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Mathematical Model on Two Phase Arterial Blood Flow of Human Hepatic Circulatory Sub-system with Special Reference to Malaria

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Abstract:
In this paper, we consider two phase arterial blood flow of human hepatic circulatory sub-system during malaria in which one phase is of blood plasma and other is that of red blood cells. In this study we apply non–Newtonian Power law model according to stress and strain rate of arteries and employing the Navier-Stoke equation and equation of continuity for cylindrical co-ordinate system. All mathematical equations are written in tensorial form and solution technique adapted is analytical as well as numerical for collected clinical data of blood pressure and hemoglobin. Resulting equation shows a linear relationship between hematocrit and blood pressure drop and graphical presentation for particular parametric value is much closer to clinical observation.

Keywords: Blood pressure drop, Hemoglobin, Non- Newtonian power law model, Stress, Strain rate.

1. Introduction

1.1 Structure and function of liver

Liver is one of the largest, anatomically and functionally most complex organ of the human body. The liver constitutes 2.5% of the human body weight and is the largest organ of the body [1, 2]. The liver is the reddish- brown in color and wedge –shaped organ with four lobes of unequal sizes and shapes. Liver lobes are enclosed by a thick capsule, generally overlapped with reflected periforinum [3]. The normal weight of a human liver is 1.44-1.66 kg and the width about 15 cm [4]. It is located in the right upper quadrant of the abdominal cavity and is situated just below the diaphragm, to the right of the stomach and covers gallbladder [5]. The liver performs main essential functions: (i) metabolic processes (ii) detoxifying harmful substance (iii) produces bile necessary for the digestion and absorption of dietary fats (iv) stores glycogen and vitamins and (v) old and damaged red blood cells are broken down [24].

1.2 Structure and the function of hepatic Circulatory sub-system

The hepatic artery originates from the celiac trunk and branches near to the portahepatis into the left hepatic artery (LHA) and the right hepatic artery (RHA). The artery may be subdivided into the common hepatic artery (CHA) from the celiac trunk to the origin of the gastro duodenal artery and the hepatic artery 'proper' (PHA) from that point to its bifurcation [6]. The common hepatic artery is one of the ultimate branches of the celiac artery. It delivers oxygen–rich blood to the liver, pylorus, pancreas and duodenum. It runs on the right inside the lesser sac, a cavity close to the middle of the abdomen. As any other artery of the body, oxygen saturation portal blood during the fasting state ranges up to 85% which is greater than other systemic veins; however, it substantially drops after food ingestion. It is generally believed that half of the oxygen requirements of the liver are provided by portal venous blood and the other half is delivered from the hepatic artery. [7].

1.3 Composition of blood

Blood is a fluid connective tissue and consists of two components – a yellow fluid, plasma and cells which are suspended in it. Plasma is that part of the extracellular fluid which is limited to the blood vessels. Plasma which constitutes 55% of blood fluid is mostly water (90%) and 7% protein by the volume [8]. Blood account for 7% of the human body weight [9] by volume; red blood cells or erythrocytes constitute about 45% of whole blood, plasma about 54.3% and white cells about 0.7% [10]. Whole blood (plasma and cells) displays non Newtonian fluid dynamics. Red blood cells comprise the blood hemoglobin and distribute oxygen [11]. These cells devoid of nucleus and organelles have unique properties of deformability. The deformability of RBC depends on three parameters :(I) the membrane elasticity that is mainly dependent on cytoskeleton components (II) the cytoplasmic viscosity that depends on intracellular ion and hemoglobin concentration and (III) the surface to volume ratio. The balance among these three parameters can be altered during malaria [22].

1.4 Description of disease

Malaria is a serious and sometimes fatal human disease caused by plasmodium parasites. Four kinds of malaria parasites infect humans: *Plasmodium falciparum*, *P. vivax*, *P. ovale* and *P. malariae*. *Plasmodium falciparum* is most dangerous species. After mosquito bite sperozoites enter the blood stream and majority of sperozoites reach to liver and infect hepatocytes. Sperozoites mature in hepatocytes and when liver cell rapture releasing merozoites into the blood stream and then merozoites invade red blood cells.

2. Real Model

2.1 Selection of Parameter and Frame of Reference

In this mathematical modeling we have choose a frame of reference for the state of a moving blood according to complexity of the problem of blood flow, we have select generalized three dimensional orthogonal curvilinear co-ordinate system, shortly prescribed as E^3, addressed as 3-dim Euclidean space and interpret the quantities related to blood flow in tensorial form. The biophysical laws thus articulated completely hold well in any co-ordinate system, which is mandatory for the veracity of the law (1990) [13]. Now let the co-ordinate axes be OX^i where O is the origin and superscript i = 1, 2, 3. let X^i be the co-ordinate of any point P in space, the mathematical description of state of a moving blood is affected by means of functions which give the distribution of blood velocity $v^i = v^k(X^i,t)$, k = 1, 2, 3 and of any two thermodynamic quantities pertaining to the blood for the pressure p = $p(X^i, t)$ and the density $\rho = \rho(X^i, T)$. Blood is the mixed fluid it is divided in two phase first is plasma and other is blood cells. The blood cells are enclosed with a semi-permeable membrane whose density is greater than that of plasma, these blood cells are uniformly distributed in plasma .Thus blood can be considered as homogeneous mixture of two phases.

2.2 Mathematical Formulation

As the hematocrit increases, the blood in arteries remote from the liver shows Power law model non-Newtonian flow. The previous researchers of this field have taken the blood to be single phased[14] .Whenever percentage of blood is reduces the blood has been supposed Newtonian but in case of increasing the hematocrit, the effective viscosity of blood flowing in the arteries remote from the heart depends upon the strain rate. The blood flow becomes non Newtonian when strain rate lie between 5 to 200 per second and the power law $T' = \eta_m e^n$. In this situation the constitutive equation of blood is as follow [14].

$$T^{ij} = -pg^{ij} + \eta_m(e^{ij})^n = -pg^{ij} + T'^{,ij} \qquad (2.1)$$

Where T^{ij} be stress tensor and $T'^{,ij}$ be shearing stress tensor.

The equation of continuity for power law flow will be as follows:

$$\frac{1}{\sqrt{g}}(\sqrt{g}v^i)_{,i} = 0 \qquad (2.2)$$

And the equation of motion in tensorial form is as follows:

$$\rho_m \frac{\partial v^i}{\partial t} + \rho_m v^j v^i{}_{,j} = T^{ij}{}_{,j} \qquad (2.3)$$

Where T^{ij} be taken from constitutive equation and

Where $\rho_m = X\rho_C + (1-X)\rho_P$ and $\eta_m = X\eta_C + (1-X)\eta_P$

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 [15]. 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. Then the volume portion covered by the plasma will be (1-X).

Since the blood vessels are cylindrical, the above governing equations have to transform into cylindrical co-ordinates. Let $x^1 = r$, $x^2 = \theta$, $x^3 = z$

Matrix of corresponding metric tensor in cylindrical form is as follow:

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

So matrix of conjugate metric tensor is

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

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

$\left\{ {1 \atop 2\ 2} \right\} = -r$, $\left\{ {2 \atop 2\ 1} \right\} = \left\{ {2 \atop 1\ 2} \right\} = \frac{1}{r}$ Except of these all are zero.

Physical components of velocity of blood flow will be related as

$$\sqrt{g_{11}}v^1 = v_r \Rightarrow v_r = v^1, \sqrt{g_{22}}v^2 = v_\theta \Rightarrow v_\theta = rv^2, \sqrt{g_{22}}v^3 = v_z \Rightarrow v_z = v^3$$

and the physical component of $-p_{,j}\, g^{ij}$ are $-\sqrt{g_{ii}}p_{,j}\, g^{ij}$

The matrix of physical component of shearing stress – tensor

$T'^{,ij} = \eta_m(e^{ij})^n = \eta_m(g^{ik}v^i_{,k} + g^{jk}v^j_{,k})^n$ Will be as follows:

$$\begin{bmatrix} 0 & 0 & \eta_m\left(dv/dr\right)^n \\ 0 & 0 & 0 \\ \eta_m\left(dv/dr\right)^n & 0 & 0 \end{bmatrix}$$

The covariant derivative of $T'^{,ij}$ is

$$T'^{,ij}_{,j} = \frac{1}{\sqrt{g}}\frac{\partial}{\partial x^j}\left(\sqrt{g}T'^{,ij}\right) + \left\{ {i \atop j\ k} \right\} T'^{,kj}$$

Keeping in view the above facts the equation of continuity and equation of motion are transformed into cylindrical co-ordinate system which is as follows:

The equation of continuity –

$$\frac{\partial v}{\partial z} = 0 \qquad (2.4)$$

The equation of motion –

$$-\frac{\partial p}{\partial r} = 0, \qquad 0 = 0, \qquad 0 = -\frac{\partial p}{\partial r} + \frac{\eta_m}{r}\frac{\partial}{\partial r}\left(r\left(\frac{dv}{dr}\right)^n\right) \qquad (2.5)$$

These are the r, θ, z components respectively

Here this fact has been taken in view that in axial flow is symmetric in artery so

$v_\theta = 0$ *and* v_r, v_z *and* p do not depend upon θ. Also the blood flows steadily, i.e.

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

On integrating equation (2.4), we get $v_z = v(r)$ (2.6)
Because v does not depend upon θ
The integration of equation of motion (2.5), we get $p = p(z)$ (2.7)
Since p does not depend upon θ
Now, with the help of equation (2.6) and (2.7), the equation of motion (2.5) transform into the following form:

$$0 = -\frac{dp}{dz} + \frac{\eta_m}{r}\frac{d}{dr}\left(r\left(\frac{dv}{dr}\right)^n\right) \qquad (2.8)$$

3. Analysis and solution

The pressure gradient $-(\frac{dp}{dz}) = P$ of blood flow in the arteries remote from liver can be supposed to be constant and hence the equation (2.8) takes the following form:

$$\frac{d}{dr}\left(r\left(\frac{dv}{dr}\right)^n\right) = -\frac{Pr}{\eta_m} \qquad (3.1)$$

On integrating equation (3.1), we get

$$r\left(\frac{dv}{dr}\right)^n = -\frac{Pr^2}{2\eta_m} + A \qquad (3.2)$$

Since the velocity of blood flow on the axis of the cylindrical arteries is maximum and constant. So that we apply the boundary condition at r=0, $v = v_0$(constant), on equation (3.2) to get the arbitrary constant A = 0. Hence the equation (3.2) takes the following form:

$$r\left(\frac{dv}{dr}\right)^n = -\frac{Pr^2}{2\eta_m} \Rightarrow -\frac{dv}{dr} = \left(\frac{Pr}{2\eta_m}\right)^{1/n} \qquad (3.3)$$

Integrating equation (3.3) we get

$$v = -\left(\frac{P}{2\eta_m}\right)^{1/n} \frac{r^{\frac{1}{n}+1}}{(n+1)/n} + B \qquad (3.4)$$

Now for we determine the arbitrary constant B, by using no-slip condition in the inner wall of the arteries: at $r = R$, $v = 0$, where R = radius of vessel, on equation (3.4) we obtain

$$B = \left(\frac{P}{2\eta_m}\right)^{1/n} \frac{nR^{\frac{1}{n}+1}}{n+1} \qquad (3.5)$$

Using equation [3.5] in the equation (3.4) then

$$v = \left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} \frac{n}{n+1}\left[R^{\frac{1}{n}+1} - r^{\frac{1}{n}+1}\right] \qquad (3.6)$$

This is the velocity of blood flow in the arteries remote from the liver where P is blood pressure gradient and η_m is the viscosity coefficient of mixture of blood.

4. Result and Discussion (Bio- Physical Interpretation)

The total flow- flux of blood through the transverse section of the arteries is [17].

$$Q = \int_0^R v.2\pi r\, dr = \int_0^R \left(\frac{P}{2\eta_m}\right)^{1/n} . \frac{n}{n+1}\left(R^{\frac{1}{n}+1} - r^{\frac{1}{n}+1}\right) 2\pi r\, dr$$

$$= \left(\frac{P}{2\eta_m}\right)^{1/n} . \frac{2\pi n}{n+1}\left(\frac{R^{\frac{1}{n}+1}.r^2}{2} - \frac{n.r^{1/n+1}}{3n+1}\right)_0^R$$

$$= \left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} . \frac{2\pi n}{n+1} . \frac{(n+1)R^{\frac{1}{n}+3}}{2(3n+1)}$$

$$Q = \left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} . \frac{\pi n R^{\frac{1}{n}+3}}{(3n+1)} \quad , \quad where\ P = -\frac{dp}{dz}$$

$$Q = \left[\frac{P_i - P_f}{2\eta_m(z_i - z_f)}\right]^{\frac{1}{n}} \cdot \frac{\pi n R^{\frac{1}{n}+3}}{(3n+1)} \qquad [4.1]$$

5. Observation:

Hemoglobin Vs Blood pressure is taken from Medical College Banda (UP)

Patient Name: Smt. Sushila **Age / Sex:** 36 Years / female, Annual No.1293/2022

Clin: Dr. Mukesh Bansal

Table-1 Clinical Hemoglobin Vs Blood Pressure Drop

S.No	Date	B.P. (In mm hg)	Hemoglobin (gm/dl)	Hematocrit (H)	B.P. (In Pascal)	Cli. BPD
1	03/08/2022	110/70	8.6	25.8	14665.2/9332.4	2666.4
2	05/08/2022	115/78	8.2	24.6	15331.8/10398.96	2466.42
3	08/08/2022	110/75	7.8	23.8	14665.2/9999	2333.6
4	11/08/2022	120/78	8.4	25.2	15998.4/10398.96	2799.72
5	13/08/2022	125/85	8.7	26.10	16665/11332.20	2666.4

Average Systolic pressure =15465.12 Pa

Average Diastolic Pressure = 10292.30 Pa

H = Average hematocrit = 25.1

P_i = Pressure in Artery = Average Systolic Pressure =15465.12 Pa

P_f = Pressure in Arterioles = $\frac{S+D}{2}$ = 12878.71 Pa

According to Glenn Elert (2010)

η_m = Viscosity of mixture = 0.035 p.s.

According to Gustafson, Daniel R. (1980)

η_p = Viscosity of plasma =0.0015 p.s [18]

Length of common hepatic arteries = 0.0347 m

Since $\eta_m = \eta_c X + \eta_p(1 - X)$

Or, $\eta_m = \eta_c \frac{H}{100} + \eta_p\left(1 - \frac{H}{100}\right)$ $where\ X = \frac{H}{100}$

$0.035 = \eta_c \frac{25.1}{100} + 0.0015\left(1 - \frac{25.1}{100}\right)$

$\eta_c = 0.134966135$ P.S =Viscosity of cells

Now putting the value of η_c $in\ \eta_m$, we have

$\eta_m = 0.134966135\frac{H}{100} + 0.0015\left(1 - \frac{H}{100}\right)$

$\eta_m = 133.466 \times 10^{-5} H + 0.0015$

Now from equation (4.1), Flow flux is given as

$$Q = \left[\frac{P_i - P_f}{2\eta_m(Z_i - Z_f)}\right]^{1/n} \cdot \frac{\pi n R^{\frac{1}{n}+3}}{(3n+1)} \quad where\ Q = 1000\frac{ml}{min} \Rightarrow 0.0167\frac{lit}{sec} = 1.67 \times 10^{-5} m^3/sec$$

$1.67 \times 10^{-5} = \left[\frac{15465.12 - 12878.71}{2 \times 0.035 \times 0.0347}\right]^{\frac{1}{n}} \cdot \frac{3.14 \times n \times (0.0025)^{\frac{1}{n}+3}}{(3n+1)}$

$340.382166 = (2662.01113)^{\frac{1}{n}}\left(\frac{n}{3n+1}\right)$

Solve above equation by Newton- Raphson method

$x_{n+1} = x_n - \frac{f(x_n)}{f'(x_n)}$

We obtain

$n = 1.0963$

$$Q = \int_0^R v.2\pi r\, dr = \int_0^R \left(\frac{P}{2\eta_m}\right)^{1/n} . \frac{n}{n+1}\left(R^{\frac{1}{n}+1} - r^{\frac{1}{n}+1}\right) 2\pi r\, dr$$

Using by Simpson one third rule

Here P = 314650.868 R = 0.0025

We divide the subinterval five equal parts, so step size h= 0.0005

a = 0, b = R = 0.0025, N = 5

h = $\frac{(b-a)}{N}$ $h = \frac{(0.0025-0}{5}$ h = 0.0005

$\frac{1}{n} = \frac{1}{1.0963} = 0.912159081$

h=0.0005, 2h=0.001, 3h=0.0015,4h=0.002 and 5h=0.0025

$$f(r) = (314650.868).(0.522969041)\left[(0.0025)^{0.912159081+1} - r^{\frac{1}{n}+1}\right] 2\,\pi\,r$$

$f(r) = 1033390.72\left[1.05790668 \times 10^{-5} r - r^{\frac{1}{n}+2}\right]$

$\int_0^{0.0025} f(r)\, dr = \frac{h}{3}$ [f(0) + 4f(h) + 2f(2h) + 4f(3h) + 2f(4h) + f(5h)]

Now

f(0) = $1033390.72\ [1.05790668 \times 10^{-5}0 - 0^{1.9121590811}]$ = 0

f(h) = $1033390.72\ [1.05790668 \times 10^{-5} \times 0.0005 - (0.0005)^{2.912159081}]$

f(2h) = $1033390.72\ [1.05790668 \times 10^{-5} \times 0.001 - (0.001)^{2.912159081}]$

f(3h) = $1033390.72\ [1.05790668 \times 10^{-5} \times 0.0015 - (0.0015)^{2.912159081}]$

f(4h) = $1033390.72\ [1.05790668 \times 10^{-5} \times 0.002 - (0.002)^{2.912159081}]$

f(5h) = $1033390.72\ [1.05790668 \times 10^{-5} \times 0.0025 - (0.0025)^{2.912159081}]$

or,

f(0) = 0

f(h) = $1033390.72\ [0.0005289534 \times 10^{-5} - 2.43711219 \times 10^{-10}]$

f(2h) = $1033390.72\ [.00105790668 \times 10^{-5} - 1.83452129 \times 10^{-9}]$

f(3h) = $1033390.72\ [0.00158686002 \times 10^{-5} - 5.97487077 \times 10^{-9}]$

(4h) = $1033390.72\ [0.00211581336 \times 10^{-5} - 1.38092468 \times 10^{-8}]$

f(5h) = $1033390.72\ [0.002644766 \times 10^{-5} - 2.64476669 \times 10^{-8}]$

$\int_0^{0.0025} f(r)\ \mathrm{dr} = \frac{0.0005}{3}\ [0 + 4 \times 1033390.72\ [0.0005289534 \times 10^{-5} - 2.43711219 \times 10^{-10}] + 2 \times 1033390.72\ [.00105790668 \times 10^{-5} - 1.83452129 \times 10^{-9}] + 4 \times 1033390.72\ [0.00158686002 \times 10^{-5} - 5.97487077 \times 10^{-9}] + 2 \times 1033390.72\ [0.00211581336 \times 10^{-5} - 1.38092468 \times 10^{-8}] + 1033390.72\ [0.002644766 \times 10^{-5} - 2.64476669 \times 10^{-8}]]$

$\int_0^{0.0025} f(r)\ \mathrm{dr} = 172.232131[0.0174554598 \times 10^{-5} - 8.26095311 \times 10^{-8}]$

$= 1.58358948 \times 10^{-5} m^3/sec$

Percentage error $= \frac{(1.67 \times 10^{-5} - 1.58358948 \times 10^{-5})}{1.67 \times 10^{-5}} \times 100$

$= 5.174282263\%$

Hence by result by numerical method differ 5.174282263% with analytical method.

Now again from equation (4.1), we will find pressure drop

$\triangle P = \left[\frac{(3n+1)Q}{\pi n R^3}\right]^n \left[\frac{2\eta_m \Delta Z}{R}\right]$

Substituting values in above equation, we have

$\Delta P = \left[\frac{(3 \times 1.0963 + 1)(1.67 \times 10^{-5})}{3.14(1.0963)(0.0025)^3}\right]^{1.0963} \cdot \left[\frac{2\eta_m (0.0347)}{0.0025}\right]$

$\Delta P = (73906.2008)(133.466 \times 10^{-5} H + 0.0015)$

$\Delta P = 98.63965\ H + 110.8593$ by analytical method

And for numerical method

$\Delta P = \left[\frac{(3 \times 1.0963 + 1)(1.58358948 \times 10^{-5})}{3.14(1.0963)(0.0025)^3}\right]^{1.0963} \cdot \left[\frac{2\eta_m (0.0347)}{0.0025}\right]$

$\Delta P = (69724.4344)(133.466 \times 10^{-5} H + 0.0015)$

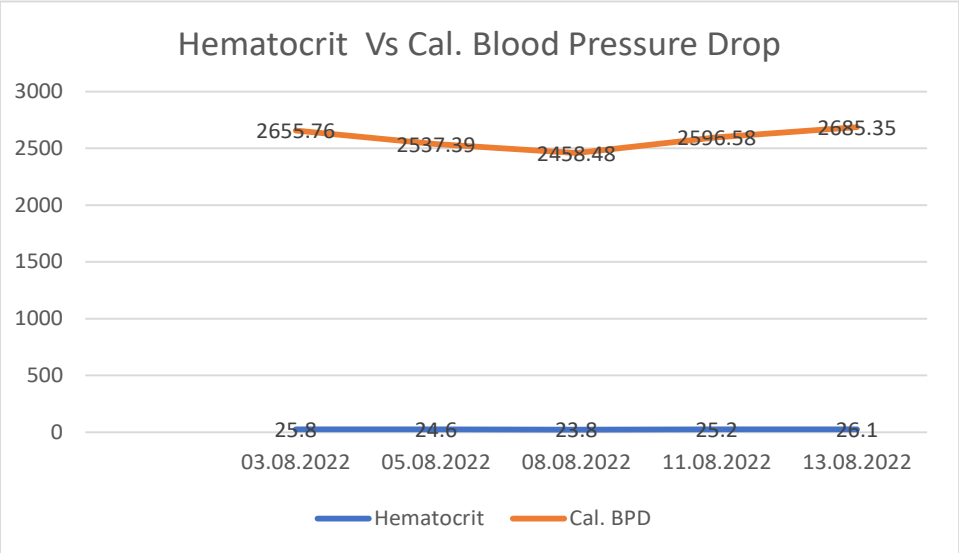
$\Delta P = 93.05841\ H + 104.586652$ by numerical method

Putting values of H in above equation .We get the following table of blood pressure drop

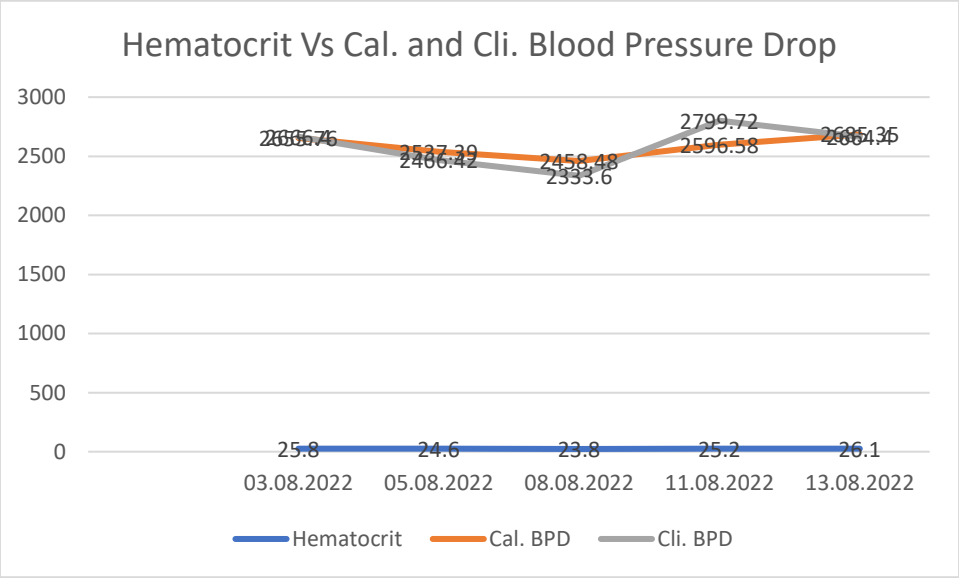
Table-2 Hematocrit Vs Modulated Blood Pressure Drop

Date	03/08/2022	05/08/2022	08/08/2022	11/08/2022	13/08/2022
Hematocrit (H)	25.8	24.6	23.8	25.2	26.1
Blood pressure drop (ΔP)	2655.76	2537.39	2458.48	2596.58	2685.35

Graph 1 Hematocrit Vs Modulated Blood Pressure Drop



Graph 2 Hematocrit Vs Modulated and Clinical Blood Pressure Drop



6. Observation of graph

The graph 1 between modulated blood pressure drop and hematocrit shows that five different dates were observed minimum blood pressure drop 2458.48 on dated 08/08/2022 and maximum value obtains 2685.35 on dated 13/08/2022. At the hematocrit value from 25.8 to 23.8 via 24.6, the blood pressure drop straightly decreases on dated from 03/08/2022 to 08/08/2022 via 05/08/2022 and hematocrit value from 23.8 to 26.1 via 25.2, the blood pressure drop straightly increases on dated from 08/08/2022 to 13/08/2022 via11/08/2022. The graph 2 hematocrit Vs modulated blood pressure drop and clinical blood pressure drop.

7. Conclusion:

In this study we observed that slope of straight line is absolute value and when hematocrit increases the blood pressure drop also increases and when hematocrit decreases the blood pressure drop also decreases. This implies that when trend of straight line decreasing sense then medicine dose slowly increases, when steepness of curve low then we can suggest high dose of medicine and when trend of straight line increasing sense then we suggest normal dose of medicine. In comparative study of graphs we found that both graph nearly have same character and mathematical model verified for clinical data.

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