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# CLINICAL INFLUENCE OF HYDROXYCHLOROQUINE WITH AZITHROMYCIN ON BLOOD FLOW THROUGH BLOOD VESSELS FOR THE PREVENTION AND TREATMENT OF COVID-19

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## ABSTRACT

COVID-19 emerges to produce genetic changes in platelets of blood. Platelets accumulated more easily in the blood of COVID-19 patient and they are more correlated with a greater risk of thrombus or blood clotting, which can cause of heart attack, stroke, organ failure and other serious complications in a number of patients, mostly among those with underlying disorders such as diabetes, obesity, or high blood pressure. Blood viscosity is directly correlated with systolic and diastolic blood pressure. Venous hematocrit and plasma viscosity are higher in the hypertensive patients. To reduce the blood-viscosity of such patient a regular dose of hydroxychloroquine with azithromycin can be given to increase flow of blood in blood vessels by building the blood slighter viscous than earlier and to reduce the infection of virus in the respiratory system. The blood flow of patients with the greater viscosity can be reduced by reducing the viscosity of plasma. Hydroxychloroquine is a glucose lowering drug which means it helps to lower the blood sugar in the patient; hence it works on lowering the blood viscosity, whereas the azithromycin is an antibiotic used to treat the respiratory infections. In presented work efforts have been initiated to investigate some result for behavior of blood flow in blood vessels and the significance of hydroxychloroquine with azithromycin for COVID-19 patient. At the end the numerical demonstration has been given to deliver the outcomes for the blood flow, pressure and viscosity. The findings of this

research work may possibly assist in the treatment and diagnosis of cardiovascular disorders as well as COVID-19 patient.

**Keywords: Stenosis, Blood flow, Blood vessels, Viscosity, Hydroxychloroquine, Azithromycin**

## INTRODUCTION

The deadly coronavirus carries on spreading throughout the globe, and mathematical models can be used to investigate the effects of virus that causes COVID-19 on blood flow. Several people those who suffered with COVID-19 can also develop a risk of blood clotting or bacterial infection as a complication. In such cases, health care provider can recommend antibiotics to the patients it may reduce the problems or the risk of heart disease. Hydroxychloroquine (Plaquenil) is a medicine that has been used for many years as a treatment of malaria, lupus, and rheumatoid arthritis. Though, Hydroxychloroquine has one more benefit to decrease the chances of making a thrombus in the blood vessels of cardiovascular system. It minimizes the chance of getting a heart attack or stroke **[7-11]**. Atherosclerosis or stenosis is a heart disorder, that can put blood flow at risk and responsible for cardiovascular diseases **[5, 10]**. In treatment of diseases, atherosclerosis is one of the primary health risks, which is the primary root cause of demise in several countries. Cardiovascular disorder is a dangerous disorder of the heart or blood vessels due to blocked blood vessels in the heart. Though, it is an actual fact, that when a doctor use this word "cardiovascular disease" it generally denotes the heart disease only or blood vessels that are due to "Atheroma", Stenosis or Atherosclerosis **[6, 12, 17]**. There are certain fatty lumps known as atheroma develops on the inner lining of some blood vessels. These diseases are because of brief interruption of blood which includes transient ischaemic attack (TIA), angina, heart attack, stroke, and peripheral arterial disease. Stenosis growth is responsible to escalate the resistance and associated changes in blood supply, gives rise to the several diseases like hypertension, cerebral strokes and myocardial infarction etc. **[1-3]**. Hence, the study of stenotic arterial flow in blood is very essential to prevent and treat an arterial diseases as well as heart problems. Several patients of cardiovascular disease normally consume suitable-dose of clopidogrel (75 mg) each day or aspirin (75 mg) each day **[4]**. This lowers the chances of getting a heart attack by about a third and minimizes the chance of getting any cardiovascular problem by about a quarter. It is also observed that by consuming daily a low dose of aspirin can also reduce the risk of developing cancer. Considering all these facts, several theoretical and mathematical models **[13, 14]** have been established to discuss the blood flow aspects because of the occurrence of stenosis in the inner layer of the blood vessel wall. In many mathematical models the effects of paired stenosis through small artery have been studied **[16]**. Various researchers **[15, 18]** have investigated the special effects of an overlapping stenosis on blood flow parameter in narrow blood vessels. In all these studies tubes of uniform cross-section have been taken to analyze the effects of stenosis through blood vessels. But, in reality it is not true, the ducts in biological, physiological systems are not horizontal they have some inclination to the axis. In the investigation of **[9]** Herschel-Bulkely fluid model with multiple stenosis through an inclined tube of non-uniform cross section have been taken in order to estimate the effects of blood flow on different parameters. In the work of **[4]** mathematical modeling has been done by considering blood as a Herschel-Bulkley fluid model of type non-Newtonian fluid to find out several effects. In a recent research, a numerical model have been taken to show the effect of stenoses on blood flow and the model used for the representation of blood behavior was Casson's fluid model. An investigation has been done to find out the effects of irregular arterial mild stenosis artery and the results were shown for viscosity. It was declared that in the presence of stenoses the velocity of fluid decreases **[6]**. In this paper the effects of blood viscosity, resistance to flow and pressure have been determined. The objective of this present research work is to treat and prevent the patient with high viscosity of blood with hydroxychloroquine and azithromycin and to study the blood flow through blood vessels for COVID-19 patient. The set of mathematical expression have been evaluated by making a use of MATLAB software.

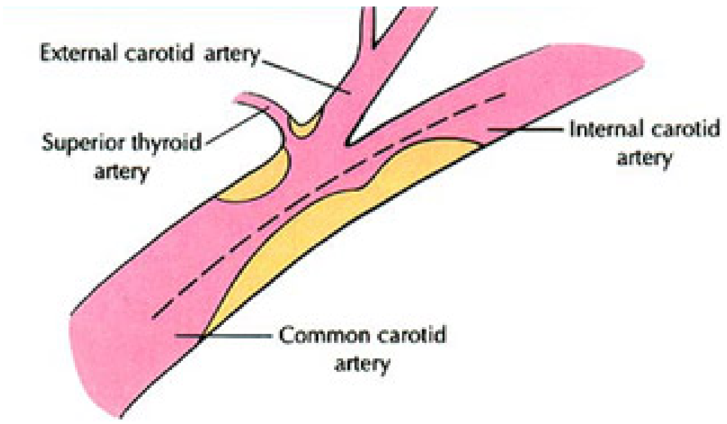


**Figure 1: Stenosed Artery**

**Formulation of the problem**

The blood flow has consider laminar, fully develop an axially symmetric, through a non-uniform cross-section cylinder with primary and secondary stenoses **(Figure 1)**.

The momentum equation is given by

$$\frac{1}{r}\frac{\partial}{\partial r}(r\tau_{rz}) = -\frac{\partial p}{\partial z} + \frac{\sin\alpha}{F}, \quad (1)$$

$$F = \frac{\mu U^n}{\rho g R_0^{n+1}} \quad (2)$$

$\tau_{rz}$ **= Shear stress,**

**Model I**

The Casson Fluid model:

$$\tau_{rz}^{\frac{1}{2}} = \left[-\mu\frac{\partial u}{\partial r}\right]^{\frac{1}{2}} + \tau_0^{\frac{1}{2}}, \qquad \tau_{rz} > \tau_0, \quad (3)$$

$$\frac{\partial u}{\partial r} = 0, \tau_{rz} < \tau_0, \quad (4)$$

**Model II**

The Power-law Fluid model:

$$\left.\begin{aligned} &\left(-\frac{du}{dr}\right) = \left(\frac{\tau}{\mu}\right)^{1/n} = f(\tau), \\ &\text{where } \tau = \left(-\frac{dp}{dz}\right)\frac{R_c}{2} \end{aligned}\right\}, \quad (5)$$

$$\frac{\partial u}{\partial r} = 0, \tau_{rz} < \tau_0, \quad (6)$$

**Boundary conditions**

By using boundary conditions:

τ is finite at r=0, **(7)**

u=0 at r=h(z) **(8)**

The non-dimensional variable are as follows:

$$\bar{z} = \frac{z}{L}, \bar{\delta} = \frac{\delta}{R_0}, \bar{R}(z) = \frac{R(z)}{R_0}, \bar{P} = \frac{p}{\left(\frac{\mu UL}{R_0^2}\right)}, \bar{\tau}_0 = \frac{\tau_0}{\mu\left(\frac{U}{R_0}\right)}, \bar{\tau}_{rz} = \frac{\tau_{rz}}{\mu\left(\frac{U}{R_0}\right)}, \bar{Q} = \frac{Q}{\pi R_0^2} \ \bar{F} = \frac{F}{\mu U\lambda} \quad (9)$$

The mathematical expression for the geometry of the primary and secondary stenoses in non-dimensional form is given by:

$$h = R(z) = \begin{cases} R_0 & : 0 \le z \le d_1, \\ R_0 - \frac{\delta_1}{2}\left(1 + \cos\frac{2\pi}{L_1}\left(z - d_1 - \frac{L_1}{2}\right)\right) & : d_1 \le z \le L_1, \\ R_0 & : d_1 + L_1 \le z \le B_1 - \frac{L_2}{2}, \\ R_0 - \frac{\delta_2}{L_2}\left(1 + \cos\frac{2\pi}{L_2}(z - B_1)\right) & : B_1 - \frac{L_2}{2} \le z \le B_1, \\ R^*(z) - \frac{\delta_1}{2}\left(1 + \cos\frac{2\pi}{L_2}(z - B_1)\right) & : B_1 \le z \le B_1 + \frac{L_2}{2}, \\ R^*(z) & : B_1 + \frac{L_2}{2} \le z \le B, \end{cases} \quad (10)$$

The following constraints for mild stenoses should be satisfied:

$\delta_i \ll \min(R_0, R_{out})$,

$\delta_i \ll L_i$, where $R_{out} = R(z)$ at $z = B$.

Here $\delta_i$ and $L_i$ are the maximum heights and lengths of two stenoses.

**Solution of the problem**

The velocity has obtained by simplifying and integrating the eqs. (1),(3) and (5) with the help of boundary conditions (7) and (8), when $P = -\frac{\partial p}{\partial z}$, and $f = \frac{\sin\alpha}{F}$.

$$u = \frac{(P+f)}{\mu}\left[\frac{r^2-h^2}{4} + \frac{\tau_0}{(P+h)}(r-h) - \frac{2^{\frac{3}{2}}\sqrt{2}}{3}\left(r^{3/2} - h^{3/2}\right)\left(\frac{\tau_0}{(P+f)}\right)^{1/2}\right] \quad (11)$$

$$u = \frac{(P+f)}{\mu}\left[\frac{r^2-h^2}{4} + \frac{\tau_0}{(P+h)}(r-h)\right] \quad \text{for } r_0 \le r \le h \quad (12)$$

Eq. (11), Eq. (12). have represented the velocity for Casson's fluid model and Power law fluid model respectively.

From equations (7) and (8), the upper limit of the plug flow region is given as follows:

$$r_0 = \frac{2\tau_0}{(P+f)} \quad (13)$$

by taking the condition $\tau_{rz} = \tau_h$ at r = h, we have

$$\frac{r_0}{h} = \frac{\tau_0}{\tau_h} = \tau, \; 0 < \tau < 1. \quad (14)$$

Using $r = r_0$ in Eqs. (11), (12) the plug core velocity is as follows:

$$u_p = \frac{(P+f)}{\mu}\left[\frac{r_0^2}{12} - \frac{h r_0}{2} + \frac{2}{3}h^{3/2}r_0^{1/2} - \frac{h^2}{4}\right] \text{ for } 0 \le r \le r_0. \quad (15)$$

$$u_p = \frac{(P+f)h^2}{\mu}\left[\frac{1}{4} + \frac{\tau_0^2}{2} - \frac{\tau_0}{2}\right] \text{for } 0 \le r \le r_0. \quad (16)$$

Eq. (15) and Eq. (16) are representing the velocity for Casson's fluid model and Power law fluid model respectively. And the flow rate is represented by the following Eq. **(17)**:

$$Q = -\frac{R_0^4 \pi}{8\mu}\frac{dp}{dz}\left(\frac{R}{R_0}\right)^4 +- \frac{\tau_0 \pi}{3\mu}\left(\frac{R}{R_0}\right)^3 +- \frac{4R_0^{7/2}\pi}{7}\left\{\frac{\tau_0}{\mu}\left(-\frac{1}{2\mu}\frac{dp}{dz}\right)\left(\frac{R}{R_0}\right)^7\right\}^{1/2} \quad (17)$$

The flow rate is given as below:

$$\lambda = -\frac{1}{Q}\int_{-1}^{1}\left[\begin{matrix} -Q\mu + 2\tau_0\left(\frac{1}{3}h^3(1-\tau_0^3) - \frac{h^3}{2}(1-\tau_0^2)\right) \\ /\tau_0^2 h^4\left(\frac{1}{4} + \frac{1}{4}\tau_0^2 - \frac{\tau_0}{2} + \frac{h^4}{4} + \right. \\ \left.(1-\tau_0^2) - \frac{h^4}{8}(1-\tau_0^4)\right) \end{matrix}\right] + f\, dz \quad (18)$$

The apparent viscosity ($\mu_{app}$) is represented as below;

$$\mu_{app} = \frac{1}{\left(R(z)/R_0\right)^4 f(\bar{y})} \quad (19)$$

$$f(\bar{y}) = \left(\bar{y}\right)^4 +- \frac{\tau_0 \pi}{3\mu}\left(\bar{y}\right)^3 +- \frac{4R_0^{7/2}\pi}{7}\left\{\frac{\tau_0}{\mu}\left(-\frac{1}{2\mu}\frac{dp}{dz}\right)\left(\bar{y}\right)^7\right\}$$

## RESULTS AND DISCUSSION

Stenosis is a very hazardous heart disease. Blood flow in the heart affects due to irregular growth of stenosis in the arteries. This irregular growth of stenosis may lead to serious cardiovascular disorders. The aggregation of lipids or fats on the inner wall of the blood vessels is the main reason for formation of the stenosis. Due to stenosis several diseases can develop like brain hemorrhage, blood pressure, heart attack atherosclerosis. In preparation to evaluate the approximate effects of several parameters evolved in the study, some programs on MATLAB have been established. And to estimate the critical results attained for pressure profile, apparent viscosity and resistance to blood flow for diseased and normal conditions have been determined. Fig 2-4 shows the findings of this research work by making use of values of parameter established tentative data in the blood vessels. Fig. 2 consists the results for resistance with stenosis size for $B_1 = 0.8$, $B = 1$, $\beta_1 = 0.01$, $d_1 = L_1 = L_2 = 0.2$. It is quite evident from the experimental results that resistance increases as stenosis size escalates or radius of artery decreases.

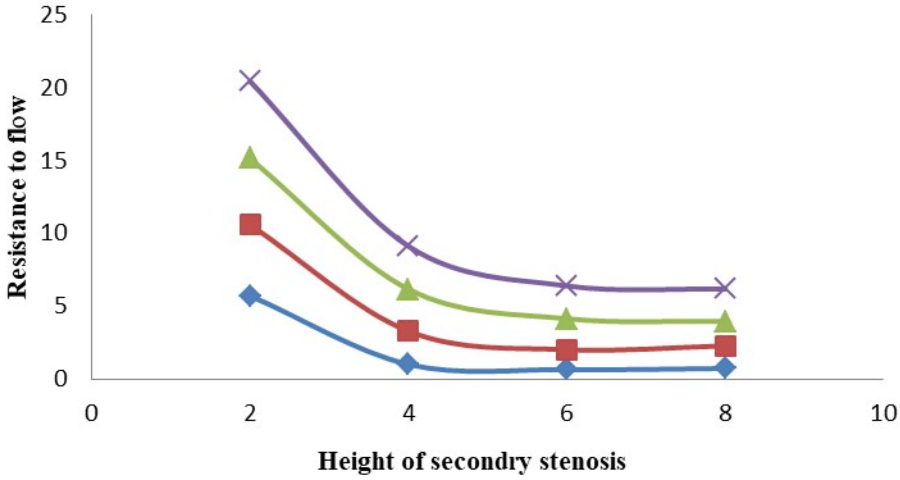


**Fig.2. Variation of Resistance to flow with height of secondry stenosis**

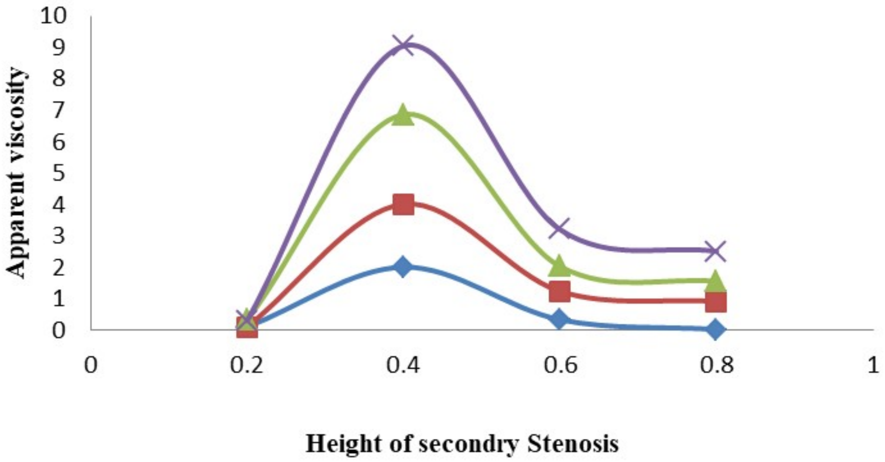


**Fig. 3. Variation of apparent viscosity for different values of height of secondry stenosis**

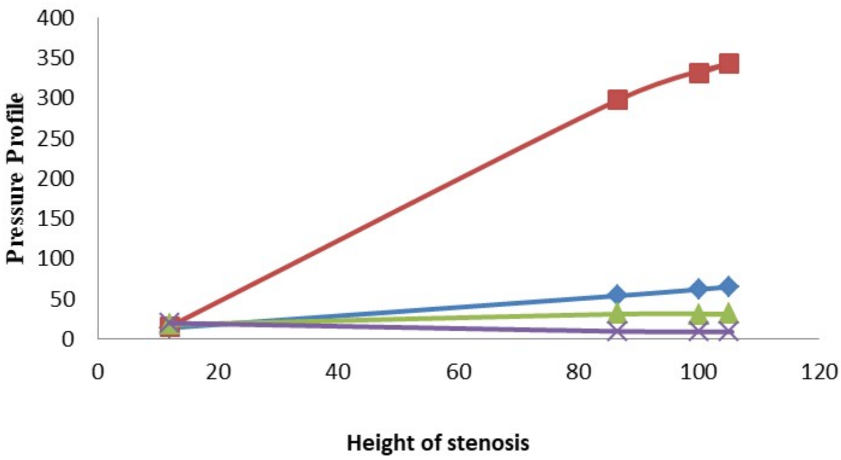


**Fig. 4. Variation of pressure for different values of secondry stenosis**

**Figure 3** reveals the deviation of viscosity with respect to shape parameter of stenosis along with $B_1 = 0.8$, $B = 1$, $\beta_1 = 0.01$, $d_1 = L_1 = L_2 = 0.2$. It has also observed that the pressure increases as shape parameter of stenosis increases. The similar results have been found in the observation of **[14]**. The variation of pressure profile with the height of the secondary stenosis has been shown in the Figure 4, for distinct values of α. It is clear from the figure that the pressure profile increases with the increasing values of $\delta_2$ and it can also be seen that it increases for the falling values of α for the Casson's fluid and Power-law fluid model **[11, 13]**. Pressure gradient, viscosity and resistance are the main aspects which are directly influenced by the flow in blood vessels. In the stenotic region the resistance elevates as the stenosis develops and it is constant in region where there is no stenosis. In the diabetic patients the resistance to flow is higher than the non-diabetic patients. Therefore, the diabetic patients with higher resistance are more susceptible to high blood pressure, heart diseases and other disorder like COVID-19. Hence, in case of such patients the resistance to blood flow and blood pressure can be maintained by reducing the viscosity of the plasma. Hydroxychloroquine is blood-viscosity reducing drugs which improve the flow of blood by lowering the blood viscosity. Blood viscosity of plasma may be reducing by giving regular dose of hydroxychloroquine.

## CONCLUSION

It is perceived in this research work that the flow raises with the height of both the primary and secondary stenosis ($\delta_1$, $\delta_2$) for both the fluid models. It is also observed that the resistance also drops with the falling value of inclination (α) in both fluid models. This analysis presents an improved study to acknowledge the flow aspects of blood having increased viscosity, and the significance of hydroxychloroquine to prevent and treat the blood clotting. The viscosity, pressure gradient and resistance to flow are the main aspects of blood flow through blood vessels. Resistance to flow rises as the radius of blood vessel decreases or in the stenotic region and remains constant outside the stenotic region. The arterial circulation is complex in the diseased condition, but the non-Newtonian nature of blood may help in the smooth circulation of diseased arteries. The blood flow in COVID-19 patients is greater in comparison to the normal patients. Thus, COVID-19 patients with greater resistance to flow are more inclined to high blood pressure and heart stoke. Therefore, the plasma viscosity may be reduced by giving medication in order to reduce the viscosity and resistance to flow of blood. Hydroxychloroquine with the combination of azithromycin is a better medication for the patient with heart disorder to reduce the viscosity of plasma and to treat any respiratory infection.

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