Anticipating Diabetic Kidney Disease Through Measurements of Albumin in Diabetes Patients

Huber Nieto-Chaupis
Universidad de Ciencias y Humanidades Center of Research E-Health
Av. Universitaria 5175, Los Olivos, Lima39, Lima Perú
huber.nieto@gmail.com

Abstract—We have proposed a system based in the continuous measurement of albumin in type-2 diabetes patients whose diagnosis was done 5 years ago or more. The main idea of this investigation consists in a plan of visits by the nurse to the localizations of the patients, in order to collect samples of urine and blood. From the results of lab, endocrinologist or nephrologist can provide an accurate prescription in order to anticipate the apparition of the diabetic kidney disease, particularly in those patients with a diagnosis of more than 10 years. We focus in those patients from Peri-urban areas of big cities, where most of them are not motivated to attend a public hospital due to the logistic involved and others aspects against the well-being of patient. When this system is used, the simulations has shown that 4 of 17 patients might surpass any type of kidney complications in the middle term.

Index Terms—Diabetes, Kidney Disease, Albumin.

I. INTRODUCTION

A. Motivation of the Paper

The disease of type-2 diabetes is nowadays one of the main causes of worldwide mortality and it seems to be that is showing a sustained increasing in the next decades [1][2][3]. For instance, in Latin American countries like Peru, new cases have been reported in young population around the thirties or even below, fact which might be perceived as the future deterioration of the quality of life of this population for the next 10 or 20 years [4]. When diabetes is not under control, it triggers irreversible and unexpected complications. One of them is the so-called diabetic kidney disease (DKD) which might be the most strong a complication of diabetes [5][6][7][8][9][10]. In most cases it has as consequence the permanent damage of kidney, so that the patients would pass to the phase of dialysis, fact which would deteriorate their quality of life imminently [11][12][13]. Due to the lack of resources, Peruvian public hospitals might not be well prepared to face future arrival of patients, concretely might exist the necessity of installing additional dialysis rooms. It would demand not only adequate infrastructure, supplies and full equipment labs of dialysis, but also the requirement that these labs are working continuously. Concretely, our interest focuses on the human groups belonging to the Peri-urban areas of Lima city showing a remarkable progress of type-2 diabetes. In praxis, these patients are potential candidates to acquire DKD in the middle term and it is expected that their quality of life is reduced drastically. Clearly, the worsening state of patient has an impact on their families deteriorating the social aspects as well.

B. Main Contribution of this Paper

We have designed an E-Health system whose objective is the probabilistic prediction of the future concentrations of albumin from the samples of urine which are collected periodically. For this end, we have proposed the methodology called "the hospital goes where patient is". It consists in visits made by nurses to the diabetes patients, after of having identified their localization and corroborated their state of health. Nurse performs glucose measurements as well as takes blood and urine samples. These samples are expected to be sent to labs in order to obtain a full analysis of the presence of albumin in urine. In addition, blood test would corroborate some aspects which might be useful for doctor in order to take actions and carry out precise interventions. When results of prediction are indicating the possible degradation of the glomerulus’s layers for a possible lapse of time, it might serve to the nephrologist to reconfigure a new pharmacological strategy and suggest new alimentary diets in order to decrease the probability of acquiring DKD in the middle term [14]. The scenario where "the hospital goes where the patient is", is featured by the acquisition of patient’s data in short periods. This is clearly advantageous in the sense that the patient has a certain comfortability as to receive medic control at home. One actually expects that the outcomes after of applying this methodology would decrease the probability for passing to the phase of dialysis. Actually, this is contrary to the common case or “standard case” where patients attend hospitals, normally. The case of those diabetes patients which are characterized by having a social and economic vulnerability, the "standard case" might be considered a reason by which the patients abandon the visits to hospital due to the confluence of undesired bureaucracy and excess of logistic as commonly one finds in public hospitals of some Latin American cities. In second section all concerning to the E-Health system is presented. In third section, is formulated a simple model which is based on the behavior of glucose and albumin. The conjunction of these variables plays a crucial role in the dynamics of the system. With this, we propose the algorithm of prediction which is sustained in the method of Monte Carlo. It is expected that the algorithm would play a crucial role as software in a modern health system, working continuously. The algorithm
has analyzed the data of 17 type-2 diabetes patients. In fourth section, results of this paper are presented. Mainly 3D histograms were plotted [15]. Finally, the conclusion of paper is drawn.

II. PROPOSAL OF THE SYSTEM

A. The E-Health Functionality

The main idea of the proposal of E-Health system is sketched in Fig. 1. Firstly, nurse has identified the address of the patient in order to make visits. According his perception and point of view, nurse collects both urine and blood samples to be sent to labs. Actually it is done same day of the visit. Results of test are expected on next day. Lab informs about the results to the doctors: nephrologist and endocrinologist. Once the doctors have received the results of the tests, they fill E-forms in order to be sent to a data server through text message. The data server makes estimates by using a predictive algorithm (see next section). According to the results of the predictions, the server sends a text message to nurse [1][3][7].

In this manner, nurse performs intervention consisting in a plan of visits continuously. Also nurse receives suggestions from doctors previous to the visits. Actually, doctors can also do recommendations to the nurse such as to program an interview in the hospital in those cases where the situation of patient is abnormal. For instance, in the case that the server gives as result a rapid increase of the values of albumin for the next six months, the nephrologist can recommend to the nurse which should be running in an unstoppable manner.

B. Patients Selection

Patients were selected under the following criteria: (i) evidence that the diabetes patients are abandoning their pharmacological treatment due to unknown reasons, (ii) evidence that the patient is showing a rapid increasing of their glucose values surpassing 250 mg/dL, (iii) evidence that the patient has a very low level of self-care. Once all this package of criteria is applied, were identified up to 17 diabetes patients. All of them are above 25 y.o, and signed the consent form as part of the ethics policy of this study. In Table I the sample containing up to 17 patients is listed. It is shown information per patient of up to 5 variables. Firstly, we can see that the ages are ranging between 38 and 75 y.o. Secondly, the weights between 71 and 100 kg. Clearly various cases of obesity can be identified. The third variable is given by the systole blood pressure (SBP) which is showing high values in conjunction with overweighted cases, anticipating that the sample is already containing cases of risk. The average of glucose measurements during the last three months are shown in fourth column. All cases are showing irregular control glucose measurements during the last three months are shown in conjunction with overweighted cases, anticipating that the sample is already containing cases of risk. The average of glucose measurements during the last three months are shown in fourth column. All cases are showing irregular control glucose measurements during the last three months are shown in fourth column. All cases are showing irregular control glucose values. If albumin test are above of the allowed ones, the nephrologist adjust the treatment to the kidney. All test results go to the server where prediction is performed. If future values of albumin are increasing then both doctors suggest to nurse to take soon intervention.

<table>
<thead>
<tr>
<th>Age/Weight/SBP</th>
<th>Glucose Average (mg/dL)</th>
<th>Nephro Risk Level</th>
<th>Years with Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/3/88/81/168</td>
<td>190 high</td>
<td>&gt; 5</td>
<td></td>
</tr>
<tr>
<td>2/4/11/100/142</td>
<td>177 middle</td>
<td>&gt; 10</td>
<td></td>
</tr>
<tr>
<td>3/4/29/100/122</td>
<td>130 low</td>
<td>≈ 4</td>
<td></td>
</tr>
<tr>
<td>4/5/30/80/118</td>
<td>196 low</td>
<td>≈ 1</td>
<td></td>
</tr>
<tr>
<td>5/6/58/61/30</td>
<td>230 middle</td>
<td>&gt; 4</td>
<td></td>
</tr>
<tr>
<td>6/5/71/11/30</td>
<td>102 low</td>
<td>≈ 5</td>
<td></td>
</tr>
<tr>
<td>7/5/33/13/66</td>
<td>122 low</td>
<td>&gt; 10</td>
<td></td>
</tr>
<tr>
<td>8/3/69/1129</td>
<td>139 low</td>
<td>≈ 5</td>
<td></td>
</tr>
<tr>
<td>9/5/48/21/30</td>
<td>164 middle</td>
<td>&gt; 10</td>
<td></td>
</tr>
<tr>
<td>10/5/79/150</td>
<td>310 middle</td>
<td>≈ 2</td>
<td></td>
</tr>
<tr>
<td>11/6/93/130</td>
<td>275 high</td>
<td>≈ 10</td>
<td></td>
</tr>
<tr>
<td>12/6/79/170</td>
<td>225 high</td>
<td>≈ 5</td>
<td></td>
</tr>
<tr>
<td>13/6/82/166</td>
<td>207 high</td>
<td>&gt; 8</td>
<td></td>
</tr>
<tr>
<td>14/6/70/155</td>
<td>249 high</td>
<td>&gt; 5</td>
<td></td>
</tr>
<tr>
<td>15/7/68/167</td>
<td>211 middle</td>
<td>≈ 8</td>
<td></td>
</tr>
<tr>
<td>16/7/11/148</td>
<td>290 high</td>
<td>&gt; 5</td>
<td></td>
</tr>
<tr>
<td>17/7/57/156</td>
<td>145 middle</td>
<td>&gt; 10</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1. Sketch of the E-Health system proposed in this paper. Nurse makes visit to the patient. Based on evidences, nurse makes the decision to extract blood and urine samples to be sent to the lab. If glucose values are above the allowed ones, the endocrinologist would work on a new strategy to put down glucose values. If albumin test are above of the allowed ones, the nephrologist adjust the treatment to the kidney. All test results go to the server where prediction is performed. If future values of albumin are increasing then both doctors suggest to nurse to take soon intervention.
SBP. Indeed, patients were asked to describe their habits of nutrition, intake of sodium, salt, and fat. Finally, last column indicates the number of years by which the patient is living with the disease, counted from the moment where patient has received the diagnosis of type-2 diabetes.

III. Monte Carlo Simulation of System and Results

A. Mathematical Model as Basis of System’s Software

In order to propose a mathematical model in according to the standard knowledge of the scales of concentration of albumin and well-known scenarios [11][12][13], we pass to define the levels of albumin as follows

\[
A = \begin{cases} 
A_1 \equiv \text{normal} & 0 < W \leq 30 \text{mg/dL} \\
A_2 \equiv \text{microalbumin} & 30 < W \leq 300 \text{mg/dL} \\
A_3 \equiv \text{macroalbumin} & W > 300 \text{mg/dL}
\end{cases}
\]

Clearly, one can see up to three phases which would appear in the next years during the progress of disease [14]. Starting from the fact that these phases are each other connected as sequences in time, then is possible to associate them a multi-step function which would be that of the Erf functions. However, it is crucial as behaves the amplitude of these functions because the progressive increasing of albumin might be strongly correlated to the temporal evolution of glucose as well. In this way, we can write below the proposal of albumin as function of time

\[
A(t) = \sum_{j=1}^{N} G_j(t) \odot \text{Erf} \left( \frac{t - \mu_j}{\varsigma_j} \right),
\]

where \(\mu_j\) and \(\varsigma_j\) denote the parameters of the step functions which are associated to the morphology of the temporal evolution. We can see that the integer number \(j\) runs up to \(N\) curves, and \(G_j(t)\) denotes the changing amplitude of the albumin curve which might be governed by the glucose behavior. It is possible to extend the meaning of \(G_j(t)\) in the sense that it can depend upon others parameters which would have direct impact on the temporal behavior of the glucose [7][8]. We can express the glucose curve as follows

\[
G_j(t, \rho_j, \gamma_j, \beta_j) = \rho_j \left[ 1 + W_j \sin^3(t/\gamma_j) \right] / \left( 1 + \exp(-\beta_j t) \right),
\]

where \(W_j, \rho_j, \gamma_j\) and \(\beta_j\) are related to the patient’s behavior. As proposed in [7], the stability of the diabetes patient would depend on the full control of these parameters in order to avoid a rapid growth of glucose in short periods of time. For instance, all of them are well determined by the psychology of patient as well as by its aptitude to face the possible apparition of unexpected complications due to the progress of disease. In Table II, the meaning and range of values of these parameters are listed. Under this view we can formulate the proposal of model. Thus, with (1) and (2) we can write down the main equation which would denote the function of albumin in time, and expressed in gr/dL.

\[
A(t) = \sum_{j=1}^{N} \rho_j \left[ 1 + W_j \sin^3(t/\gamma_j) \right] / \left( 1 + \exp(-\beta_j t) \right) \text{Erf} \left( \frac{t - \mu_j}{\varsigma_j} \right),
\]

which would define a 6-parameters model, and depending on the time. Basically it is the multiplication of the glucose’s behavior and the albumin. Clearly, we keep the basic idea that the albumin in urine might be proportional to the glucose concentration. In effect, we take for example the parameter \(\rho_j\) that in according to Table II, it would absorb the effects of the pharmacology against the progress of diabetes and other positive effects on the patients. Eq. (3) also exhibits the nonlinearity of the albumin behavior in time. In fact, the presence of the \(W_j\) which multiplies the term \(\sin^3(t/\gamma_j)\) is actually the responsible to increase or decrease the level of nonlinearity on \(A\). This is linked to the albumin disorder of patient when no any pharmacology is taken.

B. Algorithm of Prediction and E-Health System

The software which is expected to be running in the data server (Fig. 1) is based entirely in the Eq. (3). Furthermore, the simulation has contemplated the following requirements: (i) nurse visits patients at least twice per week. It means

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Meaning</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\rho)</td>
<td>Pharmacology</td>
<td>1 - 300</td>
</tr>
<tr>
<td>(\beta)</td>
<td>Diet</td>
<td>0.01 - 10</td>
</tr>
<tr>
<td>(W)</td>
<td>Alimentary disorder (without pharmacology)</td>
<td>0.01 - 1.0</td>
</tr>
<tr>
<td>(\gamma)</td>
<td>Alimentary disorder (with pharmacology)</td>
<td>1 - 5</td>
</tr>
</tbody>
</table>

\[
\text{Algorithm of System}
\]

\[
1 \text{ DO } p = 1, 17 \text{ (patients)}
2 \text{ DO } j = 1, N \text{ (unit of time)}
3 \text{ Extract a random number } r
4 \text{ Defines } p_{p,j+1}, \varsigma_{p,j+1}
5 \text{ Defines } p_{w_{p,j+1}}, \beta_{p,j+1}, \gamma_{p,j+1}, W_{p,j+1}
6 \text{ Normalizes } A(t_{p,j+1}), A_1, A_2, A_3
7 \text{ IF } A(t_{p,j+1}) > r \text{ THEN}
8 \text{ IF } A(t_{p,j+1}) \rightarrow A_1 \text{ THEN}
9 \text{ nurse makes a visit}
10 \text{ ELSEIF } A(t_{p,j+1}) \rightarrow A_2 \text{ THEN}
11 \text{ nephro and endocrino make suggestions}
12 \text{ ELSEIF } A(t_{p,j+1}) \rightarrow A_3 \text{ THEN}
13 \text{ nephro makes suggestions}
14 \text{ ENDIF}
15 \text{ } A(t_{p,j+1}) \rightarrow A(t_{p,j+2})
16 \text{ DO } q = 1, Q \text{ (future values)}
17 \text{ DO } r = 1, R \text{ (future of parameters)}
18 \text{ fills } p_{p,j+r}, \varsigma_{p,j+r}
19 \text{ fills } p_{w_{p,j+r}}, \beta_{p,j+r}, \gamma_{p,j+r}, W_{p,j+r}
20 \text{ ENDDO}
21 \text{ fills } A(t_{p,j+q})
22 \text{ ENDDO}
23 \text{ ENDDO}
24 \text{ ENDDO}
25 \text{ ENDDO}
26 \text{ END}

\]

TABLE II

<table>
<thead>
<tr>
<th>Parameter</th>
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</thead>
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<tr>
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</tr>
<tr>
<td>(\gamma)</td>
<td>Alimentary disorder (with pharmacology)</td>
<td>1 - 5</td>
</tr>
</tbody>
</table>
that the data server stores around 8 samples per months. We have considered that \( N = 3 \), which is in according to the expected levels namely normoalbumin, microalbumin, and macroalbumin [14]. The algorithm of system can be described as follows: in line-1 and line-2 the loops for the number of patients and times are initialized. Between lines 3 and 6 the parameters are defined, together with the initialization of the random number which is extracted from a generators machine (external subroutine). Doctors have received the test results from lab for both: glucose and albumin. The results go to data server continuously. In line-7 the Monte Carlo step is applied. It consists in the question of that if the amount of normalized albumin (whose values are ranging between 0 and 1) for a subsequent time of the last measurement is greater than the random number. When it is satisfied then the next task is locate the value of albumin inside the expected ranges \( A_{1,2,3} \). Depending on it, the system would start communications with nurse and/or endocrinologist and/or nephrologist, in order to make intervention if any. Actually, this is in agree with scheme of Fig. 1 where data server stores and activates warnings in those cases where there is evidence of risk of high values of albumin. In line-15 is seen that the system opts for analyzing again for a subsequent time by passing from \( t_{j+1} \) to \( t_{j+2} \). In lines 18 and 19 are filled the future values for the parameters of Eq. (3). Once the parameters were calculated for the future, we proceed to estimate the albumin value as given in line-21. Here is saved the values of glucose in order to count the number of patient with their respective predictions.

### IV. RESULTS OF SIMULATION

#### A. Simulation for Glucose and Albumin for 3 Years

In Fig. 2, up to 4 3D histograms [15] for simulations contemplating 6, 12, 24 and 36 months are displayed. In top left histogram is denoted the case for 6 months, which turns out to be insufficient for any conclusion. It is seen that the patients has not any evidence of the possible future states of diabetic nephropathy. It is because the averages are around 100 mg/dL and 120 mg/dL of albumin and glucose, respectively. It is also perceived that the E-Health predictive system might be yielding linear outputs for short terms. In top right, is shown the indication of line-21 of algorithm. The number of patients is plotted against the predicted values of glucose and albumin. The histograms denote the simulations for a time of 6 (top left), 12 (top right), 24 (bottom left) and 36 (bottom right) months.

![Fig. 2. Different 3D histograms derived from the simulation by following the indication of line-21 of algorithm. The number of patients is plotted against the predicted values of glucose and albumin. The histograms denote the simulations for a time of 6 (top left), 12 (top right), 24 (bottom left) and 36 (bottom right) months.](image)

#### B. Simulation of Albumin for 5 years

Finally, in Fig. 3, the curves corresponding to theoretical, the Monte Carlo simulation, and one which would only correspond to the transition of microalbumin to macroalbumin are plotted. The orange-line curve denotes the theoretical which is calculated with the best values for the parameters of the Eq. (3). This curve would be the template for the Monte Carlo simulation. In fact, the curve with dots (sky blue color) is the resulting after of simulating the functionality of the E-Health system with the method of Monte Carlo. We have used the orange line as the reference for the simulation. The prediction was obtained by assuming the continuous functionality of the E-Health system and focused on the patients 5, 11, 13 and 16. The resulting curve represents the average the predicted values of albumin of these patients for 5 years. We can see that there is of up to two predictions per years. The dots are superimposed to a continuous curve. Indeed, one can see the apparition of stochastic fluctuations along the horizon of prediction which can be interpreted as a limited aspect of the computational simulation. Clearly, it would reduce the quality further visits, as well as the patient would receive suggestions and conversations with doctors (through cell phones). From all histograms and after a statistical analysis, we can arrive that at least 4±1 patients would represent the subsample which might be inhibited for acquiring DKD, in contrast with the case where all patients would be in potential risk for acquiring diabetic nephropathy and dialysis. According to our predictions, the patients labeled by 5, 11, 13 and 16 might not be affected with the DKD if only if the system is working continuously through visits, prediction and doctors communications. This result encompasses the goal of the E-Health system by which is expected to reduce the number of diabetic patients from Peri-urban areas of big cities which are in constant risk for kidney’s complications.
and, at least 4 patients were identified which might acquire DKD in the upcoming 3 years, fact which would be discussed and stressed by doctors in order to improve the quality of the pharmacological prescriptions in the short and middle term.

REFERENCES


Fig. 3. Curves of temporal behavior of albumin for patients labeled by 5, 11, 13 and 16 for three cases: Monte Carlo simulation (black), theoretical (orange), and the transition from microalbumin to macroalbumin (blue sky).

of the prediction. The error attached to the simulations was of order of 18%. The fluctuations appear as result that the Monte Carlo has selected \( W_{1,2,3} \) (the parameters responsible for nonlinearities) \( \approx 0.5 \) and \( \zeta_1=2.4, \zeta_2=3.8, \) and \( \zeta_3=5.5. \) Finally, the black line is the simulated with the highest values of the parameter \( \rho, \) by which from 595 Monte Carlo steps, at least a 2% might surpass the trajectory of the orange line. This might be perceived as the origin for the transition of microalbumin to macroalbumin. This scenario might correspond to the cases where the patients are already with a diagnostic of DKD. The simulation has yielded that the patients labeled by 9, 10, 12 and 15 might be part of this scenario. In this way, the nurse can prepare an aggressive plan of visits and teleconsults aiming to maintain a constant surveillance of the albumin and glucose through successive tests. In addition, doctors can also improve the prescriptions and recommend interviews with patients in the short term [16][17][18].

V. CONCLUSION

In this paper, we have proposed and computationally tested a E-Health system that aims to be used in vulnerable and diabetic populations of Lima city. It might be a useful tool to reduce the number of patients which would be potentially users of the dialysis processes. We have formulated a mathematical methodology based on step-functions which can be interpreted as the phases of the evolution of glucose in patients. This formalism mathematical depends on parameters which are related to the lifestyle of patients. This formalism is further used as part of a software system working in a data server. The system contains an algorithm with capabilities for making predictions in the middle term up to 5 years. These predictions depend on the method of Monte Carlo, since the evolution of diabetic patients acquires certain randomness fact which is entirely attributed to the semi stochastic behavior of patient.

Clearly, the fluctuations of the evolution temporal of glucose is driven basically by an inadequate alimentation and the abandonment of pharmacology. The worsening of the state of the diabetic patient is also triggered by the lack of interviews between the patient and the health specialists. From a sample of 17 patients, our results have indicated that at least 4 of 17 might not develop the DKD for the next 5 years. On the other hand, at least 4 patients were identified which might acquire DKD in the upcoming 3 years, fact which would be discussed and stressed by doctors in order to improve the quality of the pharmacological prescriptions in the short and middle term.