Original Article **OPEN ACCESS**

CARDIOVASCULAR RISK ASSESSMENT AND SUPPORT TECHNIQUES

Whole blood viscosity assessment issues I: Extrapolation chart and reference values

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Citation: Nwose EU. Whole blood viscosity assessment issues I: Extrapolation chart and reference values. **North Am J Med Sci** 2010; 2: 165-169.
Doi: 10.4297/najms.2010.2165
Availability: www.najms.org
ISSN: 1947 – 2714

Abstract

Background: There are many different methods for the assessment of whole blood viscosity, but not every pathology unit has equipment for any of the methods. However, a validated arithmetic method exists whereby whole blood viscosity can be extrapolated from haematocrit and total serum proteins. **Aims**: The objective of this work is to develop an algorithm in the form of a chart by which clinicians can easily extrapolate whole blood viscosity values in their consulting rooms or on the ward. Another objective is to suggest normal, subnormal and critical reference ranges applicable to this method. **Materials and Methods**: Whole blood viscosity at high shear stress was determined, from various possible pairs of haematocrit and total proteins. A chart was formulated so that whole blood viscosity can be extrapolated. After determination of two standard deviations from the mean and ascertainment of symmetric distribution, normal and abnormal reference ranges were defined. **Results**: The clinicians' user-friendly chart is presented. Considering presumptive lower and upper limits, the continuum of ≤14.28, 14.29 – 15.00, 15.01 – 19.01, 19.02 – 19.39 and ≥19.40 (208 Sec^{-1}) is obtained as reference ranges for critically low, subnormal low, normal, subnormal high and critically high whole blood viscosity levels respectively. **Conclusion**: This article advances a validated method to provide a user-friendly chart that would enable clinicians to assess whole blood viscosity for any patients who has results for full blood count and total proteins. It would make the assessment of whole blood viscosity costless and the neglect of a known cardiovascular risk factor less excusable.

Keywords: Assessment chart, reference values, whole blood viscosity.

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Introduction

Whole blood viscosity (WBV) is one of Virchow's triad, which has been an established concept of three phenomena including stasis, endothelial dysfunction and atherothrombosis that ultimately lead to, and/or result from cardiovascular complications[1,2].Each phenomenon represents a subclinical vascular process, which in turn is indicated by a clinical pathology index. Specifically, WBV is the index for stasis. It is an intrinsic resistance of blood flow in the vascular system [3-5].

It is a property of the fluidity and internal friction of blood determined in part by adjacent fluidy blood cells as well as other constituents sliding past one another. Increase in WBV is subclinical risk factor for future cardiovascular

disease [4].Factors that increase WBV include haematocrit, total plasma protein, erythrocyte aggregation and erythrocyte deformability [3, 6]. Basically, increase in cell-cell or cell-macromolecule contacts leads to increase in friction and, by default, reduction in fluidity vis-à-vis increase in viscosity.

In current clinical practice, WBV is assessed mainly in the management of some diseases associated with critical hyperproteinaemia, polycythemia and retinal occlusion. Considering the implication of stasis in metabolic diseases, such usage is under-utility. Moreover, while several methods for the assessment of WBV exist, not every pathology unit has equipment for any of the diverse methods. The implication is that not many clinicians are able to assess WBV when they want to. However, a validated arithmetic method exists whereby WBV can be derived for any patient who has results for haematocrit and total serum proteins [6].

Based on the arithmetic method for WBV from haematocrit (HCT) and serum total proteins (TP), the objective of this work is develop an algorithm in the form of a chart by which clinicians can easily extrapolate WBV values in their consulting rooms or on the ward. Another objective is to suggest normal, subnormal and critical reference ranges applicable to this method.

Materials and Methods

This work is part of Translational Biomedical Science Research initiative of the author. It is supported materially by the Albury South West Pathology – a unit of Western Pathology Cluster of NSW Health Australia. Firstly, WBV at high shear stress was determined, from various possible pairs of haematocrit and total proteins, arithmetically according to validated formula [6]:

$$WBV\ (208\ Sec^{-1}) = 0.12 \times HCT + 0.17(TP - 2.07)$$

Where HCT = haematocrit (%) and TP = Serum total proteins (g/L)

In order to be able to obtain abnormally low levels through to abnormally high levels, WBV was determined with haematocrit levels 15% through to 66% and protein levels of 40g/L through to 90g/L. A chart was formulated so that WBV can be extrapolated. That is, if given any pair of haematocrit and serum protein values.

A second phase of analysis to determine standard deviations with a view to define and recommend reference ranges was performed. De-identified data (N = 76,912) from South West Pathology in the period of January 2006 to December 2008 was used. All data had available records of haematocrit and serum total protein results being concomitantly obtained from one phlebotomy point. The Ethics Committee of the Area Health Service granted request through the Operations Manager for the use of de-identified data.

Presumption of normal WBV: It was rationalized that since WBV is being derived from haematocrit and total protein, normalcy of these two parameters may be adjudged to be normal WBV. The pairs of (1) lowest acceptable level haematocrit of 37% and total protein of 60g/L corresponding to WBV value of 14.29 Sec^{-1} and (2) highest acceptable level haematocrit of 54% and total protein of 78g/L corresponding to WBV value of 19.39 Sec^{-1} were respectively taken as presumptive lower and upper limits for WBV. Subject to determination of two standard deviations from the mean and ascertainment of normal distribution based on Kurtosis, normal and subnormal ranges were defined.

Results

The chart obtained for the extrapolation of WBV is presented below (Fig. 1). As may be expected, the result demonstrates the following seven points

- Concomitant anemia and hypoproteinaemia translate to low WBV
- Concomitant normal levels of haematocrit and serum total proteins most often translates to normal WBV, but may also present subnormal levels.
- Concomitant polycythemia and hyperproteinaemia almost always translate to high WBV.
- Individuals who have anemia could still have normal WBV if total protein level is on the upper end of normalcy
- Individuals who have normal haematocrit could still have abnormally high or low WBV depending on the serum total protein level
- Critical hyperproteinaemia does not translate to hyperviscosity, if there is anemia. However, hypoviscosity is unlikely
- Polycythemia does not translate to hyperviscosity if there is hypoproteinaemia.

The central values including standard deviations for haematocrit, serum total protein and WBV obtained are provided in Table 1. The Table 1 shows that WBV in overall data is not evenly distributed (Kurtosis >3.0), whereas it is evenly distributed in the subset with normal haematocrit and total proteins (Kurtosis <1.0). Therefore, normal reference range is defined using two standard deviations from Mean of the normal subset.

$$Normal\ reference\ range = Mean \pm 2SD = 17.01 \pm (2 \times 1.00) = 15.01 - 19.01$$

Considering the presumptive lower and upper limits of 14.29 – 19.39, and obtained/recommendable normal range, the following reference values are obtained and highlighted in Fig. 1:

- ✓ Critically low level: ≤14.28 (208 Sec^{-1})
- ✓ Subnormal low level: 14.29 - 15.00 (208 Sec^{-1})
- ✓ Subnormal high level: 19.02 - 19.39 (208 Sec^{-1})
- ✓ Critically high level: ≥19.40 (208 Sec^{-1})

Whole Blood Viscosity at high shear rate (208 Sec`1) Assessment Chart: Clinician's user-friendly model

Haematocrit (%) — columns; Serum Total Proteins (g/L) — rows

Serum Total Proteins (g/L)	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
90	16.75	16.87	16.99	17.11	17.23	17.35	17.47	17.59	17.71	17.83	17.95	18.07	18.19	18.31	18.43	18.55	18.67	18.79	18.91	19.03	19.15	19.27	19.39	19.51	19.63	19.75
89	16.58	16.70	16.82	16.94	17.06	17.18	17.30	17.42	17.54	17.66	17.78	17.90	18.02	18.14	18.26	18.38	18.50	18.62	18.74	18.86	18.98	19.10	19.22	19.34	19.46	19.58
88	16.41	16.53	16.65	16.77	16.89	17.01	17.13	17.25	17.37	17.49	17.61	17.73	17.85	17.97	18.09	18.21	18.33	18.45	18.57	18.69	18.81	18.93	19.05	19.17	19.29	19.41
87	16.24	16.36	16.48	16.60	16.72	16.84	16.96	17.08	17.20	17.32	17.44	17.56	17.68	17.80	17.92	18.04	18.16	18.28	18.40	18.52	18.64	18.76	18.88	19.00	19.12	19.24
86	16.07	16.19	16.31	16.43	16.55	16.67	16.79	16.91	17.03	17.15	17.27	17.39	17.51	17.63	17.75	17.87	17.99	18.11	18.23	18.35	18.47	18.59	18.71	18.83	18.95	19.07
85	15.90	16.02	16.14	16.26	16.38	16.50	16.62	16.74	16.86	16.98	17.10	17.22	17.34	17.46	17.58	17.70	17.82	17.94	18.06	18.18	18.30	18.42	18.54	18.66	18.78	18.90
84	15.73	15.85	15.97	16.09	16.21	16.33	16.45	16.57	16.69	16.81	16.93	17.05	17.17	17.29	17.41	17.53	17.65	17.77	17.89	18.01	18.13	18.25	18.37	18.49	18.61	18.73
83	15.56	15.68	15.80	15.92	16.04	16.16	16.28	16.40	16.52	16.64	16.76	16.88	17.00	17.12	17.24	17.36	17.48	17.60	17.72	17.84	17.96	18.08	18.20	18.32	18.44	18.56
82	15.39	15.51	15.63	15.75	15.87	15.99	16.11	16.23	16.35	16.47	16.59	16.71	16.83	16.95	17.07	17.19	17.31	17.43	17.55	17.67	17.79	17.91	18.03	18.15	18.27	18.39
81	15.22	15.34	15.46	15.58	15.70	15.82	15.94	16.06	16.18	16.30	16.42	16.54	16.66	16.78	16.90	17.02	17.14	17.26	17.38	17.50	17.62	17.74	17.86	17.98	18.10	18.22
80	15.05	15.17	15.29	15.41	15.53	15.65	15.77	15.89	16.01	16.13	16.25	16.37	16.49	16.61	16.73	16.85	16.97	17.09	17.21	17.33	17.45	17.57	17.69	17.81	17.93	18.05
79	14.88	15.00	15.12	15.24	15.36	15.48	15.60	15.72	15.84	15.96	16.08	16.20	16.32	16.44	16.56	16.68	16.80	16.92	17.04	17.16	17.28	17.40	17.52	17.64	17.76	17.88
78	14.71	14.83	14.95	15.07	15.19	15.31	15.43	15.55	15.67	15.79	15.91	16.03	16.15	16.27	16.39	16.51	16.63	16.75	16.87	16.99	17.11	17.23	17.35	17.47	17.59	17.71
77	14.54	14.66	14.78	14.90	15.02	15.14	15.26	15.38	15.50	15.62	15.74	15.86	15.98	16.10	16.22	16.34	16.46	16.58	16.70	16.82	16.94	17.06	17.18	17.30	17.42	17.54
76	14.37	14.49	14.61	14.73	14.85	14.97	15.09	15.21	15.33	15.45	15.57	15.69	15.81	15.93	16.05	16.17	16.29	16.41	16.53	16.65	16.77	16.89	17.01	17.13	17.25	17.37
75	14.20	14.32	14.44	14.56	14.68	14.80	14.92	15.04	15.16	15.28	15.40	15.52	15.64	15.76	15.88	16.00	16.12	16.24	16.36	16.48	16.60	16.72	16.84	16.96	17.08	17.20
74	14.03	14.15	14.27	14.39	14.51	14.63	14.75	14.87	14.99	15.11	15.23	15.35	15.47	15.59	15.71	15.83	15.95	16.07	16.19	16.31	16.43	16.55	16.67	16.79	16.91	17.03
73	13.86	13.98	14.10	14.22	14.34	14.46	14.58	14.70	14.82	14.94	15.06	15.18	15.30	15.42	15.54	15.66	15.78	15.90	16.02	16.14	16.26	16.38	16.50	16.62	16.74	16.86
72	13.69	13.81	13.93	14.05	14.17	14.29	14.41	14.53	14.65	14.77	14.89	15.01	15.13	15.25	15.37	15.49	15.61	15.73	15.85	15.97	16.09	16.21	16.33	16.45	16.57	16.69
71	13.52	13.64	13.76	13.88	14.00	14.12	14.24	14.36	14.48	14.60	14.72	14.84	14.96	15.08	15.20	15.32	15.44	15.56	15.68	15.80	15.92	16.04	16.16	16.28	16.40	16.52
70	13.35	13.47	13.59	13.71	13.83	13.95	14.07	14.19	14.31	14.43	14.55	14.67	14.79	14.91	15.03	15.15	15.27	15.39	15.51	15.63	15.75	15.87	15.99	16.11	16.23	16.35
69	13.18	13.30	13.42	13.54	13.66	13.78	13.90	14.02	14.14	14.26	14.38	14.50	14.62	14.74	14.86	14.98	15.10	15.22	15.34	15.46	15.58	15.70	15.82	15.94	16.06	16.18
68	13.01	13.13	13.25	13.37	13.49	13.61	13.73	13.85	13.97	14.09	14.21	14.33	14.45	14.57	14.69	14.81	14.93	15.05	15.17	15.29	15.41	15.53	15.65	15.77	15.89	16.01
67	12.84	12.96	13.08	13.20	13.32	13.44	13.56	13.68	13.80	13.92	14.04	14.16	14.28	14.40	14.52	14.64	14.76	14.88	15.00	15.12	15.24	15.36	15.48	15.60	15.72	15.84
66	12.67	12.79	12.91	13.03	13.15	13.27	13.39	13.51	13.63	13.75	13.87	13.99	14.11	14.23	14.35	14.47	14.59	14.71	14.83	14.95	15.07	15.19	15.31	15.43	15.55	15.67
65	12.50	12.62	12.74	12.86	12.98	13.10	13.22	13.34	13.46	13.58	13.70	13.82	13.94	14.06	14.18	14.30	14.42	14.54	14.66	14.78	14.90	15.02	15.14	15.26	15.38	15.50
64	12.33	12.45	12.57	12.69	12.81	12.93	13.05	13.17	13.29	13.41	13.53	13.65	13.77	13.89	14.01	14.13	14.25	14.37	14.49	14.61	14.73	14.85	14.97	15.09	15.21	15.33
63	12.16	12.28	12.40	12.52	12.64	12.76	12.88	13.00	13.12	13.24	13.36	13.48	13.60	13.72	13.84	13.96	14.08	14.20	14.32	14.44	14.56	14.68	14.80	14.92	15.04	15.16
62	11.99	12.11	12.23	12.35	12.47	12.59	12.71	12.83	12.95	13.07	13.19	13.31	13.43	13.55	13.67	13.79	13.91	14.03	14.15	14.27	14.39	14.51	14.63	14.75	14.87	14.99
61	11.82	11.94	12.06	12.18	12.30	12.42	12.54	12.66	12.78	12.90	13.02	13.14	13.26	13.38	13.50	13.62	13.74	13.86	13.98	14.10	14.22	14.34	14.46	14.58	14.70	14.82
60	11.65	11.77	11.89	12.01	12.13	12.25	12.37	12.49	12.61	12.73	12.85	12.97	13.09	13.21	13.33	13.45	13.57	13.69	13.81	13.93	14.05	14.17	14.29	14.41	14.53	14.65
59	11.48	11.60	11.72	11.84	11.96	12.08	12.20	12.32	12.44	12.56	12.68	12.80	12.92	13.04	13.16	13.28	13.40	13.52	13.64	13.76	13.88	14.00	14.12	14.24	14.36	14.48
58	11.31	11.43	11.55	11.67	11.79	11.91	12.03	12.15	12.27	12.39	12.51	12.63	12.75	12.87	12.99	13.11	13.23	13.35	13.47	13.59	13.71	13.83	13.95	14.07	14.19	14.31
57	11.14	11.26	11.38	11.50	11.62	11.74	11.86	11.98	12.10	12.22	12.34	12.46	12.58	12.70	12.82	12.94	13.06	13.18	13.30	13.42	13.54	13.66	13.78	13.90	14.02	14.14
56	10.97	11.09	11.21	11.33	11.45	11.57	11.69	11.81	11.93	12.05	12.17	12.29	12.41	12.53	12.65	12.77	12.89	13.01	13.13	13.25	13.37	13.49	13.61	13.73	13.85	13.97
55	10.80	10.92	11.04	11.16	11.28	11.40	11.52	11.64	11.76	11.88	12.00	12.12	12.24	12.36	12.48	12.60	12.72	12.84	12.96	13.08	13.20	13.32	13.44	13.56	13.68	13.80
54	10.63	10.75	10.87	10.99	11.11	11.23	11.35	11.47	11.59	11.71	11.83	11.95	12.07	12.19	12.31	12.43	12.55	12.67	12.79	12.91	13.03	13.15	13.27	13.39	13.51	13.63
53	10.46	10.58	10.70	10.82	10.94	11.06	11.18	11.30	11.42	11.54	11.66	11.78	11.90	12.02	12.14	12.26	12.38	12.50	12.62	12.74	12.86	12.98	13.10	13.22	13.34	13.46
52	10.29	10.41	10.53	10.65	10.77	10.89	11.01	11.13	11.25	11.37	11.49	11.61	11.73	11.85	11.97	12.09	12.21	12.33	12.45	12.57	12.69	12.81	12.93	13.05	13.17	13.29
51	10.12	10.24	10.36	10.48	10.60	10.72	10.84	10.96	11.08	11.20	11.32	11.44	11.56	11.68	11.80	11.92	12.04	12.16	12.28	12.40	12.52	12.64	12.76	12.88	13.00	13.12
50	9.95	10.07	10.19	10.31	10.43	10.55	10.67	10.79	10.91	11.03	11.15	11.27	11.39	11.51	11.63	11.75	11.87	11.99	12.11	12.23	12.35	12.47	12.59	12.71	12.83	12.95
49	9.78	9.90	10.02	10.14	10.26	10.38	10.50	10.62	10.74	10.86	10.98	11.10	11.22	11.34	11.46	11.58	11.70	11.82	11.94	12.06	12.18	12.30	12.42	12.54	12.66	12.78
48	9.61	9.73	9.85	9.97	10.09	10.21	10.33	10.45	10.57	10.69	10.81	10.93	11.05	11.17	11.29	11.41	11.53	11.65	11.77	11.89	12.01	12.13	12.25	12.37	12.49	12.61
47	9.44	9.56	9.68	9.80	9.92	10.04	10.16	10.28	10.40	10.52	10.64	10.76	10.88	11.00	11.12	11.24	11.36	11.48	11.60	11.72	11.84	11.96	12.08	12.20	12.32	12.44
46	9.27	9.39	9.51	9.63	9.75	9.87	9.99	10.11	10.23	10.35	10.47	10.59	10.71	10.83	10.95	11.07	11.19	11.31	11.43	11.55	11.67	11.79	11.91	12.03	12.15	12.27
45	9.10	9.22	9.34	9.46	9.58	9.70	9.82	9.94	10.06	10.18	10.30	10.42	10.54	10.66	10.78	10.90	11.02	11.14	11.26	11.38	11.50	11.62	11.74	11.86	11.98	12.10
44	8.93	9.05	9.17	9.29	9.41	9.53	9.65	9.77	9.89	10.01	10.13	10.25	10.37	10.49	10.61	10.73	10.85	10.97	11.09	11.21	11.33	11.45	11.57	11.69	11.81	11.93
43	8.76	8.88	9.00	9.12	9.24	9.36	9.48	9.60	9.72	9.84	9.96	10.08	10.20	10.32	10.44	10.56	10.68	10.80	10.92	11.04	11.16	11.28	11.40	11.52	11.64	11.76
42	8.59	8.71	8.83	8.95	9.07	9.19	9.31	9.43	9.55	9.67	9.79	9.91	10.03	10.15	10.27	10.39	10.51	10.63	10.75	10.87	10.99	11.11	11.23	11.35	11.47	11.59
41	8.42	8.54	8.66	8.78	8.90	9.02	9.14	9.26	9.38	9.50	9.62	9.74	9.86	9.98	10.10	10.22	10.34	10.46	10.58	10.70	10.82	10.94	11.06	11.18	11.30	11.42
40	8.25	8.37	8.49	8.61	8.73	8.85	8.97	9.09	9.21	9.33	9.45	9.57	9.69	9.81	9.93	10.05	10.17	10.29	10.41	10.53	10.65	10.77	10.89	11.01	11.13	11.25

Serum Total Proteins (g/L)	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66
90	19.87	19.99	20.11	20.23	20.35	20.47	20.59	20.71	20.83	20.95	21.07	21.19	21.31	21.43	21.55	21.67	21.79	21.91	22.03	22.15	22.27	22.39	22.51	22.63	22.75	22.87
89	19.70	19.82	19.94	20.06	20.18	20.30	20.42	20.54	20.66	20.78	20.90	21.02	21.14	21.26	21.38	21.50	21.62	21.74	21.86	21.98	22.10	22.22	22.34	22.46	22.58	22.70
88	19.53	19.65	19.77	19.89	20.01	20.13	20.25	20.37	20.49	20.61	20.73	20.85	20.97	21.09	21.21	21.33	21.45	21.57	21.69	21.81	21.93	22.05	22.17	22.29	22.41	22.53
87	19.36	19.48	19.60	19.72	19.84	19.96	20.08	20.20	20.32	20.44	20.56	20.68	20.80	20.92	21.04	21.16	21.28	21.40	21.52	21.64	21.76	21.88	22.00	22.12	22.24	22.36
86	19.19	19.31	19.43	19.55	19.67	19.79	19.91	20.03	20.15	20.27	20.39	20.51	20.63	20.75	20.87	20.99	21.11	21.23	21.35	21.47	21.59	21.71	21.83	21.95	22.07	22.19
85	19.02	19.14	19.26	19.38	19.50	19.62	19.74	19.86	19.98	20.10	20.22	20.34	20.46	20.58	20.70	20.82	20.94	21.06	21.18	21.30	21.42	21.54	21.66	21.78	21.90	22.02
84	18.85	18.97	19.09	19.21	19.33	19.45	19.57	19.69	19.81	19.93	20.05	20.17	20.29	20.41	20.53	20.65	20.77	20.89	21.01	21.13	21.25	21.37	21.49	21.61	21.73	21.85
83	18.68	18.80	18.92	19.04	19.16	19.28	19.40	19.52	19.64	19.76	19.88	20.00	20.12	20.24	20.36	20.48	20.60	20.72	20.84	20.96	21.08	21.20	21.32	21.44	21.56	21.68
82	18.51	18.63	18.75	18.87	18.99	19.11	19.23	19.35	19.47	19.59	19.71	19.83	19.95	20.07	20.19	20.31	20.43	20.55	20.67	20.79	20.91	21.03	21.15	21.27	21.39	21.51
81	18.34	18.46	18.58	18.70	18.82	18.94	19.06	19.18	19.30	19.42	19.54	19.66	19.78	19.90	20.02	20.14	20.26	20.38	20.50	20.62	20.74	20.86	20.98	21.10	21.22	21.34
80	18.17	18.29	18.41	18.53	18.65	18.77	18.89	19.01	19.13	19.25	19.37	19.49	19.61	19.73	19.85	19.97	20.09	20.21	20.33	20.45	20.57	20.69	20.81	20.93	21.05	21.17
79	18.00	18.12	18.24	18.36	18.48	18.60	18.72	18.84	18.96	19.08	19.20	19.32	19.44	19.56	19.68	19.80	19.92	20.04	20.16	20.28	20.40	20.52	20.64	20.76	20.88	21.00
78	17.83	17.95	18.07	18.19	18.31	18.43	18.55	18.67	18.79	18.91	19.03	19.15	19.27	19.39	19.51	19.63	19.75	19.87	19.99	20.11	20.23	20.35	20.47	20.59	20.71	20.83
77	17.66	17.78	17.90	18.02	18.14	18.26	18.38	18.50	18.62	18.74	18.86	18.98	19.10	19.22	19.34	19.46	19.58	19.70	19.82	19.94	20.06	20.18	20.30	20.42	20.54	20.66
76	17.49	17.61	17.73	17.85	17.97	18.09	18.21	18.33	18.45	18.57	18.69	18.81	18.93	19.05	19.17	19.29	19.41	19.53	19.65	19.77	19.89	20.01	20.13	20.25	20.37	20.49
75	17.32	17.44	17.56	17.68	17.80	17.92	18.04	18.16	18.28	18.40	18.52	18.64	18.76	18.88	19.00	19.12	19.24	19.36	19.48	19.60	19.72	19.84	19.96	20.08	20.20	20.32
74	17.15	17.27	17.39	17.51	17.63	17.75	17.87	17.99	18.11	18.23	18.35	18.47	18.59	18.71	18.83	18.95	19.07	19.19	19.31	19.43	19.55	19.67	19.79	19.91	20.03	20.15
73	16.98	17.10	17.22	17.34	17.46	17.58	17.70	17.82	17.94	18.06	18.18	18.30	18.42	18.54	18.66	18.78	18.90	19.02	19.14	19.26	19.38	19.50	19.62	19.74	19.86	19.98
72	16.81	16.93	17.05	17.17	17.29	17.41	17.53	17.65	17.77	17.89	18.01	18.13	18.25	18.37	18.49	18.61	18.73	18.85	18.97	19.09	19.21	19.33	19.45	19.57	19.69	19.81
71	16.64	16.76	16.88	17.00	17.12	17.24	17.36	17.48	17.60	17.72	17.84	17.96	18.08	18.20	18.32	18.44	18.56	18.68	18.80	18.92	19.04	19.16	19.28	19.40	19.52	19.64
70	16.47	16.59	16.71	16.83	16.95	17.07	17.19	17.31	17.43	17.55	17.67	17.79	17.91	18.03	18.15	18.27	18.39	18.51	18.63	18.75	18.87	18.99	19.11	19.23	19.35	19.47
69	16.30	16.42	16.54	16.66	16.78	16.90	17.02	17.14	17.26	17.38	17.50	17.62	17.74	17.86	17.98	18.10	18.22	18.34	18.46	18.58	18.70	18.82	18.94	19.06	19.18	19.30
68	16.13	16.25	16.37	16.49	16.61	16.73	16.85	16.97	17.09	17.21	17.33	17.45	17.57	17.69	17.81	17.93	18.05	18.17	18.29	18.41	18.53	18.65	18.77	18.89	19.01	19.13
67	15.96	16.08	16.20	16.32	16.44	16.56	16.68	16.80	16.92	17.04	17.16	17.28	17.40	17.52	17.64	17.76	17.88	18.00	18.12	18.24	18.36	18.48	18.60	18.72	18.84	18.96
66	15.79	15.91	16.03	16.15	16.27	16.39	16.51	16.63	16.75	16.87	16.99	17.11	17.23	17.35	17.47	17.59	17.71	17.83	17.95	18.07	18.19	18.31	18.43	18.55	18.67	18.79
65	15.62	15.74	15.86	15.98	16.10	16.22	16.34	16.46	16.58	16.70	16.82	16.94	17.06	17.18	17.30	17.42	17.54	17.66	17.78	17.90	18.02	18.14	18.26	18.38	18.50	18.62
64	15.45	15.57	15.69	15.81	15.93	16.05	16.17	16.29	16.41	16.53	16.65	16.77	16.89	17.01	17.13	17.25	17.37	17.49	17.61	17.73	17.85	17.97	18.09	18.21	18.33	18.45
63	15.28	15.40	15.52	15.64	15.76	15.88	16.00	16.12	16.24	16.36	16.48	16.60	16.72	16.84	16.96	17.08	17.20	17.32	17.44	17.56	17.68	17.80	17.92	18.04	18.16	18.28
62	15.11	15.23	15.35	15.47	15.59	15.71	15.83	15.95	16.07	16.19	16.31	16.43	16.55	16.67	16.79	16.91	17.03	17.15	17.27	17.39	17.51	17.63	17.75	17.87	17.99	18.11
61	14.94	15.06	15.18	15.30	15.42	15.54	15.66	15.78	15.90	16.02	16.14	16.26	16.38	16.50	16.62	16.74	16.86	16.98	17.10	17.22	17.34	17.46	17.58	17.70	17.82	17.94
60	14.77	14.89	15.01	15.13	15.25	15.37	15.49	15.61	15.73	15.85	15.97	16.09	16.21	16.33	16.45	16.57	16.69	16.81	16.93	17.05	17.17	17.29	17.41	17.53	17.65	17.77
59	14.60	14.72	14.84	14.96	15.08	15.20	15.32	15.44	15.56	15.68	15.80	15.92	16.04	16.16	16.28	16.40	16.52	16.64	16.76	16.88	17.00	17.12	17.24	17.36	17.48	17.60
58	14.43	14.55	14.67	14.79	14.91	15.03	15.15	15.27	15.39	15.51	15.63	15.75	15.87	15.99	16.11	16.23	16.35	16.47	16.59	16.71	16.83	16.95	17.07	17.19	17.31	17.43
57	14.26	14.38	14.50	14.62	14.74	14.86	14.98	15.10	15.22	15.34	15.46	15.58	15.70	15.82	15.94	16.06	16.18	16.30	16.42	16.54	16.66	16.78	16.90	17.02	17.14	17.26
56	14.09	14.21	14.33	14.45	14.57	14.69	14.81	14.93	15.05	15.17	15.29	15.41	15.53	15.65	15.77	15.89	16.01	16.13	16.25	16.37	16.49	16.61	16.73	16.85	16.97	17.09
55	13.92	14.04	14.16	14.28	14.40	14.52	14.64	14.76	14.88	15.00	15.12	15.24	15.36	15.48	15.60	15.72	15.84	15.96	16.08	16.20	16.32	16.44	16.56	16.68	16.80	16.92
54	13.75	13.87	13.99	14.11	14.23	14.35	14.47	14.59	14.71	14.83	14.95	15.07	15.19	15.31	15.43	15.55	15.67	15.79	15.91	16.03	16.15	16.27	16.39	16.51	16.63	16.75
53	13.58	13.70	13.82	13.94	14.06	14.18	14.30	14.42	14.54	14.66	14.78	14.90	15.02	15.14	15.26	15.38	15.50	15.62	15.74	15.86	15.98	16.10	16.22	16.34	16.46	16.58
52	13.41	13.53	13.65	13.77	13.89	14.01	14.13	14.25	14.37	14.49	14.61	14.73	14.85	14.97	15.09	15.21	15.33	15.45	15.57	15.69	15.81	15.93	16.05	16.17	16.29	16.41
51	13.24	13.36	13.48	13.60	13.72	13.84	13.96	14.08	14.20	14.32	14.44	14.56	14.68	14.80	14.92	15.04	15.16	15.28	15.40	15.52	15.64	15.76	15.88	16.00	16.12	16.24
50	13.07	13.19	13.31	13.43	13.55	13.67	13.79	13.91	14.03	14.15	14.27	14.39	14.51	14.63	14.75	14.87	14.99	15.11	15.23	15.35	15.47	15.59	15.71	15.83	15.95	16.07
49	12.90	13.02	13.14	13.26	13.38	13.50	13.62	13.74	13.86	13.98	14.10	14.22	14.34	14.46	14.58	14.70	14.82	14.94	15.06	15.18	15.30	15.42	15.54	15.66	15.78	15.90
48	12.73	12.85	12.97	13.09	13.21	13.33	13.45	13.57	13.69	13.81	13.93	14.05	14.17	14.29	14.41	14.53	14.65	14.77	14.89	15.01	15.13	15.25	15.37	15.49	15.61	15.73
47	12.56	12.68	12.80	12.92	13.04	13.16	13.28	13.40	13.52	13.64	13.76	13.88	14.00	14.12	14.24	14.36	14.48	14.60	14.72	14.84	14.96	15.08	15.20	15.32	15.44	15.56
46	12.39	12.51	12.63	12.75	12.87	12.99	13.11	13.23	13.35	13.47	13.59	13.71	13.83	13.95	14.07	14.19	14.31	14.43	14.55	14.67	14.79	14.91	15.03	15.15	15.27	15.39
45	12.22	12.34	12.46	12.58	12.70	12.82	12.94	13.06	13.18	13.30	13.42	13.54	13.66	13.78	13.90	14.02	14.14	14.26	14.38	14.50	14.62	14.74	14.86	14.98	15.10	15.22
44	12.05	12.17	12.29	12.41	12.53	12.65	12.77	12.89	13.01	13.13	13.25	13.37	13.49	13.61	13.73	13.85	13.97	14.09	14.21	14.33	14.45	14.57	14.69	14.81	14.93	15.05
43	11.88	12.00	12.12	12.24	12.36	12.48	12.60	12.72	12.84	12.96	13.08	13.20	13.32	13.44	13.56	13.68	13.80	13.92	14.04	14.16	14.28	14.40	14.52	14.64	14.76	14.88
42	11.71	11.83	11.95	12.07	12.19	12.31	12.43	12.55	12.67	12.79	12.91	13.03	13.15	13.27	13.39	13.51	13.63	13.75	13.87	13.99	14.11	14.23	14.35	14.47	14.59	14.71
41	11.54	11.66	11.78	11.90	12.02	12.14	12.26	12.38	12.50	12.62	12.74	12.86	12.98	13.10	13.22	13.34	13.46	13.58	13.70	13.82	13.94	14.06	14.18	14.30	14.42	14.54
40	11.37	11.49	11.61	11.73	11.85	11.97	12.09	12.21	12.33	12.45	12.57	12.69	12.81	12.93	13.05	13.17	13.29	13.41	13.53	13.65	13.77	13.89	14.01	14.13	14.25	14.37

Color codes & Recommended reference ranges

Critical high level: ≥ 19.40
Subnormal high level: 19.02 - 19.39
Normal reference range: 15.01 - 19.01
Subnormal low level: 14.29 - 15.00
Critical low level: ≤ 14.28
Purple text zone: WBV values when both haematocrit and total protein results are within acceptable clinical normal range

Table 1 Central values for overall data and the normal subset

	Mean		Median		SD		Kurtosis	
	Overall†	Normal‡	Overall†	Normal‡	Overall†	Normal‡	Overall†	Normal‡
Haematocrit %	43	43	43	43	4.56	4.07	1.93	0.74
Total protein g/L	72	72	72	72	5.75	4.73	3.66	0.04
WBV (208 Sec^{-1})	16.94	17.01*	17.02	17.03	1.26	1.00*	3.17	-0.24

Keys: †All data set (N = 76,912), ‡Data subset with normal haematocrit and total proteins (N = 67,582); SD = standard deviation, WBV = calculated whole blood viscosity at high shear rate.

Discussion

This study has determined what should be reference values for the arithmetic method for WBV (Fig. 1). The result shows that haematocrit and total proteins are not evenly distributed in the general population of patients, except in the subset of those who have normal results (Table 1). Therefore, it would be more appropriate to decide the reference values using only the normal subset.

The clinical applicability of WBV measurements in cardiovascular risk assessment requires reference values [5]. This report presents reference ranges for WBV for the arithmetic method. It also presents a user-friendly algorithm in the form of colored chart (Fig. 1). WBV has been acknowledged as a factor in all metabolic diseases. While hyperviscosity syndrome is ideally a subclinical cardiovascular disease state [7], it remains the single component of Virchow's triad that has been most consistently neglected in general practice. Although accessibility may be an excuse, the algorithm reported here contributes to make assessment of WBV accessible and more inexcusable.

Gender factor is not included in the arithmetic formula. This is explainable by the observation from other methods of blood viscosity measurement that WBV level may be higher in men compared to women, but not correcting for haematocrit [6]. That is, even in tandem proteinaemia status, a woman may present lower WBV level due to the factor of lower normal range for haematocrit.

Clinical assessment of, and research studies on blood viscosity are discretionally based on a choice of plasma or whole blood. This implies that the choice of specimen for blood viscosity has yet to be agreed upon. Proponents of plasma viscosity discuss factors influencing blood viscosity with a discountenance or little regards for the blood flow rate and cellular/haematocrit contributions [8]. The objective of this work is not to argue against/for plasma viscosity/WBV. However, the inference from the result that critical hyperproteinaemia does not translate to hyperviscosity if there is anemia, but hypoviscosity is unlikely lends credence to the strength and weakness of plasma viscosity (Fig. 1). It is noteworthy that erythrocyte concentration (haematocrit) is a factor in deformability, which is strongly influenced by erythrocyte oxidative stress [9, 10]. Haematocrit is also a factor in erythrocyte aggregation and sedimentation rate, which influences flow rate and viscosity [11, 12].

What this report contributes is a tool by which clinicians armed with results of the routine full blood count and total protein can deduce WBV. The novelty is that it is without a cost to the patient or healthcare provider. The importance of this report lies in the usefulness for the management of diabetes and antiplatelet monitoring amongst others. For instance, it has been shown that aspirin therapy has as yet no clinical evidence-base, but with additional intervention of the underlying oxidative stress, reduces blood viscosity in diabetes [13, 14].

Limitations: Temperature is also a factor that influences WBV. The effect that temperature has on blood viscosity can be gleaned from the use of whole body hypothermia during certain surgical procedures. Basically, hypothermia increases blood viscosity, increases resistance to blood flow and reduction in blood loss in a sequential feedforward manner [15]. However, the method by which this chart has been formulated has not taken body temperature on board.

Recommendation: Beside the method adopted in this study, different methods exist for the determination of WBV and associated with this is different normal values. Further study is proposed to investigate how the reference ranges reported here compares with the reference ranges of other blood viscosity methods. Furthermore, a close central value has been observed in poorly controlled diabetes as in the excellently controlled group using this arithmetic method [16]. Further study is also proposed to investigate the degree of deviation and prevalence of abnormality at different stages of diabetes. The same investigation of the degree of deviation and prevalence of abnormality can be done for other diseases where cardiovascular complication is a concern.

Hypoviscosity syndrome has been mentioned in the literature [15], but gained little or no attention. The prevalence of low level WBV in the general population could be determined from this method. However, such statement of prevalence would be more credible after the recommended comparative analysis to corroborate this report.

Conclusion

It has been recommended that blood viscosity should be measured routinely in medical practice [7]. However, the test has yet to be accessible from every laboratory, and especially in rural areas. Given the arithmetic method, what this article contributes is a tool that enables clinicians to assess WBV for any patient who has got the need to be tested for full blood count and total proteins. The tool is simple to use in the consulting rooms or during routine ward rounds.

Acknowledgement

Receipt of an approval from HREC committee of the Greater Southern Area Health Service, NSW Health is hereby gratefully appreciated. The operations manager of the South West Pathology Service and Nathan Cann are also appreciated for their contribution in data acquisition and support in the research initiative.

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