Dynamic Modeling of Peritoneal Dialysis and Its Implementation in Children with Chronic Kidney Failure

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ABSTRACT

This study has been conducted to shed light on the dynamic interactions between the peritoneal dialysis (PD) treatment and the nutritional intake decisions, with respect to the physical development of children with chronic kidney failure. The interrelationships between the substances such as protein, albumin, calcium, phosphate, sodium and potassium -the major developmental and vital indicators of the child-patients - along with their relationships with the PD treatment have been analyzed with the help of System Dynamics methodology. To analyze the dynamics of PD treatment, the time unit of the model has been chosen as a day and the time horizon has been chosen as three years in order to better observe the differences in the growth and development of child-patients. Simulation experiments are carried out to search for effective combinations of PD and nutritional recipes for child-patients. Finally, an interactive simulation game version of the model, which represents the relationship between the diet and the ratios of accumulated toxic or beneficial materials in the body, has been designed. Such simulation game can be used to help doctors, patients and patients' families in seeking diet and treatment recipes suitable to patients' monthly needs for a better growth and physical development.

Keywords: Chronic Kidney Failure, Peritoneal Dialysis, Dialysis in Children, System Dynamics, Simulation Modelling, Simulation Gaming

1. INTRODUCTION

Human body is a collection of numerous sub-systems that cooperate in order to keep the internal balance, called "homeostasis". Among those sub-systems, urinary system comes to the forefront since it plays an important role to help maintaining vital indicators of the body with its regulatory activities. Central components of the urinary system are kidneys. When kidneys stop functioning properly, kidney failure occurs, toxic wastes accumulate in the body, and the levels of materials found in blood such as albumin, calcium, phosphate, active vitamin D, sodium and potassium go beyond their normal levels [1]. These irregularities cause serious health problems such as high blood pressure, bone deformation and protein-calorie malnutrition. In child-patients, growth retardation is one of the most frequent symptoms of kidney failure [2].

1.1 Chronic kidney failure

Chronic kidney failure (CKF) is described as the decline in filtration function of kidneys over time. Glomerular filtration rate (GFR) is used as the best measure to estimate the level of kidney functioning, described as the volume of fluid filtered from the kidneys over unit time. It can take values between 0 describing extreme failure to 100 describing full health. This scale is used to determine the five stages of the disease. The last stage is called "End Stage Renal Failure (ESRD)" in which GFR is under 15.

Organ transplantation and dialysis are two different treatments for ESRD. Former is a surgery where damaged kidney is replaced by one from a healthy donor. Latter is divided into two categories: peritoneal and haemodialysis. In child-patients, peritoneal dialysis is common due to its flexibility with respect to children's active social and school lives.

In ESRD patients, residual renal function (RRF) is important since it affects the duration of dialysis, the life quality, and morbidity. RRF is described as the remaining capacity of kidneys to remove wastes and toxic materials, or, remaining GFR capacity [3]. It is observed that RRF declines linearly to zero over time independent of patients' initial health conditions.

1.2 Peritoneal dialysis

In peritoneal dialysis (PD), a soft tube, called "catheter", is inserted into patient's abdomen to fill it with cleansing liquid, called "dialysis solution" or "dialysate". Dialysate remains in abdomen for a certain period of time until it drains toxic materials, extra fluids and wastes from the body. After draining the toxic materials, it is exchanged with a clean solution. This time period which dialysate remains in the abdomen is called "dwell time".

Dialysate is composed of some electrolytes such as sodium, and magnesium and an osmotic agent, glucose. The general diffusion principles are valid for PD and the difference in concentration between blood and dialysate determines the amount of toxic materials transmitted to dialysate. The transmission rate at which toxic wastes move to dialysate is called "clearance rate." Materials' clearance rates are almost the same for different dialysates.

1.3 Complications

CKF patients suffer from several health problems. These problems can be categorized as accumulation of toxic materials in blood, malfunctioning of protein metabolism, bone deformation and imbalance of electrolytes.

First, CKF patients experience insufficient removal of toxic materials as a result of protein metabolism such as urea and creatinine. Since protein is the main constituent of the body, its anabolism and catabolism never stops, which means the formation of urea and creatinine is inevitable in CKF patients. It is important to remove these toxic materials through PD at regular intervals to provide normal protein metabolism functioning [1].

Albumin is the most abundant protein in blood. In CKF patients, decline in blood albumin occurs due to improper protein metabolism. During dialysis, PD patients lose lots of albumin. Even though the excessive loss of albumin triggers the production in the body, the produced albumin is not enough to replace what is lost. Albumin level is used to detect and track protein malfunctioning, and also it is a vital indicator for morbidity and mortality. In order to keep and maintain the growth of child-patients at a healthy level, it is important to prevent the decline in albumin level [4].

Calcium is a vital mineral for the growth and development of bones and crucial for neural and hormonal systems in body. Another problem that CKF patients are facing is bone deformation and retardation due to abnormal transition of calcium from bones to blood [5]. Also, diseased kidneys cannot excrete excessive phosphate, which causes build-up of phosphate at fatal levels in the blood. To reduce its levels, patients use phosphate binders through oral way [6].

Vitamin D also plays an important role in bone development. It is used in its active form, called calcitriol, in the body. Calcitriol is produced in kidneys and helps reabsorbing calcium from intestines. In CKF patients, calcitriol production stops. This causes excretion of calcium directly from the intestines instead of its reabsorption. Consequently, patients with CKF suffer from calcium deficiency. The need of calcitriol can be cured by oral medication [1].

Another problem in CKF is the imbalance in sodium and potassium levels. Due to improper kidney functioning, sodium cannot be excreted from the body sufficiently and causes an increase in blood volume. This leads to high blood pressure. The removal of potassium from the body also depends on kidneys' functioning. Since CKF patients cannot excrete potassium adequately, they suffer from high levels of blood potassium. Even a small change in serum potassium levels can cause several fatal problems like heart attack. Therefore, it is important to keep its level between normal values through dialysis [7] [8].

2. RESEARCH OBJECTIVES AND OVERVIEW OF THE MODEL

System dynamics (SD) approach is a method to describe, discuss and understand the dynamics of complex systems and problems. Particularly, the complexity of medical problems arises from the dynamic interactions between sub-systems in the human body.

Improper protein regulation and bone formation, along with disturbances in electrolytes constitute the complexity and dynamics of the medical problem. Nonlinear relationships between main factors in these sub-systems and the feedback loops that they are connected with are the sources of the complexity of homeostasis. Adding the complexities of PD to this system creates an even harder and more complicated problem.

The first objective of this study is to construct a model that describes the relationships between PD, the related homeostatic activities in the body and the nutritional diets in children. After building a valid model, the second objective is to carry out simulation experiments to search the correct PD and nutritional recipes for child-patients. Final objective is to develop an interactive game version of the model to help patients and their families seeking better nutritional intake decisions.

In the study, the time unit is chosen as "a day" and simulation horizon is chosen as "three years" to be able to observe adequately the effects of the disease and alternative treatment methods on growth and development of child-patients.

2.1. Overview of the model

After a literature review, model is divided into three sectors: Bone Sector, Protein Sector and Fluid-Electrolyte Sector (see Appendix 1) [10]. First two sectors are related to the development and growth of children while the last one is important for vital indicators in the body. In Figure 1, a general simplified representation of whole model can be found. In this figure, stock variables in the model are shown in rectangle boxes. Stocks affecting all sectors in the model are shaded rectangles, written in black. Stocks in the model are chosen as the ones critical to control. These stocks are sodium (Na), potassium (K), calcium (Ca), phosphate (PO), albumin, urea, creatinine, extracellular (blood) volume, muscle protein and bone mineral content (BMC). Among these stocks, muscle protein and BMC are used as physical indicators of growth in children. Flows in and out of stocks are determined by the interactive relationships between hormones and nutrient intakes. Furthermore, the RRF, dwell time, blood volume and the patient's weight affect all sectors.

RRF level affects the loss of K, Na, water, PO, Ca, urea and creatinine through urine positively. Since RRF declines linearly over time, the urine loss of mentioned materials also declines linearly. In the model, based on the levels taken from real life patients, RRF starts from 3 ml/min and declines to zero over the simulation horizon. Therefore, the urine loss of mentioned materials also converges to zero. The second common factor is dwell time. Dwell time increases the loss of albumin, urea, water, Na, K, Ca, PO and creatinine through PD over time. Blood volume is used to calculate the concentration levels of albumin, Na, Ca, K, PO, urea and creatinine in the blood. Last common parameter is patient's weight. Since it is assumed that the weight is proportional to the child-patient's age, the amount of nutrition intake in the body is determined based on body weight according to the medical guides established for children with CKF. The loss of K, Na, Ca, creatinine, urea, PO, water and albumin during PD depends on their concentrations in the blood. It means that when their stock level increases, their PD losses also increase. Total decrease in the stock levels is calculated as the sum of the amounts lost through urine and dialysis.

Finally, some of the protein is stored in the muscles for growth. If serum albumin decreases under normal level, child-patients need extra protein to store. More protein intake causes the formation of urea and creatinin. Therefore, there is a thin line between growth maintenance and sufficient excretion of wastes.



Figure 1: The simplified version of model structure, variables, relationships and parameters

3. MODEL DESCRIPTION

PD clearance rates of all elements in the model are determined through the clearance Mass Transfer Coefficients (MTC) found in the literature. MTC has the unit of liter per time showing the permeability of the element through the peritoneal membrane. Materials' loss rate through the PD are found by multiplying their MTC by their blood concentration and then discarding it from the concentration of the material in dialysate [11]. Additionally, except calcium and sodium, for all other elements in blood, the concentration in the dialysate is equal to zero to maximize dialysis efficiency. In the model, PD clearance rates have the unit of 1/day and daily dialysis duration for kidney patients are specified as 12

hours/ day, which is the usual case.

All the concentrations are found by dividing corresponding stock level by the blood volume. The amount of loss by urine is affected positively by RRF and RRF's decrease rate is found as 0.17 ml/min/month in the literature [12]. All PD losses of the materials have linear relationships with the PD time. The dialysate is assumed constant as "1.36% glucose" and PD type is taken as Continuous Ambulatory Peritoneal Dialysis (CAPD) [4].

In the game version, body weight is taken as main input to calculate required food intakes and stock levels. In simulation runs, the weight of the child starts from 10 kg and can range between 10 and 50 (corresponding to the ages of 1 to 12) [13].

The blood test is done once a month and decision maker (DM) in the model changes the nutritional intake and oral medicine levels according to its results. DM holds medicine and nutritional prescription constant until the next month. To model the assumption that DM would increase or decrease the nutritional intake levels when the concentration levels appear to be high or low, proper functions are used affecting the nutritional intakes. Final nutritional intake levels are found by multiplying these effect functions with required intake levels. HISTORY(), MOD() and TIME() functions are used to change the decisions just once in a month in the model.

3.1. Bone sector

i. Background information

The indication of a normal growth in a child is the bone construction rate. This rate is affected by the Ca balance between the blood and bone. As mentioned previously, the blood Ca level in the children with CKF is lower than normal level. If there is not enough Ca in blood, then Ca is released from the bones through blood, which diminishes the bones' strength. The bone strength can be measured by BMC.

Ca blood level is affected by the parathyroid hormone (PTH), calcitonin and calcitriol. When Ca blood level falls beyond normal, PTH increases and triggers the Ca transfer from bones to blood. When Ca blood goes beyond normal, calcitonin hormone triggers the transfer of Ca from blood to bones.

As mentioned earlier, Vitamin D affects the bone construction in children as well and it is used in its active form, calcitriol. Since calcitriol triggers the reabsorption of Ca from intestines, a decrease in its level due to CKF also causes a decrease in the blood Ca level.

ii. Assumptions and simplifications

One of the assumptions of this sector is about osteoblasts and osteoclasts which have roles in the bone construction and destruction, continuously, non-stop during a day [1]. Since the model time unit is a day, which makes the metabolic events of these cells too micro to represent, they are not added to the model.

In the model, required calcitriol intake of the patient is satisfied with oral intake and its production in the kidneys is taken as zero. Another assumption is that the phosphate exchange between the bone and blood is negligible and it is not modelled.

iii. Bone sector model description

There are four stocks in this sector: Calcitriol, Blood Calcium, Blood Phosphate and BMC (see Appendix 1-Figure 11). Blood Phosphate has two outflows as PD loss of PO and urine loss of PO, and one inflow of absorption from the intestines. PD loss of PO is found by multiplying phosphate clearance rate with the stock. Phosphate clearance is 0.33 for 12 hours dialysis, 0.0275 per hour [14]. The other outflow is calculated by multiplying phosphate urine loss rate with the stock. Phosphate urine loss rate is 0.09 /day for a RRF of 5ml/min [14].

PO absorption from the intestines is affected by phosphate holder usage and calcitriol level. As the calcitriol increases, the absorption increases. Normal calcitriol concentration is 57.9 ng/l. The absorption is found by multiplying phosphate intake with phosphate absorption rate. The normal rate for absorption fraction is 0.65 but the phosphate holder usage decreases this level. Absorption rate is found by multiplying the normal absorption rate with a graphical function showing the effect of phosphate holder on phosphate absorption (see Appendix 2). The blood phosphate level is effective at the phosphate holder intake which is modelled by another effect function. The phosphate intake is found by multiplying normal phosphate intake with the effect function of blood phosphate level (from the results of the blood tests) at the phosphate intake (see Appendix 2). Therefore, if the blood phosphate level is higher than normal, phosphate intake is decreased.

Another stock in the sector, calcitriol has one outflow and one inflow. Calcitriol destruction rate is assumed to be 1 per day. The calcitriol intake to the body is a management decision and thus affected by the blood Ca level. The required calcitriol intake increases as the body weight increases [15]. Normal calcitriol intake for ESRD children is 10ng/kg/day [13].

Blood Calcium is another stock in the sector. Like many other stocks in the model, this stock has also a PD and a urine loss. But the Ca level in the dialysis fluid is really close to blood level [16]. Ca clearance rate is 0.7 for a 12 hours dialysis. When RRF is 5ml/min, urine loss fraction is 0.09 /day [17].

The absorption of Ca from the intestines depends on the calcitriol level [18]. As the calcitriol level increases, the absorption increases, too. The absorption rate of Ca from the intestines is taken as %11, while this level is %25 in healthy people [18]. Ca intake by the food is a managerial decision and decided by checking blood test results and affects the absorption. If the Ca level is higher than the normal level, then Ca intake is decreased for that month. There is a required Ca level for a certain body weight.

Ca absorption is a bi-flow which is positive when Ca concentration is lower than normal. This flow is formulated as classical stock adjustment formulation which has 1 as stock adjustment time. The flow rate is affected by PTH when Ca level is lower than normal and by calcitonin in the other case. These affects are shown by two effect formulations which are multiplied by stock adjustment formulation to have the complete flow function (see Appendix 2). On the other hand, PTH and calcitonin levels are affected by blood Ca level. Normal blood PTH concentration at ESRD patients is at around 200 pg/ml which is higher from healthy patients (<140 pg/ml) [15]. In blood, the normal level of calcitonin is around 200 pg/ml. This level is multiplied by the effect function of Ca to find the correct calcitonin level [15].

3.2. Protein sector

iv. Background information

Body protein is another important indication of child growth and daily protein intake should be enough to ensure a healthy growth. In children with CKF, protein intake is restricted to prevent having dangerous urea and creatinine levels.

Albumin, the most abundant protein in blood, is generally used to observe nutritional status of a child and it should be controlled frequently. In children with CKF, albumin level is generally lower than expected because of its undesired loss from the blood during PD.

Urea and creatinine are dangerous waste products of metabolic activities and are discarded via kidneys. In CKF patients, kidney function decreases by time and reaches to zero which patients can no longer produce urine.

v. Assumptions and simplifications

First, blood proteins other than albumin are not modelled since the changes in the levels of other blood proteins are too small to be added in the model. The urine loss of albumin is considerably small and thus it isn't modelled [19].

Second, the inter-processes between muscle protein synthesis, protein intake, and urea- creatinine formation are not included in the model. Muscle protein is assumed to be the only protein stock in the model as it is the biggest source of protein store.

The child patient in the model is assumed to have an average physical activity in daily life and it is assumed that the patient does not have metabolic acidosis condition.

vi. Protein sector model description

There are four stocks in the sector: albumin, urea, creatinine, and muscle protein (see Appendix 1- Figure 12). The most important parameter is the protein intake. The required protein intake is dependent on the body weight based on nutritional guidelines. If it appears that the urea level is higher than normal according to blood test, the protein intake of the patient is decreased. If the albumin level is lower than its expected level, then the protein intake is increased. These effects of albumin and urea on the protein intake are modelled via the several effect functions of which the details can be seen in the Appendix 2.

Albumin stock has two outflows of PD loss and albumin catabolism and has one inflow of albumin synthesis. 0.73 g of the protein intake via foods is converted to albumin every day [19]. On the other hand, albumin has a catabolism rate of 0.09 g/day [20]. The PD loss of albumin is found by multiplying the albumin stock with PD clearance rate of 0.008 for 12 hours of dialysis which accounts for a day [19].

Urea in blood is lost by dialysis and urine and increased by the urea synthesis. PD loss fraction is 0.07/ hour while urea loss fraction is 0.03/day/ml/min [21] [22]. Urea synthesis is found by multiplying the protein intake with a constant synthesis fraction of 0.3/day (see Appendix 2). Initial muscle protein level is linearly dependent on the body weight. For every 1 kg of body weight, there is 330 gram muscle protein for a normal child [23]. Muscle protein has just one inflow which is found by multiplying the protein intake and synthesis fraction of 0.14/day with the effect function of protein intake on the muscle synthesis. As the protein intake increases, the muscle protein synthesis increases as well.

The initial creatinine stock level is found by multiplying the blood volume with the normal creatinine concentration of a child with 10 kg body weight. Creatinine synthesis fraction is found as 0.027/day and urine loss fraction is found as 0.1/day for a 5ml/min of kidney function while the PD loss fraction is found as 0.81/day for 12 hours of dialysis [24]. Creatinine concentration is normalized by dividing the real creatinine concentration with the expected creatinine concentration for a given body weight.

3.3. Electrolyte sector

vii. Background information

Sodium affects the muscle and neural functions and the secretion of anti-diuretic hormone (ADH) besides being main stimulant of thirst. Due to its effect in the blood volume level, it indirectly affects the concentration of all other materials in the blood. As a result of CKF, sodium cannot be removed from the body and accumulates in the blood.

The control of potassium in the body should be tight since it has important roles in the water balance, muscle and neural functions like sodium [25]. For example, when potassium level goes out of its normal boundaries, the heart rhythm deforms which can cause heart attack. Potassium is excreted both via kidneys and intestines in a healthy body. Since kidneys do not function properly in CKF patients, the excretion via intestines shows a 5 to 10% increase from its normal level [25]. Yet, this increase cannot satisfy the required excretion rate of potassium. Thus dialysis has a crucial role in the prevention of the potassium accumulation in blood.

viii. Assumptions and simplifications

The first simplification is that the loss of water via sweat is not modelled since this loss does not affect any of the model parameters and its addition would not create any dynamics. Also, there are many factors affecting the water intake in the body but only ADH hormone is taken among these factors since the others aren't related to the model scope. The level of physical activity is not modelled either.

ix. Electrolyte sector model description

There are three stocks, potassium (K), sodium (Na) and blood volume in the sector (see Appendix 1-Figure 13). Potassium has inflow of absorption from intestines, outflow of gut losses, dialysis and urine losses, and cellular inflow. The loss from gut is found by

multiplying constant loss rate of 0.25/day with the K stock level. PD loss fraction is 0.073/hour of dialysis. Urine loss fraction is 0.04/day per ml/min of RRF [26]. Absorption from the intestines is equal to multiplication of K intake with the 0.75 absorption fraction. The required K intake is calculated by using the body weight. The cellular flow of K is a biflow which is formulated as a normal stock adjustment function. Normal K level is 0.17 g/l and the stock adjustment time is taken as 1 day (see Appendix 2) [25].

Sodium has one inflow of absorption from the intestines and two outflows of PD and urine losses. The absorption from the intestines is found by multiplying Na intake with the absorption fraction of 0.6/day. The required Na intake is calculated by using the body weight. Urine loss fraction is 0.003/day/RRF [27]. PD liquid has a really close Na concentration level (3.05 g/l) to the normal blood Na concentration (3.15 g/l) which makes the PD loss of Na residual [16]. The clearance rate of Na is 0.07 per hour of dialysis [28].

The initial level of blood volume stock is found by multiplying the initial body weight with 0.2 l/kg [29]. Blood volume is lost via PD and urine and it is increased by the water intake. Water intake level is found by multiplying the normal water intake with the effect function of ADH in the water intake (see Appendix 2). Normal water intake is dependent on the body weight. As the body weight increases, water requirement in the body also increases. The PD loss fraction of blood volume is 0.26/day for 12 hours of dialysis [29]. Urine loss fraction is 0.007/day per 1ml/min of RRF [30].

4. MODEL VALIDATION

4.1. Direct structure tests

In the direct structure tests, some direct tests are conducted such as unit consistency, and direct extreme condition tests, without any simulations [31]. It is tested whether each equation has unit consistency by entering the units of its input variables.

4.2. Indirect structure tests

Indirect structure (structure-oriented behavior) tests are done to compare the behavior of the model with the (expected) real life behavior, in some extreme or other special condition simulations. In the first test, all the stocks were held in their equilibrium levels [31]. The aim behind this test is to assure that the system has a balanced structure which can yield homeostasis, just like in the real life. In the second part of indirect structure tests, how the system behaves under extreme conditions was tested. No dialysis, no protein intake, or excessive protein intake can be counted as examples of extreme cases. Each of these extreme cases is designed as simulation scenarios and the results are investigated to understand whether the model gives reasonable results under these extreme scenarios [31].

The dynamics of the model in the case of no dialysis can be seen in Figure 2. The blood volume and creatinine level reach a mortal state in a few days, which is consistent with the real-life situation if no dialysis was made. These tests, demonstrate that the model structure is consistent with the real system.



Figure 2: Extreme condition test: The dynamics of blood volume, creatinine and urea when there is no dialysis

5. MODEL OUTPUT ANALYSIS

After the validation step, the base model has been run for 3 years starting with an initial weight of 10 kg for a child patient. The dynamics of the base results for 1080 days can be seen in Figures 3, 4 and 5 below. There are oscillations in the blood concentrations of most variables since the nutrient intake decisions are changed just once in a month according to the blood test results. Urea and normalized creatinine levels are a bit higher than their expected levels during simulation, which is normal for an ESRD patient. As can be seen in the Table 1, BMC and muscle protein levels at the end of the simulation are lower than those levels of a non-patient child with same age. This can be interpreted as the indicator of a growth deficiency in the child patient which is usually seen in children with ESRD.



Figure 3: Base dynamics of electrolyte sector



Figure 4: Base dynamics of bone sector



Figure 5: Base dynamics of protein sector

Table 1 The comparison of muscle protein, BMC and blood volume of the base run with a those levels of a non-patient child in the same age.

Time (day)	Body Mass(kg)	Muscle protein (g)	Expected Muscle protein(g)	BMC	Expected BMC
0	10	3300	3300	300	300
360	12	3884	3960	315	360
720	15	4521	4950	390	450
Final	18	5525	5940	516	540

6. SCENARIO ANALYSIS

In this section, the effects of initial RRF level, body mass, frequency of blood test, PD duration, and protein and calcitriol intake on the growth level of the patient are investigated through simulation runs.

6.1. The effect of initial RRF

In these runs, the effect of initial RRF level on the growth is tested. Angela et al. found that patients with zero RRF generally have worse cardiovascular, inflammatory, nutritional and metabolic profiles with a higher mortality rate [32].

Run	Initial RRF Level (ml/min)
1	0
2	10
3	20

Table 2 Initial RRF levels in different runs

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As can be seen in Figure 6, blood volume is higher in 1 run in which RRF is lower, which means higher blood pressure for such patients. This result is validated by the study of Constantin et al. investigating the relationship between RRF and blood volume [33]. Since urine loss of calcium, sodium and phosphate are negligible; they are not affected by RRF level. As the RRF falls, the final muscle protein level is lower which indicates a slowed growth. The reason behind a lower muscle protein level is the increasing urea concentration and thus decreasing protein intake as RRF falls. This shows that growth is better maintained in the uric patients (RRF is larger than zero) than the anuric patients (RRF is zero).



Figure 6: Blood volume dynamics for different initial RRF levels



Figure 7: Muscle protein dynamics for different initial RRF levels

6.2. The effect of initial weight

In this analysis, the initial weight of the patient is determined as 10 kg and 30 kg respectively in two different runs. Since the initial body weight level determines an initial age in our model, the growth patterns in child-patient can be compared for different age levels.

Run	Initial body weight
1	10 kg
2	30 kg

 Table 3 Initial body weight levels in runs

The initial level of BMC is dependent on the initial body weight as explained in the model description section. To be able to make a better comparison, BMC levels of two runs are normalized by their expected BMC levels (without the illness) for the corresponding age of the child. The same normalization process is done for muscle protein as well since it also depends on the initial body weight. As it can be seen in Figure 8, in the second run, BMC level is closer to its expected level than the 1st run. This shows that child patients who are younger are expected to be more negatively affected by the illness in terms of their growth. This finding is supported by the results found in literature as well [34].



Figure 8: Normalized BMC levels for two different initial body weights

7. GAME VERSION

After the construction, validation and verification of the model, an interactive simulation game is designed to help parents and doctors of child patients in the treatment process. The goal in the game is maintaining a normal growth level and keeping the concentration levels within their limits. The game simulates two years and decisions are entered in the interface once a month as shown in Figure 9. Before the game starts, introductory information about the game is given along with a hand-out showing normal blood concentration intervals of chemicals, required nutrient intakes and expected BMC and muscle protein levels for different ages.

Calcitriol in	30
Cain	500
PO in	0.8
Dwell time	12
Protein in	18
Initial weight	10
PO binder	6
Kin	0.6
Na in	0.7
Initial RRF	3

Figure 9: The game decision interface

The game player is expected to enter nutrient and medicine intake level decisions, and PD duration once a month while giving initial weight and RRF level only in the beginning of the game. The concentration levels as a result of the decisions entered are shown once a month to the player, while the muscle protein and BMC levels are shown just once every six months. At the end of the game, a score is calculated based on how much the concentrations have been outside their limits and how far the final growth parameters deviate from their expected levels.



Figure 10: An example of game dynamics and final score

8. CONCLUSION

In this research, a dynamic model is built to understand the effects of peritoneal dialysis and nutrient intake on growth and metabolic dynamics of child patients with chronic kidney failure. After validating the model by direct and indirect structure tests, some scenarios are tested to see the effects of important decisions like dialysis duration on the growth of a child-patient. Additionally, an interactive game is designed to help the parents of child-patients seeking a proper treatment of disease.

The model focusing on the growth of a child with chronic kidney failure comprises three sectors: protein, bone and electrolyte. Modelling approach, assumptions and principles for these sectors are explained in the model description section. Main input parameters are initial body weight, initial residual renal function level and peritoneal dialysis duration. Even though many simplifications are naturally done in modelling, validation and verification tests have shown no obvious weakness in the structure or behavior of the model.

During the scenario analysis, the effects of peritoneal dialysis duration, initial level of residual renal function and initial body weight on the growth patterns of children are investigated. According to the results, doing peritoneal dialysis less than 12 hours decreases the children's growth rate while frequency of blood tests does not affect the results. Also, it is found that if the child catches the illness at a younger age, the growth will be more negatively affected.

In future studies, the model can be expanded by adding medical details such as the effects of growth hormones and detailed nutritional components. Interactive game can also be improved by changing the nutrient intake levels from grams to more common sense real life portions. Also, the model can be enhanced to test other effects, such as alternative medication.

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APPENDIX 1: STELLA VIEW OF THE MODEL

Figure 11 Bone sector stock-flow diagram

Figure 12 Protein sector stock-flow diagram

Figure 13 Electrolyte sector stock-flow diagram