REVISTA BRASILEIRA DE
HEMATOLOGIA E HEMOTERAPIA

Article / Artigo

Clinical evaluation of the paleness: agreement between observers and comparison with hemoglobin levels

Rosemeri Maurici da Silva[1]
Carlos Alexandre Machado[2]

Introduction: Pallor is characterized by discoloring of the skin and mucous membranes due to a reduction in the amount of circulating hemoglobin. The objective of this study was to compare the degree of pallor, stratified using crosses, with hemoglobin levels and to evaluate the correlation between observers. Method: From February to April 2009, an observational cross-sectional study was carried out of over 18-year-old individuals admitted to a hospital in the south of the state of Santa Catarina, for whom the measurement of hemoglobin levels had been requested. The degree of Pallor (from absent to ++++/4) of the ocular mucosa of 96 patients was evaluated by two types of examiners (physicians and medical students). The Kappa agreement index was used to assess the agreement between observers. Results: All patients (45.8% male and 54.2% female) were Caucasian with a mean age of 57.7 years. There were statistically significant differences on comparing the mean hemoglobin levels with pallor for the medical students but no significant differences were seen for the physicians. The Kappa agreement index between the observers was low. This research demonstrates that the agreement between the observers was not good in the evaluation of pallor. The most reliable evaluation regarding the hemoglobin levels was by the physicians.

Keywords: *Pallor; Hemoglobin/analysis; Anemia/diagnosis; Physical examination; Conjunctiva/pathology; Observer variation*

Introduction

Anemia is a condition that occurs due to a reduction in the amount of circulating red blood cells in the blood, or due to a reduction of the hemoglobin below specific levels. It is defined as a hemoglobin concentration below the 95th percentile of healthy reference populations. Anemia is a condition that occurs because of different situations such as significant blood loss, excessive blood cell destruction, or reduced production of hemoglobin.[1]

Iron deficiency anemia is the most common type of anemia worldwide however there are other types of nutritional anemia, such as those of vitamin B12, folate and vitamin A deficiency.[2] A drop in hemoglobin by blood loss may result from menstruation, severe infections such as tuberculosis, malaria, HIV and parasitic infestations, among others.[3]

Anemia, according to the World Health Organization (WHO), is defined as a hemoglobin level below 13.0 g/dL for men, 12.0 g/dL for non-pregnant women and 11.0 g/dL for pregnant women and it should be considered when below 11.0 g/dL for 6- to 60-month-old infants, 11.5 g/dL for 5- to 12-year-old children, and 12 g/dL for 12- to 15-year-old adolescents.[4]

Universidade do Sul de Santa Catarina – Unisul, Tubarão (SC), Brazil

[1] *Health Sciences Post Graduation Course, Universidade do Sul de Santa Catarina – Unisul, Tubarão (SC), Brazil*
[2] *Academic Medical School, Universidade do Sul de Santa Catarina – Unisul, Tubarão (SC), Brazil*

Conflict of interest: none

Submitted: 5/6/2010
Accepted: 9/24/2010

Correspondence: *Rosemeri Maurici da Silva*
Rodovia Virgílio Várzea, 2236, Residencial Villa Vernazza, Apto 601, Bloco A – Saco Grande
88032001 – Florianópolis (SC), Brazil
E-mail: rosemaurici@hotmail.com

This condition affects around 1.6 billion people worldwide, that is, almost 25% of the population. It affects preschool children and, to a lesser extent, men, with 50% of this prevalence being due to iron deficiency anemia. However, the largest group of affected individuals is that of non-pregnant women, with about 470 million cases. According to WHO, between 40% and 50% of adult women and children in the world have anemia.[5,6]

A study carried out in Criciúma, in the state of Santa Catarina, showed that, according to WHO criteria, the prevalence of anemia among boys of 36 months old and younger was 50% and for girls of the same age it was 58%; anemia was less prevalent among white children. The total family income and father's education were associated to the prevalence of anemia in children.[7]

Anemia is a condition that is manifested by several signs and symptoms. It may present with fatigue, palpitations, astenia and sleepiness, but also with pallor, the main finding in the physical examination.[8] It is important to be aware of information attained during the medical history, physical examination and laboratory findings, as this set of data is needed for an accurate diagnosis of anemia.[9]

Pallor is characterized a lack of color of the skin and mucous membranes due to a low amount of circulating hemoglobin. It affects the entire body but it is best observed in places where blood vessels are close to the surface, such as the palms, nail beds and mucous membranes. When anemia is present, it should be quantified. The most common method is by assigning crosses to graduate pallor: from +/4 (the slightest pallor to be perceived) to ++++/4 (the most intense pallor).[8] Remember that pallor begins to be apparent to the examiner's eye at hemoglobin levels of below 9 g/dL.[10]

Several studies evaluating the accuracy of the diagnosis of anemia in physical examinations performed by physicians, medical students and residents, showed no significant difference among examiners, but also showed that the exam was not accurate when anemia is mild or moderate.[10-12]

According to some authors, to evaluate mild to moderate anemia, the method of estimating the level of hemoglobin is more accurate than the method of assigning crosses.[11]

Several anatomical sites should be evaluated to estimate pallor, and, when identified in one, anemia should be suspected, thereby maximizing the accuracy of the test.[12] Pallor of the conjunctiva is the most accurate in the case of beta thalassemia with good sensitivity and specificity, regardless of age and gender.[13] It is well known that both palmar pallor and conjunctival pallor are not very sensitive for anemia, and there is a low interobserver reliability. Palmar pallor has less sensitivity compared to conjunctiva pallor.[14] Clinical evaluation of the signs become more sensitive as the degree of anemia increases, so the absence of pallor at physical examination does not totally rule out this condition.[10]

Knowing that anemia is highly prevalent worldwide and affects people of all ages, genders, races and nationalities, that there are restrictions in some centers to do laboratory tests to detect anemia in all patients, and that most of the studies related to the symptomatic evaluation of anemia were performed in children, it is important to carry out a study in adults on the usefulness of this evaluation, which is simple and inexpensive.

Methods

A cross-sectional observational study was performed in the period from February to April 2009 of 98 over 18-year-old individuals for whom measurements of hematocrit (Ht) and hemoglobin (Hb) were requested on admission. All patients were admitted to a hospital in the south of the state of Santa Catarina, Brazil.

Study participants were enrolled and assessed under artificial light within 24 hours of admission by a student from the ninth semester of the undergraduate medical course, and a resident physician with training or physician. Without knowledge of the laboratory levels of Hb and Ht-, the evaluators noted their opinions on a questionnaire provided by the researchers. All patients gave their informed consent at enrolment. The presence or absence of conjunctival pallor was evaluated and when identified, quantification was made by the allocation of crosses (+/4 to ++++/4).

The exclusion criteria were refusal to sign the consent form, the impossibility of evaluations within 24 hours of admission and transfusions during this period.

The technique of cyanomethemoglobin was used to measure the level of hemoglobin, and an automated technique was employed to determine hematocrit levels both in an ABX 60 ® apparatus.

The research data were stored in a database and analyzed using the SPSS 16.0 ® computer program. Data were summarized as percentages or means as indicated. The degree of agreement between observers was assessed using the Kappa index, with values greater than or equal to 0.75 accepted as satisfactory. The differences between hemoglobin serum levels and pallor stratified using the cross system were evaluated with significance set at 95%.[15]

The research project was approved by the Ethics Committee on Human Research (ID# 08.511.4.01.III).

Results

A total of 98 consecutive Caucasian patients were considered for this study however two were excluded as they had been submitted to blood transfusions within 24 hours

after admission and so the study sample consisted of 96 individuals.

The average age of participants was 57.7 years [standard deviation (SD) ± 17.5] with a minimum age of 18 and maximum of 90 years old.

Forty-four (45.8%) patients were male and 52 (54.2%) were female.

The mean hemoglobin (Hb) serum level was 11.6 g/dL (SD ± 2.1 g/dL) with a minimum of 7.4 g/dL and a maximum of 17.7 g/dL.

The hematocrit (Ht) concentration ranged between 22.6% and 54.8% with a mean of was 35.4% (SD ± 6.5%).

According to physicians, 45 (46.9%) individuals were pallid and 51 (53.1%) were not. However according to the medical students, 52 (54.2%) individuals were pallid and 44 (45.8%) were not.

Table 1 shows the evaluation of patients using the crosses system according to the physicians and medical students.

Table 2 shows the evaluation of pallor (presence or absence) among physicians and medical students. The Kappa index of 0.4 was considered low.

Table 1. Classification of pallor in crosses according to physicians and medical students

Crosses	Physicians		Students	
	n	(%)	n	(%)
0	51	(53.1)	44	(45.8)
1	20	(20.8)	27	(28.1)
2	20	(20.8)	16	(16.7)
3	4	(4.2)	8	(8.3)
4	1	(1.1)	1	(1.1)
Total	96	(100)	96	(100)

Table 2. Concordance of classification of pallor in crosses according to physicians and medical students

Classification of pallor by physicians (crosses)	Classification of pallor by students (crosses)					
	0	1	2	3	4	Total
0	33	12	3	3	0	51
1	7	7	4	2	0	20
2	4	8	5	3	0	20
3	0	0	4	0	0	4
4	0	0	0	0	1	1
Total	44	27	16	8	1	96

Table 3 shows the correlation of the classification of pallor using crosses by physicians and medical students; the Kappa index was 0.2.

The hemoglobin and hematocrit levels of patients with respect to the stratification of patients by the physicians using crosses are shown in Table 3. A statistically significant difference ($p < 0.05$) was identified between the numbers of anemic and non-anemic patients in respect to the classification of physicians using crosses and hemoglobin and hematocrit levels.

Table 3. Hemoglobin and hematocrit levels of patients grouped by classification by crosses by physicians

Classification of pallor by physicians (crosses)	Hemoglobin (mean ± SD*)	Hematocrit (mean ± SD)
0	12.78 ± 1.73	39.11 ± 5.38
1	10.99 ± 1.56	33.56 ± 4.53
2	9.68 ± 1.45	29.61 ± 4.35
3	8.97 ± 1.33	26.58 ± 2.27

* SD = standard deviation

Table 4. Hemoglobin and hematocrit levels of patients grouped by classification by crosses by students

Classification of pallor by students (crosses)	Hemoglobin (mean ± SD *)	Hematocrit (mean ± SD)
0	12.39 ± 2.23	37.72 ± 6.87
1	11.04 ± 1.62	33.85 ± 5.09
2	10.31 ± 1.78	31.62 ± 5.73
3	11.6 ± 2.11	35.62 ± 5.85

* SD = standard deviation

The hemoglobin and hematocrit levels of patients in relation to the stratification of pallor by the students are shown in Table 4. There was no statistically significant difference ($p > 0.05$) between the numbers of anemic and non-anemic patients in respect to the level of pallor assigned by students using crosses compared to the hemoglobin and hematocrit levels.

Discussion

The study sample consisted of 18- and 90-year-old Caucasian patients, with a slight predominance of women (54.2%). There are no published data that attribute greater difficulty when assessing men or women in respect to pallor or in respect to different ages. In fact these demographic characteristics can not be attributed to any interference in the results shown here.

The ideal conditions to examine skin color are during the day in natural light and without direct illumination on the skin.[8] This study aimed at evaluating patients in the normal working conditions of physicians in the service in which the survey was conducted, i.e., artificial fluorescent light and during any time of day, both morning and night. This means the results are applicable to the daily medical practice, making them reproducible in other situations. Moreover, both categories, physicians and medical students, assessed the same patients under the same

conditions, thus making the difficulties equal and reducing diagnostic bias and not interfering in the inter-rater agreement. The conditions to evaluate pallor were not the primary objective of this work, but the degree of agreement among observers.

According to several authors, there is no homogeneity as to the regions of the body to be examined for pallor, nor a 'best site' to investigate.[14,16-20] For some authors, conjunctival pallor has greater sensitivity to palmar pallor.[14] Combined palmar and conjunctival pallor had a sensitivity of 74.3% to detect anemia defined as hemoglobin below 9 g/dL; pallor is not a good method to detect mild anemia.[10] Studies say that conjunctival pallor has a high sensitivity of 72.5% to detect moderate to severe anemia in children.[17] In the current study, we used only one place to evaluate pallor, as the objective was to correlate this with Hb and Ht levels and not to reflect on which is the best place to assess pallor. The conjunctiva was chosen to evaluate pallor categorized using crosses (from 0 to ++++/4). For the examiners (physicians and medical students), the most frequent response was zero, that is, no pallor.

For medical students, Hb levels were not correlated with the number of crosses, that is, the lowest Hb levels were not consistent with a greatest number of crosses. As for the physicians, there was a significant correlation between the Hb value and the number of allocated crosses, indicating a better accuracy in the assessment by the physicians. A study carried out at Hospital das Clinicas in Sao Paulo, 14 medical students and physicians were randomly selected to assess pallor in five hospitalized patients who had moderate to severe anemia at the time of the examination. The examiners had to estimate the Hb level of the patient and to stratify pallor using crosses; it was seen that the examiner's experience is not so important in the evaluation of anemia by clinical examination.[10] This result differs from the current study, in which physicians, with more experience in the clinical practice, had better results than medical students. A positive correlation was observed between the mean Hb level and categorization by crosses according to physicians suggesting some improvement in the diagnostic skill over time.

In another study of thirty patients admitted and assessed by a fifth-year medical student and by a physician to detect anemia by palmar, conjunctiva and nail bed pallor, no relationship was found between the sites evaluated (the presence or absence was stratified by crosses) with Ht and Hb values. Nor was it verified whether the evaluation of anemia by clinical examination [16] makes the experience more precise.

Final considerations

The results of this study showed there was a significant difference in the evaluation of anemia by conjunctival pallor of patients by physicians compared to medical students, who have little experience in semiological examinations. It is estimated from these data that the length of experience of physicians, who use conjunctival pallor as a method to identify anemia, significantly influences the validity of the diagnosis and for professionals with greater clinical experience the results tend to be more accurate.

Resumo

Introdução: A palidez é caracterizada pelo descoramento da pele e mucosas, decorrente da pouca quantidade de hemoglobina circulante. Objetivo: O objetivo é comparar o grau de palidez, estratificada em cruzes, com os níveis séricos de hemoglobina, e avaliar o grau de concordância entre observadores. Métodos: Foram avaliados, no período de fevereiro a abril de 2009, por meio de estudo transversal observacional, os indivíduos com idade superior a 18 anos internados em um hospital no sul do estado de Santa Catarina, para os quais haviam sido solicitadas dosagens de hemoglobina. Os pacientes foram avaliados por dois observadores (médicos e estudantes de medicina) quanto à presença e grau de palidez (de ausente a ++++/4) na conjuntiva ocular. O índice de concordância Kappa foi utilizado para avaliar a concordância entre observadores. Foram avaliados 96 pacientes, caucasianos, com idade média de 57,7 anos, sendo 45,8% do gênero masculino e 54,2% do gênero feminino. Resultados: A comparação entre os níveis médios de hemoglobina com a palidez graduada em cruzes não apresentou diferença estatisticamente significativa para os profissionais medicos, sendo a diferença significativa para os estudantes de medicina. O índice de concordância Kappa entre os observadores foi baixo. Conclusão: Esta pesquisa demonstrou que não houve boa concordância entre os observadores na avaliação de palidez estratificada em cruzes, sendo a avaliação mais fidedigna com relação aos níveis séricos de hemoglobina entre os profissionais médicos.

Descritores: *Palidez; Hemoglobina/análise; Anemia/diagnóstico; Exame físico; Conjuntiva/patologia; Variações dependentes do observador*

References

1. Mahan LK, Escott-Stump SK. Alimentos, nutrição e dietoterapia. 11a ed. São Paulo: Roca; 2005.
2. Comité Nacional de Hematología. [Iron deficiency anemia. Guideline for diagnosis and treatment]. Arch Argent Pediatr. 2009; 107(4):353-61. Spanish.
3. Zago MA, Falcão RP, Pasquini R. Hematologia: fundamentos e prática. São Paulo: Atheneu; 2004.
4. World Health Organization. Prevention and control of iron deficiency anaemia in women and children. Geneva: WHO/ UNICEF; 2001.
5. World Health Organization. Worldwide prevalence of anaemia 1993-2005. WHO global database on anaemia [Internet]. Geneva: WHO/ CDC; 2008. [cited 2010 Aug 24]. Available from: http:// whqlibdoc.who.int/publications/2008/9789241596657_eng.pdf
6. Organización Mundial de la Salud. La anemia como centro de atención. Hacia un enfoque integrado para el control eficaz de la

anemia [Internet]. Geneva: OMS/UNICEF; 2005. [cited 2009 Sep 15]. Available from: http://www.paho.org/Spanish/AD/FCH/NU/OMS04_Anemia.pdf

7. Neuman NA, Tanaka OY, Szarfarc SC, Guimarães PR, Victora CG. [Prevalence and risk factors for anemia in Southern Brazil]. Rev Saúde Pública. 2000;34(1):56-63. Portuguese.
8. Porto CC. Exame clínico. 5a ed. Rio de Janeiro: Guanabara Koogan; 2004.
9. Goldman L, Ausiello D, editores. Tratado de medicina interna. 2a ed. São Paulo: Saunders Elsevier; 2004.
10. Leal LP, Osório MM. Validação e reprodutibilidade de sinais clínicos no diagnóstico de anemia em crianças. Cad Saude Pública [Internet] 2005 [citado 2008 Jul 21];21(2):565-72. Disponível em: http://www.scielosp.org/pdf/csp/v21n2/23.pdf
11. Benseñor IM, Calich AL, Brunoni AR, Espírito-Santo FF, Mancini RL, Drager LF, et al. Accuracy of anemia diagnosis by physical examination. São Paulo Med J. 2007;125(3):170-3.
12. Stoltzfus RJ, Edward-Rai A, Dreyfuss ML, Albonico M, Montresor A, Dhoj Thapa M, et al. Clinical pallor is useful to detect severe anemia in population where anemia is prevalent and severe. J Nutr. 1999;129(9):1675-81.
13. Yalçin SS, Unal S, Gümrük F, Yurdakök K.The validity of pallor as a clinical sign of anemia in cases with beta-thalassemia. Turk J Pediatr. 2007;49(4):408-12.
14. Spinelli MG, Souza JM, Souza SB, Sesoko EH. Confiabilidade e validade da palidez palmar e de conjuntivas como triagem de anemia. Rev Saúde Pública [Internet]. 2003 [citado 2008 Fev 12];37(4):404-8. Disponível em: http://www.scielosp.org/pdf/rsp/v37n4/16773.pdf
15. Sackett DL, Haynes RB, Guyatt GH, Tugwell P. Clinical epidemiology. A basic science for clinical medicine. 2a ed. Boston: Little Brown; 1991.
16. Silva RM, Bittencourt L, Sakae TM. Avaliação clínica de palidez estratificada em cruzes: concordância entre observadores e comparação com níveis séricos de hemoglobina. Arq Bras Ciênc Saúde. 2008;33(2):79-82.
17. Sdepanian VL, Silvestrini WS, Morais MB. Limitação diagnóstica do exame físico na identificação de crianças com anemia. Rev Assoc Med Bras. 1996;42:169-74.
18. Zucker JR, Perkins BA, Jafari H, Otieno J, Obonyo C, Campbell CC. Clinical signs for the recognition of children with moderate or severe anaemia in western Kenya. Bull World Health Organ. 1997;75 Suppl 1:97-102.
19. Chalco JP, Huicho L, Alano C, Carreazo NY, Bada CA. Accuracy of clinical pallor in the diagnosis of anaemia in children: a meta-analysis. BMC Pediatr. 2005;5:46.
20. Sheth TN, Choudhry NK, Bowes M, Detsky AS. The relation of conjunctival pallor to the presence of anemia. J Gen Intern Med. 1997;12(2):102-6. Comment in: J Gen Intern Med. 1997; 12(7):455.