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Application of Differential Equation in the Design of Dialysis Machine

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Abstract

In this work, I have discussed the application of differential equations in the design of a dialyzer machine. A dialyzer is a device through which blood flows from the patient's body into the machine. A substance called dialysate flows through the machine in the opposite direction to the blood. This aids in separating waste materials with the help of a semipermeable membrane attached to the machine. This membrane possesses minute pores that allow the passage of waste matter, which has much smaller molecules than the blood cells, but restrict the passage of blood itself. The design of the dialyzer machine concerns the flow rate of the waste material through the membrane. This flow-rate is determined by the differences in concentration of waste material on either side of the membrane, where, the flow occurs from high concentration to low concentration.

Keywords: Dialyzer, Dialysate, Permeable membrane, Differential equation.

1. Introduction

The kidney is the most important organ in the human body. Its primary purpose is to filter out waste products such as urea, creatinine, and excess fluid from the blood. When the kidneys malfunction, waste accumulates in the blood, potentially reaching dangerous levels and becoming poisonous to the system. The main causes of chronic kidney failure worldwide are hypertension (high blood pressure) and diabetes mellitus [1] [2]. About one-fourth of all patients requiring kidney dialysis have diabetes. A common issue with kidney malfunction and renal failure is water retention, often necessitating the removal of several pints of fluid from the patient's blood. Dialysis machines serve as artificial kidneys, performing most, though not all, of the kidney's functions for patients with permanent or temporary renal failure. These machines use hemodialysis to cleanse the blood and balance its constituents. During this process, the patient's blood is circulated through the machine, where it is filtered and balanced for electrolytes, pH, and fluid concentration before being returned to the patient. There are two basic classes of dialysis machines: clinical

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units, which are typically cabinet-sized machines operated by trained technicians; and home-use dialysis machines, which are smaller and sometimes portable [3],[4],[5].

Normally, patients with complete loss of kidney function would need to visit the clinic at least three times per week and spend about four hours connected to the machine. With home-use machines, patients have more flexibility in scheduling dialysis, and they can dialyze for longer periods and more frequently. Thus, home-use machines are growing in popularity because they offer greater convenience and better clinical outcomes. Doctors use a kidney dialysis machine or dialyzer to assist the kidneys in the cleansing process. Kidney dialysis removes waste products from the blood of patients with improperly working kidneys. During the dialysis process, the patient's blood is pumped through a dialyzer, usually at a rate of 1 to 3 deciliters per minute. The patient's blood is separated from the cleaning fluid by a semipermeable membrane, which permits waste but not blood cells to diffuse to the cleaning fluid. The cleaning fluid contains some substances beneficial to the body, which diffuse into the blood. The cleaning fluid, called the dialysate, flows in the opposite direction to the blood, usually at a rate of 2 to 6 deciliters per minute. Waste products from the blood diffuse into the dialysate through the membrane at a rate proportional to the difference in concentration of the waste products in the blood and dialysate. Diffusion occurs when there is a higher concentration of a dissolved substance on one side of a semi-permeable membrane than on the other. Particles of the dissolved substance will move from the more concentrated side across the membrane to the less concentrated side until the concentration on both sides is the same. Our main approach is to study how the dialyzer works and to analyze the design of the dialysis machine with theoretical results versus experimental data [6],[7],[8].Top of Form

The kidneys function to maintain water, electrolyte, and acid-base balance in the body, as well as to excrete waste products such as urea and uric acid. They receive approximately 20 percent of the cardiac output, which amounts to about 1200ml of blood flow per minute. On average, 1.5- 2 liters of urine are produced per day. A semi-permeable membrane, like a cellulose membrane, contains numerous pores with an average size of 40 angstroms, allowing the passage of substances with a molecular weight up to 56,000. However, substances with a molecular weight greater than 56,000, such as albumin and hemoglobin, cannot pass through. Additionally, red and white blood cells are too large to traverse these pores. To prevent substances like electrolytes and dextrose from passing through the membrane, the concentration of these substances in the dialysate is maintained at levels equivalent to those found in the blood of a healthy human being. In 1943, a Dutch physician named Willem Johan Kolff constructed the first operational dialyzer. Over the subsequent two years (1943-1945), Kolff used his machine to treat 16 patients suffering from acute kidney failure, but the results were unsuccessful. It wasn't until 1945 that a 67-year-old woman became the first patient successfully treated with dialysis [9],[10].

Various efforts are under investigation to synthesize new membrane materials which are expected to decrease the treatment time and to increase biocompatibility/hemocompatibility of the membranes. In addition, new module designs are considered to increase the efficiency of the hemodialysis operation. The test of performance of new membranes or module designs requires extensive trial and error experimentations. To eliminate this difficulty several mathematical models have been developed to investigate the dialyzer performance and patient's clearance values. The main purpose of the study is to give mathematical model of dialysis of blood.

This paper is organized as follows: In section 2, I discuss about the design of dialysis machine. In section 3, I present the model in which the design of dialysis machine is formulated and I also analyse the model. In section 4, I present the interpretation of the model and lastly in section 5, I present our conclusions.

2 Design of a Dialysis Machine:

Dialysis machines are medical equipment whose design and manufacture are regulated by the Food and Drug Administration (FDA). This means that their design and construction must follow precisely documented processes, and their performance must meet stringent documentation, development testing, production testing, and field maintenance requirements. The equipment also must contain comprehensive self-test and fault-indication capabilities, which require additional circuitry and the use of components that include self-test features. Electrical leakage to the patient is a significant concern. Medical device developers must meet the requirements of the IEC 60601-1 product safety standard for electrical medical equipment. Given the time and expense required to achieve FDA approval, manufacturers must ensure the long-term availability of system components. Thus, it is important to select a supplier with a customer-oriented discontinuance policy to ensure that system components will be available for many years [1] [11]

Dialysis machines have three basic functions: (1) circulation of blood from the patient's access through the dialyzer and back to the access using a blood pump and a disposable tubing set; (2) preparation of dialysate from purified water and one or more concentrates and circulation of that dialysate through the dialyzer using a system that also controls the rate of fluid removal, and (3) monitoring for any loss of integrity in either the blood or dialysate circuit or any excursion of an operating parameter outside a predefined range. The basic systems that provide these functions have been well established for more than 15 years and are described elsewhere. Developments in dialysis machines over the past 10 years have been directed at improving dialysis efficiency and at improving safety and ease of use [12][13][14].

The patient's blood is continuously pumped from an artery, a large vein, or a surgically modified vein to allow high blood flow rates. Its pressure is monitored both upstream and downstream from the peristaltic blood pump. Before the blood enters the dialyzer, heparin is added to prevent clotting. A syringe pump is used to deliver the heparin at a precisely controlled rate. The blood then enters the dialyzer where it passes across a large-surface-area, semipermeable membrane with a dialysate solution on the other side. A pressure gradient is maintained across the membrane to ensure the proper flow of compounds out of and into the blood. After cleansing and balancing within the dialyzer, the blood is passed through an air trap to remove any air bubbles before it is returned to the patient. An air bubble sensor ensures that no air bubbles remain. Blood-pressure, oxygen-saturation, and sometimes hematocrit levels (blood cell concentration) are monitored for proper operation of the machine and to ensure patient safety. For maximum effectiveness, fresh dialysate is continually pumped through the dialyzer during operation.

Blood flows from the patient’s body into the dialyzer machine. There is a cleansing fluid, called the dialysate, which flows through the machine in the opposite direction to the blood. The blood and the dialysate are separated by a semipermeable membrane. The membrane in the dialyzer has minute pores that will not allow the passage of blood but will allow the passage of the waste matter which has much smaller molecules than the blood cells. The design of dialysis machine concerns the flow rate of the waste material throws the membrane. The flow is determined by the differences in concentration of waste material on either side of the membrane. The flow is from the high concentration to low concentration.

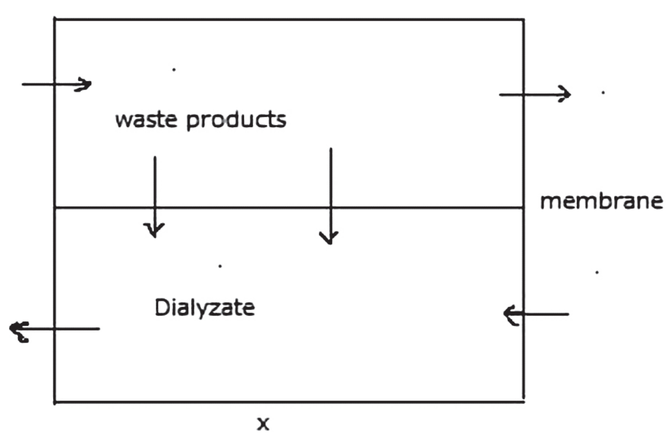
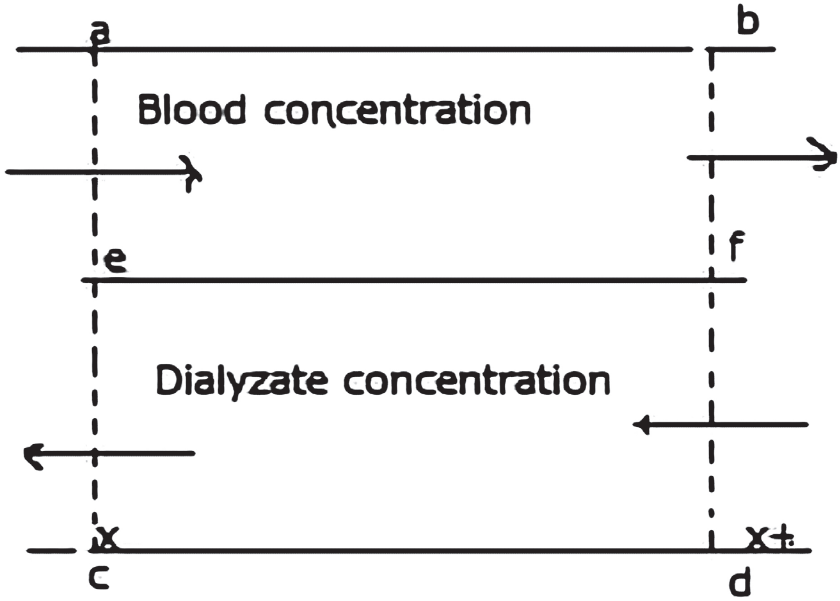


Figure 1. Simple Dialyzer Machine

3.Model Formulation and Analysis:

Dialysis machine (Dialyzer) is used to assist the kidneys in the cleansing process. In dialyzer, blood flows from the patient's body and there is a cleansing fluid, that flows in dialyzer in the opposite to that of blood, with this dialysate (cleansing fluid) waste materials from the blood are removed. The physician and the patient care about the rate at which the waste material is removed. This rate will depend on (a) the flow rate of blood through the dialyzer. (b) The flow rate of dialysate through the dialyzer. (c) the capacity of the dialyzer, and (d) the permeability of the membrane. Here, in this paper for convenient and plausible our analysis is to take the capacity of the dialyzer and the permeability of the membrane to be fixed constants and will focus on the dependence of the removal rate of the waste on the flow rate [2][4][5][15][16][17].

Let x denote the horizontal position in the dialyzer. Let x+Δx be the nearest position. Here we take a small cross section of the dialyzer from position x to x+Δx. We refer to the cross-section of the total flow as an 'element' of the flow which can be express in the following figure.



Let *p(x)* represents the concentration of wastes in blood; *q(x)* represents the concentration of wastes in the dialysate, where *x* is the distance along the dialyzer. From Fick's law we get "The amount of material passing through the membrane is proportional to the difference in concentration." From the above figure we can analysis the movement of concentration of waste. The difference in concentration across *ae* i.e., one moves from the upper half of the figure to the lower half is *p(x)-q(x)*; therefore, the transfer of waste mass through a section of the membrane of width 1 and length Δx from blood solution to dialysate solution in unit time is approximately

$$k[p(x)-q(x)]\Delta x$$

Where k is proportionality constant and independent of x. We must consider the mass change in the 'element' a b d c in unit time. Now,

Mass flow across ea into element = mass passing through membrane *ef* + mass flow across *bf* out of element,

Let F_B denote the constant rate of flow of blood through the dialyzer. Then we may express this relationship in mass balance equation as:

$$F_B.p(x) = k[p(x)-q(x)]\Delta x + F_B.p(x+\Delta x)$$

$$F_B.p(x+\Delta x) - F_B.p(x) = - \quad k[p(x)-q(x)]\Delta x$$

$$F_B[\frac{p(x+\Delta x)-p(x)}{\Delta x}] = -k[p(x)-q(x)]$$

Taking limit as $\Delta x \to 0$ on both sides we get,

$$\lim_{\Delta x \to 0} F_B[\frac{p(x+\Delta x)-p(x)}{\Delta x}] = -\lim_{\Delta x \to 0} k[p(x)-q(x)]$$

This gives the differential equation

$$F_B\frac{dp}{dx} = -k(p-q). \qquad (1)$$

This is the case on an examination of the flow of the blood.

For the case of the flow of the dialysate,

We must consider the mass change in the 'element' *bdca* in unit time. Now,

Mass flow across *df* into element = mass added through membrane *fe* + mass flow across *ce* out of element,

Let F_D denote the constant rate of flow of dialysate through the dialyzer. Then we may express this relationship in mass balance equation as:

$$F_D.q(x) = k[p(x) - q(x)]\Delta x + F_D.q(x + \Delta x)$$

$$F_D.q(x + \Delta x) - F_D.q(x) = k[p(x) - q(x)]\Delta x$$

$$-F_D[\frac{q(x+\Delta x)-q(x)}{\Delta x}] = k[p(x) - q(x)]$$

Taking limit as $\Delta x \rightarrow 0$ on both sides we get,

$$\lim_{\Delta x \to 0} -F_D[\frac{q(x + \Delta x) - q(x)}{\Delta x}] = \lim_{\Delta x \to 0} k[p(x) - q(x)]$$

This gives the differential equation

$$-F_D \frac{dq}{dx} = k(p - q). \qquad (2)$$

The minus sign comes from the fact that the blood flows in the opposite direction as the dialysate. From equations (1) and (2) we have,

$$\frac{dp}{dx} = -\frac{k}{F_B}(p - q).$$

$$-\frac{dq}{dx} = \frac{k}{F_D}(p - q).$$

Now adding we get,

$\frac{dp}{dx} - \frac{dq}{dx} = -\frac{k}{F_B}(p - q) + \frac{k}{F_D}(p - q)$ Notice that p and q occur in this equation in an antisymmetric manner. Let $r = p - q$ then we obtain

$\frac{dr}{dx} = -\alpha r$ Where $\alpha = \frac{k}{F_B} - \frac{k}{F_D}$

Solving with separation of variables, $\frac{dr}{r} = -\alpha dx$ and integrating $\alpha = \frac{k}{F_B} - \frac{k}{F_D}$

$$\log r = -\alpha x + \log A$$

$$\log r - \log A = -\alpha x$$

$$\log\frac{r}{A} = -\alpha x$$

$$\frac{r}{A} = e^{-\alpha x} \quad \text{i.e.,} \quad r(x) = Ae^{-\alpha x} \tag{3}$$

Where A is the arbitrary constant.

Putting the value of r in equation (1) and (2) we get

$$\frac{dp}{dx} = -\frac{k}{F_B}(p-q) = -\frac{k}{F_B}r = -\frac{k}{F_B}Ae^{-\alpha x} \quad \text{and}$$

$$\frac{dq}{dx} = -\frac{k}{F_D}(p-q) = -\frac{k}{F_D}r = -\frac{k}{F_D}Ae^{-\alpha x}$$

Integrating, $\int dp = \int -\frac{k}{F_B}Ae^{-\alpha x}dx$

$$p(x) = B + \frac{k}{\alpha F_B}Ae^{-\alpha x} \tag{4}$$

And $\int dq = \int -\frac{k}{F_D}Ae^{-\alpha x}dx$

$$q(x) = B + \frac{k}{\alpha F_D}Ae^{-\alpha x} \tag{5}$$

Where B is an arbitrary constant.

We suppose that the blood has initial waste concentration p_0 and the dialysate initial waste concentration 0. Thus, at the initial condition $p(0)=p_0$ at $x=0$ and $q(0)=0$ at $x=L$. Where L is the length of the dialysis machine. With this initial condition equation (4) and equation (5) becomes,

$$p(0) = B + \frac{k}{\alpha F_B}Ae^{-\alpha 0} \quad \text{i.e.,} \quad p(0) = B + \frac{k}{\alpha F_B}A \tag{6}$$

$$q(0) = B + \frac{k}{\alpha F_D}Ae^{-\alpha L} \quad \text{i.e.,} \quad 0 = B + \frac{k}{\alpha F_D}Ae^{-\alpha L} \tag{7}$$

From (6) and (7) we get, $p(0) = -\frac{k}{\alpha F_D}Ae^{-\alpha L} + \frac{k}{\alpha F_B}A$

$$= \frac{-kA}{\alpha}\left(\frac{e^{-\alpha L}}{F_D} - \frac{1}{F_B}\right)$$

$$= \frac{-kA}{\frac{k}{F_B}-\frac{k}{F_D}}\left(\frac{e^{-\alpha L}}{F_D} - \frac{1}{F_B}\right)$$

$$= \frac{-A}{\frac{1}{F_B}-\frac{1}{F_D}}\left(\frac{e^{-\alpha L}}{F_D} - \frac{1}{F_B}\right)$$

Therefore $A = -\frac{p_0\left(\frac{1}{F_B}-\frac{1}{F_D}\right)}{\left(\frac{e^{-\alpha L}}{F_D}-\frac{1}{F_B}\right)}$ and $B = -\frac{k}{\alpha F_D} A e^{-\alpha L} = \frac{-A}{\frac{1}{F_B}-\frac{1}{F_D}}\left(\frac{e^{-\alpha L}}{F_D}\right) = \frac{p_0\left(\frac{1}{F_B}-\frac{1}{F_D}\right)}{\left(\frac{e^{-\alpha L}}{F_D}-\frac{1}{F_B}\right)} \frac{1}{\left(\frac{1}{F_B}-\frac{1}{F_D}\right)}\left(\frac{e^{-\alpha L}}{F_D}\right)$

Therefore $B = \frac{p_0}{\left(\frac{e^{-\alpha L}}{F_D}-\frac{1}{F_B}\right)} \frac{1}{F_D} e^{-\alpha L}$

Now putting the value of A and B from above in equations (4) and (5)

$p(x) = B + \frac{k}{\alpha F_B} A e^{-\alpha x}$ And $q(x) = B + \frac{k}{\alpha F_D} A e^{-\alpha x}$

$= \frac{p_0}{\left(\frac{e^{-\alpha L}}{F_D}-\frac{1}{F_B}\right)} \frac{1}{F_D} e^{-\alpha L} - \frac{p_0\left(\frac{1}{F_B}-\frac{1}{F_D}\right)}{\left(\frac{e^{-\alpha L}}{F_D}-\frac{1}{F_B}\right)} \frac{1}{\left(\frac{1}{F_B}-\frac{1}{F_D}\right)}\left(\frac{e^{-\alpha x}}{F_B}\right)$ And

$= \frac{p_0}{\left(\frac{e^{-\alpha L}}{F_D}-\frac{1}{F_B}\right)} \frac{1}{F_D} e^{-\alpha L} - \frac{1}{\left(\frac{1}{F_B}-\frac{1}{F_D}\right)}\left(\frac{e^{-\alpha x}}{F_D}\right) \frac{p_0\left(\frac{1}{F_B}-\frac{1}{F_D}\right)}{\left(\frac{e^{-\alpha L}}{F_D}-\frac{1}{F_B}\right)}$

$= p_0 \left(\frac{\frac{1}{F_D}e^{-\alpha L}}{\left(\frac{e^{-\alpha L}}{F_D}-\frac{1}{F_B}\right)} - \frac{\frac{1}{F_B}e^{-\alpha x}}{\left(\frac{e^{-\alpha L}}{F_D}-\frac{1}{F_B}\right)}\right)$ and $= \frac{p_0}{F_D}\left(\frac{e^{-\alpha L}-e^{-\alpha x}}{\left(\frac{e^{-\alpha L}}{F_D}-\frac{1}{F_B}\right)}\right)$

Hence $p(x) = p_0 \left(\frac{\frac{1}{F_D}e^{-\alpha L}-\frac{1}{F_B}e^{-\alpha x}}{\left(\frac{e^{-\alpha L}}{F_D}-\frac{1}{F_B}\right)}\right)$ (8) and $q(x) = \frac{p_0}{F_D}\left(\frac{e^{-\alpha L}-e^{-\alpha x}}{\left(\frac{e^{-\alpha L}}{F_D}-\frac{1}{F_B}\right)}\right)$ (9)

These equations (8) and (9) represent a definitive analysis of the concentration of waste in the blood and in the dialysate.

4.Interpretation:

To interpret these, we observe that the amount of waste removed from the blood in unit time is:

Now from equation (1)

$$\int_0^L k[p(x) - q(x)]dx = -F_B \int_0^L \frac{dp}{dx} dx$$

$$= -F_B \int_{p_0}^{p_L} dp$$

$$= F_B[p_0 - p_L]$$

Hence to design dialyzers we must focus our attention on $\frac{F_B}{p_0}[p_0 - p_L]$. This term is called the Clearance (Cl) i.e.,

$Cl = \frac{F_B}{p_0}[p_0 - p_L]$ With the help of equation (8) and (9)

$$= \frac{F_B}{p_0}\left(p_0 - p_0 \quad \left(\frac{\frac{1}{F_D}e^{-\alpha L} - \frac{1}{F_B}e^{-\alpha L}}{\left(\frac{e^{-\alpha L}}{F_D} - \frac{1}{F_B}\right)}\right)\right)$$

$$= F_B\left(1 - \quad e^{-\alpha L}\left(\frac{\frac{1}{F_D} - \frac{1}{F_B}}{\left(\frac{e^{-\alpha L}}{F_D} - \frac{1}{F_B}\right)}\right)\right)$$

$$= F_B\left(\frac{\frac{e^{-\alpha L}}{F_D} - \frac{1}{F_B} - \frac{e^{-\alpha L}}{F_D} + \frac{e^{-\alpha L}}{F_B}}{\frac{e^{-\alpha L}}{F_D} - \frac{1}{F_B}}\right)$$

$$= F_B\left(\frac{\frac{1}{F_B}(e^{-\alpha L} - 1)}{\frac{1}{F_B}(\frac{F_B}{F_D}e^{-\alpha L} - 1)}\right)$$

$$= F_B\left(\frac{(1 - e^{-\alpha L})}{(1 - \frac{F_B}{F_D}e^{-\alpha L})}\right)$$ And $\alpha L = \left(\frac{k}{F_B} - \frac{k}{F_D}\right)L = kL\left(\frac{1}{F_B} - \frac{1}{F_D}\right) = \frac{kL}{F_B}(1 - \frac{F_B}{F_D})$.

5.Conclusion

Mathematical procedure related to the working process of a dialyzer is presented in this work. Mostly people are affected by the malfunction of Kidney. It is required to wipe out these malfunctions. To remove these malfunctions properly there are two chances either transplant the kidney or to use a dialyzer. Now a days use of dialyzer is essential and its demand is increasing day by day. For this, it is necessary to understand the function of dialyzer and the working manual with the help of differential equation. Thus, the actual design of a dialyzer would entail testing these theoretical results against experimental data, taking into account factors like the variation of k with x, the depth of the channels, variations in the membrane. Additionally, it is crucial to consider the patient's individual requirements and medical history when determining the most suitable treatment option. Factors like age, overall health, and any potential complications must be taken into account in order to ensure the best possible outcome. Furthermore, ongoing research and advancements in dialyzer technology are continuously shaping the landscape of kidney treatment, promising even more effective and efficient solutions in the future. This underscores the importance of a multidisciplinary approach, involving medical professionals, engineers, and researchers, in the development and refinement of dialyzer designs. By synergizing theoretical knowledge with practical experimentation, we can pave the way for more refined and personalized dialyzer solutions, ultimately improving the quality of life for individuals affected by kidney malfunction by the use of differential equation.

References:

1. Ahmed J., Besarab A., Lubkowski T, Frinak S: Effect of differing blood lines on delivered blood flow during hemodialysis, *Am J Kidney Dis*; 44: 498–508, 2004.

2. Cheung A.K., Levin N.W., Greene T., Agodoa L., Bailey J, Beck G., Clark W., Levey A.S., Leypoldt J.K., Ornt D.B., Rocco M.V., Schulman G., Schwab S., Teehan B., Eknoyan G., Effects of high- flux hemodialysis on clinical outcomes: results of the HEMO study *J Am Soc Nephrol*, 14: 3251-3263, 2003.

3. Leypoldt J.K., Cheung A.K., Agodoa L.Y., Daugirdas J.T., Greene T., Keshaviah PR., Hemodialyzer mass transfer-area coefficients for urea increase at high dialysate flow rates. *Kidney Int,* 51: 2013–2017, 1997.

4. Maggiore Q., Pizzarelli F., Santoro A., Panzetta G., Bonforte G., Hannedouche T., Alvarez de Lara M.A., Tsouras I., Loureiro A., Ponce P., Sulkovà S., Van Roost G., Brink H., Kwan J.T.C, The effects of control of thermal balance on vascular stability in hemodialysis patients: results of the European randomized clinical trial, Am *J Kidney Dis,* 40: 280–290, 2002.

5. Polaschegg H.D., Levin N.W., Hemodialysis machines and monitors; in Jacobs C., Kjellstrand C.M., Koch K.M., Winchester J.F. (eds), Replacement of Renal Function by Dialysis, ed 4. *Dordecht, Kluwer,* pp 333–379, 1996.

6. Ronco C., Clark W.R., Hollow-fiber dialyzers: technical and clinical considerations; in Nissenson

7. A.R, Fine R.N (eds): Clinical Dialysis*, ed 4. New York, McGraw-Hill*, pp 85–100, 2005.

8. Ronco C., Brendolan A., Crepaldi C., Rodighiero M., Scabardi M. Blood and dialysate flow distributions in hollow-fiber hemodialyzers analyzed by computerized helical scanning technique. *J Am Soc Nephrol,* 13: S53–S61, 2002.

9. Ronco C., Bowry S.K., Brendolan A., Crepaldi C., Soffi ati G., Fortunato A., Bordoni V., Granziero A., Torsellon G., La Greca G., Hemodialyzer: from macro-design to membrane nanostructure; the case of the FX-class of hemodialyzers, *Kidney Int*, 61(suppl 80): S126–S142., 2002.

10. Richard A., Ward C.R. Dialyzer and Machine Technologies: Application of Recent Advances to Clinical Practice Blood *Purif*, 24: 6 –10, 2006.

11. Schwab S.J., Oliver M.J., Suhocki P., McCann R., Hemodialysis arteriovenous

access: detection of Stenosis and response to treatment by vascular access blood flow. *Kidney Int*, 59: 358–362, 2001.

12. Barnes B., and G.R. fulford, Mathematical Modelling with case studies, *CRC press*, 2009.

13. Depner T.A., Rizwan S., Stasi T.A., Pressure effects on roller pump blood flow during hemodialysis, *ASAIO Trans,* 31: M456– M459, 1990.

14. Eknoyan G., Beck G.J., Cheung A.K., Daugirdas J.T., Greene T., Kusek J.W., Allon M., Bailey J., Delmez J.A., Depner T.A., Dwyer J.T., Levey A.S., Levin N.W., Milford E., Ornt D.B., Rocco M.V., Schulman G., Schwab S.J., Teehan B.P., Toto R., Effect of dialysis dose and membrane flux in maintenance hemodialysis*, N Engl J Med*, 347: 2010–2019, 2002.

15. Hoenich N.A., Stamp S., Clinical performance of a new high-flux synthetic membrane. *Am J Kidney Dis,* 36: 345–352, 2000.

16. George F., and Steven G., Differential Equations Theory, Technique, and Practice, *McGraw Hill Education (India) Pvt.,* 2014.

17. George F., Differential Equations with Applications and Historical Notes, TATA *McGraw*

Hill Publishing Company Ltd. New Delhi, 1992.

18. Kapur J.N., Mathematical modeling, Wiley *Eastern Limited*, 1994.