; 2002.

4. Modell B, Darlison M. *Global epidemiology of haemoglobin disorders and derived service indicators*. Bull World Health Organ. 2008;86(6):480-487.

5. Ministério da Sáude do Brasil. *Doença Falciforme Atenção Integral À Saúde Das Mulheres*. Brasilía; 2015.

6. Ministério da Sáude do Brasil. *TRIAGEM NEONATAL Manual de Normas Técnicas E Rotinas Operacionais Do Programa Nacional de Triagem Neonatal*. 1ª. Brasília; 2002.

7. Ministério da Saúde. Nota técnica: Detecção de Doença Falciforme no pré-natal. 2013:1-5.

8. Coordenação Geral de Sangue e Hemoderivados, Departamento de Atenção Especializada, Ministério da Saúde do Brasil. Nota técnica no 035/2011 Inserção da Eletroforese de hemoglobina nos exames de Pré-natal - Rede Cegonha. Brasília; 2011.

9. Ministério da Saúde. *PNDS 2006 - Pesquisa Nacional de Demografia e Saúde da Criança e da Mulher*. Brasília; 2008.

10. Sato APS, Fujimori E, Szarfarc SC. *Hemoglobin curves during pregnancy before and after fortification of flours with iron*. Rev da Esc Enferm da USP. 2014;48(3):409–14.

11. World Health Organization (WHO). *Iron deficiency anaemia: assessment, preventing, and control*. A Guide for Programme Managers. Geneva: WHO; 2001.

12. Bandeira FMGC, Leal MC, Souza RR, Furtado VC, Gomes YM, Marques NM. *Hemoglobin S positice newborn detected by cord blood and its characteristics.* Jornal de Pediatria vol. 75, nº3. Sociedade Brasileira de Pediatria; 1999.

13. Vichinsky EP, Mahoney DH. *Diagnosis of sickle cell disorders*. UpToDate. www.uptodate.com. Published 2018. Accessed May 15, 2018.

14. West MS, Wethers D, Smith J, Steinberg M. *Laboratory profile of sickle cell disease: a cross-sectional analysis*. The Cooperative Study of Sickle Cell Disease. J Clin Epidemiol 1992; 45:893.

Tabela 1: Características sociodemográficas de gestantes que realizaram exame de eletroforese de hemoglobina na rotina de pré-natal, entre abril de 2017 e abril de 2019, IMIP, Recife.

Variáveis	**N=1791**	**%**
I*dade*: média (DP) 27,2 (± 6,9) anos		
11-19 anos	260	14,5
20-34 anos	1190	66,4
35-40 anos	246	13,7
Acima de 40 anos	51	2,8
Sem informação	43	2,4
Raça/cor		
Negra/parda	1232	68,8
Outras	469	26,2
Sem informação	90	5,0
Procedência		
Recife	775	43,3
RMR	410	22,9
Interior do estado	404	22,6
Outros estados	99	5,5
Sem informação	103	5,8
Situação conjugal		
Solteira	468	26,1
Casada/união consensual	1233	68,8
Divorciada/viúva	21	1,2
Sem informação	67	3,7

Fonte: IMIP 2017/2019

Tabela 2: Características obstétricas de gestantes que realizaram exame de eletroforese de hemoglobina na rotina de pré-natal, entre abril de 2017 e abril de 2019, IMIP, Recife.

Variáveis	**N=1791**	**%**
Pré-natal de alto risco		
Sim	976	54,5
Não	746	41,7
Sem informação	69	3,9
Gestação anterior		
Sim	1070	59,8
Não	689	38,5
Sem informação	31	1,7
Número de gestações anteriores		
0	689	38,5
1	505	28,2
2 ou mais	565	31,6
Sem informação	31	1,7
Idade gestacional na 1ª consulta de pré-natal: média±DP = 19,9 (± 7,41) sem		
Até 14 semanas	343	19,1
15-28 semanas	746	41,7
Acima 28 semanas	183	10,2
Sem informações da DUM*, dela paciente	364	20,3
Sem informação no prontuário	155	8,7

Fonte: IMIP 2017/2019
*DUM = data da última menstruação.

Tabela 3: Associação entre cor da pele e presença de HbS entre gestantes que realizaram exame de eletroforese de hemoglobina na rotina de pré-natal, entre abril de 2017 e abril de 2019, IMIP, Recife

Cor da pele	**Eletroforese de Hb**		Teste quiquadrado de Pearson (Valor de p)
	Ausência de HbS N (%)	Presença de HbS N (%)	
Negra/Parda	1.180 (95,8)	52 (4,2)	0,107
Outras	457 (97,4)	12 (2,6)	

Fonte: IMIP 2017/2019

Tabela 4: Associação entre cor da pele e resultado de eletroforese de Hb de gestantes que realizaram exame de eletroforese de hemoglobina na rotina de pré-natal, entre abril de 2017 e abril de 2019, IMIP, Recife

Cor da pele	**Resultado da eletroforese de Hb**				Teste quiquadrado de Pearson (valor de p)
	Normal	DF	TF	Outras hemoglobinopatias	
Negra/Parda	1166 (94,6)	7 (0,6)	43 (3,5)	16 (1,3)	
Outras	455 (97)	2 (0,4)	10 (2,2)	2 (0,4)	**0,188**
Total	**1621 (95,3)**	**9 (0,5)**	**53 (3,1)**	**18 (1,1)**	

Fonte: IMIP 2017/2019

Tabela 5: Comparação dos valores da concentração da Hb entre as gestantes que realizaram exame de eletroforese de hemoglobina na rotina de pré-natal, por grupo e na amostra total, entre abril de 2017 e abril de 2019, IMIP, Recife.

Concentração de Hb (g/dL)	**Eletroforese de Hb**				Todas os grupos juntos	Teste Sidak (valor de p)
	Normal[a]	TF	DF[a]	Outros resultados		
	11,7 (±1,1)	11,7 (±1,5)	10,2 (±2,5)	11,3 (±1,2)	11,7 (±1,2	***p=0,011***

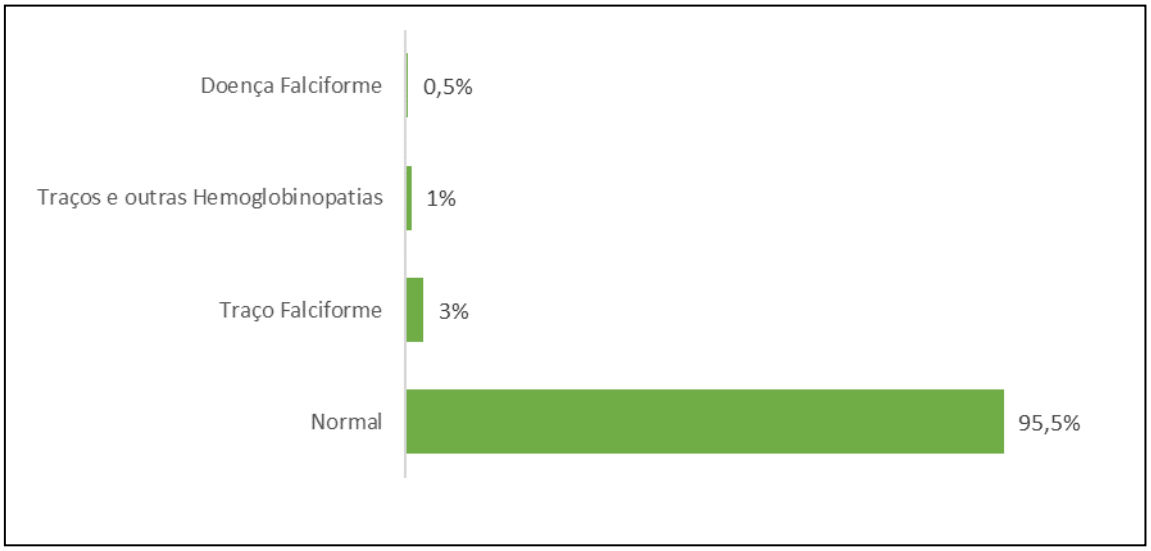

Gráfico 1: Resultado da Eletroforese de Hb entre gestantes que realizaram exame de eletroforese de hemoglobina na rotina de pré-natal, entre abril de 2017 e abril de 2019, IMIP, Recife.

HEMATOLOGY, TRANSFUSION AND CELL THERAPY

AUTHOR INFORMATION PACK

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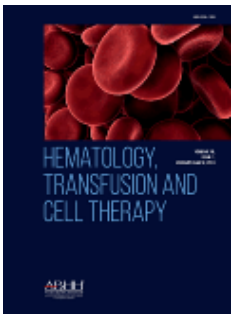

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DESCRIPTION

Hematology, Transfusion and Cell Therapy is a quarterly scientific publication of the Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular (ABHH), Sociedade Brasileira de Transplante de Medula Óssea (SBTMO), Associazione Italo-Brasiliana di Ematologia (AIBE), and Sociedade Brasileira de Oncologia Pediátrica (SOBOPE).

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Hematology, Transfusion and Cell Therapy, the official scientific publication of the Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular, aims to promote scientific development in Hematology, Transfusion Medicine and related areas. All manuscripts, after initial acceptance by the editors, will be sent for analysis by two peer reviewers. Anonymity is guaranteed throughout the evaluation process. When considered necessary, a list of modifications will be sent to authors to correct their work or justify their decision not to do so.

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