Measurement of human blood viscosity a using Falling Needle Rheometer and the correlation to the Modified Herschel-Bulkley model equation

Hideki Yamamoto a,*, Takafulmi Yabuta a, Yusuke Negi a, Daiki Horikawa a, Kimito Kawamura b, Eiji Tamura c, Katsuhiro Tanaka d, Fujimaro Ishida d

a Faculty of Environmental and Urban Engineering, Department of Chemical, Energy and Environmental Engineering, Kansai University, Suita, Osaka, Japan
b Nippon Steel Technology Co. Ltd., Amagasaki, Hyogo, Japan
c Nippon Steel Technology Co. Ltd., Ibaraki, Japan
d Department of Neurosurgery, NHO Mie Chuo Medical Center, Hisai, Mie Japan

ABSTRACT

We measured the blood viscosity of 25 male and 25 female healthy people (total 50) using a compact-sized falling needle viscometer (Falling Needle Rheometer) capable of highly accurate measurements. Based on the analysis of the flow characteristics, most of the blood specific non-Newtonian fluid (Casson fluid) behavior was confirmed. Additionally, the blood from males has a higher apparent viscosity and Casson yield value than that from women. Furthermore, a new Herschel-Bulkley type model equation representing the relationship between the shear rate and apparent viscosity of human blood was proposed based on the measured blood flow characteristics. The proposed model improved the exponential term on the shear rate and added the constant term on the yield stress so that the measured value can be correlated with a high accuracy. Using the proposed model equation, the correlation accuracy of all of the measured human blood viscosities was better than in the Herschel-Bulkley model equation and Casson model in a wide range of shear rate regions. By incorporating numerical flow analysis (computational fluid dynamics), this model equation may contribute to analyses considering the non-Newtonian fluidity of human blood.

1. Introduction

Blood is composed of cellular and plasma components. Previous reports have indicated that the blood viscosity greatly affects the number of erythrocytes, which are the main cellular components of blood, and their aggregate dispersion. The plasma components in blood are fibrinogen, globulin, water, and various other proteins and inorganic salts [1]. The importance of understanding the flow characteristics of human blood has increased in the medical field in recent years. An accurate understanding of the blood viscosity and flow state in blood vessels is also very important from the viewpoint of cardiovascular diseases, such as stroke and myocardial infarction, preventive medicine, and health management [2, 3]. However, blood has multiphase flow characteristics in which cellular components and plasma components are mixed, and the fluid behavior is complicated due to the aggregation and dispersion of cellular components. Additionally, measurement is not easy because blood has coagulation properties outside the body [4]. In currently rotary viscometers and capillary viscometers, accurate measurement in the low shear rate region and rapid measurement after blood sampling are affected by red blood cell agglutination and blood coagulation.

We reported the development of a compact-sized falling needle viscometer (Falling Needle Rheometer) (Asahi Quality Innovations, Ltd., Ibaraki, Japan, Nippon Steel Technology Co., Ltd., Tokyo, Japan) capable of measuring blood in a small amount (4 ml) with high accuracy, and reported the human blood flow characteristics and non-Newton analysis methods. However, the number of blood specimens by gender (male/female) for examining human blood viscosity characteristics is still small and not fully evaluated [5, 6, 7]. In the present study, viscosity measurements were conducted on blood from 50 healthy volunteers (25 males, 25 females) from a database of blood viscosity, and a new flow analysis model equation was developed. The database of blood viscosity was created to examine individual differences and differences in blood viscosity between male and female.

In recent years in the medical field, when fluid flow characteristics are used as numerical values in numerical flow analysis (computational fluid dynamics, CFD), Newtonian fluid conditions are often applied as the
blood viscosity parameters, primarily to simplify the analysis [8, 9]. However, blood exhibits non-Newtonian characteristics by increasing the viscosity in low shear rate regions, and this cannot be ignored in computational fluid dynamics [10]. Therefore, a fluid viscosity model representing the shear rate and apparent viscosity of blood is required for aneurysm analysis [11]. In general, fluid viscosity models that represent shear rates and apparent viscosities of various fluids include blood are Newton’s model, power law model, Curry-type model, Carreau-Yasuda model, bi-exponential function models, Casson model and Herschel-Bulkley (HB) model [12]. Among these, the Casson or HB models are considered for correlation to human blood flow characteristics [13, 14]. However, measurements show that a region exists where the model equation does not sufficiently correspond to the actual blood viscosity in the specific shear rate region with respect to the blood flow characteristics. Therefore, the available shear rate region is limited. Although the HB model shows high fitting accuracy at the low shear rate region, the viscosity decreases without reaching a constant value in the high shear region. Furthermore, the Casson model shows high fitting accuracy in the high shear rate region but tends to be less than the original viscosity at the low shear rate region. A new model equation that can adapt to a wide range of shear rate regions is considered necessary to improve the applicability and versatility of human blood viscosity measurements in the medical field. Additionally, in CFD, if it is possible to use a model equation with blood as a non-Newtonian fluid, then it is possible to simulate blood flow according to the actual conditions. For instance, this makes the simulation more accurate for evaluating the rupture point of a cerebral aneurysm.

The purpose of this study is to improve the fitting accuracy of the calculated value obtained by the new model equation and the measured value obtained by the experiment. In this study, we measured the viscosity of human blood from 50 healthy subjects and developed a flow analysis model from the results. We also improved the HB model equation and developed a model equation for blood viscosity corresponding to a wide range of shear rates.

2. Analysis theory of Falling Needle Rheometer

A small dropping needle type viscometer (FNR) is a viscometer that can measure the viscosity and flow characteristics of a fluid from the terminal velocity of a small cylindrical needle (weight) that naturally falls within the fluid. FNR was developed for blood viscosity measurement. The measurements are shown in Figure 1 and the measurement principle was obtained from the fluid model shown in Figure 2 [5] [10].

Table 1. Average density values of Needle.

| Needle number | Density [kg/m³] |
|---------------|-----------------|
| 1             | 1087.5          |
| 2             | 1112.8          |
| 3             | 1117.3          |
| 4             | 1139.8          |
| 5             | 1155.1          |
| 6             | 1165.2          |
| 7             | 1191.7          |
| 8             | 1220.0          |
| 9             | 1285.5          |
| 10            | 1351.4          |
| 11            | 1419.9          |
| 12            | 1483.1          |

Figure 1. Experimental apparatus of Falling Needle Rheometer (FNR).

Figure 2. Fluid model around of falling needle in the fluid.
Figure 3. Measured value area and average values of blood for male, female and all people with anticoagulant at 305 K.
As shown in Figure 2, consider a case in which a cylindrical needle with a radius kR (m) and length L (m) falls freely in a circular tube container with a radius R (m). Eq. (1) was derived from the equilibrium relationship acting on the microcylindrical shell of the inner diameter r (m), outer diameter r + dr (m), and length L (m).

\[
\frac{1}{r} \frac{d}{dr} \left( \frac{P_1 - P_2}{L} \right) = \frac{d}{dr}\left( \frac{1}{r} \right)
\]

(1)

An upward stress \( \tau \) (Pa) is exerted on the needle wall surface, the pressures \( P_1 \) (Pa) and \( P_2 \) (Pa) act on the upper and lower surfaces, and gravity and buoyancy forces on the needle. \( \rho_1 \) and \( \rho_2 \) are the density of fluid and Needle, respectively. Eq. (2) is thus obtained from the balance of the forces acting on the needle. Here, it is assumed that \( \Delta P = P_1 - P_2 \) (\( \Delta P \leq 0 \)).

\[
\begin{align*}
\left( \rho_1 - \rho_2 \right) g \pi (kR)^2 L + \pi (kR)^2 \Delta P &= 2 \pi k R \ell \gamma (r=0) \\
\end{align*}
\]

(2)

The amount of fluid flow \( Q \) (m³/s) to transfer between the falling needle surface and the container wall due to falling of the needle can be calculated by Eq. (3).

\[
Q = 2 \pi \int_{kR}^{\infty} w r dr = \pi (kR)^2 U_t
\]

(3)

Here, \( U_t \) (m/s) is the terminal falling speed of the needle. The boundary condition is expressed by Eq. (4) [4].

\[
\begin{align*}
\dot{u}_{r=kR} &= -U_t \\
\dot{u}_{r=0} &= 0
\end{align*}
\]

(4)

The derived Eqs. (1), (2), (3), and (4) are basic equations for flow analysis. Simultaneously with Eqs. (1), (2), (3), and (4) and the corresponding constituent equations of fluid, analysis of the shear rate and shear stress on the needle surface becomes possible. In the present study, analysis was performed by applying the relational expression of the shear rate and shear stress, which is the constitutive equation of Newtonian fluid, to Eqs. (1), (2), (3), and (4). The analysis results are shown below as Eqs. (5), (6), (7), and (8). The viscosity \( \mu \) (mPa s) of the Newtonian fluid is expressed by Eq. (6). In Equation (6), \( G \) is a value particular to the device determined by the radius ratio \( k \) (·) of the needle and cell and the cell radius \( R \) (m), expressed by Eq. (6).

\[
\mu = \frac{\left( \rho_1 - \rho_2 \right) g \pi (kR)^2 L + \pi (kR)^2 \Delta P}{2 \pi k R \ell \gamma (r=0)}
\]

(5)

\[
G = \frac{2 \left( k^2 + 1 \right)}{(kR)^2 \left\{ (k^2 + 1) \ln k + k - k^2 \right\}}
\]

(6)

The shear rate \( \gamma \) (s⁻¹) and shear stress \( \tau \) (Pa) at the surface \( r = kR \) of the needle are shown in Eqs. (7) and (8), respectively [4].

\[
\dot{\tau}_{r=kR} = \frac{du}{dr} = \frac{(k^2 - 1) U_t}{kR \left\{ (k^2 + 1) \ln k + k - k^2 \right\}}
\]

(7)

\[
\tau_{r=kR} = \frac{(\rho_1 - \rho_2) g (1 - k^2) kR}{2 (k^2 + 1)}
\]

(8)

3. Herschel-Bulkley model equation (HB model)

A HB model was used as a basic equation to develop a model equation of the shear rate-apparent viscosity dependence. The general equation of the HB model is shown below.

\[
\mu = K \gamma^{n-1} + \tau_0 \gamma
\]

(9)

In Eq. (9), \( \mu \) (mPa s) is the viscosity, \( K \) (mPa s^n) is the non-Newtonian viscosity coefficient, \( \gamma \) (s⁻¹) is the shear rate, \( \tau_0 \) (mPa) is the yield stress, and \( n \) is the fluid behavior index (·). This model shows good fitting in the low shear rate region of human blood viscosity [16]. However, the blood viscosity decreases without showing the typical constant value in the high shear rate region.

4. Experimental methods

This study was approved and conducted by the Ethics Review Committee of Mie Central Medical Center on April 18, 2016, based on an application by Dr. Fujimaro Ishida (application number 2016–09). Also, informed consent was obtained from all the people who took blood in the experiment. In the blood viscosity measurement, the blood samples were obtained from 50 volunteers under the approval of the ethics committee of Mie Central Medical Center.

In the experiment, an ethylenediaminetetraacetic acid dipotassium salt dihydrate (EDTA-2K)-containing vacuum blood collection tube (Japan Becton Dickinson Co., Ltd., Tokyo, Japan) was used to sample blood. The 50 volunteers comprised of 25 males and 25 females in their 20 s–60 s (5 of each sex for each age group). As a required condition for measurement of the blood viscosity, blood was taken at 7:30 AM if the

Table 2. Average flow analysis values of male, female, and all people.

| Needle number | Shear rate \( \gamma \) [s⁻¹] | Shear stress \( \tau \) [Pa] | Viscosity \( \mu \) [mPa s] |
|---------------|------------------------------|-----------------------------|-----------------------------|
| (a) male       |                              |                             |                             |
| 1             | 13.7                         | 0.151                       | 12.1                        |
| 2             | 28.4                         | 0.258                       | 9.63                        |
| 3             | 29.3                         | 0.278                       | 10.0                        |
| 4             | 49.0                         | 0.375                       | 7.89                        |
| 5             | 58.7                         | 0.444                       | 7.71                        |
| 6             | 66.5                         | 0.484                       | 7.50                        |
| 7             | 85.3                         | 0.600                       | 7.21                        |
| 8             | 108                          | 0.723                       | 6.82                        |
| 9             | 158                          | 1.01                        | 6.46                        |
| 10            | 209                          | 1.29                        | 6.27                        |
| 11            | 263                          | 1.59                        | 6.12                        |
| 12            | 314                          | 1.86                        | 5.98                        |
| (b) female    |                              |                             |                             |
| 1             | 20.6                         | 0.168                       | 9.11                        |
| 2             | 40.2                         | 0.275                       | 7.12                        |
| 3             | 41.1                         | 0.294                       | 7.43                        |
| 4             | 61.8                         | 0.393                       | 6.50                        |
| 5             | 74.6                         | 0.460                       | 6.29                        |
| 6             | 83.4                         | 0.501                       | 6.11                        |
| 7             | 104                          | 0.617                       | 6.02                        |
| 8             | 130                          | 0.740                       | 5.76                        |
| 9             | 190                          | 1.02                        | 5.45                        |
| 10            | 247                          | 1.31                        | 5.35                        |
| 11            | 309                          | 1.61                        | 5.25                        |
| 12            | 363                          | 1.87                        | 5.21                        |
| (c) all people|                              |                             |                             |
| 1             | 17.2                         | 0.159                       | 10.6                        |
| 2             | 34.3                         | 0.266                       | 8.37                        |
| 3             | 35.2                         | 0.286                       | 8.72                        |
| 4             | 55.4                         | 0.384                       | 7.20                        |
| 5             | 66.7                         | 0.452                       | 7.00                        |
| 6             | 74.9                         | 0.492                       | 6.81                        |
| 7             | 94.8                         | 0.609                       | 6.61                        |
| 8             | 119                          | 0.731                       | 6.29                        |
| 9             | 174                          | 1.02                        | 5.96                        |
| 10            | 228                          | 1.30                        | 5.81                        |
| 11            | 286                          | 1.60                        | 5.69                        |
| 12            | 339                          | 1.87                        | 5.60                        |
The patient had not had breakfast that morning or intense exercise the previous day. Flow analysis was performed with a total of 12 needles using our developed FNR viscosity method. Since the densities of the needle and blood are necessary for the flow analysis, each density was measured. The average density of the needles used in the experiment is shown in Table 1. The density was measured using a portable densitometer (DMA35; Anton Paar Co., Ltd., Graz, Austria). The measurement temperature was 305 K. And the hematocrit, which indicates the proportion of red blood cells in whole blood was also measured.

5. Results and discussion

The range and average values obtained from viscosity measurements of male samples, female samples, and all samples are shown in Figure 3. The average flow analysis values are shown in Table 2. The flow curves and Casson plots are shown in Figures 4 and 5. As shown in Figure 4, the Casson fluid region, a transition region, and a Newtonian fluid region were confirmed in the total specimens according to the shear rate. As shown in Figure 5, the behavior of the Casson fluid specific to blood was confirmed in each case. The values of the yield stress $\tau_y$ based on the Casson plot were 0.0207, 0.0139 and 0.0160 (Pa) for male, female and all specimens, respectively. The yield stress of the blood from males was slightly greater than that from females given that men generally have higher blood viscosity, that is, a higher average value of hematocrit.

An equation with a high correlation to the viscosity measurement value of all specimens was created.

The Modified Herschel-Bulkley (mHB model) model with the improved shear rate-apparent viscosity, addressing the limitations of Eq. (9), is shown below.

$$\mu = a\tau_y + b(\gamma + \phi e^{-15})^n + \left(\frac{C}{\gamma + \phi e^{-15}}\right) + d$$  (10)

Here, $a$ (mPa $\cdot$ s), $b$ (mPa $\cdot$ s$^2$), $m$ (s), $n$ (-) and $\phi$ (s$^{-1}$) ($\phi = 1$); $c$ is the shear stress (Pa); and $d$ is the viscosity (mPa $\cdot$ s) at shear rate infinity. The main improvement of the mHB model is that a new natural exponential function term was added to the first term so that the fitting improves in the low shear rate region. In addition, the constant viscosity term at infinite shear rate was added to the fourth term to improve fitting in the high shear rate region. Moreover, the $e^{-15}$ term was incorporated to prevent divergence when the shear rate is low, such as during flow simulations. The following calculation conditions were set for the improved mHB equation.
1. \( \tau \) is the value of the shear stress used when measuring the minimum shear rate.
2. \( \dot{\gamma} \) is the viscosity when measuring the maximum shear rate.
3. \( \dot{\gamma} \) is the shear rate measured with needles of different densities.

Next, the least squares method was executed using an Excel solver to determine the values of \( a, b, m, \) and \( n \) parameters of the approximation equation for all 50 specimens. The range setting of each parameter when performing the solver was set as follows: \( a: a \geq 0, b: b \geq 0, m: -0.05 \leq m \leq -0.01, \) and \( n: -2.0 \leq n \leq -0.5. \) The initial values were \( a = b = 5, m = -0.03, \) and \( n = -1.25. \) The applicable range was based on the actually measured value, and \( 5 < \dot{\gamma} < 400. \)

A comparison of the HB, the mHB, and Casson models using the calculation results of the 50 specimens are shown in Figure 6. The mHB model improved the decrease in viscosity in the high shear rate region by introducing a constant into the fourth term. In addition, the low shear rate region showed high correlation due to the addition of the first natural exponential term. In addition, the mHB model showed a high correlation over all ranges, from low to high shear rates, compared to the Casson model. Furthermore, the total error was 53.5, 16.4, 49.8, 53.6 when the measured values by FNR and the calculated values of the HB equation, mHB and Casson and Power-law models were subtracted. The value calculated from the mHB equation was closest to the measured value.

The values of \( a \) and \( b \) calculated from all specimens using the mHB model were applied as constants to the model for males and females, and...
the constants \( m \) and \( n \) were calculated for each male and female by least squares using the Excel solver. From the calculation results of the 50 specimens, \( a \) and \( b \) in the 50 samples were fixed at \( a = 3.27 \) and \( b = 58.7 \), and \( m \) and \( n \) in the approximate expressions of the male and female averages were calculated. The \( m \) and \( n \) for male and female were \( m = -0.0201, n = -1.05 \) and \( m = -0.0211, n = -1.17 \), respectively. Graphs of the approximations of male, female, and all samples to which the parameters obtained by the solver were substituted are shown in Figure 7, and the results combining the male, female, and all samples are shown in Figure 8. The correlations between the flow analysis and the approximate expressions all showed strong correlations exceeding \( R^2 = 0.98 \). Additionally, comparing the approximate expressions of the average values of the male and female specimens, the male has a higher apparent viscosity value regardless of the low shear rate and high shear rate, likely due to the higher hematocrit of the males.

Figure 9 shows the relationship between the blood viscosity and the shear rate of the individual sample calculated using the mHB equation. The correlation between the flow analysis value and the approximate expression for individual specimens was \( R^2 = 0.89 \) (average of 50 specimens). From the results of this study, it is thought that the mHB equation can be used as one of the equations that can be used for correlation and estimation of blood viscosity.
Figure 9. Relationship between shear rate and apparent viscosity for male and female samples assigning individual values to average approximate expression.
6. Conclusion

Blood viscosity measurements using FNR were performed on blood from healthy subjects. From the obtained results, Casson fluid behavior specific to blood was confirmed. Blood from males tended to have higher apparent viscosity and yield stress than that from females. Using the viscosity measurements measured by FNR, a new HB type model equation for shear rate and apparent viscosity was proposed.

The modified HB model improved the viscosity decrease at high shear rates, which was a problem with the HB model. High correlation accuracy was obtained by substituting the viscosities of the individual specimens in the high shear rate region into the approximation formula for each gender. As a result, the model can estimate the viscosity in a wide shear region of human blood.

Declarations

Author contribution statement

Hideki Yamamoto: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Takafumi Yabuta: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Yusuke Negi: Performed the experiments.

Daiki Horikawa: Conceived and designed the experiments; Performed the experiments.

Kimito Kawamura, Eiji Tamura, Katsuhiro Tanaka & Fujimaro Ishida: Contributed reagents, materials, analysis tools or data.

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Competing interest statement

The authors declare no conflict of interest.

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