Mathematical models of two phase human hepatic blood flow in venules with special reference to liver cirrhosis

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Abstract: *Present paper visualize a model of two phased blood flow in hepatic venules, keeping in view the nature of hepatic blood circulationin human body. The viscosity increases in the venules due to formation of rouleaux along axis of red bloodcells. We have applied the Herschel Bulkley Non-Newtonian model in Bio- fluid mechanical setup with thehelp of clinical data in case of Liver Cirrhosis for hemoglobin versus blood pressure. The overall presentationis in tensorial form and the solution technique adopted is analytical as well as numerical. The role ofhematocrit is explicit in the determination of blood pressure in case of Hepatic disease Liver Cirrhosis thegraphical presentation for particular parametric value is much close to the clinical observation.*

Keywords*-Structure of the Liver, Hematocrit, Liver Cirrhosis, Hepatic Blood Flow, Herschel Bulkley Non-Newtonian model etc.*

INTRODUCTION (DESCRIPTION OF BIO-PHYSICAL PROBLEM)

Globally, liver cirrhosis was estimated to be responsible for over one million deaths in 2010, which equates to approximately 2% of all deaths worldwide It is estimated that in 2013, liver cirrhosis resulted in 170,000 deaths in Europe **[1].**Cirrhosis is the leading cause of adult liver transplants in Europe with 58,357 carried out between 1988 and 2013**[2].**Here this work will focus on two phase hepatic blood flow in venules with special reference to Liver Cirrhosis. There are many work is available in that field, but P.N.Pandey and V. Upadhyay (2001) discussed a some phenomenon in two phase blood flow gave an idea on the two phase hepatic blood flow inLiver disease Cirrhosis.**Liver** is the largest glandular organ in the body and performs multiple critical functions to keep the body pure of toxins and harmful substances. When something attacks and damages the liver, liver cells are killed and scar tissue is formed. This scarring process is called **fibrosis** and it happens slowly over many years. When the whole liver is scarred, it shrinks and hardens. This is called **cirrhosis**, and usually this damage cannot be undone. Any illness that affects the liver over a long period of time may lead to fibrosis and, eventually, cirrhosis. Heavy drinking and viruses (like hepatitis C or B) are common causes of cirrhosis**[3].** Because the liver becomes lumpy and stiff in cirrhosis, blood cannot flow through it easily, so pressure builds up in a vein, called the portal vein, which brings blood to the liver. Platelets are blood cells that help in blood clotting. With cirrhosis, blood is blocked from entering the liver and toxic substances that the liver normally filters escapes into general blood circulation.The Liver receive a dual blood supply from the hepatic portal vein and hepatic arteries supplying approximately 75% OF Liver blood supply. Liver volume and portal blood flow decreases after the age of 50.Human circulatory system was divided systemic circulation and hepatic circulation.

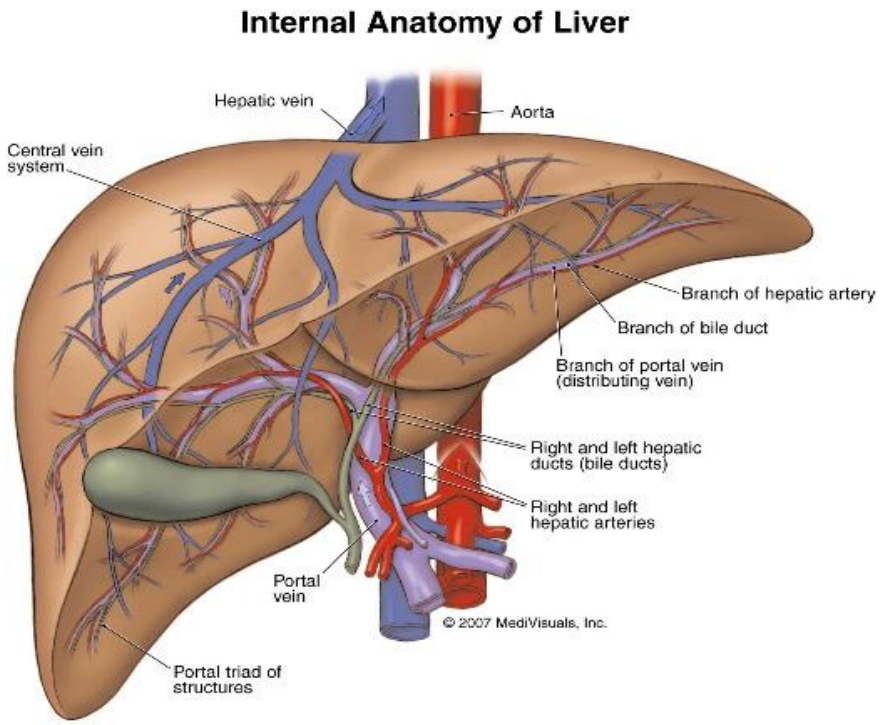


Fig.1. Internal Anatomy of Liver

Because in this proposed research work based on human hepatic blood circulation so we have focused only human hepatic blood circulation. Human hepatic blood circulation is a sub system of human circulatory system. According to Upadhyay and Pandey we have considered two phase blood which is one of the red blood cells and other is plasma. We have collected clinical data in case of Liver Cirrhosis for hemoglobin versus blood pressure for in this study. We have selected a frame of reference for mathematical modeling of two phase blood flow of the state of a moving blood· the work of P.N. Pandey and V. Upadhyay in whole circulatory system but this work will focus on Hepatic circulatory system, and Hepatic circulatory system is a sub system of whole circulatory system. In this work, applied the Herschel Bulkley non-Newtonian model.

Blood is a complex fluid consisting of particular corpulse suspended in a non-Newtonian fluid. The particular solids are red blood cells (RBCs), white blood cells (WBCs) and platelets. The fluid is plasma, which itself is a complex mixture of proteins and other intergradient in an aqueous base. In blood 98% RBC and remaining 2% WBC and platelets cells i.e. there are a few part of the other cells. Which are ignorable, so one phase of the blood is plasma and 2nd phase of the blood is RBCs.According to Singh P. and Upadhyay K.S. The flow of blood is affected by the presence of blood cells. This effect is directly proportional to the volume occupied by blood cells.

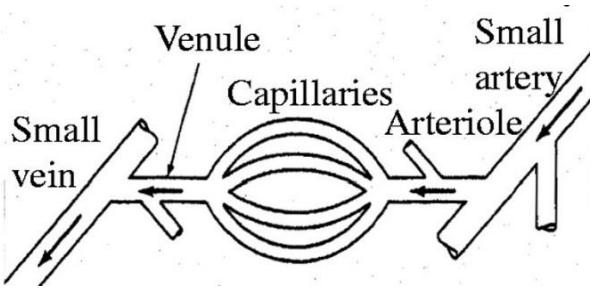


Fig.2. a typical routs of hepatic blood flow

Let the volume portion covered by blood cells in unit volume be X , this X is replaced by H/100, where H is the Hematocrit the volume percentage of blood cells .Then the volume portion covered by the plasma will be 1 -X . If the mass ratio of blood cells to plasma is r then clearly.

$$\boldsymbol{r} = \frac{\boldsymbol{X}\boldsymbol{\rho_c}}{(\boldsymbol{1}-\boldsymbol{X})\boldsymbol{\rho_p}} (1)$$

Where $\boldsymbol{\rho_c}$ and $\boldsymbol{\rho_p}$are densities of blood cells and blood plasma respectively .usually this mass ratio is

not a constant , even then this may be supposed to constant in present context.**[4]**

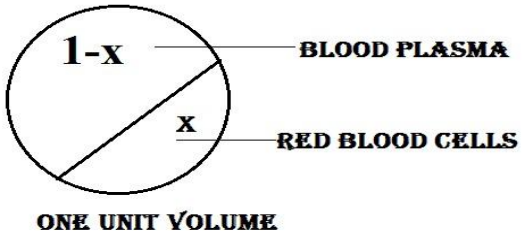


Fig.3. Blood Volume

MATHEMATICAL MODEL/FORMULATION:

Upadhyay and Pandey (*Upadhyay et al., 2012*) **[5].**Recommended that blood flow in vessels is a peristaltic transport system because they thought blood is having two layers of fluid while in the peripheral reasons of vessels blood flow is a Newtonian phenomenon. Blood is in the liquid form and it is non-Newtonian. Though blood is not an ideal fluid, even to develop the equation of motion. We start with a model of ideal fluid. The second important principle of fluid dynamics is that of conservation of momentum. The equation of motion is based on this principle According to this principle, the total momentum of any fluid system is conserved in absence of external force.

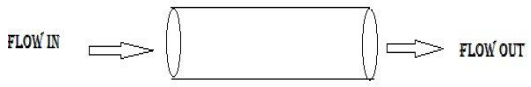


Fig.4. Hepatic venules blood flow

$$\frac{dp}{dt} + P - F_{v(viscosity)} = 0 \ (External\ force)$$

The blood can be considered as homogeneous mixtures of two phases. We derive the fundamental equation of continuity, which is a mathematical expression of principal of conservation of matter.

EQUATION OF CONTINUITY:

According to Campbell and Pitcher (Campbell and Pitcher, 1957), Upadhyay and Pandey have already discuss two phase modal. It has been transformed in to bio fluid mechanical set up. For this purpose, blood has been assumed to be constituted by plasma and blood cells which is realistic so for (*Upadhyay et al., 2012*) **[4].**The principles of conservation of mass in hepatic circulatory system, equation of continuity for two phases are following as:

$$\frac{\partial(X\rho_c)}{\partial t} + (X\rho_c v^i)_{,i} = 0 \quad (2)$$

$$and \ \frac{\partial[(1-X)\rho_p]}{\partial t} + \left[(1-X)\rho_p v^i\right]_{,i} = 0 (3)$$

Where v^i= Common velocity of two phase blood cells and plasma. And again $(X\rho_c v^i)_{,i}$ co-Variant derivative of $(X\rho_c v^i)$with respect toX^i .In the same way $\left[(1-X)\rho_p v^i\right]_{,i}$is co-variant Derivative of $(1-X)\rho_p v^i$with respect toX^i.

If we define the uniform density of the blood $\boldsymbol{\rho_m}$as follows

$$\frac{1+r}{\rho_m} = \frac{r}{\rho_c} + \frac{1}{\rho_p} (4)$$

Then equation (2) and (3) can be combined together as follow

$$\frac{\partial \rho_m}{\partial t} + (\rho_m v^i)_{,i} = 0 \ (5)$$

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

EQUATION OF MOTION FOR BLOOD FLOW:

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. Taking viscosity coefficient of blood cells to beη_c and applying the principle of conservation of momentum, we get the equation of motion for two phase of blood cells as follows:

$$X\rho_c \frac{\partial v^i}{\partial t} + (X\rho_c v^i)v^i_{,j} = -X_{P,j}\,g^{ij} + X_{\eta_c}\left(g^{jk} v^l_{,k}\right)_{,j} \quad (6)$$

Similarly equation of motion for plasma will be as follows:

$$(1-X)\rho_p \frac{\partial v^i}{\partial t} + \left((1-X)\rho_p v^i\right)v^i_{,j} = -(1X)_{P,j}\,g^{ij} + (1-X)_{\eta_c}\left(g^{jk} v^l_{,k}\right)_{,j} (7)$$

Now adding equation (6) and (7) and using relation (4), the equation of motion for blood flow with the both phases will be as follows:

$$\rho_m \frac{\partial v^i}{\partial t} + (\rho_m v^i)v^i_{,j} = -P_{,j}\,g^{ij} + \eta_m\left(g^{jk} v^i_{,k}\right)_{,j} \quad (8)$$

Where $\eta_m = X\eta_c + (1-X)\eta_P$are the viscosity coefficient of blood as a mixture of two phases.

As the velocity of Blood flow decreases, the viscosity of blood increases. The velocity of blood deceases because venules away from heart in relatively other blood vessels. Hence the pumping of the heart on

these vessels is relatively low. Secondly these vessels relatively narrow down more rapidly. In this situation, the blood cells line up on the axis to build up rouleaux. Hence a yield stress is produced. Though this yield stress is very small, even then the viscosity of blood is increased nearly ten times.

The Herschel Bulkley law holds good on the two phase blood flow through venules and whose constitutive equation is as follows:

$$T^{*} = \eta_m e^n + T_P\left(T^* \geq T_p\right) \; where \; T_p \text{ isyield stress.}$$

When strain rate. $e = 0\ (T^* < T_p)$ A core region is formed which flow just like a plug. Let the radius of the plug be r_p. the stress acting on the surface of plug will be T_p. equating the forces on the plug, we get

$$P\pi r_p^2 = T_p 2\pi r_p$$

$$\Longrightarrow r_p = 2\frac{T_p}{P} \quad (9)$$

The Constitutive equation for test part of blood vessel is

$$T^* = \eta_m e^n + T_P \text{ Or } T^* - T_p = \eta_m e^n = T_e$$

Where T_e =effective Stress
Whose generalized form will be as follows:

$$T^{ij} = -P\mathrm{g}^{ij} + T_e^{ij}$$

Where $T_e^{ij} = \eta_m (e^{ij})^n$ While $e^{ij} = \mathrm{g}^{jk} V_{,k}^{i} + \mathrm{g}^{ik} V_{,k}^{j}$ where the symbols have their usual meanings.
Now we describe the basic equations for Herschel Bulkley blood flow as follows:

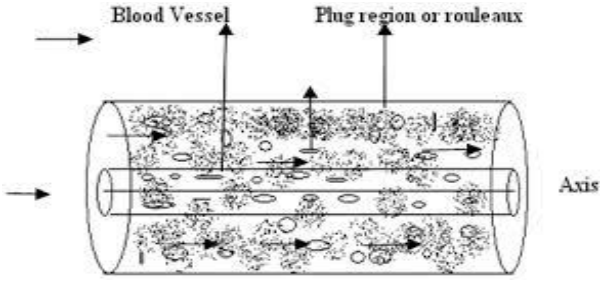


Fig.5. Herschel Bulkley blood flow

EQUATION OF CONTINUITY-

$$\frac{1}{\sqrt{\mathrm{g}}}\left(\sqrt{\mathrm{g}}v^i\right)_{,i} = 0 (10)$$

EQUATION OF MOTION-

$$\rho_m \frac{\partial v^i}{\partial t} + (\rho_m v^j) v_{,j}^{i} = -T_{e,j}^{ij} (11)$$

Where all the symbols have their usual meaning

ANALYSIS:

Since the blood vessels are cylindrical; the above governing equations have to transform 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: $[\mathrm{g}_{ij}] = \begin{bmatrix} 1 & 0 & 0 \\ 0 & r^2 & 0 \\ 0 & 0 & 1 \end{bmatrix}$ while matrix of Conjugate metric tensor is as follows:

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

Whereas the chritoffel's symbols of 2nd kind are as follows:

$\left\{ \begin{matrix} 1 \\ 2 \end{matrix} \; \begin{matrix} 1 \\ 2 \end{matrix} \right\} = -r, \left\{ \begin{matrix} 1 \\ 2 \end{matrix} \; \begin{matrix} 1 \\ 2 \end{matrix} \right\} = \left\{ \begin{matrix} 1 \\ 2 \end{matrix} \; \begin{matrix} 1 \\ 2 \end{matrix} \right\} = \frac{1}{r}$ Remaining others are zero.
Relation between contravarient and physical components of velocity of blood flow will be as follows:

$\sqrt{\mathrm{g}_{11} v^1} = v_r \Longrightarrow v_r = v^1, \sqrt{\mathrm{g}_{22} v^2} = v_\theta$

$\Longrightarrow v_\theta = r v^2, \sqrt{\mathrm{g}_{33} v^3} = v_z \Longrightarrow v_z = v^3$

Again the physical components of $P_{,j}\mathrm{g}^{ij}$ are $\sqrt{\mathrm{g}_{ij}} P_{,j}\mathrm{g}^{ij}$ and now
Equation (9) and (10) are transformed into cylindrical form so as to solve them as power law modal to get

$$\frac{dv}{dr} = \left(\frac{pr}{2\eta_m}\right)^{\frac{1}{n}} (12)$$

Where, pressure gradient $\frac{dp}{dz} = P$
Replace $r \; to \; r - r_p$ for non-plug region

$$-\frac{dv}{dr} = \left(\frac{P(r - r_p)}{2\eta_m}\right)^{\frac{1}{n}}$$

$$-\frac{dv}{dr} = \left(\frac{\frac{Pr}{2} - \frac{Pr_p}{2}}{\eta_m}\right)^{\frac{1}{n}}$$

From equation no (9)

$$-\frac{dv}{dr} = \left(\frac{\frac{Pr}{2}}{\eta_m}\right)^{\frac{1}{n}}$$

Substituting the value of from (7) into (12), we get

$$-\frac{dv}{dr} = \left(\frac{\frac{Pr}{2} - \frac{Pr_p}{2}}{\eta_m}\right)^{\frac{1}{n}}$$

$$\frac{dv}{dr} = -\left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} (r - r_p)^{\frac{1}{n}} (13)$$

Integrating above equation (12) under the no slip boundary condition: $v = 0 \; at \; r = R$ so as we get

$$v = -\left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} \frac{n}{n+1}\left[(R-r_p)^{\frac{1}{n}+1} - (r-r_p)^{\frac{1}{n}+1}\right] \quad (14)$$

This is formula for velocity of blood flow in venules. Putting $r = r_p$ to we get the velocity v_p of plug flow as follows:

$$v_p = \left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} \frac{n}{n+1}\left[(R-r_p)^{\frac{1}{n}+1}\right] (15)$$

Where the value r_p of is taken from (9).

RESULT (bio-physical interpretation)

OBSERVATIONS:

Hematocrit v/s. Blood pressure in during liver cirrhosis patient. It is taken from **Gastro liver Hospital Swaroop Nagar Kanpur UP**

By**Dr. V.K. Mishra.**

Patient Name: Mr. SohanAge: 64 yr.

Diagnosis-Liver Cirrhosis (hepatic disease)

Hemoglobin in gm. /dl and blood pressure in (mmhg)

The flow flux of two phased blood flow in venule is

$$Q = \int_0^{r_p} 2\pi r v_p \, dr + \int_{r_p}^{R} 2\pi r v \, dr$$

$$= \int_0^{r_p} 2\pi r \frac{n}{n+1}\left(\frac{p}{2\eta_m}\right)^{\frac{1}{n}} (R-r_p)^{\frac{1}{n}+1} dr + \int_{r_p}^{R} 2\pi r \frac{n}{n+1}\left(\frac{p}{2\eta_m}\right)^{\frac{1}{n}} \left[(R-r_p)^{\frac{1}{n}+1} - (r-r_p)^{\frac{1}{n}+1}\right] dr$$

Using (12) and (14)

$$= \frac{2\pi n}{(n+1)}\left(\frac{p}{2\eta_m}\right)^{\frac{1}{n}} (R-r_p)^{\frac{1}{n}+1}\left[\frac{r^2}{2}\right]_0^{r_p} + \frac{2\pi n}{(n+1)}\left(\frac{p}{2\eta_m}\right)^{\frac{1}{n}}\left[\frac{r^2}{2}(R-r_p)^{\frac{1}{n}+1} - \frac{r(r-r_p)^{\frac{1}{n}+2}}{\frac{1}{n}+2} + \frac{r(r-r_p)^{\frac{1}{n}+3}}{\left(\frac{1}{n}+2\right)\left(\frac{1}{n}+3\right)}\right]_{r_p}^{R}$$

$$= \frac{\pi n}{(n+1)}\left(\frac{p}{2\eta_m}\right)^{\frac{1}{n}} R^{\frac{1}{n}+3}\left[\frac{r_p^2}{R^2}\left(1-\frac{r_p}{R}\right)^{\frac{1}{n}+1} + \left(1+\frac{r_p}{R}\right)\left(1-\frac{r_p}{R}\right)^{\frac{1}{n}+2} - \frac{2\left(1-\frac{r_p}{R}\right)^{\frac{1}{n}+2}}{\left(\frac{1}{n}+2\right)} + \frac{2\left(1-\frac{r_p}{R}\right)^{\frac{1}{n}+3}}{\left(\frac{1}{n}+2\right)\left(\frac{1}{n}+3\right)}\right]$$

Now, we have, *Q = 1000 ml/min, Q = 0.00000167 m^3/second* and let $R = 1, and\ r_p = \frac{1}{3}$ *and we get*

$$Q = \frac{\pi n}{(n+1)}\left[\frac{p}{2\eta_m}.\frac{2}{3}\right]^{\frac{1}{n}} \frac{2}{27}\left[\frac{26n^2+33n+9}{6n^2+5n+1}\right]$$

$$\frac{27Q}{2\pi} = \left[\frac{p}{3\eta_m}\right]^{\frac{1}{n}}\left[\frac{26n^3+33n^2+9n}{6n^3+11n^2+6n+1}\right]$$

According to Gustafson, Daniel R. (1980)

$$\eta_p = 0.0013\ (pascal\ sec)$$

$\eta_m = 0.0271\ (pascal\ sec)$ According to Glenn Elert (2010) [7]

Date	Hemoglobin (HB) in (gram/dl)	Hematocrit(3*HB) In (kg/m^3)	Blood Pressure (BP) In (mmhg)	Venules Pressure Drop in Pascal-second $\frac{2}{3}\left(\frac{\frac{S+D}{2}+D}{3}\right) - \frac{\frac{S+D}{2}+D}{3}$
13-06-17	9.2	0.2604	110/60	-2147.9655
17-06-17	9.6	0.2716	110/70	-2370.1688
18-6-17	9.8	0.2773	120/80	-2666.4400
24-6-17	10.5	0.2971	130/70	-2518.3044
29-6-17	10.2	0.2886	125/60	-2259.0672

Table-01

H= 0.2604 and $P_f - P_i$=2147.9655 Pascal second,
Terminal hepatic venules average length
$0.15\ cm = 0.15 \times 10^{-9} m^3$[8] Then

$$\frac{27 * 0.00000167}{2 * 3.14}$$

$$= \left(\frac{2147.9655}{3 * 0.0271}\right)^{\frac{1}{n}} \left[\frac{26n^3 + 33n^2 + 9n}{6n^3 + 11n^2 + 6n + 1}\right] 0.000007180$$

$$= (26420.23985)^{\frac{1}{n}} \left[\frac{26n^3 + 33n^2 + 9n}{6n^3 + 11n^2 + 6n + 1}\right]$$

Solve by numerical method, we get

$$n = -0.882304$$

Terminal hepatic venules average length $0.15\ cm = 0.15 \times 10^{-9} m^3$[6] then

$$\Longrightarrow\ z_f - z_i = 0.15 \times 10^{-9} m^3$$

By using relation

$\eta_m = X\eta_c + (1 - X)\eta_P$where $X = \frac{H}{100}$, we get

$\eta_c = 9.9091$ And again using same above relation

$\eta_m = 0.099091H + 0.0013$

Now let $A = \frac{26n^3+33n^2+9n}{6n^3+11n^2+6n+1}$

$$\frac{P}{3\eta_m} = \left(\frac{27Q}{2\pi A}\right)^n \Longrightarrow P = 3\eta_m \left(\frac{27Q}{2\pi A}\right)^n$$

$$P = -\frac{dP}{dZ} \Longrightarrow dP = -PdZ$$

$$\Longrightarrow -\int_{p_f}^{p_i} dP = -\int_{Z_i}^{Z_f} 3\eta_m \left(\frac{27Q}{2\pi A}\right)^n dZ$$

Where $P_i - P_f$ pressure drop and
$Z_f - Z_i$Length of hepatic arterioles

$$P_i - P_f = 3\eta_m \left(\frac{27Q}{2\pi A}\right)^n (Z_f - Z_i)$$

Substituting the value of $Q, \eta_m, Z_f - Z_i, and\ n$, we get

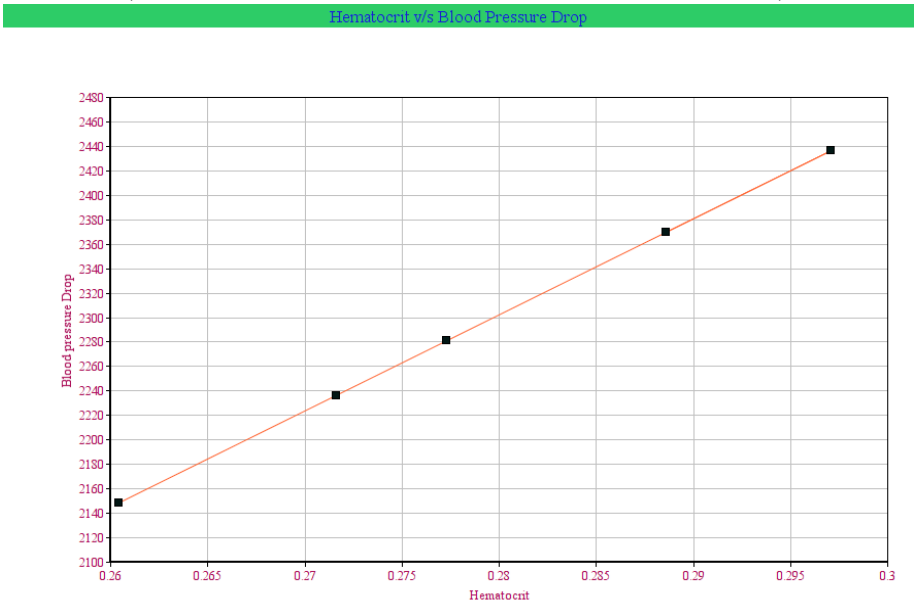
$$\boldsymbol{P_i - P_f = 7854.3686H + 103.0434}$$

We get, values of blood pressure drop if hematocrit is known by using above relation.

RELATION BETWEEN BLOOD PRESSURE DROP AND HEMATOCRIT:

Date	Hematocrit	Blood Pressure Drop
13-06-17	0.2604	2148.32098
17-06-17	0.2716	2236.2899
18-06-17	0.2773	2281.0504
24-06-17	0.2971	2436.5763
29-06-17	0.2886	2369.8141
Table-02		

BIOPHYSICAL INTERPRETATION:
(GRAPHICAL PRESENTATION OF CLINICAL DATA)



OBSERVATION:

A mathematically investigation of the graph shows increasing sense.

CONCLUSION:

A simple survey of the graph between blood pressure and hematocrit in Liver Cirrhosis patient shows that when hematocrit increased then Blood pressure is also increased, That is the hematocrit is proportional to blood pressure. When blood pressure drop is increased then we cannot suggest for operation but when blood pressure drop is decreased we suggest for successful operation.

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