Computers in Biology and Medicine 69 (2016) 226–233

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

Age and gender effects on 15 platelet phenotypes in a Spanish population

Miquel Vázquez-Santiago [a], Andrey Ziyatdinov [b], Núria Pujol-Moix [a,c], Helena Brunel [b], Agnès Morera [a], José Manuel Soria [b], Juan Carlos Souto [a,*]

[a] Unitat d'Hemostàsia i Trombosi, Hospital de la Santa Creu i Sant Pau, Sant Antoni Maria Claret, 167, Barcelona 08025, Spain
[b] Unit of Genomics of Complex Diseases, Sant Pau Institute of Biomedical Research (IIB-Sant Pau), Sant Antoni Maria Claret, 167, Barcelona 08025, Spain
[c] Department of Medicine, Universitat Autònoma de Barcelona, Hospital de la Santa Creu i Sant Pau, Sant Antoni Maria Claret, 167, Barcelona 08025, Spain

ARTICLE INFO

Article history:
Received 13 October 2015
Accepted 26 December 2015

Keywords:
Age
Gender
Immature platelet fraction (IPF)
Platelet counts
Platelet indices
Platelet function assay (PFA)

ABSTRACT

Introduction: Several studies have analysed the platelet parameters in human blood, nevertheless there are no extensive analyses on the less common platelet phenotypes. The main objective of our study is to evaluate the age and gender effects on 15 platelet phenotypes.
Methods: We studied 804 individuals, ranging in age from 2 to 93 years, included in the Genetic Analysis of Idiopathic Thrombophilia 2 (GAIT 2) Project. The 15 platelet phenotypes analysed were the platelets counts, platelet volumes, plateletcrits, immature platelet fraction (IPF) and platelet function assay (PFA). A regression-based method was used to evaluate the age and gender effects on these phenotypes.
Results: Our results were consistent with the previously reported results regarding platelet counts and plateletcrit (PCT). They showed a decrease with increasing age. The mean platelet volume (MPV), platelet distribution width (PDW) and platelet-large cell ratio (P-LCR) increased with age, but did not present any gender effect. All the IPF phenotypes increased with age, whereas the PFA phenotypes did not show any relation to age or gender.
Discussion: To sum up, our study provides a comprehensive analysis of the age and gender effects on the platelet phenotypes in a family-base sample. Our results suggest more reasonable age stratification into two distinct groups: childhood, ranging from 2 to 12 years, and the mature group, from 13 to 93 years. Moreover, the PFA phenotypes were maintained constant while the platelet counts, the MPV and IPF levels vary with age.

1. Introduction

Platelets are anucleated blood cells that play an important role in different physiological functions such as haemostasis, wound healing and inflammation [1,2]. Their intrinsic features include size, metabolic capacity, ability to aggregate and relative short lifespan (8–10 days). These features determine their functional properties [3,4]. Megakaryocytes maintain the platelet population and functionality, producing about 10^{11} platelets per day [4,5].

The haematological status of individuals is currently based on the assessment of different clinical phenotypes such as platelet counts, platelet volumes and plateletcrits [6–8]. These phenotypes are used to determine the thrombopoietic status of patients and quantitative variations in platelet phenotypes [9–11]. The platelet distribution width (PDW) describes how uniform the platelets are in size, and it has been proposed as a marker of platelet activation [7,12]. The platelet-large cell ratio (P-LCR) is defined as the percentage of large platelet volume, and it has been associated with higher platelet reactivity and cardiovascular risk [13–15]. The immature platelet fraction (IPF) phenotypes are an indirect measurement of the reticulated platelets and the thrombopoiesis turnover [7,9,16,17]. The platelet function assay (PFA) phenotypes estimate the platelet function [18,19]. All of these platelet phenotypes are measured using either haematological analysers [6,8,9] or *in vitro* assays [19–21].

In the healthy human population, normal platelet counts range from 150 to 400 · 10^9/L of whole blood [4,5,22]. The mean platelet volume (MPV) ranges from 7.8 to 11.0 fL [23] and the reference PDW values range from 2 to 30 fL [11]. The IPF values range from 0.70% to 6.1% or 8% [6,7,24]. These phenotypes have previously been studied with respect to the effects of age and gender [25–27].

* Corresponding author. Tel.: +34 9335537151; fax: +34 9335537153.
E-mail addresses: MVazquezS@santpau.cat (M. Vázquez-Santiago), AZiyatdinov@santpau.cat (A. Ziyatdinov), NPujol@santpau.cat (N. Pujol-Moix), helena.brunel@gmail.com (H. Brunel), ambnesi@gmail.com (A. Morera), JSoria@santpau.cat (J.M. Soria), JSouto@santpau.cat (J.C. Souto).

http://dx.doi.org/10.1016/j.compbiomed.2015.12.023
0010-4825/

Some studies have compared also many different haematological analysers [8,9,24,28], intervals of age [25,29,30], and the ethnicity or habitat [31–35]. There are also studies that have reported incomplete or partial analyses of the platelet blood count (PBC) [16,23,25].

The main aim of our study is to provide a comprehensive analysis of the influence of age and gender on 15 platelet phenotypes. An underlying aim is to determine statistical differences among the results obtained using two different automated haematological analysers on these 15 platelet phenotypes and, finally, our third aim was to develop a single statistical model to evaluate the age and gender effects on each these phenotypes.

2. Methods

2.1. Sample

We studied a subset population of the GAIT 2 Project at the Hospital de la Santa Creu i Sant Pau of Barcelona, Spain. The main aim of the GAIT 2 Project was to identify genetic factors of thrombophilia using family-based analyses and variance component statistical methods [36]. The GAIT 2 population consisted of 935 individuals from 35 extended Spanish families. Each family consisted of at least 10 members over 3 generations and was ascertained through a proband with idiopathic thrombophilia.

To be included in the present study, an individual had to present normal haematological values, including normal iron metabolism. The exclusion criteria were any venous or arterial thrombosis event (previous or present), apparent illness, signs or symptoms of acute illness, inflammatory or infectious disease in the last four weeks, active malignancy and antiaggregant drugs intake in the last two weeks before onset of the study. Individuals with haemorrhagic diathesis also were excluded of the study. Thus, the total analysed population consisted of 804 healthy Caucasian individuals and 131 individuals were excluded. The ages of our population ranged from 2 to 93 years and it included 389 males and 415 females, who were divided into the following four age groups: childhood (Group 1), adolescence (Group 2), adulthood (Group 3) and elders (Group 4), as listed in Table 1.

Our study complied with the Declaration of Helsinki. Written informed consent was obtained from all adult patients and by parents of children. All procedures were approved by the Institutional Review Board at the Hospital de la Santa Creu i Sant Pau.

Table 1
Age groups in the GAIT2 subset population included in the study.

Groups (years)	Males		Females		Total	
	N	Age ± SD[a]	*N*	Age ± SD[a]	*N*	Age ± SD[a]
Childhood group 1 (2–12 years)	66	7.8 ± 2.9	59	8.8 ± 2.7	125	8.3 ± 2.8
Adolescence group 2 (13–18 years)	42	16.1 ± 1.7	25	15.9 ± 1.8	67	16.0 ± 1.7
Adulthood group 3 (19–64 years)	243	41.9 ± 11.8	269	41.1 ± 11.6	512	41.5 ± 11.7
Elders group 4 (65–93 years)	38	74.0 ± 6.7	62	74.4 ± 6.6	100	74.3 ± 6.6
Total (2–93 years)	389	36.5 ± 20.9	415	40.0 ± 21.1	804	38.3 ± 21.1

[a] Means and standard deviations (SD) are given in years.

Table 2
Platelet phenotypes analysed in our study by automated haematological analyser and methodology.

Phenotype groups	Sysmex XE-2100®		Sysmex KX-21N®	PFA-100®
	Impedance	Optical	Impedance	*In vitro*
Platelet counts	PLT	PLTOP	PLT40	
Platelet volumes	MPV PDW	P-LCR	MPV40	
Plateletcrits	PCT		PCT40	
Immature platelet fraction	IPF%		HIPF%	
	IPF#		IPF-X	
Platelet function assay				PFAadp
				PFAepi

Table 3
Pairwise comparison of phenotypes measured by different automated haematological analysers and/or methodology using the *Sign test*.

Phenotype groups	Sysmex XE-2100®				Sysmex KX-21N®		*p*-values
	Impedance		Optical		Impedance		
Platelet counts[a]	PLT	232 (240 ± 55)			PLT40	235 (246 ± 63)	$3.1 \cdot 10^{-3}$
	PLT	232 (240 ± 55)	PLTOP	230 (237 ± 55)			$1.76 \cdot 10^{-13}$
			PLTOP	230 (237 ± 55)	PLT40	235 (246 ± 63)	$< 2.2 \cdot 10^{-16}$
Platelet volumes	MPV	11.0 (10.5 ± 1.5)			MPV40	12.1 (12.3 ± 1.5)	$< 2.2 \cdot 10^{-16}$
Plateletcrit[b]	PCT	0.25 (0.25 ± 0.05)			PCT40	0.28 (0.30 ± 0.08)	$< 2.2 \cdot 10^{-16}$

Platelet counts, volumes and plateletcrits show the median (mean ± standard deviation). **(*)** Median and mean in platelet volumes (MPV and MPV0) are given in fL.

[a] Median and mean in platelet counts (PLT, PLTOP and PLT40) are given in $\times 10^9$/L.

[b] Median and mean in plateletcrit (PCT and PCT40) are given in percentage (%).