Haematological Profile in Healthy Urban Population (8 to 70 Years of Age)

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A B S T R A C T

Haematological profile for 17 constituents of blood were determined in 998 healthy school children (8–19 years old) and 2246 healthy adult persons (20–70 years old) residing permanently or at least 5 years in a defined geographic region of Zagreb, Croatia.

Physiological variations corresponding to age and sex were studied as the most important factors affecting biological variation in haematological constituents of blood. In our study erythrocytes, haemoglobin and haematocrit values were not sex dependent until the age of 13 after which the values were higher in men than in women. Sedimentation rate showed sex and age related differences in the adult age with higher values in women especially after 50 years. Total leukocyte count declined with age and in adults the values were slightly lower in women. Segmented neutrophil granulocytes showed the upward trend with age whereas the lymphocyte and monocyte counts declined. Women showed slightly higher platelet count in the adult age.

Based on biological variation, we have estimated the reference intervals for 17 haematological constituents of blood in order to provide medically reliable evaluation of haematological laboratory results.

Introduction

Only a limited number of haematological constituents of blood and small number of individuals of different age groups had been the subject of investigation of few clinical laboratories in Croatia[1,2] and foreign countries[3–8].

For the first time in our country we have produced population based reference intervals for 17 haematological constituents of blood in the representative reference sample group of 3244 healthy subjects, 998 school children and adolescents aged 8–19 years and 2246 adults aged 20–70 years. The study was performed under strictly controlled conditions according to the IFCC recommendations[12–17] comprised in the National Committee for Clinical Laboratory Standards Document C28-P[18].

The aim of this study was to determine the profile of haematological constituents of blood throughout the period of intensive growth and development during puberty and adolescence, and in the adult age in order to provide medically reliable evaluation of laboratory haematological results owing to age and sex by paediatricians and clinicians in our country.

Participants and Methods

The local school children and adolescents (8–19 years old) as well as the adults (20–70 years old) were carefully selected and declared healthy by specialists according to the medical check-ups (according to the »International statistical classification of diseases and related health problems«[19]) as well as on the basis of a questioner pertinent to the personal and family anamnesis, drug use and abuse, physical exercise, food preferences, cigarettes smoking, alcohol consumption and anthropometrical studies. Population based representative sample group according to age and sex is presented in Table 1. This study was performed after a permission by the Ethical Committee of Medical School University of Zagreb, Croatia was issued, and after a written parent's and child's consent was obtained.

For the production of haematological reference values we have collected the venous blood from the children according to the standardised procedure recommended for adults[14] and for children[20]. All haematological constituents of blood were determined within 2 to 3 hours after collection. Venipuncture blood was collected into vacutainer tubes (Becton Dickinson) containing tri-potassium EDTA as the anticoagulant.

The measurement of haematological constituents of blood were performed by an automated haematology analyser

TABLE 1
POPULATION BASED REFERENCE
SAMPLE GROUPS (n = 3244) ACCORDING
TO AGE AND SEX

Age group (yrs)	Females n	Males n
8	23	26
9	61	63
10	66	62
11	112	82
12	27	19
13	48	31
14	36	38
15	61	28
16	35	35
17	31	21
18–20	40	53
20–30	258	243
31–40	340	277
41–50	280	230
51–60	169	147
61–70	109	51
>70	114	28
Total	1810	1434

»Coulter«[21] which is an impendance-type analyser. The calibration status of the analyser was checked according to the manufacturer's recommendations, each time before samples were run. In addition each blood smear was stained according to Pappenheim-May-Grünwald-Giemsa[22] and microscopically differentiated 100 leukocytes. Westergreen method[23] was used for measurement of sedimentation rate.

Corresponding analytical inaccuracy (bias) and coefficients of variations for long-term analytical imprecision during the production of reference values, achieved analytical goals based on biological variations[24,25], for haematology tests (Table 2). All tests were performed by the Institute of Clinical Chemistry Clinical Hospital »Merkur« which has been en-

TABLE 2
QUALITY-CONTROL DATA FOR HAEMATOLOGICAL INDICES

	Inaccuracy, bias %	Imprecision, CV_A %
Erythrocytes	1.42	0.58
Haemoglobin	0.02	0.49
Haematocrit	0.02	0.64
MCV– mean cell volume	0.70	0.65
MCH – mean cell haemoglobin	0.02	0.83
MCHC – mean cell haemoglobin concentration	0.28	0.88
RDW – red cell distribution width	1.44	0.73
Platelets	2.34	2.12
MPV – mean platelet volume	1.94	1.49
Total leukocytes	13.70	0.61
Leukocytes – differential		
Eosinophil granulocytes	7.50	3.18
Basophil granulocytes	1.17	1.16
Neutrophil granulocytes	1.84	0.35
Lymphocytes	4.18	0.48
Monocytes	5.06	1.34
Sedimentation rate	5.00	4.00

CV_A = analytical coefficient of variation

rolled as a World Health Organisation sponsored member of the International External Quality Assessment Scheme for Haematology since September 1985.

Our data were analysed by Statistical Program »Statistics«, Window 3.1 according to the recommendations of the Expert Panel on Theory of Reference Values[16]. Accordingly the reference intervals reflected our estimate of 0.025 – 0.975 percentiles of non-parametric distributions. Results that differed for more than 3 standard deviations (SD) were eliminated. In order to reduce maximally interindividual variations the non-parametric method was estimated on one-year age groups, total 11 age groups for each sex. Mann Whitney U-test was used for statistically significant differences between sex and age groups. The error probability P < 0.05 was considered significant. In the absence of significant sex and age related differences the groups were combined and analysed as a single group.

Results and Discussion

Reference intervals (0.025 – 0.975 percentiles) for the red cell indices are presented in Table 3. Sex and age groups were combined when the differences among them were not statistically significant. Figure 1 shows age and sex dependent variations of median concentrations for erythrocytes, haemoglobin, haematocrit, MCV (mean cell volume), MCH (mean cell haemoglobin), MCHC (mean cell haemoglobin concentration), RDW (red cell distribution width) and sedimentation rate for all age groups.

According to our results during childhood and adolescence the concentrations of erythrocytes and haematocrit remained for girls on the same level as the adult population while concentrations of

TABLE 3
REFERENCE INTERVALS (0.025 – 0.975 PERCENTILES) FOR RED CELL INDICES

Red cell indices	N	Age (yrs)	0.025–0.975 percentiles	Units
Females				
Erythrocytes	538	8 – 19	4.07 – 5.42	x 1012/L
	1270	20 – 70	3.86 – 5.08	
Haemoglobin	538	8 – 19	118 – 149	g/L
	1270	20 – 70	119 – 157	
Haematocrit	538	8 – 19	0.354 – 0.450	L/L
	1270	20 – 70	0.356 – 0.470	
Sedimentation rate	538	8 – 19	2 – 20	mm/3.6 ks
	878	20 – 50	4 – 24	
	392	> 50	5 – 28	
Males				
Erythrocytes	252	8 – 12	4.34 – 5.47	x 1012/L
	206	13 – 19	4.43 – 5.88	
	976	20 – 70	4.34 – 5.72	
Haemoglobin	252	8 – 12	121 – 145	g/L
	206	13 – 19	129 – 166	
	976	20 – 70	138 – 175	
Haematocrit	252	8 – 12	0.366 – 0.452	L/L
	206	13 – 19	0.390 – 0.487	
	976	20 – 70	0.415 – 0.530	
Sedimentation rate	321	8 – 14	2 – 21	mm/3.6 ks
	132	15 – 19	2 – 12	
	750	20 – 50	2 – 13	
	226	> 50	3 – 23	
Males and females				
MCV	998	8 – 19	76.5 – 92.1	fL
	2246	20 – 70	83.0 – 97.2	
MCH	998	8 – 19	24.3 – 31.5	pg
	2246	20 – 70	27.4 – 33.9	
MCHC	998	8 – 19	304 – 346	g/L
	2246	20 – 70	320 – 345	
RDW	998	8 – 19	11.6 – 14.3	/
	2246	20 – 70	9.0 – 13.8	

MCV = mean cell volume; MCH = mean cell haemoglobin
MCHC = mean cell haemoglobin concentration; RDW = red cell distribution width

haemoglobin and MCV have shown upward trend toward the adults values. After the age of 12 boys have shown increasing concentrations of erythrocytes, haemoglobin, haematocrit and MCV values, whereas below the age of 12 no sex differences were observed. Throughout the adult age erythrocytes, haemoglobin and haematocrit concentrations were higher in men than in women what is in agreement with other investigations[7,8].

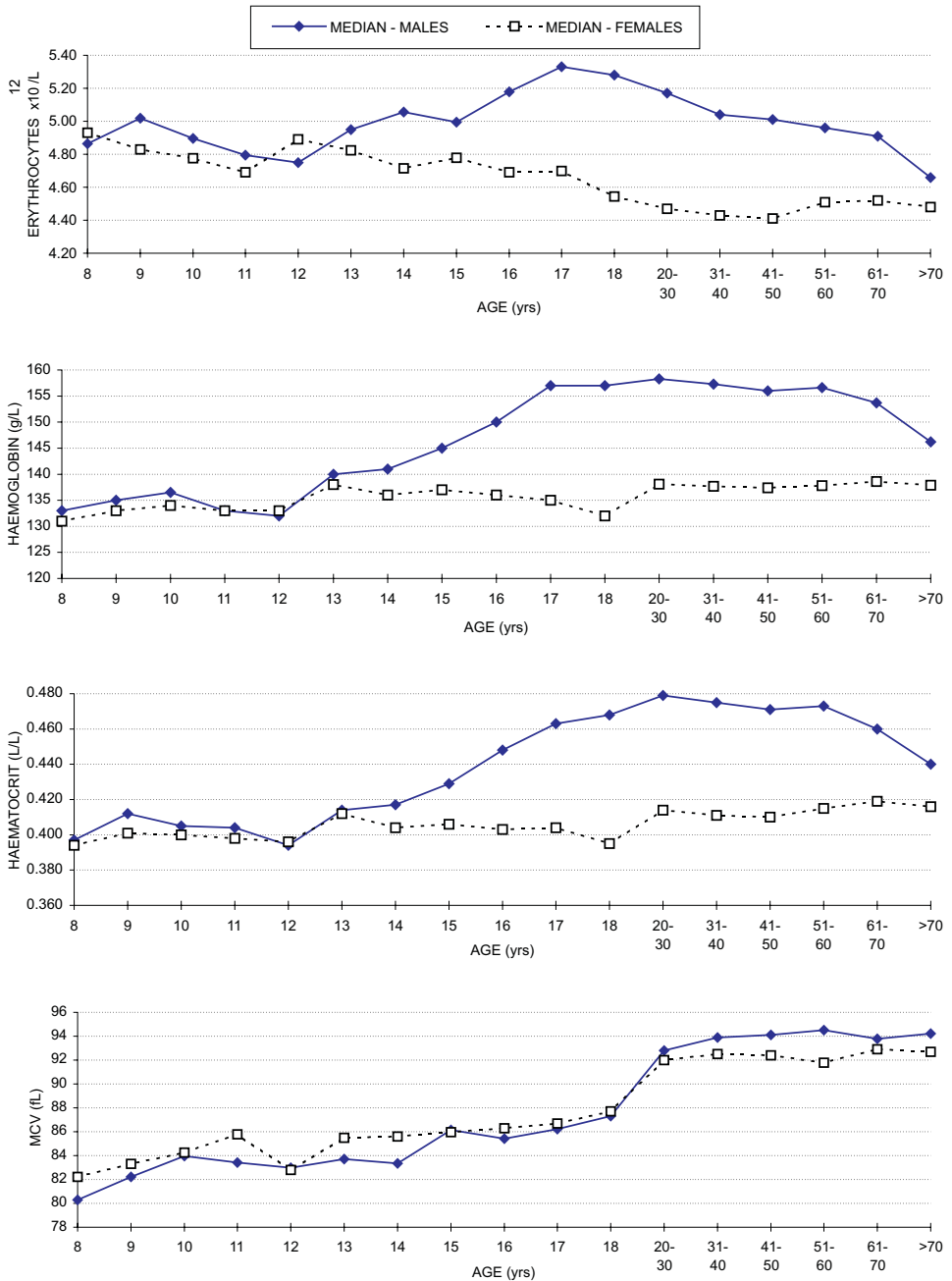MCH rose throughout puberty and adolescence although the differences were not significant between sexes at all ages.

Fig. 1. Age and sex related changes in median concentrations for red cell indices in healthy population sample aged 8–70 years.
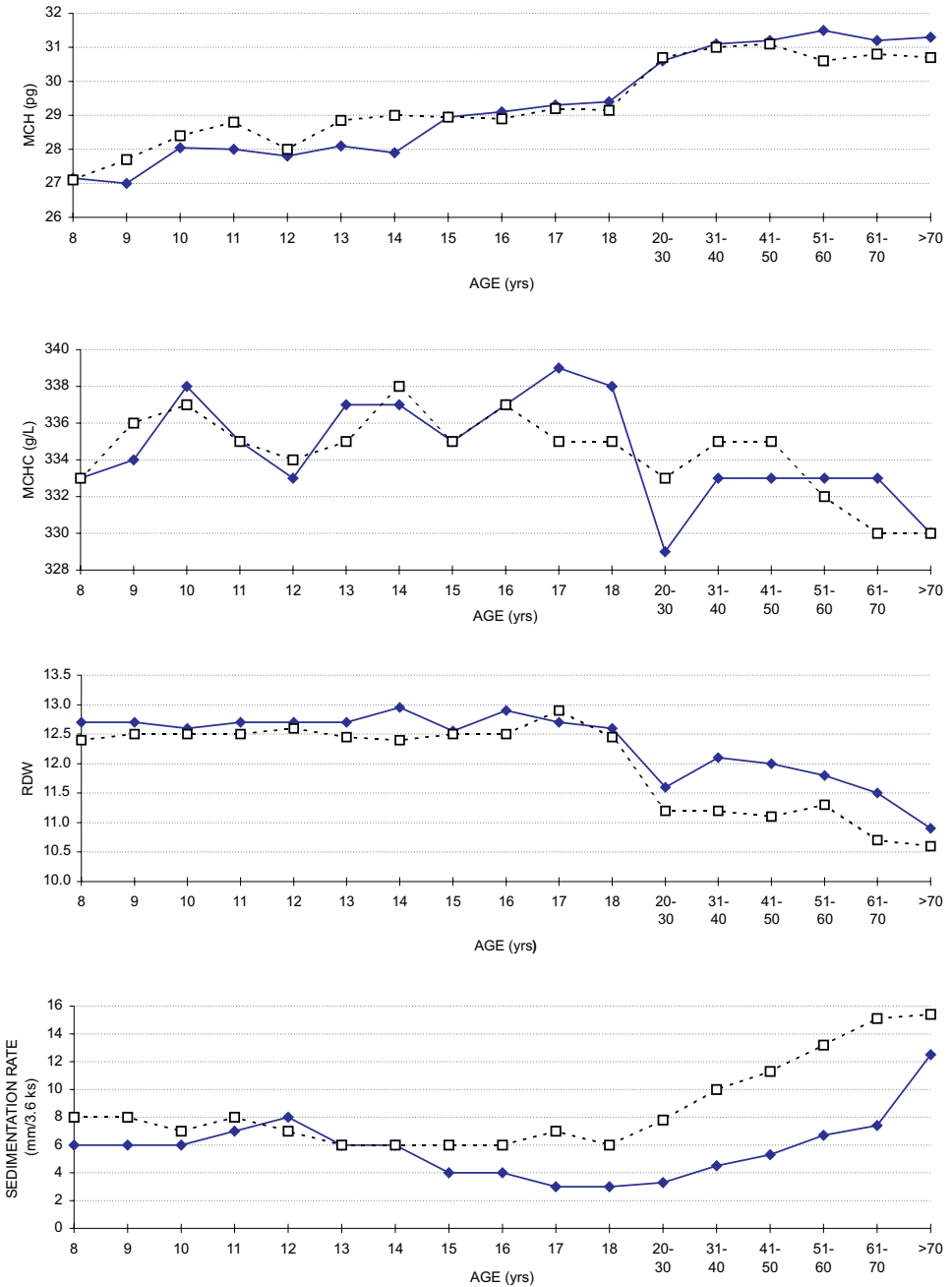
Fig. 1. Continued.

TABLE 4
REFERENCE INTERVALS (0.025 – 0.975 PERCENTILES) FOR LEUKOCYTE INDICES

Leukocytes	N	Age (yrs)	0.025–0.975 percentiles	Units
Males and females				
Total leukocytes	998	8 – 19	4.4 – 11.6	10^9 /L
	2246	20 – 70	3.4 – 9.7	
Eosinophil granulocytes	998	8 – 19	0 – 9	%
			0 – 1.04	10^9 /L
	2246	20 – 70	0 – 7	%
			0 – 0.43	10^9 /L
Basophil granulocytes	998	8 – 19	0 – 3	%
			0 – 0.23	10^9 /L
	2246	20 – 70	0 – 1	%
			0 – 0.06	10^9 /L
Unsegmented neutrophil granulocytes	998	8 – 19	0 – 2	%
			0 – 0.35	10^9 /L
	2246	20 – 70	0 – 2	%
			0 – 0.19	10^9 /L
Segmented neutrophil granulocytes	998	8 – 19	34 – 69	%
			1.49 – 8.01	10^9 /L
	2246	20 – 70	44 – 72	%
			2.06 – 6.49	10^9 /L
Lymphocytes	998	8 – 19	19 – 52	%
			0.84 – 6.03	10^9 /L
	2246	20 – 70	20 – 46	%
			1.19 – 3.35	10^9 /L
Monocytes	998	8 – 19	5 – 13	%
			0.22 – 1.51	10^9 /L
	2246	20 – 70	2 – 12	%
			0.12 – 0.84	10^9 /L

In contrast, there were virtually no age or sex related changes for MCHC.

Our results are in agreement with other authors[4,6,26,27] while Giorno[28] found statistically significant rises in the MCH with age and sex. According to Yip[27] the higher haemoglobin and haematocrit values in boys than in girls is largely a consequence of a larger number of red cells.

According to our results the sedimentation rate showed no age or sex related difference during childhood and adolescence whereas in the adult age women showed higher values especially after 50 years what is in agreement with other authors[7,8].

Table 4 shows reference intervals (0.025 – 0.975 percentiles) for the leuko-
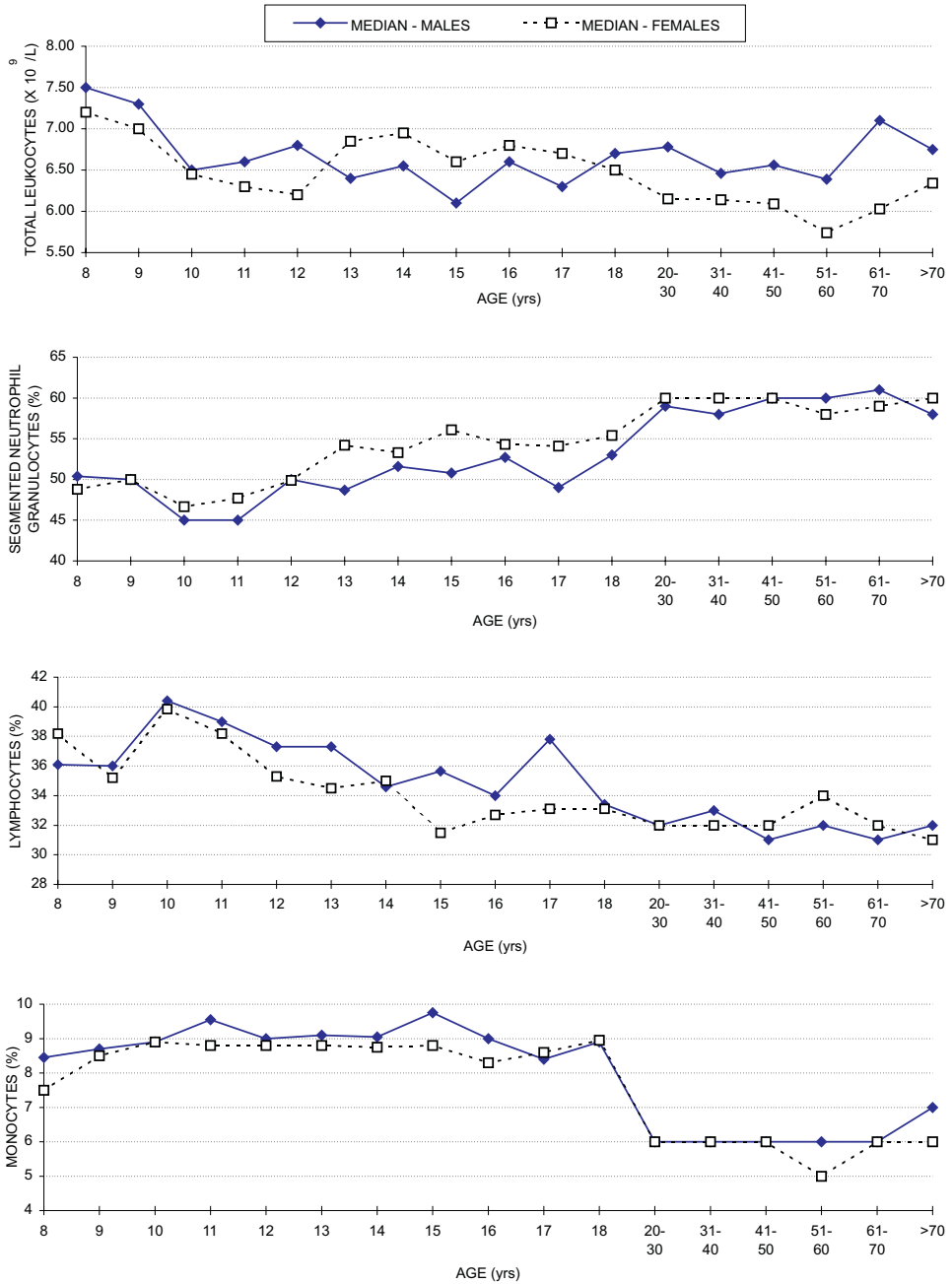
Fig. 2. Age and sex related changes in median concentrations for leukocyte indices in healthy population sample aged 8–70 years.

cyte indices. We have combined and analysed two age groups for school children and adolescents and for adults, since the difference between them were not significant. Figure 2 shows age and sex dependent variations of median concentrations for total leukocytes, neutrophil granulocytes, lymphocytes and monocytes for all age groups.

We have shown that concentrations of total leukocytes were gradually decreasing during childhood and adolescence. From 13 until 17 years girls showed higher values than boys and than the values steadily decreased towards lower values in women than in men in the adult age.

Our results showed that neutrophil granulocytes were linearly increasing with the age for both sexes, without significant sex related differences.

We have shown that concentrations of lymphocytes were gradually decreasing from the age of 8–18 years without apparent sex-differences reaching the constant adult level at the age of 15 years for girls and 18 years for boys.

According to our results the concentrations of monocytes are slightly lower in the adult age than during childhood and adolescence.

We have shown that the concentrations of eosinophil granulocytes are higher in the childhood and adolescence with 0.975 upper reference interval up to 9% of total leukocyte count than in adult age with 0.975 upper reference interval up to 7%.

No significant age or sex differences were found for basophilic granulocytes during the age of 8–70 years.

Our results are mostly in agreement with other authors[4,26,29] for total leukocytes and leukocyte differential. Only Taylor[4] found higher monocyte counts for girls while study of Swaanenburg[26] indicated higher values for boys. Cranendonk[30] found higher value for eosinophil granulocytes during childhood and adolescence than in our study.

Table 5 shows reference intervals (0.025 – 0.975 percentiles) for platelets and MPV (mean platelet volume). As the sex and age related differences were not significant the groups were combined and analysed as two age groups, for school children and adolescents and for adults. Figure 3 shows age and sex dependent variations of median concentrations for platelets and MPV for all age groups.

We have shown that the concentrations of platelets were age dependent and declined steadily toward the age of 17 years. Girls showed a distinct peak at the age of 12 years. After that girls showed slightly higher values than boys, whereas below the age of 12 no difference was observed. After the age of 17 the concentra-

TABLE 5
REFERENCE INTERVALS (0.025 – 0.975 PERCENTILES) FOR PLATELETS INDICES

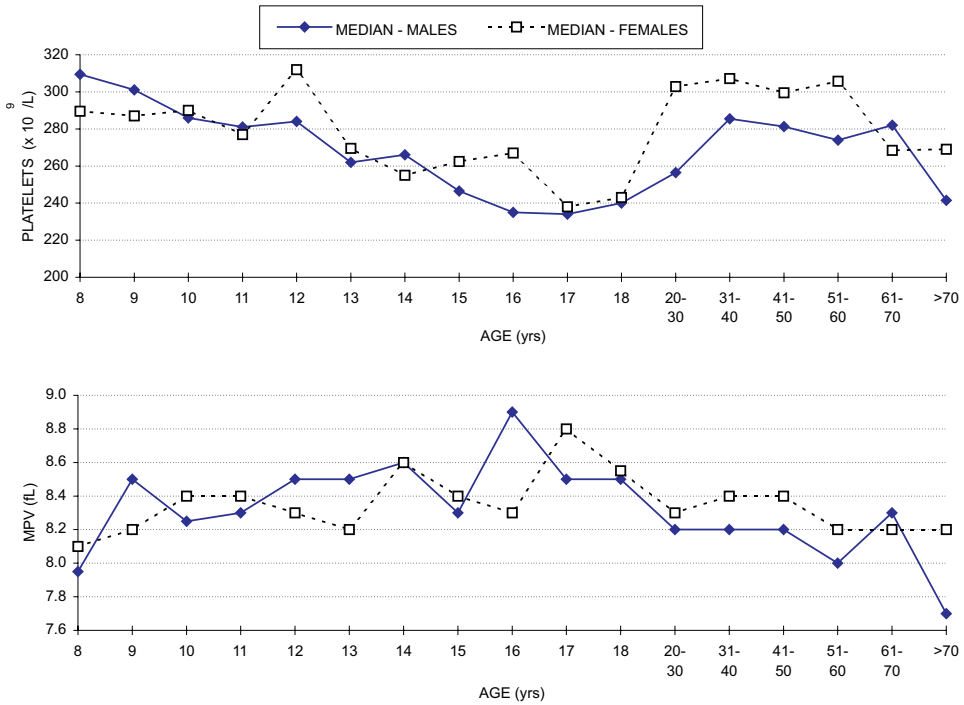| Platelets	N	Age (yrs)	0.025–0.975 percentiles	Units
Males and females				
Platelets	998	8 – 19	178 – 420	x10^9/L
	2246	20 – 70	158 – 424	
MPV	998	8 – 19	7.0 – 10.4	fL
	2246	20 – 70	6.8 – 10.4	

MPV = mean platelet volume

Fig. 3. Age and sex related changes in median concentrations for platelet indices in healthy population sample aged 8–70 years.

tions of platelets showed slightly higher values for women than for men.

According to our results the MPV slightly rose and at the age of 16 showed a peak for boys and at the age of 17 years for girls. In the adult age and sex depending differences were not significant.

Our results are in agreement with Taylor[4] while Swaanenburg[26] found significant sex differences for platelet count after age of 15 and Tsang[7] in the older population.

Conclusions

Variations according to age and sex are the most important factors affecting biological variation in haematological constituents of blood. The established profile of haematological constituents of blood may therefore be a contribution to better understandings of physiological changes throughout the period of intensive growth and development during puberty and adolescence, and in the adult age.

The estimated haematological reference ranges presented in this study are derived from a large representative population sample. Therefore the results may be used in other urban parts of our country where similar laboratory methods are in use in order to provide medically reliable evaluation of haematological laboratory results.

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PROFIL HEMATOLOŠKIH SASTOJAKA KRVI ZDRAVE URBANE POPULACIJE U DOBI OD 8–70 GODINA

S A Ž E T A K

Određen je profil fizioloških promjena za 17 hematoloških sastojaka krvi u 998 zdrave školske djece i adolescenata u dobi od 8–19 godina i 2246 zdravih odraslih osoba u dobi od 20–70 godina koji stalno žive ili najmanje 5 godina na području Zagreba, Hrvatska.

Veličina fiziološke varijacije ovisno o dobi i spolu najviše utječe na veličinu ukupne biološke varijacije hematoloških sastojaka krvi. U provedenom ispitivanju utvr đeno je da se do 13 godina vrijednosti za broj eritrocita, hemoglobin i hematokrit ne razlikuju po spolu, a zatim su više u muškaraca nego u žena. Brzina sedimentacije eritrocita ovisna je o dobi i spolu u odrasloj dobi, kada su vrijednosti kod žena više posebno nakon 50 godina života. Ukupan broj leukocita se smanjuje s dobi, a u odrasloj dobi vrijednosti su nešto niže kod žena. Segmentirani neutrofilni granulociti pokazuju trend porasta s dobi dok se broj limfocita i monocita smanjuje. U odrasloj dobi žene imaju nešto viši broj trombocita od muškaraca.

Temeljem utvrđene veličine biološke varijacije, prema preporukama IFCC-a, primjenom neparametarske metode, određeni su referentni intervali hematoloških sastojaka krvi koji omogućuju medicinski pouzdanu evaluaciju hematoloških laboratorijskih rezultata.