Gender difference among blood donors: should laboratory ranges be changed?

Samantha Pasca, Sonia Secchi, Luca Postal, Paola Boccagni

Immunohematology and Transfusion Department, APSS of Trento, Italy

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Correspondence: Samantha Pasca
e-mail: sampasca27@gmail.com

Dear Editor,

clinical history and laboratory data define suitability for blood donation. However, many laboratory results have identical normal ranges for males and females, despite the proven differences described in the medical field today. As early as 2009, Ceriotti and Panteghini[1] suggested that a correct interpretation of laboratory data should not be defined in terms of "normality," but rather by considering the reference limits of individual laboratories, which, in order to have clinical and scientific relevance, must necessarily be associated with other factors, such as age and gender. However, these suggestions are not always followed.

In our analysis, we collected laboratory data from 345 potential blood donors. Among these, 41 (11.9%) were excluded from subsequent analysis as they were not suitable to become blood donors; 16 (8.7%) were women and 25 (15.4%) were men. Finally, the data from 304 potential blood donors-167 (54.9%) females and 137 (45.1%) males-were compared and described. The mean age was 30 years (range 18-62) for females and 34 years (range 18-64) for males (p=0.003, Cohen's d=0.39). In 2022, a report from our Centro Nazionale Sangue (CNS) declared: "In Italy, only 33% of those who donate blood are women, while, for example, in Spain, it is 51%. Moreover, in other European countries, the number of donors is significantly higher". What emerges from our evaluation is that in the Autonomous Province of Trento (Italy), the number of potential female blood donors exceeds that of males, with a lower mean age at presentation, thus reaching levels more similar to European standards.

In 2017, Natasha Karp[2] and her team stated that "gender medicine begins in the laboratory. Sex indeed has a significant impact on the course and severity of many common diseases and the subsequent side effects of treatments". In our study, a comparison was conducted only on laboratory parameters with the same normal range for both sexes.

Overall, white blood cells (WBC), platelets, prothrombin time (PT), and serum protein electrophoresis values were not significant between the two groups, while all the others were. Large or very large effect sizes (Cohen's d) were found for creatinine, alanine transferase (ALT), aspartate transferase (AST), and A/G ratio, while small to moderate effect sizes were reported for platelet count, activated partial thromboplastin time (aPTT), glucose, cholesterol, and triglycerides; similar data were reported in previous studies[3,4]. Complete data are shown in **Table I**. A more pronounced presence of hypercholesterolemia in males of all ages was also found, which places them at greater cardiovascular risk, similar to findings reported by Dell'Anna *et al*.[5]

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Table I - *Comparison between laboratory data of potential female and male blood donors*

	Females	Males	p<0.05	Cohen's "d"
Number	167 (54.9%)	137 (45.1%)	/	
White blood cells (10^9/L) Mean (range) Median (SD)	5.9 (3.5-12.0) 5.6 (±1.4)	5.9 (3.3-9.3) 5.7 (±1.4)	0.934	/
Platelets (10^9/L) Mean (range) Median (SD)	249 (152-486) 237 (±54.2)	231 (128-364) 226 (±49.6)	0.025	0.35
Glucose (mg/dL) Mean (range) Median (SD)	84 (60-113) 83 (±7.8)	87 (70-112) 86 (±8.0)	0.0002	0.38
Creatinine (mg/dL) Mean (range) Median (SD)	0.75 (0.50-1.10) 0.70 (±0.11)	0.94 (0.70-1.40) 0.90 (±0.13)	<0.00001	1.58
Cholesterol (mg/dL) Mean (range) Median (SD)	177 (103-290) 177 (±30.0)	185 (117-285) 179 (±34.6)	0.036	0.25
Triglycerides (mg/dL) Mean (range) Median (SD)	79 (23-256) 73 (±35.4)	97 (24-527) 82 (±57.1)	0.0008	0.49
ALT (UI/L) Mean (range) Median (SD)	23 (12-66) 21 (±7.6)	33 (11-75) 29 (±12.0)	<0.00001	1.00
AST (UI/L) Mean (range) Median (SD)	16 (5-32) 16 (±4.7)	21 (7-46) 20 (±6.7)	<0.00001	0.86
PT (ratio) Mean (range) Median (SD)	1.01 (0.84-1.22) 1.01 (±0.07)	1.00 (0.82-1.22) 1.00 (±0.07)	0.237	/
aPTT (ratio) Mean (range) Median (SD)	1.03 (0.62-1.27) 1.03 (±0.09)	1.06 (0.90-1.25) 1.05 (±0.07)	0.0034	0.37
Total protein (g/L) Mean (range) Median (SD)	74 (65-88) 74 (±3.8)	74 (64-84) 74 (±3.5)	0.919	/
Albumin (g/L) Mean (range) Median (SD)	45.16 (37.83-51.44) 45.07 (±2.73)	47.00 (41.22-52.88) 47.03 (±2.47)	0.235	/
γ-globulin (g/L) Mean (range) Median (SD)	11.68 (7.72-27.19) 11.40 (±2.38)	10.75 (5.95-16.13) 10.61 (±1.81)	0.443	/
A/G rate Mean (range) Median (SD)	1.57 (0.96-2.09) 1.56 (±0.20)	1.73 (1.30-2.15) 1.70 (±0.17)	0.048	0.86
α1-globulin (g/L) Mean (range) Median (SD)	2.83 (1.87-4.45) 2.73 (±0.45)	2.55 (1.82-3.79) 2.52 (±0.30)	0.250	/
α2-globulin (g/L) Mean (range) Median (SD)	6.65 (4.86-9.75) 6.53 (±0.89)	5.96 (4.15-8.62) 5.91 (±0.80)	0.913	/
β1-globulin (g/L) Mean (range) Median (SD)	4.55 (3.60-6.09) 4.50 (±0.51)	4.33 (3.32-5.61) 4.33 (±0.41)	0.483	/
β2-globulin (g/L) Mean (range) Median (SD)	3.56 (2.16-5.91) 3.49 (±0.67)	3.79 (2.44-5.37) 3.78 (±0.58)	0.567	/

Statistically significant values are underlined. ALT: alanine aminotransferase; AST: aspartate aminotransferase; PT: prothrombin time; aPTT: activated partial thromboplastin time; A/G: albumin/ γ-globulin. Cohen's (d) effect size definition: 0.2 = small effect, 0.5 = moderate effect, 0.8 = large effect, 1.5 = very large effect.

Gender medicine is increasingly gaining traction in clinical practice, diagnostics, and scientific research. While women and men should be treated equally and have the same right to access healthcare, their physiopathological, genetic, and biochemical characteristics should not be disregarded. The fact that this study has found statistically significant differences and moderate to large effect sizes for many parameters analyzed suggests that a review of reference limits is necessary, and that these new limits should clearly be indicated in laboratory reports.

The Authors declare no conflicts of interest.

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