Available online at http://scik.org
Commun. Math. Biol. Neurosci. 2023, 2023:123
https://doi.org/10.28919/cmbn/8264
ISSN: 2052-2541

A NEW MODEL OF THE SPREAD OF COVID-19 AMONG DIABETES POPULATION: A MATHEMATICAL ANALYSIS AND OPTIMAL CONTROL APPROACH FOR INTERVENTION STRATEGIES

IKRAM IMKEN[1,*], NADIA IDRISSI FATMI[1], SALOUA ELAMARI[2]

[1]LIPIM Laboratory ENSA Khouribga, Sultan Moulay Slimane University, Beni Mellal, Morocco

[2]Department of Endocrinology, Diabetology, Metabolic Disease and Nutrition, Mohammed VI University of Health Sciences, Casablanca, Morocco

Abstract. In this work, we study an original mathematical model which describe the dynamic of transmission of Covid-19 virus in population with diabetes. Firstly, we analysis the mathematical model by using Routh-Hurwitz criteria to obtain the local stability of Covid-Diabetes-free equilibrium and Covid-Diabetes equilibrium. The second aim of this paper is to reduce the number of infected people with complications by control strategies using three variables of controls: the awareness program to diabetic people, also the strict glycemic control with a multidisciplinary medical follow-up in hospital and early diagnosis for diabetic people. We prove the existence of optimal controls, and a characterization of the controls in terms of states and adjoint functions principally based on Pontryagin's maximum principle. A numerical simulations for different scenarios affirm the performance of the optimization approach.

Keywords: diabetes; Covid-19; mathematical model; local stability; optimal control.

2020 AMS Subject Classification: 92C60.

*Corresponding author

E-mail address: ikramimken@gmail.com

Received October 07, 2023

1. INTRODUCTION

According to World Health Organization(WHO), the novel coronavirus disease 2019 or simply Covid-19 is an infectious disease caused by SARS-CoV-2 i.e Severe Acute Respiratory Syndrome Coronavirus-2 [1]. In fact of the last virus the transmission can occur from infected individuals to susceptible individuals via direct communication (contaminated hands) or through droplets spread by coughing or sneezing from an infected person or airborne spread. The symptoms of Covid-19 include fatigue, dry cough, fever, diarrhoea, chest pain, loss of smell and taste senses, shortness of breath, and breathing difficulties. Covid-19 has been declared as a public health emergency on January 30, 2020 [2] and pandemic on March 11 2020 [3] by WHO, due to its exponential worldwide growth.As of May 31, 2021, the total confirmed cases of Covid-19 have reached over 169 597 415 with more than 3 530 852 deaths reported [4]. The morbidity and mortality vary across countries of the world with the highest reported in the United States [5](39 672 729 confirmed cases with 650 526 deaths), India [6] (32 988 673 confirmed cases with 440 533 deaths), Brazil [7] (20 856 060 confirmed cases with 582 670 deaths), France [8] (6 627 205 confirmed cases with 113 013 deaths), Russia [9] (7 012 599 confirmed cases with 187 200 deaths) and Turkey [10] (6 478 663 confirmed cases with 57 604 deaths). Mortality rates are higher in older people and patients with pre-existing medical conditions like diabetes, chronic lung disease, hypertension, malignancy, cardio-vascular disease, and cerebrovascular diseases [11]. Recently, epidemiological studies are focusing on the co-infection of Covid-19 and comorbidities, because comorbidities have been recognized as a risk factor for increased Covid-19 cases and higher fatality [12], [13]. Also, various studies have shown that diabetes is one of the major co-morbidity associated with severe illness and death from Covid-19 infection [14].

Diabetes is a chronic condition that occurs when there is an imbalanced level of glucose in the blood [15]. According to the report of the International Diabetes Federation (IDF), [16] and WHO [17], 463 million adults are having diabetes; nearly 760 billion USD was spent on healthcare; more than 310 million diabetes patients are living in urban areas and about 11.3 % of deaths were due to diabetes.

According to the Center for Disease Control and Prevention (CDC)[18], the rate of fatality from Covid-19 is up to 50 % higher in patients with diabetes than in the individual who does not have diabetes [19]. In [20, 21], it was reported that 20,30 % of patients who died from Covid-19 had diabetes. A survey conducted in China showed that the higher prevalent co-morbidity in Covid-19 patients was diabetes with 8.2 % [22]. However, the above attestations demonstrate the fact that co-infection of diabetes and Covid-19 have a poor prognosis and increased death rate. So, analysing how diabetes aggravates Covid-19 outcomes can give us better insight to restrain the disease and development of effective public health policies. At a recent time, several researchers tried to study the effects of co-infection of diabetes and Covid-19 through their respective fields.

For example Rimesh Pal and Sanjay [23] studied an unholy interaction of Covid-19 and diabetes. They found that concurrent Covid-19 makes glucose control difficult to treat due to fluctuations in blood with diabetes patients.

Furthermore, in [24] authors have presented co-infection related worries and subsequent outcomes. Here authors have suggested that improving knowledge and precaution measures are necessary for people with diabetes during the Covid-19 pandemic

On the other hand, in mathematical modelling, there is a lack of research focus on studies dealing with co-infection of diabetes and Covid-19. Although, many mathematical models have been derived to understand the patterns of each disease (Covid-19 [25] and diabetes), the study [26] has explored diabetes and Covid-19 co-infection. This paper [26] emphasizes that the negative impact of quarantine and several strategies to the lifting of the quarantine. In addition, the author worked on the optimal control techniques to provide an optimal treatment guideline for diabetes and Covid-19 co-infected patients.

The originality of our work in its distinction from previous mathematical studies presented to date by analysing the specific interactions between Covid-19 and individuals with pre-existing chronic conditions, focusing on diabetes as a case study. More precisely, the main contributions of this paper are summarized as follows:

- Proposing a new compartemental model $DD_CD_{C+}H_{D,C}R_D$ based on a study, it is among the first studies in the Kingdom of Morocco and North Africa to describe the clinical presentation and outcomes in Moroccan diabetic patients since the beginning of the Covid-19 pandemic [27] which D, D_C, D_{C+} , $H_{D,C}$, R_D stand for susceptible diabetic, diabetic infected by Covid-19 with mild complication, diabetics infected by Covid-19 with severe complication, diabetic hospitalized due a contamination by Covid-19, recovered from the virus. The five compartemental are modeled by creating a system of differential equation which we can analyse the associated temporal dynamics by studying the equilibrium point and its stability using the Routh-Hurwitz criteria.
- Seeking effective optimal control strategies that minimize the amount of infected population with mild and severe complications. To satisfy this objective, we introduce optimal control strategies related to three sorts of controls: awareness for diabetic people, early diagnosis and strict glycemic control with a multidisciplinary medical follow up.
- Presenting numerical simulations for two cases with stability and intervention strategies. we observe a strong correlation between the theoretical results for stability and the numerical results. On the other hand, the results indicate that the implementation of the strategy that combines all the control variables adopted, and reinforces the clinical outcomes.

This paper is organized as follows in Section 2, we presented our mathematical model, and we discuss basic properties and positivity of solutions, aslo we analyse the local stability and we give some numerical simulation, in Section 3.we presented the optimal control problem for the proposed model where we gave some results concerning the optimal controls and we characterized these optimal controls using Pontryagin's maximum principle, with numerical simulations through MATLAB are given in the end of this section.

2. Mathematical Model

2.1. Description of the model. A mathematical model which describe the dynamic of transmission of Covid-19 virus in diabetic population is the following:

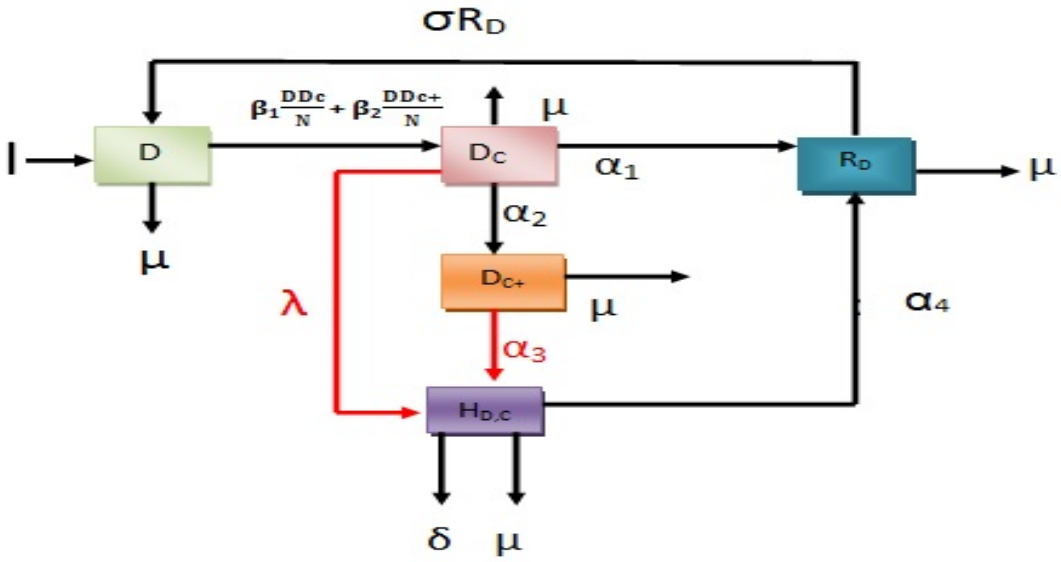


FIGURE 1. Compartments Model

Let N denotes the population size. This population is formed by:

Compartment D:

Represents the number of people with diabetes without complications who may be infected with Corona virus. The Compartment D increases by I (the incidence of Covid19-Diabetes), σR_D(people who will be infected again). This compartment decreases by the amount μ (natural mortality), $\beta_1 \frac{DD_C}{N}$ (the number of people who were infected with the virus by contacting with infected patients with mild complications) , $\beta_2 \frac{DD_{C+}}{N}$ (the number of people who were infected with the virus by communicating with the infected patients with severe complications).

This compartment is represented by the following equation:

$$\frac{dD(t)}{dt} = I - \beta_1 \frac{D(t)D_C(t)}{N(t)} - \beta_2 \frac{D(t)D_{C+}(t))}{N(t)} + \sigma R_D(t) - \mu D(t) \tag{1}$$

Compartment D_C:

Represents the number of people infected with mild complications. The compartment increases by $\beta_1 \frac{DD_C}{N}$ and $\beta_2 \frac{DD_{C+}}{N}$ and decreases by: μ (natural mortality); $\alpha_2 D_C$ (people become

infected with serious complication), $\alpha_1 D_C$ (people will only recover from the virus) and λD_C (people who will hospitalized for not be infected with severe complications).
For this compartment, we have the following equation:

$$\frac{dD_C(t)}{dt} = \beta_1 \frac{D(t)D_C(t)}{N(t)} + \beta_2 \frac{D(t)D_{C+}(t)}{N(t)} - (\lambda + \alpha_1 + \alpha_2 + \mu)D_C(t) \tag{2}$$

Compartment D_{C+} :

Represents the number of individual infected with severe complications. It is increased by $\alpha_2 D_C$ and decreased by $\alpha_3 D_{C+}$ (people who will be hospitalized) and also by μ (natural mortality).
We have:

$$\frac{dD_{C+}(t)}{dt} = \alpha_2 D_C(t) - (\mu + \alpha_3)D_{C+}(t) \tag{3}$$

Compartment $H_{D,C}$:

Represents the number of people who are hospitalized with mild and serious complications, it is increased by $\alpha_3 D_{C+}$ and λD_C and decreased by $\alpha_4 H_{D,C}$ and δ: Mortality due complications.
So we have:

$$\frac{dH_{D,C}(t)}{dt} = \lambda D_C(t) + \alpha_3 D_{C+}(t) - (\alpha_4 + \delta + \mu)H_{D,C}(t) \tag{4}$$

Compartment R_D:

Rrepresents the number of recovered. The compartment R_D is increased by $\alpha_4 H_{D,C}$ and $\alpha_1 D_C$. It is also decreased by μ, and σR_D(people who will be infected by the virus again).
Then we obtain:

$$\frac{dR_D(t)}{dt} = \alpha_1 D_C(t) + \alpha_4 H_{D,C}(t) - (\sigma + \mu)R_D(t) \tag{5}$$

Finally, we present the Diabetes-Covid-19 mathematical model is governed by the following system of differential equation:

$$
(6)\qquad \begin{cases} \dfrac{dD(t)}{dt} = I - \beta_1 \dfrac{D(t)D_C(t)}{N(t)} - \beta_2 \dfrac{D(t)D_{C+}(t)}{N(t)} + \sigma R_D(t) - \mu D(t) \\ \dfrac{dD_C(t)}{dt} = \beta_1 \dfrac{D(t)D_C(t)}{N(t)} + \beta_2 \dfrac{D(t)D_{C+}(t)}{N(t)} - (\lambda + \alpha_1 + \alpha_2 + \mu) D_C(t) \\ \dfrac{dD_{C+}(t)}{dt} = \alpha_2 D_C(t) - (\mu + \alpha_3) D_{C+}(t) \\ \dfrac{dH_{D,C}(t)}{dt} = \lambda D_C(t) + \alpha_3 D_{C+}(t) - (\alpha_4 + \delta + \mu) H_{D,C}(t) \\ \dfrac{dR_D(t)}{dt} = \alpha_1 D_C(t) + \alpha_4 H_{D,C}(t) - (\sigma + \mu) R_D(t) \end{cases}
$$

where $D(0) > 0$, $D_C(0) > 0$, $D_{C+}(0) > 0$, $H_{D,C}(0) > 0$, $R(0) > 0$.

With the condition $D(t) + D_C(t) + D_{C+}(t) + H_{D,C}(t) + R_D(t) = N(t)$, $t \in [0,T]$ the previous system becomes:

$$
(7)\qquad \begin{cases} \dfrac{dN(t)}{dt} = I - \mu N(t) - \delta H_{D,C}(t) \\ \dfrac{dD_C(t)}{dt} = (N(t) - D_C(t) - D_{C+} - H_{D,C}(t) - R_D(t))(\beta_1 \dfrac{D_C(t)}{N(t)} \\ \qquad\qquad + \beta_2 \frac{D_{C+}(t)}{N(t)}) - (\lambda + \alpha_1 + \alpha_2 + \mu) D_C(t) \\ \dfrac{dD_{C+}(t)}{dt} = \alpha_2 D_C(t) - (\mu + \alpha_3) D_{C+}(t) \\ \dfrac{dH_{D,C}(t)}{dt} = \lambda D_C(t) + \alpha_3 D_{C+}(t) - (\alpha_4 + \delta + \mu) H_{D,C}(t) \\ \dfrac{dR_D(t)}{dt} = \alpha_1 D_C(t) + \alpha_4 H_{D,C}(t) - (\sigma + \mu) R_D(t) \end{cases}
$$

2.2. Boundedness of the solution. The following result prove the boundedness and positivity of the solution.

Theorem 1. *The set of* $\Omega = \left\{ \left(N,D_C,D_{C+},H_{D,C},R_D\right) \in \mathbb{R}^5_+ / \ 0 \leq N,D_C,D_{C+},H_{D,C},R_D \leq \frac{I}{\mu} \right\}$ *is positively invariant under system* (7)*. Thus the model is epidemiologically and mathematically well posed.*

Proof. We have

$$\frac{dN}{dt} = I - \mu N - \delta H \geq -\big(\mu + \delta\big)N$$

Using Gronwall's inequality:

$$N(t) \geq N(0)\exp\big(-\int_0^t (\mu+\delta)dt\big)$$

$$\Longrightarrow N(t) > 0$$

On the other hand,we have

$$\frac{dD_C(t)}{dt} = \frac{D(t)}{N(t)}(\beta_1 D_C(t) + \beta_2 D_{C+}(t)) - D_C(t)(\lambda + \alpha_1 + \alpha_2 + \mu)$$

we note

$$\delta_1 = \lambda + \alpha_1 + \alpha_2 + \mu.$$

Assume that there exist sometime $t^* > 0$ such that $D_C(t^*) = 0$,other variable are positive and $D_C(t) > 0$ for t∈[0,t^*[.

So, we have:

$$\frac{dD_C(t)e^{\delta_1 t}}{dt} = e^{\delta_1 t}\left[\frac{D(t)}{N(t)}\big(\beta_1 D_C(t) + \beta_2 D_{C+}(t)\big)\right]$$

Integrating this equation from 0 to t^*, we have:

$$D_C(t^*) = e^{-\delta_1 t^*}\left[D_C(0) + e^{\delta_1 t}\int_0^{t^*}\frac{D(t)}{N(t)}\big(\beta_1 D_C(t) + \beta_2 D_{C+}(t)\big)\right]$$

Consequently $D_C(t^*) > 0$ which contradicts $D_C(t^*) = 0$. It follows that $D_C(t) > 0 \ \forall t \in \big[0,T\big]$

In the same way we prove $D_{C+}(t), H_{D,C}(t), R_D(t) > 0$

On the other hand ,

$$\frac{dN(t)}{dt} = I - \mu - \delta H_D \leq I - \mu N$$

$$N^{'}(t)+\mu N \leq I$$

We multiple by $exp(\mu s)$

$$\int_0^t \left(N^{'}+\mu N\right)(\mathrm{s})exp(\mu s)ds \leq \int_0^t exp(\mu s)\,(\mathrm{ds})$$

$$\implies N(t)exp(\mu t) \leq \frac{I}{\mu}exp(\mu t)-\frac{I}{\mu}+N(0)$$

$$\implies N(t) \leq \frac{I}{\mu}+(N(0)-\frac{I}{\mu})exp(-\mu t)$$

$$\implies \lim_{t\to\infty} N(t) \leq \frac{I}{\mu}$$

□

2.3. Stability analysis.

2.3.1. *Equilibrium points and* R_0. For the model above, equilibrium points are defined such that there is no variation in N, D_C, D_{C+}, $H_{D,C}$, R_D with respect to t. Then we have:

$$D^*_{C+} = \frac{\alpha_2}{\alpha_3+\mu}D^*_C \tag{8}$$

$$H^*_{D,C} = \left[\left(\lambda+\frac{\alpha_3\alpha_2}{\alpha_3+\mu}\right)\times\frac{1}{\alpha_4+\mu+\delta}\right]D^*_C \tag{9}$$

Using (8) and (9)

$$R^*_D = \frac{1}{\sigma+\mu}\left[\alpha_4\left(\lambda+\frac{\alpha_3\alpha_2}{\alpha_3+\mu}\right)\times\frac{1}{\alpha_4+\mu+\delta}+\alpha_1\right]D^*_C \tag{10}$$

On the other hand

$$N^* = \frac{I}{\mu}-\frac{\delta}{\mu}\left[\left(\lambda+\frac{\alpha_3\alpha_2}{\alpha_3+\mu}\right)\times\frac{1}{\alpha_4+\mu+\delta}\right]D^*_C \tag{11}$$

We denote

$$d_1 = \left(\lambda+\frac{\alpha_3\alpha_2}{\alpha_3+\mu}\right)\times\frac{1}{\alpha_4+\mu+\delta}$$

Hence

$$D^*_{C+} = \frac{\alpha_2}{\alpha_3+\mu}D^*_C \ , H^*_{D,C} = d_1D^*_C \quad , R^*_D = \frac{\left(d_1\alpha_4+\lambda\right)}{\sigma+\mu}D^*_C \quad , N^* = \frac{I}{\mu}-\frac{\delta}{\mu}d_1D^*_C$$

Using the definition of N

$$D^* = \frac{I}{\mu} - \left[\frac{\delta}{\mu}d_1 D_C^* + D_C^* + \frac{\alpha_2}{\alpha_3+\mu}D_C^* + d_1 D_C^* + \frac{d_1\alpha_4+\alpha}{\sigma+\mu}D_C^*\right] = \frac{I}{\mu} - D_C^* d_2$$

where

$$d_2 = \frac{\delta}{\mu}d_1 + 1 + \frac{\alpha_2}{\alpha_3+\mu} + d_1 + \frac{d_1\alpha_4+\alpha_1}{\sigma+\mu}$$

By substitution of (8),(9),(10),(11) in

$$(N(t) - D_C(t) - D_{C+} - H_{D,C}(t) - R_D(t))(\beta_1\frac{D_C(t)}{N(t)} + \beta_2\frac{D_{C+}(t)}{N(t)}) - (\lambda+\alpha_1+\alpha_2+\mu)D_C(t) = 0$$

we obtain

$$D_C^*\left[\beta_1\big(\frac{I}{\mu} - d_2 D_C^*\big) + \beta_2\big(\frac{I}{\mu} - d_2 D_C^*\big)\frac{\alpha_2}{\alpha_3+\mu} - \big(\frac{I}{\mu} - \frac{\delta}{\mu}d_1 D_C^*\big)\big(\lambda+\alpha_1+\alpha_2+\mu\big)\right] = 0$$

$$\Longrightarrow D_C^* = 0 \qquad Or \qquad D_C^* = \frac{I\big(R_0-1\big)}{d_2\mu R_0 - \delta d_1}$$

where

$$R_0 = \frac{\beta_1\big(\alpha_3+\mu\big) + \alpha_2\beta_2}{\big(\alpha_1+\alpha_2+\lambda+\mu\big)\big(\alpha_3+\mu\big)}$$

is the basic reproduction number for the model $\big($see Appendix A$\big)$.

- If $D_C^* = 0$ then , $D_{C+}^* = H_{D,C}^* = R_D^* = 0 \Longrightarrow N^* = D^* = \frac{I}{\mu}$.

  Consequently the first equilibrium point is

$$E_0 = \big(\frac{I}{\mu}, 0, 0, 0, 0\big)$$

- If $D_C^* = \frac{I\left(R_0-1\right)}{d_2\mu R_0 - \delta d_1}$ then

$$D_{C+}^* = \frac{\alpha_2 I\big(R_0-1\big)}{\big(\alpha_3+\mu\big)\big(d_2\mu R_0 - \delta d_1\big)} \qquad H_{D,C}^* = \frac{d_1 I\big(R_0-1\big)}{d_2\mu R_0 - \delta d_1}$$

$$R_D^* = \frac{I\big(d_1\alpha_4+\alpha_1\big)\big(R_0-1\big)}{\big(\delta+\mu\big)\big(d_2\mu R_0 - \delta d_1\big)} \qquad N^* = \frac{I}{\mu}\left(\frac{R_0\big(d_2\mu - \delta d_1\big)}{d_2\mu R_0 - \delta d_1}\right)$$

We collecte the precedent result in the following theorem:

Theorem 2. *The previous system* (7) *admits two equilibrium points:*

1- If $R_0 < 1$ *, the system admits a trivial equilibrium* $E_0\left(\frac{I}{\mu},0,0,0,0\right)$.

2- If $R_0 > 1$ *, then there exist an endemic equilibrium* $E_1\left(N^*,D_C^*,D_{C+}^*,H_{D,C}^*,R_D^*\right)$.

where:

$$N^* = \frac{I}{\mu}\left(\frac{R_0\left(d_2\mu - \delta d_1\right)}{d_2\mu R_0 - \delta d_1}\right) \quad , \quad D_C^* = \frac{I\left(R_0-1\right)}{d_2\mu R_0 - \delta d_1} \quad , \quad D_{C+}^* = \frac{\alpha_2 I\left(R_0-1\right)}{\left(\alpha_3+\mu\right)\left(d_2\mu R_0 - \delta d_1\right)}$$

$$R_D^* = \frac{I\left(d_1\alpha_4+\alpha_1\right)\left(R_0-1\right)}{\left(\delta+\mu\right)\left(d_2\mu R_0 - \delta d_1\right)} \quad , \quad H_{D,C}^* = \frac{d_1 I\left(R_0-1\right)}{d_2\mu R_0 - \delta d_1}$$

Remark 1. *The basic reproduction number of the system* (7) *is given by:*

$$R_0 = \frac{\beta_1}{\alpha_1+\alpha_2+\lambda+\mu} + \frac{\alpha_2\beta_2}{\left(\alpha_3+\mu\right)\left(\alpha_1+\alpha_2+\lambda+\mu\right)} = R_{D_C}(t) + R_{D_{C+}}(t)$$

$R_{D_C}(t)$*: the contribution of infectious with mild complication individuals .*

$R_{D_{C+}}(t)$*: the contribution of infectious with serious complication individuals .*

2.3.2. *Local stability of* E_0. The local stability of the equilibrium points is based on the matrix of linearisatin (Jacobian Matrix) given by:

$$J = \begin{pmatrix} -\mu & 0 & 0 & -\delta & 0 \\ \left(\beta_1 D_C^* + \beta_2 D_{C+}^*\right)\frac{D^*}{N^{*2}} & \beta_1\frac{D^*}{N^*} - \left(\lambda+\alpha_1 \right. & & & \\ & \left. +\alpha_2+\mu\right) & \beta_2\frac{D^*}{N^*} & 0 & 0 \\ 0 & \alpha_2 & -\left(\alpha_3+\mu\right) & 0 & 0 \\ 0 & \lambda & \alpha_3 & -\left(\delta+\alpha_4+\mu\right) & 0 \\ 0 & \alpha_1 & 0 & \alpha_4 & -\left(\sigma+\mu\right) \end{pmatrix}$$

For E_0, the matrix of linearisation

$$J(E_0) = \begin{pmatrix} -\mu & 0 & 0 & -\delta & 0 \\ 0 & \beta_1 - \left(\lambda+\alpha_1+\alpha_2+\mu\right) & \beta_2 & 0 & 0 \\ 0 & \alpha_2 & -\left(\alpha_3+\mu\right) & 0 & 0 \\ 0 & \lambda & \alpha_3 & -\left(\delta+\alpha_4+\mu\right) & 0 \\ 0 & \alpha_1 & 0 & \alpha_4 & -\left(\sigma+\mu\right) \end{pmatrix}$$

Then the characteristic polynomial of $J(E_0)$ is given by

$$P_0(X) = \big(-\mu - X\big)\big(-\big(\sigma+\mu\big) - X\big)\big(\delta+\mu+\alpha_4\big) - X\big)Q_0(X) \tag{12}$$

where

$$Q_0(X) = X^2 + X\big(\alpha_3+\alpha_1+\alpha_2+\lambda+2\mu-\beta_1\big) + \big(1-R_0\big)d_3$$

and

$$d_3 = \big(\alpha_3+\mu\big)\big(\lambda+\alpha_1+\alpha_2+\mu\big)$$

We have the following result.

Theorem 3. *E_0 point disease free equilibrium is stable if $R_0 < 1$*

Proof. It is easy to prove that the eigenvalue of $P_0(X)$ are: $-\mu, -\big(\delta+\mu+\alpha_4\big), -\big(\sigma+\mu\big)$ and the roots of Q_0 are $a = \alpha_3+\alpha_1+\alpha_2+\lambda+2\mu-\beta_2$ and $b = \big(1-R_0\big)d_3$.
By Routh Hurwitz Criterion, system (7) is stable if $a > 0$ and $b > 0$, which leads to $R_0 < 1$ □

2.3.3. *Local Stability of E_1.*

Theorem 4. *equilibrium point E_1 is stable if*

$$\begin{cases} R_0 > 1 \\ \beta_1 < \alpha_2 \end{cases}$$

Proof.

$$J(E_1) = \begin{pmatrix} -\mu & 0 & 0 & -\delta & 0 \\ (\beta_1 D_C^* + \beta_2 D_{C+}^*)\frac{D^*}{N^{*2}} & \beta_1\frac{D^*}{N^*} - (\lambda+\alpha_1+\alpha_2+\mu) & \beta_2\frac{D^*}{N^*} & 0 & 0 \\ 0 & \alpha_2 & -(\alpha_3+\mu) & 0 & 0 \\ 0 & \lambda & \alpha_3 & -(\delta+\alpha_4+\mu) & 0 \\ 0 & \alpha_1 & 0 & \alpha_4 & -(\sigma+\mu) \end{pmatrix}$$

We note

$$Y = (\beta_1 D_C^* + \beta_2 D_{C+}^*)\frac{D^*}{N^{*2}}, \qquad \frac{D^*}{N^*} = \frac{1}{R_0}$$

$$P_1(X) = \big(-\mu - X\big)\Big(-\big(\sigma+\mu\big) - X\Big)\Big(-\big(\delta+\mu+\alpha_4\big) - X\Big)Q_1(X)$$

where

$$Q_1(X) = X^2 + X(\alpha_3 + 2\mu + \lambda Y\delta + \lambda + \alpha_1 + \alpha_2 - \frac{\beta_1}{R_0}) + \frac{1}{R_0}(R_0 - 1)$$

We discuses the roots of following equation

$$X^2 + aX + b = 0$$

where $a = \alpha_3 + 2\mu + \lambda Y\delta + \lambda + \alpha_1 + \alpha_2 - \frac{\beta_1}{R_0}$ and $b = \frac{1}{R_0}(R_0 - 1)$.

By Routh Hurwitz Criterion, system (7) is stable if $a > 0$ and $b > 0$ then

$$\begin{cases} R_0 > 1 \\ \beta_1 < \alpha_2 \end{cases}$$

□

2.4. Numerical simulation. In this section, we present some numerical solutions of system (6) for different values of the parameters. The resolution of system (6) was created using the Gauss implicit finite difference method develped by LaSalle [28]) presented in Gumel et al. [29] and denoted the GSS1 method. We use the different initial values for each variable of state, and we use the following parameters:

$\beta_1 = 0.07$, $\beta_2 = 0.01$, $\alpha_1 = 0.04$, $\alpha_2 = 0.66$, $\alpha_3 = 0.1$, $\alpha_4 = 0.009$, $\lambda = 0.01$, $\sigma = 0.28$, $\delta = 0.3$, $\mu = 0.04$; then we have $R_0 = 0.45 < 1$,we obtained:

i) The number of suscuptible diabetics increases and approaches the number $D = 225$ (Figure 2c)

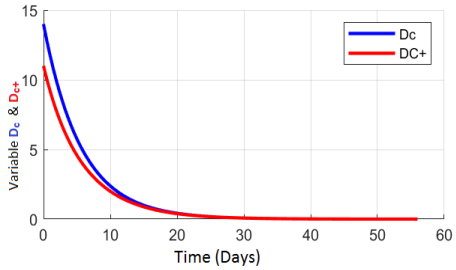
ii) The number of infected with mild complications decreases and approaches the number $D_C = 0$ (Figure 2a)

iii) the number of infected of severe complication decreases and approaches the number $D_{C+} = 0$ (Figure 2a)

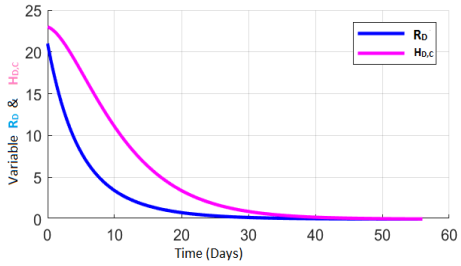
iv) The number of hospitalized decreases and approaches the number $H_{D,C} = 0$ (Figure 2b)

v) The number of recorved from the Corona virus decreases and approaches the number $R_D = 0$ (Figure 2b)

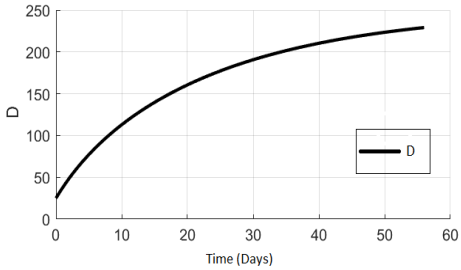
Therefore, the solution curves to the equilibrium E_0 $(D, 0, 0, 0)$ when $R_0 < 1$. Hence, model (Figure 1) is stable.



(A) infected with mild and severe compli



(B) hospitalized and recorved

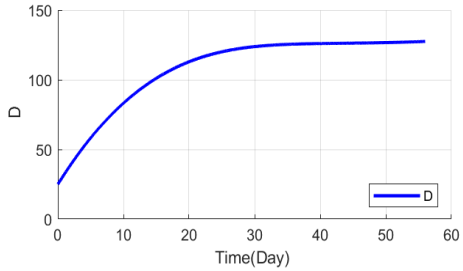


(C) scusptible

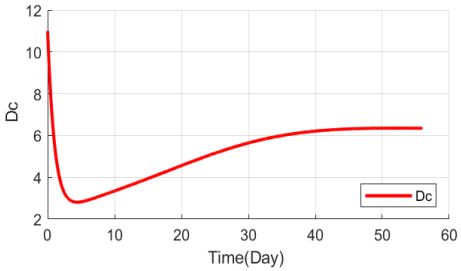
FIGURE 2. When $R_0 < 1$ the Covid19-Diabetes equilibrium E_0 is localy asymptotically stabe

Also, for the different initial values for each variable of state, and the following parameters:$\beta_1 = 0.47$ $\beta_2 = 0.28$ $\alpha_1 = 0.08$, $\alpha_2 = 0.66$, $\alpha_3 = 0.1$, $\alpha_4 = 0.09$; $\lambda = 0.2$; $\sigma = 0.04$; $\delta = 0.004$; $\mu = 0.04$; and $R_0 = 1.82 > 1$.

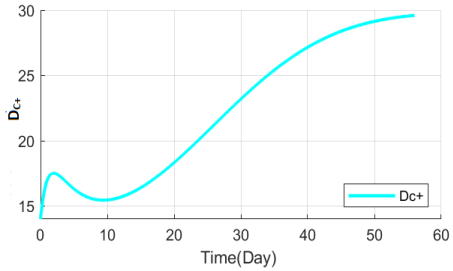
In this case, we obtained:



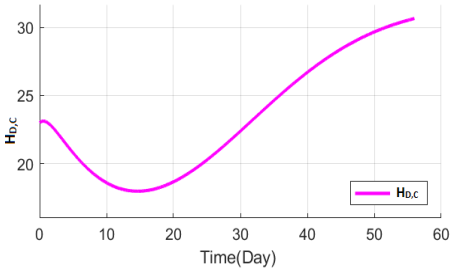
(A) suscptible



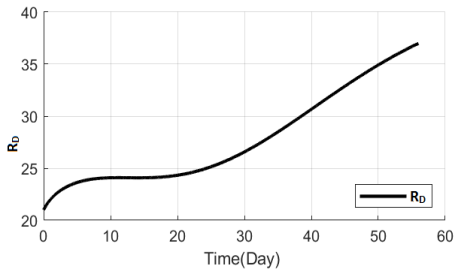
(B) infected with mild compli



(C) infected with severe compli



(D) hospitalized



(E) recorved

FIGURE 3. When $R_0 > 1$ the Covid19-Diabetes equilibrium E_1 is localy asymptotically stable

i) The number of suscuptible diabetics increases and approaches the number $D = 135,82$ (Figure 3a)

ii) The number of infected with mild complications decreases at first and it increases and approaches the number $D_C = 6,4$ (Figure 3b)

iii) the number of infected of severe complication increases and approaches the number $D_{C+} = 30,34$ (Figure 3c)

iv) The number of hospitalized increases and approaches the number $H_{D,C} = 32,06$ (Figure 3d)

v) The number of recorved from the Corona virus increases and approaches the number $R_D = 42,24$ (Figure 3e)

Therefore the solution curves to the equilibrium point $E_1$when $R_0 > 1$. Hence the model is locally asymptotically stable .

In general, people with diabetes are more likely to experience symptoms and complications when infected with a virus, especially the Coronavirus. People who have diabetes don't have a higher chance of contracting the virus but they may have worse outcomes.

The results below are the fruit of conducted study in collaboration with prof.Saloua Elamari [27]. The study, which is the first to exist in North Africa, was done in Sheikh Khalifa hospital in Casablanca Morocco.

- Acute respiratory distress syndrome: acute respiratory failure that has been evolving for a week or less(it appeared in (Figure 3c) the curve increases in the 3rd day) associating:bilateral opacities visible on thoracic imaging and pulmonary edema in which hydrostatic involvement is not predominant.
- Bacterial superinfection: presumed on clinical evidence (purulent sputum, high fever, increased oxygen requirements).
- Septic shock: persistent hypotension despite fluid resuscitation.
- Vascular events represented by the occurrence of a myocardial infarction diagnosed by electrocardiogram or stroke: confirmed by cerebral MRI or by MRI or cerebral CT.
- Heart failure: known decompensated or revealed during hospitalization.

So, these results require a real need to find an effective strategy to control the spread of virus in diabetic population.

3. THE OPTIMAL CONTROL PROBLEM

3.1. Formulation of the optimal control problem. The strategy of control that has been adopted consists to minimize the spread of the virus Covid-19 among diabetic people. In this model, we included three control $u(t)$,$v(t)$ and $w(t)$ for $t \in [0,\mathrm{T}]$. The First control $u(t)$ can be interpreted as the proportion to be subjected to sensitization and prevention so we note that is the awareness program to diabetic people at time t. The second control $v(t)$ can be interpreted as

early diagnosis in hospital with follow up. The third control can be interpreted as the proportion to be subjected to strict glycemic control with a multidisciplinary medical follow-up, so the controlled mathematical system is given by the following system of differential equations

$$
(13)\quad \begin{cases}
\dfrac{dD(t)}{dt} = I - \beta_1\big(1-u(t)\big)\dfrac{D(t)D_C(t)}{N(t)} - \beta_2\big(1-u(t)\big)\dfrac{D(t)D_{C+}(t)}{N(t)} + \sigma R_D(t) - \mu D(t) \\
\dfrac{dD_C(t)}{dt} = \beta_1\big(1-u(t)\big)\dfrac{D(t)D_C(t)}{N(t)} + \beta_2\big(1-u(t)\big)\dfrac{D(t)D_{C+}(t)}{N(t)} - \big(\lambda+\alpha_1+\alpha_2+\mu\big)D_C \\
\qquad\qquad -w(t)D_C(t) - v(t)D_C(t) \\
\dfrac{dD_{C+}}{dt} = \alpha_2 D_C(t) - (\mu+\alpha_3)D_{C+}(t) - w(t)D_{C+}(t) \\
\dfrac{dH_{D,C}}{dt} = \lambda D_C(t) + \alpha_3 D_{C+}(t) - (\alpha_4+\delta+\mu)H_{D,C}(t) + w(t)(D_{C+}(t)+D_C(t)) + v(t)D_C(t) \\
\dfrac{dR_D(t)}{dt} = \alpha_1 D_C(t) + \alpha_4 H_{D,C}(t) - (\sigma+\mu)R_D(t)
\end{cases}
$$

3.2. The optimal control: existence and characterization. Our main aim is to minimize the number of infected with mild and severe complications. Mathematically, it can be interpreted by optimisation of the objective functional:

$$
(14)\quad J\big(u,v,w\big) = D_C(T) + D_{C+}(T) + \int_0^T \left(D_C(t) + D_{C+}(t) + \frac{A}{2}u^2(t) + \frac{B}{2}v^2(t) + \frac{G}{2}w^2(t) \right) dt
$$

where $A \geq 0$, $B \geq$, $G \geq 0$ are the cost coefficient. They are selected to weight the relative importance of $u(t)$, $v(t)$ and $w(t)$ at time t. T is the final time . In other words, we seek the optimal controls u^* ,v^*, w^* such that:

$$
(15)\qquad J(u^*,v^*,w^*) = \min_{u,v,w\in U} J(u,v,w)
$$

where U is the set of admissible controls defined by:

$$
(16)\quad \begin{aligned} U = \big\{ u,v,w/is \quad & measurable, 0 \leq u_{min} \leq u(t) \leq u_{max} \leq 1, 0 \leq v_{min} \\ & \leq v(t) \leq v_{max} \leq 1, 0 < w_{min} \leq w(t) \leq w_{max} \leq 1, t \in \big[0,T\big] \big\} \end{aligned}
$$

3.2.1. *Existence of an optimal Control.* We first show the existence of solutions of the system (6), After that, we will prove the existence of the optimal control [30].

Theorem 5. *Considered the control problem with system* (13)*, there exists an optimal control* $\left(u^*, v^*, w^*\right) \in U^3$ *such that* $J(u^*, v^*, w^*) = \min_{u,v,w \in U} J(u, v, w)$.

Proof. The existence of the optimal control can be obtained using a result by Fleming and Rishel[30], checking the following steps:

- The set of controls and corresponding state variables is nonempty. To prove this condition we use a simplified version an existence result of Boyce and Diprima [31]. Let $X_i^{'} = F_{X_i}(t, X_1, X_2, X_3, X_4, X_5)$ with $i = 1, \cdots, 5$ where $(X_1^{'}, X_2^{'}, X_3^{'}, X_4^{'}, X_5^{'}) = (D, D_C, D_{C+}, H_{D;C}, R_D)$ where $X_1 \cdots X_5$ from the right hand side of the system of equation (13), let u, v, w for some constant and since all parameters are constants and $X_1, \cdots X_5$ are continuous, then $F_D, F_{D_C}, F_{D_C+}, F_{H_{D,c}}, F_{R_D}$ are also continuous.

  Additionally, the partial derivatives $\frac{\partial F_{X_i}}{\partial X_i}$ with $i = 1 \cdots 5$, are all continuous. There are exists a unique solution $\left(D, D_c, D_{C+}, H_{D,C}, R_D\right)$ that satisfies the initial conditions. Therefore the set is nonempty and condition is satisfied.
- The control space $U = \left\{ \left(u, v, w\right) / \left(u, v, w\right) \right.$ is measurable, $0 \leq u_{min} \leq u(t) \leq u_{max} \leq 1$, $0 \leq v_{min} \leq v(t) \leq v_{max} \leq 1$ and $0 \leq w_{min} \leq w(t) \leq w_{max} \leq 1$, $t \in \left[0, T\right] \left. \right\}$ is convex and closed by definition.
- All the right hand sides of equations of system are continuous, bounded above by a sum of bounded control and state and can be written as a linear function of u, v and w with coefficients depending on time and state .
- The integrand in the objective fonctional $D_C(t) + D_{C+}(t) + \frac{A}{2}u^2(t) + \frac{B}{2}v^2(t) + \frac{G}{2}w^2(t)$ is clearly convex on U.

It rest to show that there exist constant $\zeta_1, \zeta_2, \zeta_3, \zeta_4 > 0$, and ζ such that

$$D_C(t) + D_{C+}(t) + \frac{A}{2}u^2(t) + \frac{B}{2}v^2(t) + \frac{G}{2}w^2(t) \geq \zeta_1 + \zeta_2|u|^{\zeta} + \zeta_3|v|^{\zeta} + \zeta_4|w|^{\zeta}$$

The state variables being bounded, let

$\zeta_1 = \inf_{t \in [0,T]} \left(D_C(t) + D_{C+}(t)\right)$, $\zeta_2 = \frac{A}{2}, \zeta_3 = \frac{B}{2}, \zeta_4 = \frac{G}{2}$ and $\zeta = 2$, then it follows that:

$$D_C(t)+D_{C+}(t)+\frac{A}{2}u^2(t)+\frac{B}{2}v^2(t)+\frac{G}{2}w(t)\geq \zeta_1+\zeta_2|u|^{\zeta}+\zeta_3|v|^{\zeta}+\zeta_4|w|^{\zeta}$$

Then from Fleming and Rishel [31], we conclude that there exists an optimal control. □

3.2.2. *Characterization of the optimal control.* Now we apply Pontryagin's maximum [30] to derive the necessary conditions for the optimal control, wich converts into a problem of minimizing a Hamiltonian H(t) at time t defined by:

$$\hat{H}(t)=D_C(t)+D_{C+}(t)+\frac{A}{2}u^2(t)+\frac{B}{2}v^2(t)+\frac{G}{2}w^2(t)+\sum_{i=1}^{5}\lambda_i(t)f_i\big(D,D_C,D_{C+},H_{D,C},R_D\big)$$

where f_i is the right side of the difference equation of the i^{th} state variable at time t.

Theorem 6. *Given the optimal control* $\big(u^*,v^*,w^*\big)$ *and the solutions* D^*, D_C^*, D_{C+}^*, $H_{D,C}^*$, R_D^* *of the corresponding state system* (13)*, there exists adjoint variables* λ_1, λ_2, λ_3, λ_4, λ_5 *satisfying:*

$$\lambda_1^{'}(t)=\lambda_1(t)\bigg(\mu+\beta_1\big(1-u(t)\big)\frac{D_C(t)}{N(t)}+\beta_2\big(1-u(t)\big)\frac{D_{C+}(t)}{N(t)}\bigg)$$
$$-\lambda_2(t)\bigg(\beta_1\big(1-u(t)\big)\frac{D_C(t)}{N(t)}+\beta_2\big(1-u(t)\big)\frac{D_{C+}(t)}{N(t)}\bigg)$$

$$\lambda_2^{'}(t)=-1+\lambda_1(t)\beta_1\big(1-u(t)\big)\frac{D(t)}{N(t)}-\lambda_2(t)\big(\beta_1\big(1$$
$$-u(t)\big)\frac{D(t)}{N(t)}-\lambda-\alpha_1-\alpha_2-\mu-w(t)-v(t)\big)-\lambda_3(t)\alpha_2-\lambda_4(t)(\lambda+w(t)+v(t))-\alpha_1\lambda_5(t)$$

$$\lambda_3^{'}(t)=-1+\lambda_1(t)\beta_2\big(1-u(t)\big)\frac{D(t)}{N(t)}-\lambda_2(t)\beta_2\big(1-u(t)\big)\frac{D(t)}{N(t)}+\lambda_3(t)\big(\mu+\alpha_3-w(t)\big)-\lambda_4(t)(\alpha_3+w(t))$$

$$\lambda_4^{'}(t)=\big(\alpha_4+\delta+\mu\big)\lambda_4(t)-\alpha_4\lambda_5(t)$$

$$\lambda_5^{'}(t)=-\sigma\lambda_1(t)+\big(\sigma+\mu\big)\lambda_5(t)$$

With the transversality conditions at time T

$$\lambda_1(T)=0,\lambda_2(T)=-1,\lambda_3(T)=-1,\lambda_4(T)=0,\lambda_5(T)=0$$

Further more, for $t\in\big[0,T\big]$ *the optimal control* u^*, v^*, w^* *are given by*

$$u^*=min\bigg(1,max\bigg(0,\frac{(\lambda_2(t)-\lambda_1(t)}{A}\big(\beta_1\frac{D(t)D_C(t)}{N(t)}+\beta_2\frac{D(t)D_{C+}(t)}{N(t)}\big)\bigg)\bigg) \tag{17}$$

$$v^*=min\bigg(1,max\big(0,\frac{\big(\lambda_2(t)-\lambda_4(t)\big)}{G}D_C(t)\big)\bigg) \tag{18}$$

$$w^* = min\left(1, max\big(0, \frac{\lambda_2(t)D_C(t) + \lambda_3(t)D_{C+} - \lambda_4(t)\big(D_C(t) + D_{C+}(t)\big)}{B}\big)\right) \tag{19}$$

Proof. The Hamiltonian $\hat{H}$ is defined as follows:

$$\hat{H}(t) = D_C(t) + D_{C+}(t) + \frac{A}{2}u^2(t) + \frac{B}{2}v^2(t) + \frac{G}{2}w^2(t) + \sum_{i=1}^{5}\lambda_i(t)f_i\big(D, D_C, D_{C+}, H_{D,C}, R_D\big).$$

where:

$$f_1\big(D, D_C, D_{C+}, H_{D,C}, R_D\big) = I - \beta_1\big(1-u(t)\big)\frac{D(t)D_C(t)}{N(t)} - \beta_2\big(1-u(t)\big)\frac{D(t)D_{C+}(t)}{N(t)} + \sigma R_D(t) - \mu D(t)$$

$$\begin{aligned} f_2\big(D, D_C, D_{C+}, H_{D,C}, R_D\big) &= \beta_1\big(1-u(t)\big)\frac{D(t)D_C(t)}{N(t)} - \beta_2\big(1-u(t)\big)\frac{D(t)D_{C+}(t)}{N(t)} \\ &\quad - \big(\lambda + \alpha_1 + \alpha_2 + \mu\big)D_C(t) - w(t)D_C(t) - v(t)D_C(t) \\ f_3\big(D, D_C, D_{C+}, H_{D,C}, R_D\big) &= \alpha_2 D_C(t) - \big(\mu + \alpha_3\big)D_{C+} - w(t)D_{C+}(t) \\ f_4\big(D, D_C, D_{C+}, H_{D,C}, R_D\big) &= \lambda D_C(t) + \alpha_3 D_{C+}(t) - \big(\alpha_4 + \delta + \mu\big)H_{D,C}(t) + v(t)D_C(t) \\ &\quad + w(t)\big(D_C(t) + D_{C+}(t)\big) \\ f_5\big(D, D_C, D_{C+}, H_{D,C}, R_D\big) &= \alpha_4 H_{D,C}(t) + \alpha_1 D_C(t) - \big(\sigma + \mu\big)R_D(t) \end{aligned}$$

For $t \in \left[\ 0, \mathrm{T}\ \right]$; the adjoint equation and transversality conditions can be obtained by using pontrygain's maximum principal [32], such that:

$$\begin{cases} \lambda_1'(t) = \dfrac{-\partial \hat{H}(t)}{\partial D(t)} & \lambda_1(T) = 0 \\ \lambda_2'(t) = \dfrac{-\partial \hat{H}(t)}{\partial D_C(t)} & \lambda_2(T) = -1 \\ \lambda_3'(t) = \dfrac{-\partial \hat{H}(t)}{\partial D_{C+}(t)} & \lambda_3(T) = -1 \\ \lambda_4'(t) = \dfrac{-\partial \hat{H}(t)}{\partial H_{D,C}(t)} & \lambda_4(T) = 0 \\ \lambda_5'(t) = \dfrac{-\partial \hat{H}(t)}{\partial R_D(t)} & \lambda_5(T) = 0 \end{cases}$$

For $t \in [0\ ,\ \mathrm{T}]$, the optimal control u^*, v^*, w^* can be solved from the optimality condition

$$\begin{cases} \dfrac{\partial \hat{H}}{\partial u} = 0 \\ \dfrac{\partial \hat{H}}{\partial v} = 0 \\ \dfrac{\partial \hat{H}}{\partial w} = 0 \end{cases}$$

Then we have :

$$u(t) = \frac{\big(\lambda_2(t) - \lambda_1(t)\big)}{A}\left(\beta_1 \frac{D(t)D_C(t)}{N(t)} + \beta_2 \frac{D(t)D_{C+}(t)}{N(t)}\right)$$

$$v(t) = \frac{\big(\lambda_2(t) - \lambda_4(t)\big)}{G} D_C(t)$$

$$w(t) = \frac{D_C(t)(\lambda_2(t) - \lambda_4(t) + D_{C+}(t)(\lambda_3(t) - \lambda_4(t))}{B}$$

By the bounds in U of the controls, it is easy to obtain, u^*, v^*, w^* are given in ((17), (18), (19)) in the form of system. □

3.3. Numerical simulation. In this section, we present the results obtained by numerically solving the optimality system. In our control issue a problem, we have initial conditions for the variables state and terminal conditions for the adjoints. That is, the optimality system is a two-point boundary value problem with separated boundary conditions at times step $i = 0$ and $i = T$. We solve the optimality system by an iterative method with forward solving of the state system followed by back- ward solving of the adjoint system. We start with an initial guess for the controls at the first iteration and then before the next iteration, we update the controls by using the characterization. We continue until convergence of successive iterates is achieved. Different simulations can be carried out using various values of parameters. In the present numerical approach, we use the following parameters values taken in (Table 1) and (Table 2) as a case study in Sheikh Khalifa hospital [27]. Since control and state functions are on different scales, the weight constant value is chosen as follows: $A = 10^7$, $B = 10^7$ $G = 10^7$.

The proposed control strategies in this work help to achieve several objectives:

Paramter	Description	Value in d^{-1}
μ	Natural Mortality	0.04
β_1	The rate of Diabetic people who were infected by contact with infected by mild compli	0.28
β_2	The rate of Diabetic people who were infected by contact with infected by severe compli	0.2
α_1	The rate of Diabetic people who recovered from the Corona-virus	0.2
α_2	The rate of Diabetic people who develop the severe complications	0.66
α_3	The rate of people with severe comp were hospitalized	0.04
α_4	The rate of people who recovered and get out of the hospital	0.07
δ	The rate of people who died under quarantine and under severe compl	0.123
σ	The rate of Diabetic people who return infected by Corona virus	0.1
λ	The rate of people with mild complication who have been quarantined in hospital	0.001
I	Incidence	10

TABLE 1. Parameters values.

Population	Description	Value	source
$D(0)$	susceptible diabetic	25	[27]
$D_C(0)$	Diabetic infected by mild compl	11	[27]
$D_{C+}(0)$	Diabetic infected by severe compl	14	[27]
$H_{D,C}(0)$	Diabetic hospitilized	23	[27]
$R_D(0)$	Diabetic recorved from the virus	21	[27]

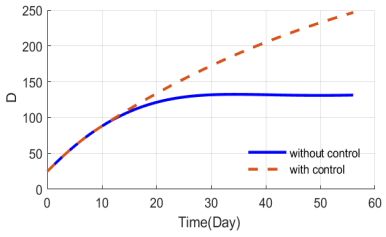
TABLE 2. Population values

Objective 1: Preventing susceptible diabetic from becoming infected individuals and early diagnosis for infected people with mild and severe complications.

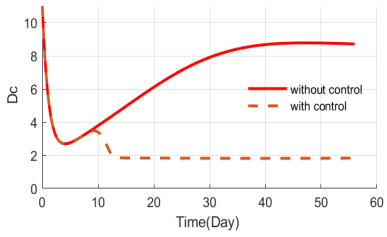
Given the major role of contact in transmitting Covid-19 among susceptible and infected people and the importance of prevention programs in limiting the number of new cases and the benefits of early diagnosis, we propose two optimal strategies based on the control u and w. Recall that u represents any measurement that can reduce contact between susceptible and infected individuals, such as awareness programs, distancing, or isolation, and w is the early diagnosis.

We noted that after applying both strategies, the number of susceptible increases positively (Figure 4a), combining two strategy results in an obvious decreased in the number of diabetics with different complications.

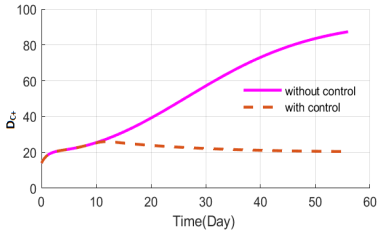
So according (Figure 4) and (Table 3), the strategy of prevention and early diagnosis has been adopted.



(A) suscptible



(B) Infected with mild compli



(C) Infected with severe compli

FIGURE 4. Number of D,D_C and D_{C+} with control u and w

Infected after 56 days	without control	with control	Pourcentage
Infected with mild compli	8,7	1,8	-79,31 %
Infected with severe compli	87,37	20	-77,1 %
scusptible diabetic	131,4	244	+ 46,31 %

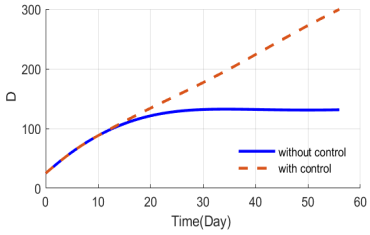
TABLE 3. Evolution of the number of diabetics with controls u and w after 65 days.

Objective 2: Preventing susceptible diabetic from becoming infected individuals and early diagnosis for infected people with mild and severe complication and strict glycemic control

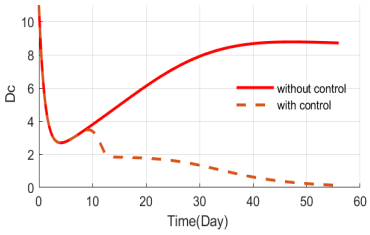
People with diabetes may get more severe COVID-19 because high blood glucose levels can increase the risk of infections. The infection itself affect the immune system, group of researchers [33, 34] found that a particular protein, called angiotensin-converting enzyme 2, or ACE2, may play a role. ACE2 is produced in the kidneys, intestines, heart, blood vessels, lungs and pancreas. ACE2 makes it easier for the coronavirus to enter the body as one of the spikes of the coronavirus binds to ACE2. When there is a sudden rise in the blood glucose levels the body may become more sensitive to ACE2.This can make it easier for the Coronavirus to enter to the cells.

Although Covid-19 enters the body through the lungs, it can easily spread throughout the body once it is connected to this ACE2. As the pancreas is one of the organs in which ACE2 is made it is possible that it damages the islet cells in the pancreas that are responsible for making insulin. Concerning the risk of glycemic imbalance induced by insulin resistance in connection with the infectious, we recommend third optimal control which is strict glycemic control for people with diabetes, HbA1c and serum ketone should be also measured in patients with elevated blood sugar levels.

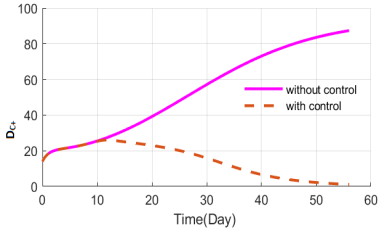
In this scenario, we use the three optimal control. We combine the 3 previous strategies, to achieve better result. According to the (Table 4) and (Figure 5) we almost see a total disappearance of infected individuals with mild and severe complications, and a positive increase in number of susceptible diabetic. At this point,it can be concluded that combining three controls is potentially more effective than using any one alone. Different combinations of optimal controls and strategies (u with v, w with v, . . .) can be used to achieve other objectives depending on the particularity of the disease in each country.



(A) suscptible



(B) Infected with mild compli



(C) Infected with severe compli

FIGURE 5. Number of D,D_C and D_{C+} with control u and v and w.

Infected after 56 days	without control	with control	Percentage
Infected with mild compli	8,7	0,1	-98,85%
Infected with severe compli	87,37	1,3	-98,51 %
susceptible diabetic	131,4	297	+55,81%

TABLE 4. Evolution of the number of diabetics with controls u and v and w after 65 days

A. APPENDIX

Reproduction number

The basic reproduction number R_0, is defined as the average number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible [35].

Using notations in [36], the matrices F and V and their Jacobian matrices for the new infection terms and the remaining transfer term evaluated at the disease free equilibrium are respectively given by;

$$F = \begin{pmatrix} -\beta_1 \dfrac{DD_C}{N} - \beta_2 \dfrac{DD_{C+}}{N} \\ \beta_1 \dfrac{DD_C}{N} + \beta_2 \dfrac{DD_{C+}}{N} \\ 0 \end{pmatrix} \qquad V = \begin{pmatrix} -I - \sigma R_D + \mu D \\ D_C\big(\lambda + \alpha_1 + \alpha_2 + \mu\big) \\ -\alpha_2 D_C + \big(\mu + \alpha_3\big) D_{C+} \end{pmatrix}$$

For trivial equilibrium E_0, we have $D^* = N^*$ so:

$$J_F = \begin{pmatrix} 0 & -\beta_1 & -\beta_2 \\ 0 & \beta_1 & \beta_2 \\ 0 & 0 & 0 \end{pmatrix} \qquad J_V = \begin{pmatrix} +\mu & 0 & 0 \\ 0 & \lambda + \alpha_1 + \alpha_2 + \mu & 0 \\ 0 & -\alpha_2 & \mu + \alpha_3 \end{pmatrix}$$

$$\Longrightarrow \qquad J_V^{-1} = \begin{pmatrix} \frac{1}{\mu} & 0 & 0 \\ 0 & \dfrac{1}{\lambda + \alpha_1 + \alpha_2 + \mu} & 0 \\ 0 & \dfrac{\alpha_2}{\big(\mu + \alpha_3\big)\big(\lambda + \alpha_1 + \alpha_2 + \mu\big)} & \dfrac{1}{\alpha_3 + \mu} \end{pmatrix}$$

$$J_F J_V^{-1} = \begin{pmatrix} 0 & \dfrac{-\beta_1}{\lambda_1 + \alpha_1 + \alpha_2 + \mu} - \dfrac{\beta_2 \alpha_2}{\big(\lambda + \alpha_1 + \alpha_2 + \mu\big)\big(\alpha_3 + \mu\big)} & \dfrac{-\beta_2}{\alpha_3 + \mu} \\ 0 & \dfrac{\beta_1}{\lambda_1 + \alpha_1 + \alpha_2 + \mu} + \dfrac{\beta_2 \alpha_2}{\big(\lambda + \alpha_1 + \alpha_2 + \mu\big)\big(\alpha_3 + \mu\big)} & \dfrac{\beta_2}{\alpha_3 + \mu} \\ 0 & 0 & 0 \end{pmatrix}$$

It follows that the basic reproduction, denoted by R_0, is given by:

$$R_0 = \rho\big(J_F J_V^{-1}\big) = \frac{\beta_1}{\lambda + \alpha_1 + \alpha_2 + \mu} + \frac{\beta_2 \alpha_2}{\big(\alpha_3 + \mu\big)\big(\lambda + \alpha_1 + \alpha_2 + \mu\big)} = R_{D_C} + R_{D_{C+}}$$

4. CONCLUSION

For future work, it would be interesting to extend the structure of our model by incorporating age effect and/or spatial diffusion, and observe how this can affect the optimal dynamics of our model. In addition, we intend to propose a direct method to optimal control based on the viability theory.

ACKNOWLEDGMENTS

The authors are thankful to the anonymous reviewers for their constructive comments and suggestions which helped in significant improvement of this work.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

REFERENCES

[1] Q. Li, X. Guan, P. Wu, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia, N. Engl. J. Med. 382 (2020), 1199–1207. https://doi.org/10.1056/nejmoa2001316.

[2] World Health Organization, COVID 19 public health emergency of international concern (PHEIC). Global research and innovation forum: towards a research roadmap. (2020). https://www.who.int/publications/m/item/covid-19-public-health-emergency-of-international-concern-(pheic)-global-research-and-innovation-forum, Accessed: 30 JUL 2021.

[3] World Health Organization, WHO director-general's opening remarks at the media briefing on COVID-19 - 11 March 2020, https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020, Accessed: 11 March 2020.

[4] World Health Organization, Weekly operational update on COVID-19 - 31 May 2021, https://www.who.int/publications/m/item/weekly-operational-update-on-covid-19-31-may-2021, Accessed: 31 May 2021.

[5] World Health Organization, United States of America Situation, https://covid19.who.int/region/amro/country/us, Accessed: 30 Aug 2021.

[6] World Health Organization, India situation, https://covid19.who.int/region/searo/country/in, Accessed: 30 Aug 2021.

[7] World Health Organization, Brazil situation, Available at: https://covid19.who.int/region/amro/country/br, Accessed: 30 Aug 2021.

[8] World Health Organization, France situation, https://covid19.who.int/region/euro/country/fr, Accessed: 30 Aug 2021.

[9] World Health Organization, Russian Federation situation, https://covid19.who.int/region/euro/country/ru, Accessed: 30 Aug 2021.

[10] World Health Organization, Turkey situation, https://covid19.who.int/region/euro/country/tr, Accessed: 30 Aug 2021.

[11] C. Huang, Y. Wang, X. Li, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, The Lancet. 395 (2020), 497–506. https://doi.org/10.1016/s0140-6736(20)30183-5.

[12] D. Wang, B. Hu, C. Hu, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China, JAMA. 323 (2020), 1061–1069. https://doi.org/10.1001/jama.2020.1585.

[13] J. Yang, Y. Zheng, X. Gou, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis, Int. J. Infect. Dis. 94 (2020), 91–95. https://doi.org/10.1016/j.ijid.2020.03.017.

[14] Q. Shi, X. Zhang, F. Jiang, et al. Clinical characteristics and risk factors for mortality of COVID-19 patients with diabetes in Wuhan, China: a two-center, retrospective study, Diabetes Care. 43 (2020), 1382–1391. https://doi.org/10.2337/dc20-0598.

[15] International Diabetes Federation, IDF diabetes atlas, 8th edition, International Diabetes Federation, Brussels, Belgium, 2017.

[16] International Diabetes Federation, IDF diabetes atlas, 9th edition, International Diabetes Federation, Brussels, Belgium, 2019.

[17] G. Roglic, WHO global report on diabetes: a summary, Int. J. Noncommun. Dis. 1 (2016), 3–8. https://doi.org/10.4103/2468-8827.184853.

[18] Centers for Disease Control and Prevention (CDC), Coronavirus disease 2019 (COVID-19), https://www.cdc.gov/coronavirus/2019-ncov/index.html, Accessed on 30 Jul 2021.

[19] A. Remuzzi, G. Remuzzi, COVID-19 and Italy: what next?, The Lancet. 395 (2020), 1225–1228. https://doi.org/10.1016/s0140-6736(20)30627-9.

[20] F. Zhou, T. Yu, R. Du, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study, The Lancet. 395 (2020), 1054–1062. https://doi.org/10.1016/s0140-6736(20)30566-3.

[21] T. Chen, D. Wu, H. Chen, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study, BMJ. 368 (2020), m1091. https://doi.org/10.1136/bmj.m1091.

[22] W. Guan, W. Liang, Y. Zhao, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis, Eur. Respir. J. 55 (2020), 2000547. https://doi.org/10.1183/13993003.00547-2020.

[23] R. Pal, S.K. Bhadada, COVID-19 and diabetes mellitus: An unholy interaction of two pandemics, Diabetes Metab. Syndr.: Clin. Res Rev. 14 (2020), 513–517. https://doi.org/10.1016/j.dsx.2020.04.049.

[24] A.A. Lukito, R. Pranata, J. Henrina, et al. The effect of metformin consumption on mortality in hospitalized COVID-19 patients: a systematic review and meta-analysis, Diabetes Metab. Syndr.: Clin. Res Rev. 14 (2020), 2177–2183. https://doi.org/10.1016/j.dsx.2020.11.006.

[25] P. Samui, J. Mondal, S. Khajanchi, A mathematical model for COVID-19 transmission dynamics with a case study of India, Chaos Solitons Fractals. 140 (2020), 110173. https://doi.org/10.1016/j.chaos.2020.110173.

[26] A. Kouidere, L.E. Youssoufi, H. Ferjouchia, et al. Optimal Control of Mathematical modeling of the spread of the COVID-19 pandemic with highlighting the negative impact of quarantine on diabetics people with Cost-effectiveness, Chaos Solitons Fractals. 145 (2021), 110777. https://doi.org/10.1016/j.chaos.2021.110777.

[27] S. Elamari, I. Motaib, S. Zbiri, et al. Characteristics and outcomes of diabetic patients infected by the SARS-CoV-2, Pan Afr. Med. J. 37 (2020), 32. https://doi.org/10.11604/pamj.2020.37.32.25192.

[28] J.P. LaSalle, The stability of dynamical systems, CBMS-NSF Regional Conference Series in Applied Mathematics, 25, SIAM, Philadelphia, PA, USA, (1976). https://doi.org/10.1137/1.9781611970432.

[29] A.B. Gumel, P.N. Shivakumar, B.M. Sahai, A mathematical model for the dynamics of HIV-1 during the typical course of infection, Nonlinear Anal.: Theory Methods Appl. 47 (2001), 1773–1783. https://doi.org/10.1016/s0362-546x(01)00309-1.

[30] W.H. Fleming, R.W. Rishel, Deterministic and stochastic optimal control, Springer, New York, NY, USA, (1975).

[31] W.E. Boyce, R.C. DiPrima, Elementary differential equations and boundary value problems, John Wiley & Sons, New York, (2009).

[32] L.S. Pontryagin, V.G. Boltyanskii, R.V. Gamkrelidze, et al. The mathematical theory of optimal processes, Wiley, New York, NY, USA, (1962).

[33] H. Hofmann, M. Geier, A. Marzi, et al. Susceptibility to SARS coronavirus S protein-driven infection correlates with expression of angiotensin converting enzyme 2 and infection can be blocked by soluble receptor, Biochem. Biophys. Res. Commun. 319 (2004), 1216–1221. https://doi.org/10.1016/j.bbrc.2004.05.114.

[34] K. Kuba, Y. Imai, J. Penninger, Angiotensin-converting enzyme 2 in lung diseases, Curr. Opin. Pharmacol. 6 (2006), 271–276. https://doi.org/10.1016/j.coph.2006.03.001.

[35] P. van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, Math. Biosci. 180 (2002), 29–48. https://doi.org/10.1016/s0025-5564(02)00108-6.

[36] H.W. Hethcote, The mathematics of infectious diseases, SIAM Rev. 42 (2000), 599–653. https://doi.org/10.1137/s0036144500371907.