Mathematical model on two layered hepatic blood flow in capillaries due to hepatitis A

JP Singh, AK Agrawal, V Upadhyay, PN Pandey, and Mohd. Abdul Ahad

Abstract
The study of mathematical model of two phase blood flow in capillary in the case of hepatitis A infection presented here. P.N. Pandey and V. Upadhyay have considered the blood flow has two phased, one of which is that of red blood cells and other is plasma. According to Fahreaus-Lindqvist affect the blood flow in two separated layers while passing through capillaries. The plasma layer which flows along the surface of the capillaries contains almost no blood cells. The second layer the core layer containing blood cells which float in plasma along the axis of capillary. They have also applied the non-Newtonian power law model in bio fluid mechanical set-up. We have collected a clinical data in the case of Hepatitis A. The overall presentation is in tensorial form and solution technique adapted is analytical as well as numerical. The role of Hematocrit is explicit in the determination of blood pressure in case of Hepatitis A infection.

Keywords: Hepatitis A, hematocrit, hepatic blood flow, Non-Newtonian power law model, circulatory system, liver

1. Introduction
1.1 Structure and Function of Liver: The liver is a vital organ of vertebrates and some other animals [1]. The liver is a reddish-brown wedge-shaped organ with four lobes of unequal size and shape. A human liver normally weighs 1.44–1.66 kg (3.2–3.7 lb) [2]. It is both the heaviest internal organ and the largest gland in the human body. Located in the right upper quadrant of the abdominal cavity, it rests just below the diaphragm, to the right of the stomach and overlies the gallbladder [3]. The gallbladder, a small pouch that sits just under the liver, stores bile produced by the liver [3]. The liver has a wide range of functions, including detoxification of various metabolites, protein synthesis, and the production of biochemical necessary for digestion [4].

The liver is connected to two large blood vessels: the hepatic artery and the portal vein. The hepatic artery carries oxygen-rich blood from the aorta, whereas the portal vein carries blood rich in digested nutrients from the entire gastrointestinal tract and also from the spleen and pancreas [5]. These blood vessels subdivide into small capillaries known as liver sinusoids, which then lead to a lobule. The liver can be divided into functional units called lobules. The liver has 2 main lobes: the larger right lobe and smaller left lob. Each lobe is divided into segments. The lobes are separated by a band of tissue called the falciform ligament, which help attach the liver to the diaphragm. Liver lobes are surrounded by a thick capsule, mostly overlaid with reflected periforirum [6].

1.2 Structure and Function of Capillaries
Capillaries are the smallest of blood vessels. They serve to distribute oxygenated blood from arteries to the tissues of the body and to feed deoxygenated blood from the tissues back into the veins. Their walls consist of a single layer of endothelial cells and the smallest have a single endothelial cell wrapped around to join with itself. These permit a single red blood cell to pass through them but only by deforming itself.

Sinusoidal capillaries are a special type of open-pore capillary also known as a discontinuous capillary that have larger openings (30 - 40μm in diameter) in the endothelium. These types of blood vessels allow red and white blood cells (7.5 μm - 25 μm diameter) and various
serum proteins to pass, aided by a discontinuous basal lamina. These capillaries lack pinocytosis vesicles, and therefore utilize gaps present in cell junctions to permit transfer between endothelial cells, and hence across the membrane. Sinusoid blood vessels are primarily located in the bone marrow, lymph nodes, and adrenal glands. Some sinusoids are distinctive in that they do not have the tight junctions between cells. They are called discontinuous sinusoidal capillaries, and are present in the liver and spleen.

### 1.3 Description of Disease
The liver is a vital organ and supports almost every other organ in the body. Because of its strategic location and multidimensional functions, the liver is also prone to many diseases [7]. The bare area of the liver is a site that is vulnerable to the passing of infection from the abdominal cavity to the thoracic cavity. Hepatitis is a common condition of inflammation of the liver. The most usual cause of this is viral, and the most common of these infections are hepatitis A, B, C, D, and E.

Hepatitis A (formerly known as infectious hepatitis) is an acute infectious disease of the liver caused by the hepatitis A virus (HAV), an RNA virus, usually spread by the fecal-oral route; transmitted person-to-person by ingestion of contaminated food or water or through direct contact with an infectious person. Hepatitis A, a term first introduced by Krugman et al. in 1967 [8], is now known to be caused by infection with hepatitis A virus (HAV), one of five viruses, each belonging to a different family, whose primary site of replication is the liver. In 1973, HAV was identified in the stools of infected persons [9], which eventually led to development of diagnostic tests, propagation in cell culture, molecular characterization, and development of a vaccine [9,10]. HAV is a no enveloped RNA virus 27 to 32 nm diameter in size, with an icosahedral symmetry, which belongs to the genus Hepatovirus of the Picornaviridae family. Unlike other members of the family, HAV requires a long adaptation period to grow in cell culture, replicates slowly, and rarely produces acytopathic effect [11,12,13]. HAV is stable in the environment for at least 1 month [14].

### 2. Real Model
#### 2.1 Constitution of blood
Blood is a complex fluid consisting of particulate corpuscles suspended in a non-Newtonian fluid. The particulate solids are red blood cells (RBCs), white blood cells (WBCs) and platelets. 55% of the plasma and 45% of the blood cells in a whole blood, thus the mass ratio of blood cells to plasma is a then clearly

\[
r = \frac{\rho_c}{(1-X)\rho_p}
\]

Where \( \rho_c \) and \( \rho_p \) are densities of blood cells and blood plasma respectively. Usually this mass ratio is not constant, even then it may be supposed to constant in present context [15].

#### 2.2 Choice of frame of reference
Boundary conditions are as follows:
1. The velocity of blood flow on the axis of capillary at \( r = 0 \) will be maximum and finite, say \( V_0 \)
Maximun velocity \( = V_0 \)
2. The velocity of blood flow on the wall of the blood vessels at \( r = R \), Where, \( R \) is the radius of capillary, will be zero.
This condition is well known as no-slip condition.
The Newtonian power law equation-

\[
\tau = \eta \mu^n
\]

Where, \( \eta \) is the viscosity of coefficient. This is found to hold in broad blood vessels where there is low hematocrit [16].

### 3. Mathematical Modelling
Let us problem of blood flow in hepatic circulatory system is different from the problems in cylindrical tube and select generalized three dimensional orthogonal curvilinear coordinate system. Briefly described as E³ called as Euclidean space. According to Mishra the biophysical laws thus expressed fully hold good in any co-ordinate system which is a compulsion for the truthfulness of the laws [17].

According to the Sherman I.W. and Sherman V.G. blood is mixed fluid [18]. Mainly there are two phases in blood. The first phase is plasma, while the other phase is that of the blood cells are enclosed with semipermeable membranes whose density is greater than that of plasma. These blood cells are uniformly distributed in plasma. Thus, blood can be considered as a homogeneous mixture of two phases [18].

#### 3.1 Equation of Continuity
The both phase of blood, i.e. blood cells and plasma move with the common velocity. Campbell and Pitcher have presented a model for two phase of blood separately [18]. The equation of continuity for two phases according to the principle of conservation of mass defined by Kapur J. N. and Gupta R.C. [20][as follow:
\[ \frac{\partial (\rho_c v^i)}{\partial t} + (\rho_c v^i) j = 0 \]  \hspace{1cm} (3.2)

And \[ \frac{\partial (1 - \rho_p)}{\partial t} + \left( (1 - X) \rho_p v^i \right) j = 0 \]  \hspace{1cm} (3.3)

Where, \( v \) is the common velocity of two phase blood cells and plasma. If we define the uniform density of the blood \( \rho_m \) as follow:

\[ \frac{1 + \tau}{\rho_m} = \frac{\rho_c}{\rho_c} + \frac{1}{\rho_p} \]  \hspace{1cm} (3.4)

From equation (3.2) and (3.3) we can written as,

\[ \frac{\partial \rho_m}{\partial t} + (\rho_m v^i) j = 0 \]  \hspace{1cm} (3.5)

Where \( \rho_m = \rho_c + (1 - X) \rho_p \)

3.2 Equation of motion

The hydro dynamical pressure \( P \) between the two phases of blood can be supposed to be uniform because the both phases i.e. blood cells and plasma are always in equilibrium state in blood \(^{(21)}\). Taking viscosity coefficient of blood cells to be \( \eta_c \) and applying the principle of conservation of momentum, we get the equation of motion for the phase of blood cells as follows:

\[ \rho_c \frac{\partial v^i}{\partial t} + (\rho_c v^i) v^j = -\rho_c g^i j + \eta_c (g^i k \nu^k)_j \]  \hspace{1cm} (3.6)

The equation of motion for plasma will be as follows:

\[ (1 - X) \rho_p \frac{\partial v^i}{\partial t} + \left( (1 - X) \rho_p v^i \right) v^j = -X \rho_p g^i j + (1 - X) (\eta_c (g^i k \nu^k))_j \]  \hspace{1cm} (3.7)

Now adding equation (3.6) and (3.7) and using relation (3.4), the equation of motion for blood flow with the both phases will be as follows:

\[ \rho_m \frac{\partial v^i}{\partial t} + (\rho_m v^i) v^j = -p^j + \eta_m (g^i k \nu^k)_j \]  \hspace{1cm} (3.8)

Where \( \eta_m = \rho_c + (1 - X) \rho_p \) is the viscosity coefficient of blood as a mixture of two phases.

4. Analysis

Equation of continuity for power law flow will be as follows:

\[ \frac{1}{\sqrt{g^i g^i)} j = 0 \]  \hspace{1cm} (4.1)

Again the equation of the motion is extended as follows:

\[ \rho_m \frac{\partial v^i}{\partial t} + \rho_p \nu^i j = T^i j \]  \hspace{1cm} (4.2)

Where \( T^i j \) is taken from constitutive equation of power law flow. Where \( \rho_m = \rho_c + (1 - X) \rho_p \), is the density of blood and \( \eta_m = \rho_c + (1 - X) \rho_p \) is the viscosity of mixture of the blood. \( X = \frac{\theta}{100} \) is volume ratio of blood cells. \( H \) is hematocrit. Other symbols have their usual meanings.

Since the blood vessels are cylindrical, the above governing equations have to be transformed into cylindrical co-ordinates. As we know earlier:

\[ X^1 = r, X^2 = \theta, X^3 = z, \]

Matrix of metric tensor in cylindrical co-ordinates is as follows:

\[ [g_{ij}] = \begin{bmatrix} 1 & 0 & 0 \\ 0 & r^2 & 0 \\ 0 & 0 & 1 \end{bmatrix} \]
While matrix of conjugate metric tensor is as follows:

\[
[g^{ij}] = \begin{bmatrix}
1 & 0 & 0 \\
0 & 1/r^2 & 0 \\
0 & 0 & 1
\end{bmatrix}
\]

Where, as Christoffel’s symbols of 2nd kind are as follows

\[
\left\{ \begin{array}{c}
n \\
2 \\
2 \\
\end{array} \right\} = -r, \left\{ \begin{array}{c}
n \\
2 \\
1 \\
\end{array} \right\} = \frac{1}{r}, \text{remaining other are zero.}
\]

Relation between contravariant physical components of the velocity of the blood flow will be as follows:

\[
\sqrt{g_{11}}v^1 = v_r \Rightarrow v_r = v^1
\]

\[
\sqrt{g_{22}}v^2 = v_\theta \Rightarrow v_\theta = r v^2
\]

\[
\sqrt{g_{33}}v^3 = v_z \Rightarrow v_z = v^3
\]

Again the physical components of \( p_{ij}g^{ij} \) is 

The matrix of the physical components of shearing stress-tensor

\[
T^{ij} = \eta_m(e^{ij}) = \eta_m(g^{ik}v^j_k + g^{jk}v^i_k)^n
\]

Will be as follows

\[
\begin{bmatrix}
0 & 0 & \eta_m(dv/dr)^n \\
0 & 0 & 0 \\
\eta_m(dv/dr)^n & 0 & 0
\end{bmatrix}
\]

The covariant derivative of \( T^{ij} \)

\[
T^{ij}_{\alpha \beta} = \frac{1}{\sqrt{g}} \frac{\partial}{\partial X^\alpha} \left( \sqrt{g} T^{ij} \right) + \left\{ \begin{array}{c}
\alpha \\
\beta \\
\gamma \\
\end{array} \right\} T^{\alpha j}
\]

Keeping in view the above facts, the governing tonsorial equations can be transformed into cylindrical forms which are as follows: the equation of continuity –

\[
\frac{\partial v_z}{\partial z} = 0 \text{ ........................................................... (4.3)}
\]

Equation of motion –

\[
-\frac{\partial p}{\partial r} = 0 \text{ ........................................................... (4.4)}
\]

\[
0 = 0 \text{ ........................................................... (4.5)}
\]

\[
0 = -\frac{\partial p}{\partial z} + \eta_m \frac{\partial}{\partial r} \left\{ r \left( \frac{\partial v_z}{\partial r} \right) \right\} \text{ ........................................................... (4.6)}
\]

Here this is fact has been taken in the view that the blood flow is axially symmetric in capillary concerned i.e. \( v_\theta = 0 \) and \( v_r, v_z \) and \( p \) do not depend upon \( \theta \). Also blood flows steadily, i.e.

\[
\frac{\partial p}{\partial t} = \frac{\partial v_z}{\partial t} = \frac{\partial v_\theta}{\partial t} = \frac{\partial v_r}{\partial t} = 0
\]

On integrating equation (4.3) we get

\[
v_z = v(r) \text{ because } v \text{ does not depend upon } \theta \text{ ........................................................... (4.7)}
\]

The integrating of equation of motion (4.4) yields:

\[
p = p(z) \text{ since } p \text{ does not depend upon } \theta \text{ ........................................................... (4.8)}
\]
Now, with the help of equations (4.7) and (4.8), the equation of motion (4.6) converts in the following form

$$0 = - \frac{dp}{dz} + \frac{\eta_m}{r} \left\{ r \left( \frac{dv}{dr} \right)^n \right\} \quad \text{................................................................. (4.9)}$$

The pressure gradient $-(dp/dz) = p$ of blood flow in the capillary remote from heart can be supposed to be constant and hence the equation (4.9) takes the following form:

$$\frac{d}{dr} \left\{ r \left( \frac{dv}{dr} \right)^n \right\} = - \frac{pr}{\eta_m} \quad \text{................................................................. (4.10)}$$

On integrating equation (4.10), we get

$$r \left( \frac{dv}{dr} \right)^n = - \frac{pr^2}{2\eta_m} + A \quad \text{................................................................. (4.11)}$$

We know that the velocity of blood flow on the axis of cylindrical capillary is maximum and constant. So that we apply the boundary condition: $r = 0, v = V_0$(constant), on equation (4.11) to get the arbitrary constant $A=0$. Hence the equation (4.11) takes the following form:

$$r \left( \frac{dv}{dr} \right)^n = - \frac{pr^2}{2\eta_m} \quad \text{................................................................. (4.12)}$$

Integrating equation (4.13) once again, we get

$$v = - \left( \frac{p}{2\eta_m} \right)^{1/n} \frac{r^{1/n+1}}{(n+1)/n} + B \quad \text{................................................................. (4.13)}$$

To determine the arbitrary constant $B$, we apply the no-slip condition on the inner wall of the capillary: at $r = R, v = 0$, where $R$= radius of vessel, on equation (4.13) so as to get

$$B = \left( \frac{p}{2\eta_m} \right)^{1/n} \frac{n}{(n+1)} \left( R^{1/n+1} - \frac{r^{1/n+1}}{(n+1)} \right) \quad \text{................................................................. (4.14)}$$

Which determine the velocity of the blood flow in capillary remote from heart. Where, $p$ is gradient of blood pressure and $\eta_m$ is the viscosity of blood mixture.

Now the formula for velocity of blood flows can be obtained by replacing $\eta_m$ with $\eta_p$ of Newtonian model as follows:

$$v_p = \frac{P}{4\eta_p}(R^2 - r^2); R - \delta \leq r \leq R$$

Where, $\delta$ is the radius of core layer.

The velocity of core layer is obtained as the formula of power law model as follows:

$$v_m = \left( \frac{p}{2\eta_m} \right)^{1/n} \frac{n}{(n+1)} \left( R^{1/n+1} - \frac{r^{1/n+1}}{(n+1)} \right) + \left[ \frac{p}{4\eta_p} (R^2 - (R - \delta)^2) - \left( \frac{p}{2\eta_m} \right)^{1/n} \frac{n}{(n+1)} \left( R^{1/n+1} - (R - \delta)^{1/n+1} \right) \right] \quad \text{................................................................. (4.15)}$$

Where, the 2nd term is the relative velocity of plasma layer with respect to core layer.

5. Result (Bio-Physical Interpretation)
Observations: Hematocrit Vs blood pressure is taken from Santosh Hospital Meerut (U.P.)

Patient name- Anita Singh Age – 36 Years

Diagnosis-Dr. P.C. Sharma
Table 1: For Hemoglobin v/s blood pressure in Clinical data

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Date</th>
<th>HB in (gm/dl)</th>
<th>Hematocrit in(kg/m³)</th>
<th>Blood Pressure in (mm hg)</th>
<th>Capillary pressure Drop in Pascal-second</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11/8/2017</td>
<td>9.2</td>
<td>276</td>
<td>130/80</td>
<td>-2666.4</td>
</tr>
<tr>
<td>2</td>
<td>13/8/2017</td>
<td>10.5</td>
<td>315</td>
<td>110/75</td>
<td>-2481.09</td>
</tr>
<tr>
<td>3</td>
<td>15/8/2017</td>
<td>9.8</td>
<td>294</td>
<td>135/95</td>
<td>-3110.36</td>
</tr>
<tr>
<td>4</td>
<td>16/8/2017</td>
<td>9.4</td>
<td>282</td>
<td>140/90</td>
<td>-3035.70</td>
</tr>
</tbody>
</table>

We know that,

Viscosity of mixture= \( \eta_m = 0.035 \text{ p.s.} \)

Viscosity of plasma= \( \eta_p = 0.0015 \text{ p.s.} \)

Radius of capillary= \( R = 35 \times 10^{-6} \text{m} \)

Thickness of RBC layer = \( \delta = \frac{1}{2} R = 11.67 \times 10^{-6} \text{m} \)

Flow flux of blood = \( Q = 1000 \text{ ml/min} = 1.67 \times 10^{-5} \text{ m}^3/\text{s} \)

Length of capillary=\( \Delta z = 615 \times 10^{-6} \text{m} \)

Hematocrit (H) = 27.6 gm./dl = 276 kg/m

Pressure drop \( p_f - p_l = 2666.4 \) Pascal second

\[
\begin{align*}
P &= - \frac{dp}{dz} \\
\Rightarrow P &= \frac{p_f - p_l}{\Delta z} = \frac{2666.4}{615 \times 10^{-6}} = 4.3356 \times 10^6
\end{align*}
\]

\[
\eta_m = \eta_c \left( \frac{H}{100} \right) + \left( 1 - \frac{H}{100} \right) \eta_p
\]

\[
\eta_m = 0.035 \times \frac{276}{100} + \left( 1 - \frac{276}{100} \right) \times 0.0015
\]

\[
\eta_c = 0.0136
\]

Again

\[
\eta_m = 0.0136 \times \frac{H}{100} + \left( 1 - \frac{H}{100} \right) \times 0.0015
\]

The flow flux in capillaries is:

\[
Q = \int_0^{R-\delta} \left[ \frac{P}{2\eta_m} \left( \frac{1}{n} \right) \left( n R^{n+1} - n R^{n+1} \right) + \frac{P}{4\eta_p} \left( R^2 - (R - \delta)^2 \right) - \frac{P}{n \eta_m} \left( \frac{n}{n+1} \right) \left( n R^{n+1} - (R - \delta)^{n+1} \right) \right] 2\pi r \, dr
\]

\[
+ \int_{R-\delta}^{R} \frac{P}{4\eta_p} \left( R^2 - r^2 \right) 2\pi r \, dr
\]

\[
= 2\pi \int_0^{R-\delta} \left[ \frac{P}{2\eta_m} \left( \frac{1}{n+1} \right) \left( R - \delta \right)^{n+1} - \frac{n}{3n+1} + \frac{P}{4\eta_p} \left( R^2 - (R - \delta)^2 \right) (R - \delta)^2 \right] 2\pi r \, dr
\]

\[
= 2\pi \left[ \frac{P}{2\eta_m} \left( \frac{1}{n+1} \right) \left( R - \delta \right)^{n+1} - \frac{n}{3n+1} + \frac{P}{8\eta_p} \left( R^2 - (R - \delta)^2 \right) (R - \delta)^2 \right]
\]

\[
1.67 \times 10^{-5} = 6.28 \times \left[ \frac{4.3356 \times 10^6}{0.07} \right] \left( \frac{n}{n+1} \right) \left( 23.33 \times 10^{-6} \right)^{\frac{3n+1}{n}} \left( \frac{1}{2} - \frac{n}{3n+1} \right)
\]

\[
+ \frac{4.3356 \times 10^6}{0.012} \left( (35 \times 10^{-6})^2 - (23.33 \times 10^{-6})^2 \right) \times (23.33 \times 10^{-6})^2
\]

\[
+ 3.14 \times 4.3356 \times 10^6 \times \frac{0.024}{0.012} \left( (35 \times 10^{-6})^2 - (23.33 \times 10^{-6})^2 \right)^2
\]

\[
4.2382 \times 10^8 = \frac{n}{3n+1} (144.9925)^{\frac{1}{2}}
\]
Solving for $n$, we get 

\[ n = 0.2276 \]

Putting the value of $n$ in equation (4.16) we get

\[ 1.67 \times 10^{-5} = 2.3969 \times 10^{-35} \left( \frac{P}{2 \eta_m} \right)^{\frac{1}{10.2276}} + 2.5451 \times 10^{-16} P \]

Neglected $2.5451 \times 10^{-16} P$, then we get,

\[ 1.67 \times 10^{-5} = 2.3969 \times 10^{-35} \left( \frac{\Delta P}{1230 \times 10^{-6} \eta_m} \right)^{\frac{1}{10.2276}} + 2.5451 \times 10^{-16} P \]

\[ \Delta P = 7624.0689 n_m \]
\[ \Delta P = 7624.0689 (0.000121H + 0.0015) \]
\[ \Delta P = 0.9225H + 11.436 \]

From the above relation we get, values of blood pressure drop if hematocrit known.

### Table 2: For Hematocrit v/s blood Pressure drop in Clinical data

<table>
<thead>
<tr>
<th>S.no.</th>
<th>Hematocrit in kg/m³</th>
<th>Blood Pressure drop in pascal-second</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>276</td>
<td>266.046</td>
</tr>
<tr>
<td>2</td>
<td>315</td>
<td>302.024</td>
</tr>
<tr>
<td>3</td>
<td>294</td>
<td>282.651</td>
</tr>
<tr>
<td>4</td>
<td>282</td>
<td>271.581</td>
</tr>
</tbody>
</table>

![Fig 1: Cross section of Liver](image1)

![Fig 2: Discontinuous Sinusodial Capillary Structure](image2)
6. Conclusion
A relationship between blood pressure drop and hematocrit for Non-Newtonian flow and draw a graph between blood pressure drop and hematocrit, this graph shows the linear and equation of relationship defined as $0.9225H + 11.436$ above equation compared by the general equation of straight line $\gamma = mx + c$ where $m$ is slope and we get slope of line of a graph is $m = 0.9225$. Slope represents the fluctuation of blood pressure drop with respect to hematocrit.

7. References