SHORT COMMUNICATION

Reference interval establishment of full blood count extended research parameters in the multi-ethnic population of Malaysia

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SUMMARY

Haematological cellular structures may be elucidated using automated full blood count (FBC) analysers such as Unicel DxH 800 via cell population data (CPD) analysis. The CPD values are generated by calculating volume, conductivity, and five types of scatter angles of individual cells which would form clusters or populations. This study considered 126 CPD parameter values of 1077 healthy Malaysian adults to develop reference intervals for each CPD parameter. The utility of the CPD reference interval established may range from understanding the normal haematological cellular structures to analysis of distinct cellular features related to the development of haematological disorders and malignancies.

KEY WORDS:
Cell population data; CPD; full blood count; reference interval; Unicel DxH 800

INTRODUCTION

Cell Population Data (CPD) generated in recent generations of automated full blood count (FBC) analysers measure the characteristics of cells based on multiple light scatter angles derived from flow cytometric digital morphology (FCDM) technology. The CPD generated by Unicel DxH 800 provides information on the volume (V), conductivity (C), and five light scatter angles as follow: Axial Light Loss A° (AL2), Low Angle Light Scatter 5.1° (LALS), Lower Median Angle Light Scatter 10°-20° (LMALS), Upper Median Angle Light Scatter 20o-42o (UMALS), and a fifth scatter channel called MALS, being the sum of Upper Median Angle Light Scatter 20°-42° and Lower Median Angle Light Scatter 10°-20° regions as depicted in Figure 1.[1]

Based on these CPD parameters, structural information and internal complexity of the cells are identified including individual cell's granularity as FCDM principles are being adapted in the analysis. Given the integration of such feature in widely available laboratory equipment, laboratory personnel may utilise this exact feature to better comprehend haematological cellular structures and how CPD might be affected in varying aetiologies. In this study, we have established the largest and most comprehensive reference intervals of CPD on Unicel DxH 800 in a multi-ethnic population of Malaysian adults.

This is an extension study of our previously published work whereby 2,725 apparently healthy adults comprising both genders and three principal races in Malaysia were recruited through voluntary participations.[2] We selected 1,077 healthy Malaysian adults aged 19 and above, both genders (403 male and 675 female), and three principal racial groups (Malay, Chinese, and Indian) who had complete data for all CPD parameters in this study. All clinical aspects of this study has been approved by the Medical Research Ethics Committee of the Ministry of Health of Malaysia (Research ID 10-277-5480). FBC analysis was performed on the Unicel DxH 800 FBC analyser and CPD was retrieved for further analysis. Morphological H inclusion review, haemoglobin analysis, serum ferritin and serum soluble transferrin receptor assays were performed on all cases. All CPD parameters in this study were tested for normality using the Shapiro-Wilk test in total and according to the predefined subgroups followed by determination of reference intervals, measures of central tendency, and dispersion along the point estimates for each subgroup. One-way analysis of variance (ANOVA) was used to compare mean values between gender, age and ethnicity.

As we did not find any clinically significant differences between the age group, gender, and racial groups for any CPD parameter upon conducting ANOVA, the data was combined. Reference intervals for 126 CPD parameters based on the volume, conductivity, and five light scatter angles of the laser (MALS, UMALS, LMALS, LALS, AL2) which encompass neutrophils, lymphocytes, monocytes, eosinophils, nucleated red blood cells, reticulocytes and early granulocyte cells were generated and each of their respective reference intervals are elaborated in Table I.

Based on reports, the utility of CPD extends from the proper diagnosis of aetiologies, including sepsis,[3] dengue fever,[4] and even lymphoproliferative disorders.[5] Due to the nature of the disorders that affect the morphologies of blood cells, CPD analysis generate values which are distinguishable from normal subjects, and thus, it is worth noting that there is an interest in establishing reference intervals of CPD in different populations as genetic or geographical factors may

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Table I: Cell population data (CPD) reference intervals in Malaysian adults.

Parameters	Mean	S.D.	Reference Interval	Parameters	Mean	S.D.	Reference Interval	Parameters	Mean	S.D.	Reference Interval
MN-V-NE	139.77	5.28	129.42 - 150.12	MN-V-EO	155.18	5.96	143.51 - 166.86	MN-V-RET	54.65	3.23	48.33 - 60.98
SD-V-NE	16.31	1.10	14.15 - 18.48	SD-V-EO	16.50	1.87	12.83 - 20.17	SD-V-RET	13.33	1.22	10.93 - 15.72
MN-C-NE	152.23	3.64	145.09 - 159.38	MN-C-EO	154.83	3.57	147.82 - 161.83	MN-C-RET	69.86	2.85	64.27 - 75.44
SD-C-NE	5.49	0.97	3.58 - 7.40	SD-C-EO	6.04	3.02	0.11 - 11.96	SD-C-RET	19.52	1.36	16.86 - 22.19
MN-MALS-NE	134.58	5.78	123.25 - 145.91	MN-MALS-EO	200.21	4.85	190.71 - 209.71	MN-MALS-RET	113.51	6.04	101.67 - 125.35
SD-MALS-NE	11.99	1.76	8.55 - 15.44	SD-MALS-EO	9.01	1.11	6.83 - 11.19	SD-MALS-RET	19.64	2.26	15.21 - 24.08
MN-UMALS-NE	130.62	6.56	117.77 - 143.48	MN-UMALS-EO	210.67	5.21	200.46 - 220.88	MN-UMALS-RET	119.87	5.36	109.37 - 130.37
SD-UMALS-NE	12.98	1.66	9.73 - 16.23	SD-UMALS-EO	10.22	1.70	6.89 - 13.54	SD-UMALS-RET	18.55	2.44	13.77 - 23.33
MN-LMALS-NE	132.43	7.50	117.73 - 147.12	MN-LMALS-EO	186.11	4.94	176.43 - 195.79	MN-LMALS-RET	103.09	7.79	87.81 - 118.36
SD-LMALS-NE	14.56	2.76	9.14 - 19.98	SD-LMALS-EO	10.49	1.53	7.49 - 13.48	SD-LMALS-RET	22.55	2.03	18.56 - 26.54
MN-LALS-NE	156.64	16.04	125.21 - 188.07	MN-LALS-EO	177.23	12.91	151.93 - 202.53	MN-LALS-RET	96.59	8.56	79.82 - 113.36
SD-LALS-NE	28.68	4.34	20.17 - 37.18	SD-LALS-EO	43.65	3.31	37.16 - 50.14	SD-LALS-RET	26.70	3.51	19.82 - 33.59
MN-AL2-NE	163.54	19.96	124.43 - 202.66	MN-AL2-EO	129.75	10.41	109.33 - 150.16	MN-AL2-RET	142.38	27.79	87.92 - 196.84
SD-AL2-NE	12.76	2.41	8.05 - 17.48	SD-AL2-EO	11.49	2.85	5.91 - 17.07	SD-AL2-RET	22.65	4.99	12.88 - 32.42
MN-V-LY	83.88	3.09	77.82 - 89.93	MN-V-NNRBC	139.90	12.72	114.98 - 164.83	MN-V-EGC	150.78	56.03	8.61 - 22.08
SD-V-LY	13.51	1.20	11.15 - 15.87	SD-V-NNRBC	56.42	4.31	47.98 - 64.87	SD-V-EGC	24.27	12.08	8.61 - 22.09
MN-C-LY	121.74	3.42	115.04 - 128.44	MN-C-NNRBC	124.14	12.55	99.55 - 148.74	MN-C-EGC	128.37	46.01	8.61 - 22.10
SD-C-LY	8.42	1.29	5.88 - 10.96	SD-C-NNRBC	31.00	3.23	24.67 - 37.33	SD-C-EGC	2.25	1.14	8.61 - 22.11
MN-MALS-LY	55.80	7.52	41.06 - 70.54	MN-MALS-NNRBC	192.60	10.88	171.27 - 213.93	MN-MALS-EGC	126.04	45.35	8.61 - 22.12
SD-MALS-LY	16.43	1.69	13.11 - 19.75	SD-MALS-NNRBC	42.84	2.62	37.70 - 47.97	SD-MALS-EGC	5.98	2.96	8.61 - 22.13
MN-UMALS-LY	41.75	14.16	13.99 - 69.52	MN-UMALS-NNRBC	186.56	12.12	162.81 - 210.32	MN-UMALS-EGC	134.13	48.15	8.61 - 22.14
SD-UMALS-LY	20.32	2.46	15.51 - 25.14	SD-UMALS-NNRBC	50.55	3.25	44.19 - 56.91	SD-UMALS-EGC	9.39	4.31	8.61 - 22.15
MN-LMALS-LY	58.51	4.71	49.28 - 67.74	MN-LMALS-NNRBC	199.39	8.75	182.23 - 216.54	MN-LMALS-EGC	114.19	41.52	8.61 - 22.16
SD-LMALS-LY	18.81	1.12	16.61 - 21.01	SD-LMALS-NNRBC	38.58	1.63	35.39 - 41.77	SD-LMALS-EGC	7.95	3.83	8.61 - 22.17
MN-LALS-LY	37.08	3.34	30.53 - 43.63	MN-LALS-NNRBC	82.55	9.13	64.66 - 100.45	MN-LALS-EGC	109.61	42.23	8.61 - 22.18
SD-LALS-LY	10.16	1.12	7.96 - 12.36	SD-LALS-NNRBC	33.97	4.11	25.91 - 42.04	SD-LALS-EGC	20.06	9.75	8.61 - 22.19
MN-AL2-LY	97.22	21.47	55.12 - 139.31	MN-AL2-NNRBC	207.39	27.43	153.64 - 261.15	MN-AL2-EGC	131.50	47.86	8.61 - 22.20
SD-AL2-LY	11.82	1.74	8.41 - 15.23	SD-AL2-NNRBC	33.16	6.79	19.86 - 46.47	SD-AL2-EGC	16.06	8.26	8.61 - 22.21
MN-V-MO	161.59	5.21	151.38 - 171.80	MN-V-RET	54.65	3.23	48.33 - 60.98				
SD-V-MO	18.17	1.97	14.30 - 22.04	SD-V-RET	13.33	1.22	10.93 - 15.72				
MN-C-MO	129.17	3.50	122.31 - 136.03	MN-C-RET	69.86	2.85	64.27 - 75.44				
SD-C-MO	6.49	1.53	3.50 - 9.49	SD-C-RET	19.52	1.36	16.86 - 22.19				
MN-MALS-MO	73.20	6.14	61.15 - 85.24	MN-MALS-RET	113.51	6.04	101.67 - 125.35				
SD-MALS-MO	13.08	1.78	9.59 - 16.56	SD-MALS-RET	19.64	2.26	15.21 - 24.08				
MN-UMALS-MO	74.35	10.16	54.45 - 94.26	MN-UMALS-RET	119.87	5.36	109.37 - 130.37				
SD-UMALS-MO	14.74	3.11	8.65 - 20.82	SD-UMALS-RET	18.55	2.44	13.77 - 23.33				
MN-LMALS-MO	67.01	5.37	56.48 - 77.54	MN-LMALS-RET	103.09	7.79	87.81 - 118.36				
SD-LMALS-MO	16.69	1.92	12.92 - 20.45	SD-LMALS-RET	22.55	2.03	18.56 - 26.54				
MN-LALS-MO	87.30	13.79	60.28 - 114.32	MN-LALS-RET	96.59	8.56	79.82 - 113.36				
SD-LALS-MO	25.56	3.34	19.01 - 32.12	SD-LALS-RET	26.70	3.51	19.82 - 33.59				
MN-AL2-MO	163.76	32.40	100.24 - 227.27	MN-AL2-RET	142.38	27.79	87.92 - 196.84				
SD-AL2-MO	13.40	2.12	9.26 - 17.55	SD-AL2-RET	22.65	4.99	12.88 - 32.42				

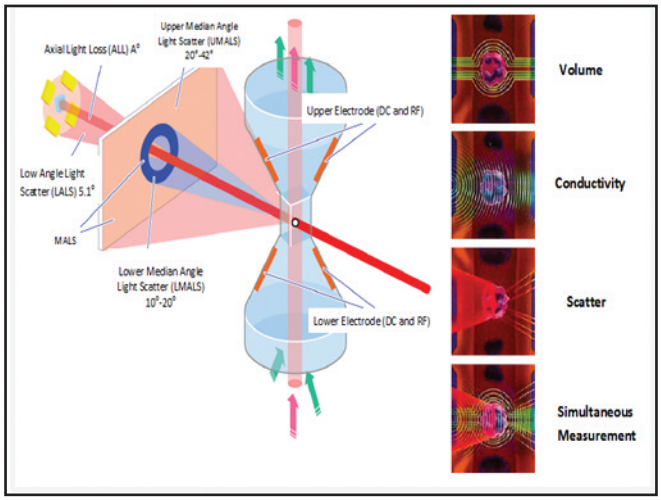

Fig. 1: Simultaneous measurement of cell volume, conductivity and scatter using Unicel DxH 800 technology. (Courtesy of Beckman Coulter).

contribute to differences between the values. Currently, only very few studies considered the establishment of CPD reference intervals in other population settings such as one conducted by Park et al., to assess 57 CPD parameters in Sysmex XN-2000.[6] This should thus call for more attention to be given in establishing CPD reference intervals which have beneficial future implications especially in the diagnostics sector.

As a conclusion to this study, our group has ascertained the most comprehensive CPD reference intervals in the largest multi-ethnic study in the region of Malaysia. CPD data have been proven very useful in classifying different diseases, and thus, we aim to use these CPD data generated from this study to distinguish haematological diseases from normal subjects in future studies.

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