Universidade de Lisboa

Faculdade de Farmácia

O Impacto da Pandemia no Doente Diabético em Portugal

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Monografia orientada pela Professora Doutora Catarina Pinto Reis, Professora Auxiliar, Coorientada pela Professora Doutora Carla Torre, Professora Auxiliar

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Resumo

A COVID-19 (doença de coronavirus), caracterizada por infeções respiratórias agudas causadas pelo Coronavírus 2 (SARS-CoV-2), trouxe consigo uma inesperada pandemia, e com ela uma mudança brusca nas nossas vidas. Especialmente notório durante os confinamentos ocorridos em todo o mundo, houve um impacto generalizado na sociedade, do qual na área da saúde não foi exceção. Os serviços de saúde tiveram de se adaptar e focar os seus recursos na luta contra esta pandemia, que se evidenciou como a prioridade número 1 ao longo de 2020 e 2021. Este foco, retirou inevitavelmente recursos alocados ao diagnóstico e tratamento de outras doenças.

À data de 2018, em Portugal, a Diabetes assumia uma elevada prevalência com cerca de -13,6% da população diagnosticada com diabetes mellitus (DM). No passado mais recente, em 2020, com o Sistema Nacional de Saúde (SNS) largamente focado no combate à COVID-19, e a consequente deslocalização de recursos humanos, financeiros e materiais, os restantes programas de saúde foram parcial ou totalmente interrompidos. Esta decisão poderá ter tido consequências que começamos hoje a avaliar, nomeadamente na limitação no acesso a cuidados de saúde por parte dos doentes.

Apesar do aparentemente óbvio impacto, avaliações oficiais do impacto da COVID-19 são ainda raras no panorama nacional. Os relatórios anuais como o "*Diabetes – Factos e Números*" deixaram de ser publicados. Devido à alarmante falta de informação oficial nesta matéria, o impacto da COVID-19 em doentes da com DM em Portugal é ainda desconhecido.

Até à data de publicação da presente dissertação, e nas bases de dados que foram utilizadas, existe um único estudo publicado de domínio público. Este estudo consistiu numa análise preliminar do panorama nacional no que toca a doentes da diabetes DM em 2020 *versus* 2019. Neste contexto, o objetivo desta dissertação foi descrever e interpretar o impacto da COVID-19 na gestão da diabetes nos hospitais do SNS em Portugal recorrendo ao estudo referido e no período de tempo compreendido entre 2019 e 2020.

Os resultados desta pesquisa demostram um aumento dos recursos e do peso relativo da diabetes na atividade hospitalar, apesar da diminuída "produção" do SNS em tempos de pandemia. Este aumento é principalmente devido ao escalar de complexidade e gravidade do doente diabético hospitalizado médio. Em última análise, este aumento observado durante a

pandemia, poderá ter conduzido a um eventual aumento das taxas de mortalidade e de letalidade em meio hospitalar para o doente diabético em Portugal.
Palavras-chave: COVID-19, Diabetes, Portugal, Impacto da pandemia

Abstract

The coronavirus disease (COVID-19) pandemic resulting from acute infections by the severe acute respiratory syndrome - Coronavirus 2 (SARS-CoV-2) brought an unexpected change in our daily lives. Specially in the lockdowns noted across the world, a halt in production and activities was felt, in which healthcare was not an exception. Healthcare providers had to shift their focus and resources to fighting this pandemic, making it the number one priority all throughout 2020 and 2021. This of course resulted in a decline of treatments and diagnoses of other diseases.

In Portugal, Diabetes has higher prevalence of 13.6% pouplation diagnosed cases of diabetes mellitus (DM), up to 2018. So, in 2020, with the *Serviço Nacional de Saúde* (SNS) focused on fighting COVID-19, with consequent concentration of human, material and financial resources, other national health programs were either partially or completely halted. With this, other patients may have suffered from a lack of healthcare. This decision might have had consequences with today we are starting to evaluate, namely in healthcare access limitations by DM patients.

However, no evaluation was made so far. Yearly reports such as *Diabetes – Factos e Números*, stopped being published, due to COVID-19 restrictions. No further reports got published, either from official or independent sources. So, the impact of COVID-19 on DM patients in Portugal is currently unknown.

So far, until the date of this publication, only one public domain study has been published, and it comprises a preliminary evaluation of the DM landscape in 2020, in comparison to the homologous period in 2019. As such, the scope of this dissertation is to describe and interpret Impacto da COVID-19 na Gestão da Diabetes nos Hospitais do SNS in Portugal, according to the study mentioned between 2019 and 2020.

The results of this research showed a higher relative weight in hospital activity and resources allocated to these patients, despite a lower healthcare production of SNS overall. This increase was due to an increase in complexity and severity of the average DM hospitalisation, as a rise in complications related to DM increased. Ultimately suggesting an increase of mortality rates, and in-hospital lethality for DM patients.
Keywords : COVID-19, Diabetes, Portugal, Impact of the pandemic

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Abbreviations

ACP Average Cost per Patient

ADA American Diabetes Association

COVID-19 Coronavirus Disease

CVD Cardiovascular Disease

DF Diabetic Foot

DGS *Direção Geral de Saúde*

DM Diabetes Mellitus

GDM Gestational Diabetes Mellitus

GDP Gross Domestic Product

HbA1c Glycated haemoglobin

LEA Lower-extremity Amputation

MD Main diagnose

MI Acute Myocardial Infarction

OGTT Oral Glucose Tolerance Test

PVD Peripheral Vascular Disease

SARS-CoV-2 Severe Acute Respiratory Syndrome - Coronavirus 2

SD Secondary diagnose

SNS *Serviço Nacional de Saúde*

SPD *Sociedade Portuguesa de Diabetologia*

WHO World Health Organisation

T1DM Type 1 Diabetes

T2DM Type 2 Diabetes

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1. Introduction

On December 31st, 2019, in Wuhan, China, an outbreak of, later described as coronavirus disease (COVID-19) resulting from infection by the severe acute respiratory syndrome - Coronavirus 2 (SARS-CoV-2), pneumonia was reported. This deadly new disease quickly spread throughout the world. On January 30th, 2020, it was declared a "public health emergency of international concern" by the *World Health Organisation* (WHO) and later on March 11th, it was declared as a pandemic (1). In Portugal, the first case was reported on March 2nd, signalling the start of the COVID pandemic in Portugal. The number of infected increased quickly and on March 18th the first lockdown was stated. During this lockdown, the Serviço Nacional de Saúde (SNS) hospitals shifted their focus to treat COVID-19 patients, as many surgical procedures, consultations, secondary diagnosis (SD) means, and treatments were suspended (2).

Due to this reshaped SNS structure, and lockdown, the access to healthcare was affected, with the number of either scheduled or emergency healthcare procedure reduced (3). The number of consultations in SNS decreased in March, by 16%, and the following 2 months by 35% and 31%, when compared to the homologous period in 2019. The number of surgeries in SNS also registered a sharp decrease in March, following the trend of a more accentuated decline in the following months, of 78% and 57% respectively (2). So, healthcare access was diminished in this period.

Currently, in 2021, it is estimated that 537 million people worldwide have DM, with a projected growth to more than 750 million by the year 2045 (4). Children and adolescents are also affected in large numbers by this disease, with 1.2 million living with type 1 DM in 2021. These high numbers lead to an inevitable high healthcare expenditure worldwide, with close to one trillion USD spent yearly. Nevertheless, there are still many registered deaths related to diabetes in 2021, with an estimate of around 6.7 million, adults with age comprised between 20 and 79 years (4).

DM is present in almost 15% of the Portuguese population, as data from 2018 suggests (5). And as such, this disease has a tremendous impact in both the daily lives of many Portuguese, and on Portuguese economy, with total spendings coming close to 1% of the Gross Domestic Product (GDP) (5).

Despite the importance of DM in Portugal, there is little to no published data by the official authorities about the national epidemiologic state of DM population since the start of

the pandemic. The last available data comes from Sociedade Portuguesa de Diabetologia (SPD) report '*Diabetes Factos e Números'* (5). This report comprises data from a specific year, having started in 2009, and the last report released being about the years 2016, 2017, and 2018, all pre-pandemic years. This report collects data from the Continental Portugal SNS provider institutions, for hospital related data.

2. Objectives

Because of a lack of information, an evaluation on the access to healthcare and health outcomes of the DM patient in Portugal must be made due to several reasons; not only to better understand the current situation, but to also better implement future policies and programs to improve these outcomes for the DM patient. Thus, the aim of this master thesis is to describe an overview of the impact of COVID in DM, including the prevalence of DM patients in SNS hospitals, including the prevalence of DM patients in hospitals, the average complexity and severity of each DM hospitalisation case, both in hospital mortality and lethality of DM patients and finally the prevalence of Diabetic Foot (DF), Lower extremity amputations (LEA), stroke and Acute Myocardial Infarction (MI).

3. Methodology

This research was based on electronic resources mainly Science Direct, PubMed and Google Scholar databases Certain keywords were used for the information gathering, such has COVID-19, Diabetes Mellitus, Type 1, Type 2, Epidemiology, Pathophisiology, Impact, Patient, Medical Care. Relative to epidemiologic data, the most recent publications, or ones with data referring to 2019 and 2020, were the ones given preference. Some publications from journals and magazines were also selected. The search was performed between January and August 2022. The cited papers were published between 1988 and 2022, as DM has been studied for a long time.

Furthermore, a review of guidelines and reports from national and international official entities such as WHO, *Direção Geral de Saúde* (DGS), SPD, and American Diabetes Association (ADA) were also included.

To the best of our knowledge, this search aims to include the most representative reports, available in the public domain.

4. Diabetes

4.1. Definition

Diabetes Mellitus (DM), also referred simply as diabetes, is described as a metabolic disease characterized by a chronic hyperglycaemia resultant of an inefficient secretion either or action of insulin, produced in pancreatic β cells. To this chronic hyperglycaemia is associated a continuous loss of function, damage or even failure of either organs or tissues, mainly the heart, kidneys, eyes, nerves, and blood vessels. The most common and characteristic symptoms include polydipsia, polyuria, weight loss e retinopathy. Acute events such as ketoacidosis or non-ketotic hyperosmolar state are the ones that occur with a higher frequency in diabetic patients, presenting a state of dehydration, possibly coma, and if not treated, it can evolve to death.

4.2. Historical Background

Recognized in antiquity from its excessive urine output and described as a disease of the urinary tract, by the I century ad Galen described it as a disease specific to the kidneys because of a weakness in their retentive faculties (6). A century later, Aretaeus of Cappadocia first described it as diabetes, which in Greek meant siphon, referring to most apparent symptom at the time, the polyuria (6). It is only in the XVII century that diabetes mellitus was first described as such by Thomas Willis. With mellitus referring to the honey like taste of urine in these patients (7,8).

4.3. Main classification

Diabetes results mainly of a loss β cell number, or function (9), leading to the defining hyperglycaemia. The characterization of different paths to β cell loss or dysfunction, from autoimmunity, insulin resistance, epigenetic processes, genetic predisposition, concurrent illnesses, and environmental factor (10), help differentiate patients and identify the best therapeutic approach for each one. So, in 2019, the WHO released a new classification for the different types of diabetes (11), being the Type 1 diabetes, Type 2 diabetes, and Gestational diabetes mellitus the most common ones (6), and as such will be the ones described in more detail

Table 1. Types of diabetes, adapted from WHO. (11)

Type 1 diabetes
Type 2 diabetes
Hybrid forms of diabetes
Slowly evolving immune-mediated diabetes of adults
Ketosis prone type 2 diabetes
Other specific types
Monogenic diabetes
Monogenic defects of β-cell function
Monogenic defects in insulin action
Diseases of the exocrine pancreas
Endocrine disorders
Drug- or chemical-induced
Infections
Uncommon specific forms of immune-mediated diabetes
Other genetic syndromes sometimes associated with diabetes
Unclassified diabetes
This category should be used temporarily when there is not a clear diagnostic category especially close to the time of diagnosis of diabetes
Hyperglycaemia first detected during pregnancy
Diabetes mellitus in pregnancy
Gestational diabetes mellitus

4.3.1. **Type 1 Diabetes**

Type 1 diabetes (T1DM), accounting for 5% to 10% of diabetes diagnosed (12), is an immune mediated diabetes, an autoimmune disorder involving the destruction of the β cells by activated CD4+ and CD8+ T cells and macrophages infiltrating the pancreatic tissue. This process is mediated through autoantibodies directed to β cells antigens, glutamic acid decarboxylase-65 antibody, insulinoma antigen-2 antibody or insulin autoantibody being the most common (12–15). This type is also described as Insulin-dependent DM as the patients diagnosed with it, are dependent on insulin treatment for the rest of their lives (16).

4.3.2. **Type 2 Diabetes**

Type 2 diabetes (T2DM), accounting for 90% to 95% of diabetes diagnosed (17), consists of either β cell dysfunction or insulin resistance. There are numerous different aetiologies, with some still being unclear (11), for this type of diabetes, from increased insulin resistance due to obesity (18,19), to genetic predisposition (ethnicity (20), familial history (14), and age (22)). This form of diabetes frequently goes undiagnosed for many years because the hyperglycaemia develops gradually and at earlier stages is often not severe enough for the patient to notice any of the classic symptoms of diabetes (23). For most people with T2DM, insulin treatment is not required for survival but may be required to lower blood glucose to prevent chronic complications (24).

4.3.3. **Gestational diabetes mellitus**

Gestational diabetes mellites (GDM) has mainly 2 aetiological origins, physiologic insulin resistance of late pregnancy induced by human placental lactogen and tumour necrosis factor α, and insufficient insulin secretion for the registered insulin resistance (15), due to genetic predisposition. This definition applies to women who develop hyperglycaemia during the pregnancy, which usually resolves postpartum (13).

4.3.4. **Other types of diabetes**

As shown in Table 1, there are many different subtypes of diabetes. These result mainly from the discovery of the underlying molecular genetics, pathophysiological processes of previously unknown DM aetiologies. The subtypes include monogenic diabetes, which results from a diagnosed and identified mutation on a specific gene (25) , secondary diabetes (15), resulting from other diagnosed diseases such as chronic pancreatitis, cystic fibrosis, pancreatic neoplasia (26); many different drugs or chemicals can induce DM (27); and resultant of infectious diseases (28,29) .

4.4. Epidemiology of DM

Portugal was the fifth OCDE country with highest prevalence of DM (9.8%), only behind Mexico (13.5%) , Turkey (11.1%) United States of America (10.8%) and Germany (10.4%) (30). So, as mentioned before, few studies relate the epidemiologic state of DM in Portugal in 2019, with the latest numbers being from 2018, and, as such the Portuguese DM landscape, before COVID-19, will be described using data from 2018.

4.4.1. Prevalence

In 2018, from a population of 7.7 million, with ages comprised between 20 and 79 years, more than one million has DM (31). This number means that 13.6% of this population has DM. Also, in the last 10 years, 44% of the cases were newly diagnosed, while 55% were already diagnosed cases. It is also notable that, at the ages of 60 to 79 years, more than a quarter of the population has DM, with 30.4% for men and 24.2% for women, being this the age group with the highest prevalence.

4.4.2. Mortality of DM

Portugal registered a decrease in mortality in the past 10 years due to DM, with 2018 registering 4305 deaths directly due to DM, with the average age at death being 81.1 years. Despite this being a relatively low value, it still represents a 3.8% of total deaths resulted from DM.

4.4.3. In-Hospital Lethality

From a universe of 40.300 total deaths in Continental Portugal SNS hospitals, 10 701 were of people diagnosed with DM, representing a 26.6%, which means that more than 1 in 4 that died in a hospital, had DM (31). When observed more in depth, only 318 died with DM as the main diagnose (MD), 1.0%. While the in-hospital lethality for DM, either has main diagnose or secondary diagnose (SD), was of 6.0% (31).

4.4.4. Hospitalisations

2018 marked a decrease in number of discharges from hospital, when compared to 2017, from 165 747 discharges to 144621. Compared to the total number of discharges, DM represents 12.4%.

Each hospitalization for DM has a main diagnosis lasted on average 12.0 days, reflecting a total number of days spent hospitalised of 63 661 days. Meanwhile the average time spent hospitalised for DM as either primary or secondary diagnose was 10.7 days.

It is important to relay the 3 major complications, relevant to this study, numbers. In 2018, diabetic foot had a total number of 1378 hospitalizations, which lead to a total number of 928 amputations, with 583 and 345 minor and major amputations, respectively. The numbers

for stroke were a total of 6 317 hospitalizations, with DM has either main or secondary diagnosis, presenting a combined lethality, DM plus stroke, of 12.6%. Meanwhile, MI had a combined number of 3 608 hospitalisations, with DM, and a combined lethality of 7.0%.

4.5. Diagnosis

According to *Direção Geral de Saúde* (DGS) (32), since 2011, DM is diagnosed if one of the 4 criteria showed in Table 2 is verified. Clinical observations are made, and further criteria are added. If there is a single abnormal value (above the threshold) of either criteria a) or c), there should be made a second test after 2 weeks to confirm a DM diagnosis. Also, it is advised to only use one test of the 4 in Table 2, but in the case of both having above threshold values, DM diagnosis is confirmed, and in case of one discordant value, one above the threshold and one below, the abnormal value should be repeated in a second test.

Table 2. Diagnosis Criteria for DM according to DGS.

a) Fasting plasma glucose values of ≥ 7.0 mmol/L (126 mg/dL)
b) Characteristic symptoms random blood glucose ≥ 11.1 mmol/L (200 mg/ dL)
c) Glycated haemoglobin (HbA1c) ≥ 6.5% (48 mmol/mol)
d) 2-hour post-load plasma glucose ≥ 11.1 mmol/L (200 mg/dL), on oral glucose tolerance test (OGTT)

Furthermore, GDM has different threshold for fasting plasma glucose and different follow-up guidelines for the diagnosis. In the first pregnancy appointment, a fasting plasma glucose test is made, and the thresholds are ≥ 5.1 and < 7.0 mmol/L (≥ 92 mg/dL and < 126 mg/dL). If the fasting glucose level is lower than 92 mg/dL, a OGTT test is made at the 24 to 28 gestation weeks. If one or more of the following values are met, then it is a confirmed GDM diagnose.

Table 3. OGTT values for GDM Diagnosis according to DGS

At 0 hours, glucose value ≥ 5,1 mmol/L (≥ 92 mg/dL)
At 1 hour, glucose value ≥ 5,1 mmol/L (≥ 92 mg/dL)
At 2 hours, glucose value ≥ 5,1 mmol/L (≥ 92 mg/dL)

4.6. Complications e Comorbidities of DM

Uncontrolled hyperglycaemia resultant from DM can lead to different complications, through different mechanisms and depending on the chronicity of it. It can result in acute symptomatology, and in the most severe cases to ketoacidosis or a non-ketotic hyperosmolar state. However, if hyperglycaemia is present for a longer time, mainly 3 types of complications may emerge, depending on the mechanism of development (33). These three types are macrovascular, microvascular, and neurologic complications. As mentioned before, this will result in different organs or tissue damage, which lead to different comorbidities, with peripheral vascular disease (PVD), diabetic neuropathy, diabetic foot problems, diabetic retinopathy, and nephropathy (34).

In addition, another three major complications are Acute Myocardial Infarction (MI), stroke, and Diabetic Foot (DF) (35), and this matter will be further described.

Both MI and stroke result from cardiovascular disease (CVD), which develops from the formation of atherosclerotic plaques, resulting in atherosclerosis of blood vessels (36). DM alone, increases the chance of hospitalisation and death because of CVD by fourfold, when compared to non-DM patients (37,38).

Diabetic Foot results from a triad of complications, neuropathy, trauma with secondary infection, and arterial occlusive disease, all the above resulting or accentuated by DM (39). Due to a decreased sensation and proprioception of the foot, a repetitive trauma can lead to skin injury and perforation, with further development to ulceration and infection. If in an advanced state, with acute foot sepsis, a lower-extremity amputation (LEA) may be required, along with antibiotic treatment and arterial intervention (39). LEA can be subdivided into minor and major amputation, with minor amputation involving the foot or toes, and major amputation occurring more proximally to the leg (40).

5. Evaluating the Impact of COVID-19 in DM patients :2019 versus 2020 Data

This present section aims to compare data collected from continental Portugal SNS hospitals between 2020 and 2019. Before other official sources are made available, this report allows for a preliminary evaluation of the impact of COVID in the DM patients treatment landscape.

5.1. Casuistry

Concerning the number of patients that accessed SNS, a decline in hospital discharges between 2019 and 2020 was observed. In pre-COVID phase, 7 107 with diabetes as MD, were discharged, while in 2020 only 6 079 were (41). This represents a 14.5% difference. As shown in , in the first lockdown there was a sudden decrease in number of patients that accessed SNS hospitals, suggesting this was due to a focus shift to COVID-19 patients treatment, with a resulting cancellation and rescheduling of complementary diagnosis means, medical's appointments, surgical procedures and treatments. Throughout the rest of the year, as shown in Figure 1, the number of patient's discharges was still lower, when compared to the homologous period in pre-COVID.

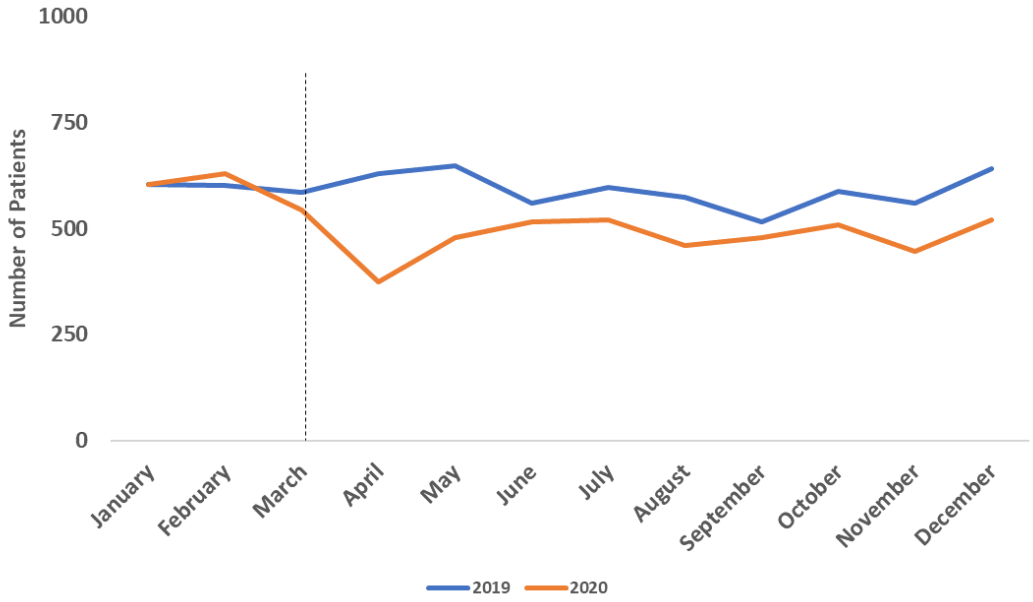

Figure 1. Number of discharges for patients with diabetes as MD, monthly variation in 2019-2020. The dashed line corresponds to March 18th, the beginning of COVID induced lockdown in Portugal (38). to

While with SD diabetes patients a 14.3% decrease was registered, from 144 662 discharged patients to 123 978 (34). The decrease was noted when the first lockdown was imposed, as shown in Figure 2.

In ambulatory care, there was also a decrease, with -12.0% number of patients with diabetes as MD. As in 2019 a total of 34 700 patients versus 30 524 patients in 2020 were in ambulatory care (34). In the first lockdown, a high drop on the number of patients in ambulatory care was registered, with a return to similiar numbers to the homologous period in 2019 in the summer months (Figure 3).

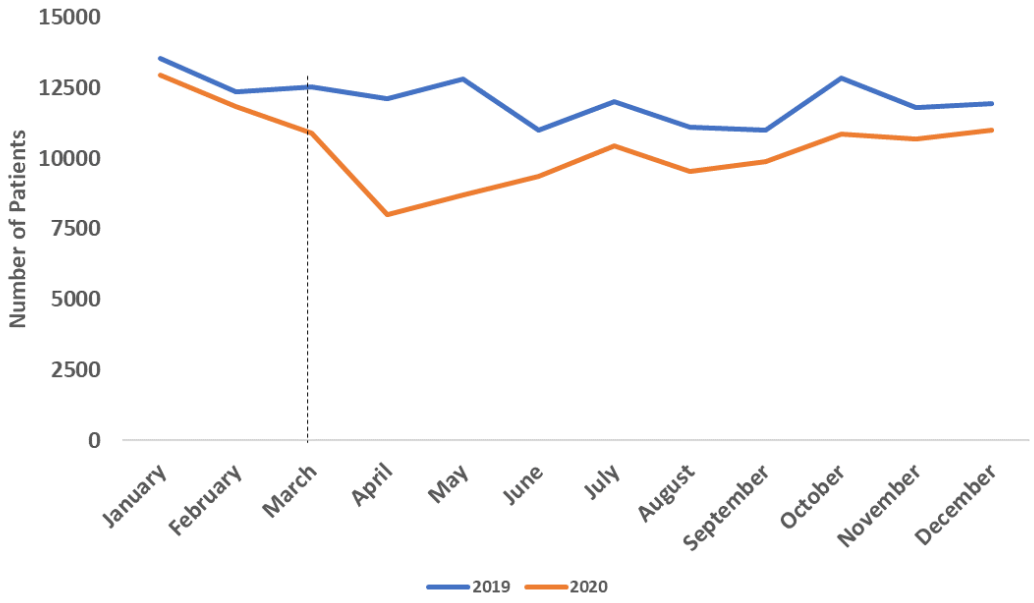

Figure 2. Number of discharges patients with diabetes as SD, monthly variation in 2019-2020. The dashed line corresponds to March 18th, the beginning of COVID induced lockdown in Portugal. Portugal.

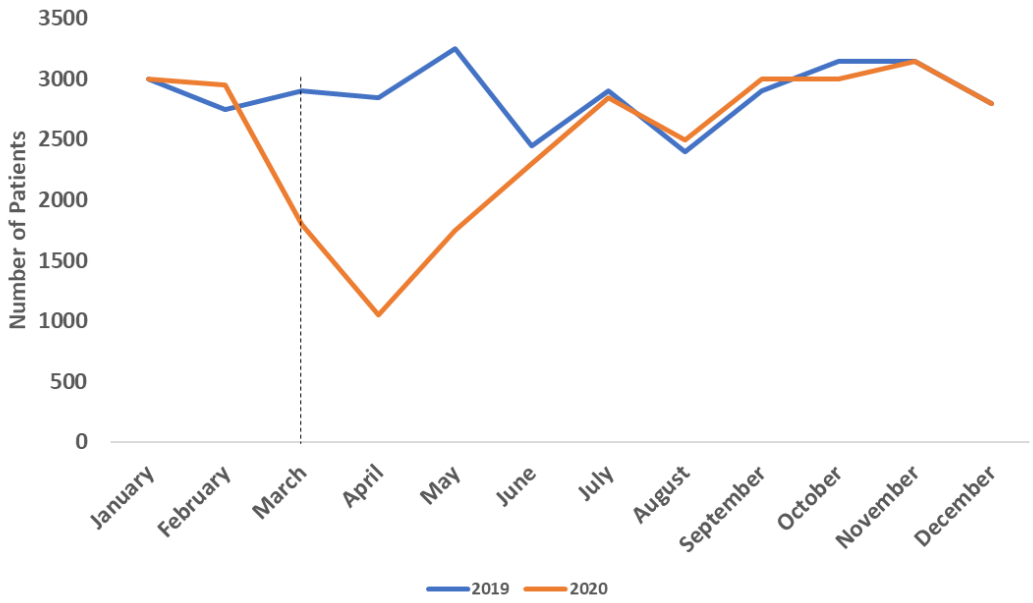

Figure 3. Number of patients with diabetes as MD in ambulatory care, monthly variation in 2019-2020. The dashed line corresponds to March 18th, the beginning of COVID induced lockdown in Portugal.

However, the difference was greater with diabetes as SD patients. With a decrease from one year to the other, from 32 809 to 25 373, a 22.7% variation in the numbers (41). The same trend as hospital discharges was seen in SD diabetes patients in ambulatory care, throughout 2020, with a higher drop in the months following the first lockdown (Figure 4).

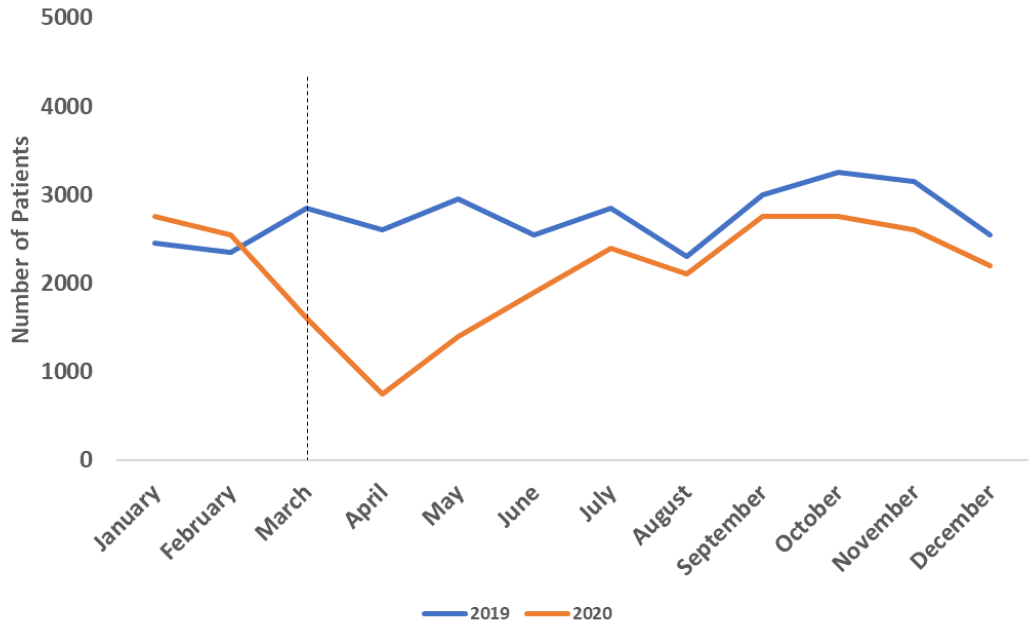

Figure 4. Number of patients with diabetes as SD in ambulatory care, monthly variation in 2019-2020. The dashed line corresponds to March 18th, the beginning of COVID induced lockdown in Portugal.

When comparing to the amount of procedures made on DM patients in SNS hospitals, to the amount of total procedures in SNS hospitals (given as activity percentage), between 2019 and 2020, there is a clear decline in activity in March and April (Figure 5), especially in ambulatory patients, due to the first lockdown. However, throughout the rest of the year, a clear increase was noted in activity, between years, meaning that despite the lower ?? numbers of DM patients in SNS in 2020, when comparing the relative amount of DM to the total number of SNS patients, there were more DM related patients than in 2019, if the total number of SNS patients were the same in 2019 and 2020.

The percentage of DM in hospitalizations as MD, suffered a minor change, in both years presenting a 0.8% of activity, while in ambulatory care there was a change from 4.6% to 5.5%, an increase of 18.2% in a year (41).

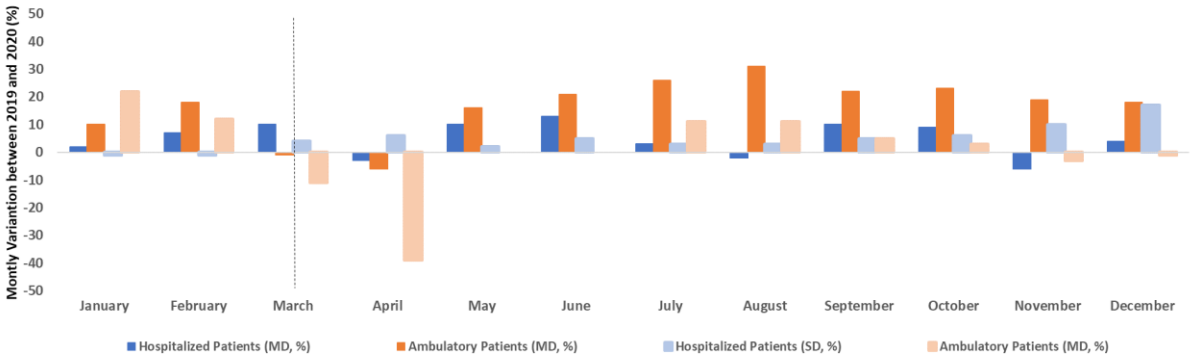

Figure 5. Variation in activity percentage of DM patients in relation to total SNS patients, from 2019-2020. The dashed line corresponds to March 18th, the beginning of COVID induced lockdown in Portugal.

In SD, a similar change as MD was shown in hospitalisations activity percentage, with an increase from 4.4% to 4.5%, a 4.8% variation. While in ambulatory care, a different variation was present, a much lower increase amounting to only 3.9 in percentage points, from 16.4% in 2019, to 17.2% in 2020 (34). In total, when considering either MD or DS in DM patients, there was a 4.8% increase in hospitalised DM activity percentage (17.2% in 2019 vs 18.1% in 2020), and a 11.2% increase in ambulatory care activity percentage for DM patients (9.0% in 2019 vs 10.0% in 2020) (34).

5.2. The complexity of each case of DM patient

In the present study, the complexity of each case of DM patient in SNS will be shown through the case mix index and the average cost per patient.

The index case mix for DM saw an increase in both MD and SD patients, from 1.402 to 1.520 for SD (2019-2020), a 14.4% increase, and from 1.273 to 1.456 for SD (2019-2020), an 8.4% increase. Meaning a higher complexity and resource allocated to DM patients, when compared to 2019. In terms of average cost per patient (ACP), a clear increase in cost was noted in both DP and SD patients, with DP rising from 2 909€ per patient to 3 327€ per patient (14.4% of increase), and a 3 203€ per patient to 3 474€ per patient (8.4% of increase), respectively (41). These values are in accordance with the increases seen in case mix index, indicating an actual increase in complexity of DM patients care in 2020, when compared to 2019. In Figure 6 there is a clear correlation in the increase of the case mix index and ACP, further supporting this hypothesis.

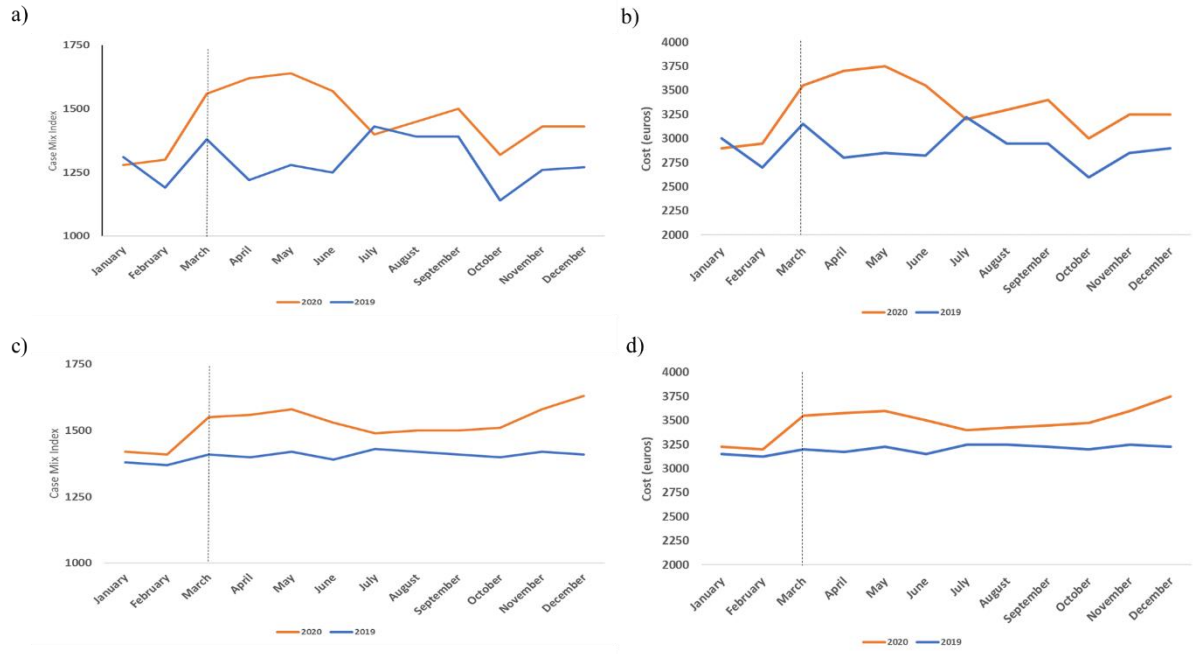

Figure 6. Case mix and ACP monthly variation in 2019 and 2020. a) Case mix monthly variation for MD patients; b) ACP monthly variation for MD patients; c) Case mix monthly variation for SD patients; d) ACP monthly variation for SD patients. The dashed line corresponds to March 18th, the beginning of COVID induced lockdown in Portugal.

Even when compared to the total ACP, there is a tendency that DM patients cost more than the average patient, further reinforcing the increase of complexity of the DM patient case in the SNS, when compared to pre-COVID times. This increase in complexity implies an

increase in the severity of each hospitalisation, with the higher cost per patient corroborating this analysis.

5.3. Hospitalisation Period

Hospitalisation period and average hospitalisation period data corroborates the previous hypothesis about the complexity of each case of DM patient during COVID increased when compared to the pre-COVID.

Starting with the total amount of hospitalisation days, on MD patients, a decrease was registered, from a total of 90 719 days in 2019 to 79 500 days in 2020, a 12.4% decrease. In the same direction were the SD patients, with a 11.0% of decrease, from 1 567 000 days to 1 394 476 days, from 2019 to 2020 respectively (41). The total amount of days goes in tandem with the lower number of DM patients in SNS after the first lockdown.

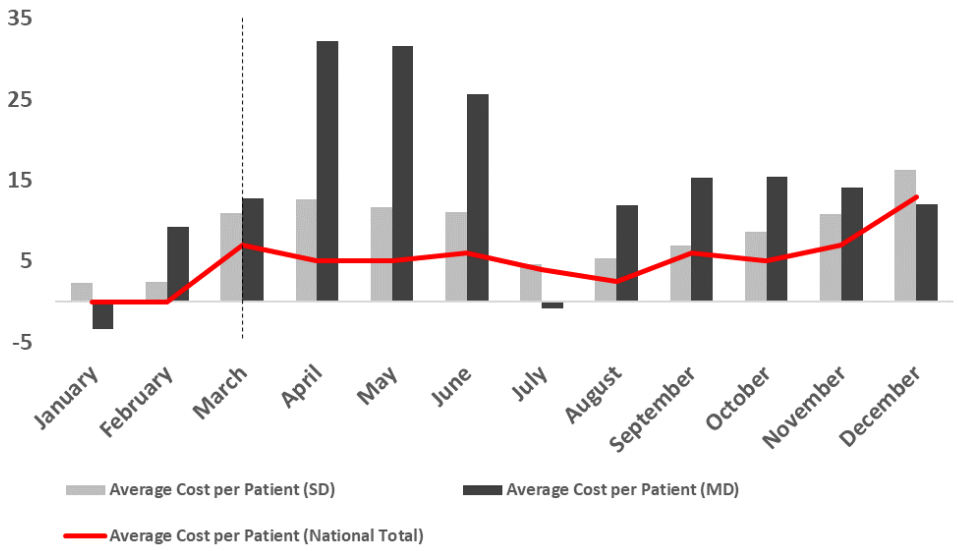

Figure 7. Average cost per patient variation comparison between 2019 and 2020, with the total ACP nationally variation, in the same period. The dashed line corresponds to March 18th, the beginning of COVID induced lockdown in Portugal.

Despite the decrease in of total hospitalisation days on MD patients, when compared to the total amount of hospitalisation in SNS (Figure 8), a smaller variation is present, with only a 4.0% of increase on the weight of DM hospitalisation day in total hospitalisation days, from 1.27% to 1.32%, in 2019 and 2020, respectively (41).

Only a slightly variation was noted on SD patients, where a rise from 21.9% in 2019 to 23.1%, meant a 5.6% variation (41) as seen in Figure 10.

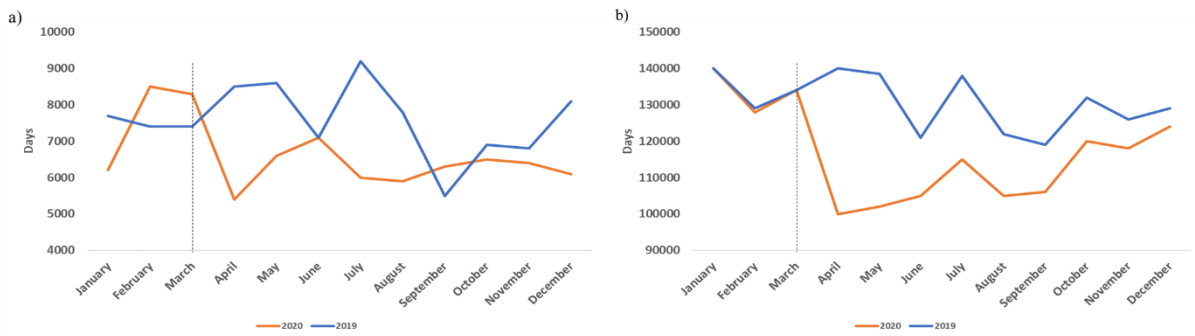

Figure 8. Total Hospitalisation period, in days, of DM patients from 2019 and 2020. a) Total hospitalisation period for MD patients; b) Total hospitalisation period for SD patients. The dashed line corresponds to March 18th, the beginning of COVID induced lockdown in Portugal.

Lastly, the average hospitalisation period further strengthens this trend of an increased severity of the average DM hospitalisation. The average hospitalisation period for MD patients increased from 12.8 days to 13.1 days, in 2019 and 2020, respectively (41). For SD patients this value changed from 10.8 days to 11.2 days, respectively. Although a lower increase when compared to pre-COVID data, nevertheless there was an increase (Figure 11).

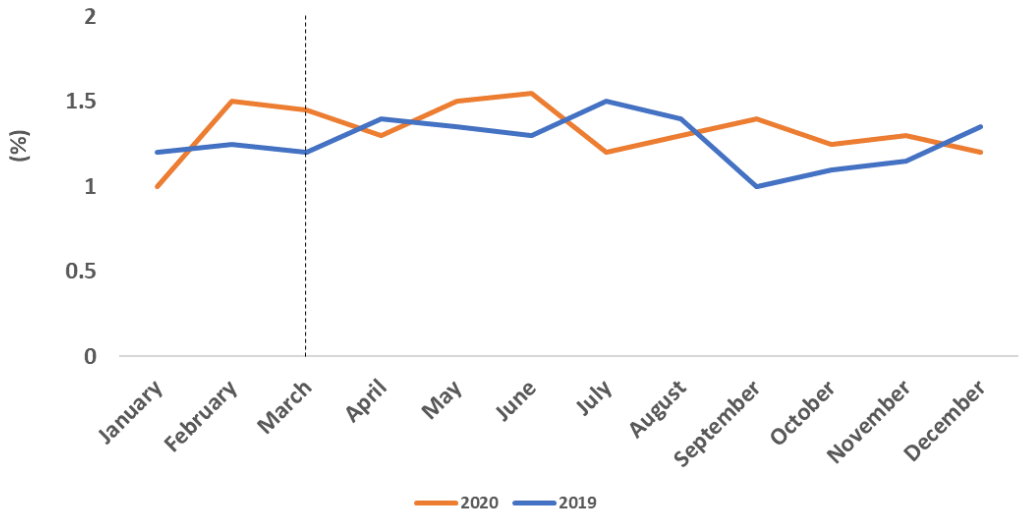

Figure 9. Diabetes as MD related hospitalisation days weight in total hospitalisation days from 2019 and 2020. The dashed line corresponds to March 18th, the beginning of COVID induced lockdown in Portugal.

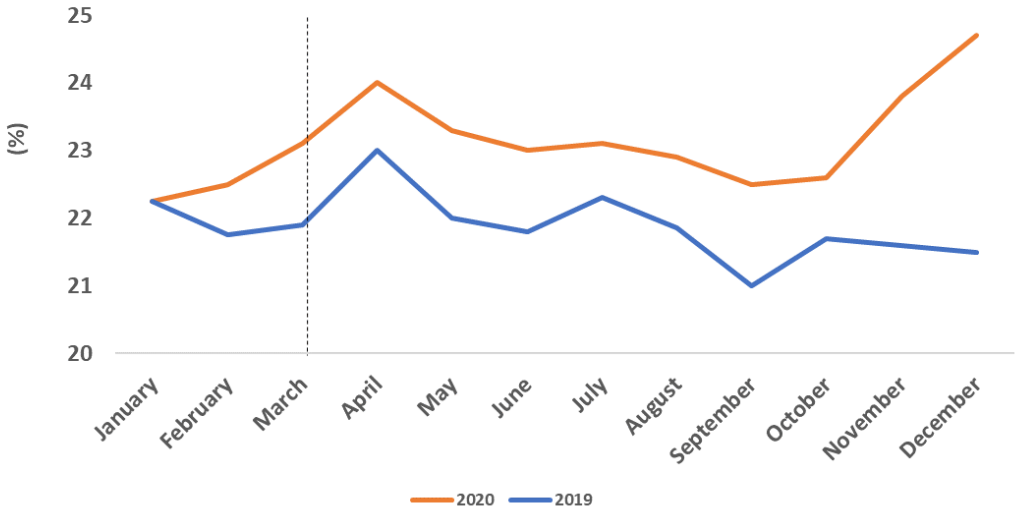

Figure 10. Diabetes as SD related hospitalisation days weight in total hospitalisation days from 2019 and 2020. The dashed line corresponds to March 18th, the beginning of COVID induced lockdown in Portugal.

5.4. Mortality

To further support the hypothesis of increased severity in DM patients in SNS in the first pandemic year, both the absolute number and the relative number of deaths in SNS due to DM increased, with the absolute number reaching 452 and 14 995, for MD or SD patients respectively, in 2020. When compared to 2019 values, of 423 and 14 235 for MD diabetes and SD diabetes patients.

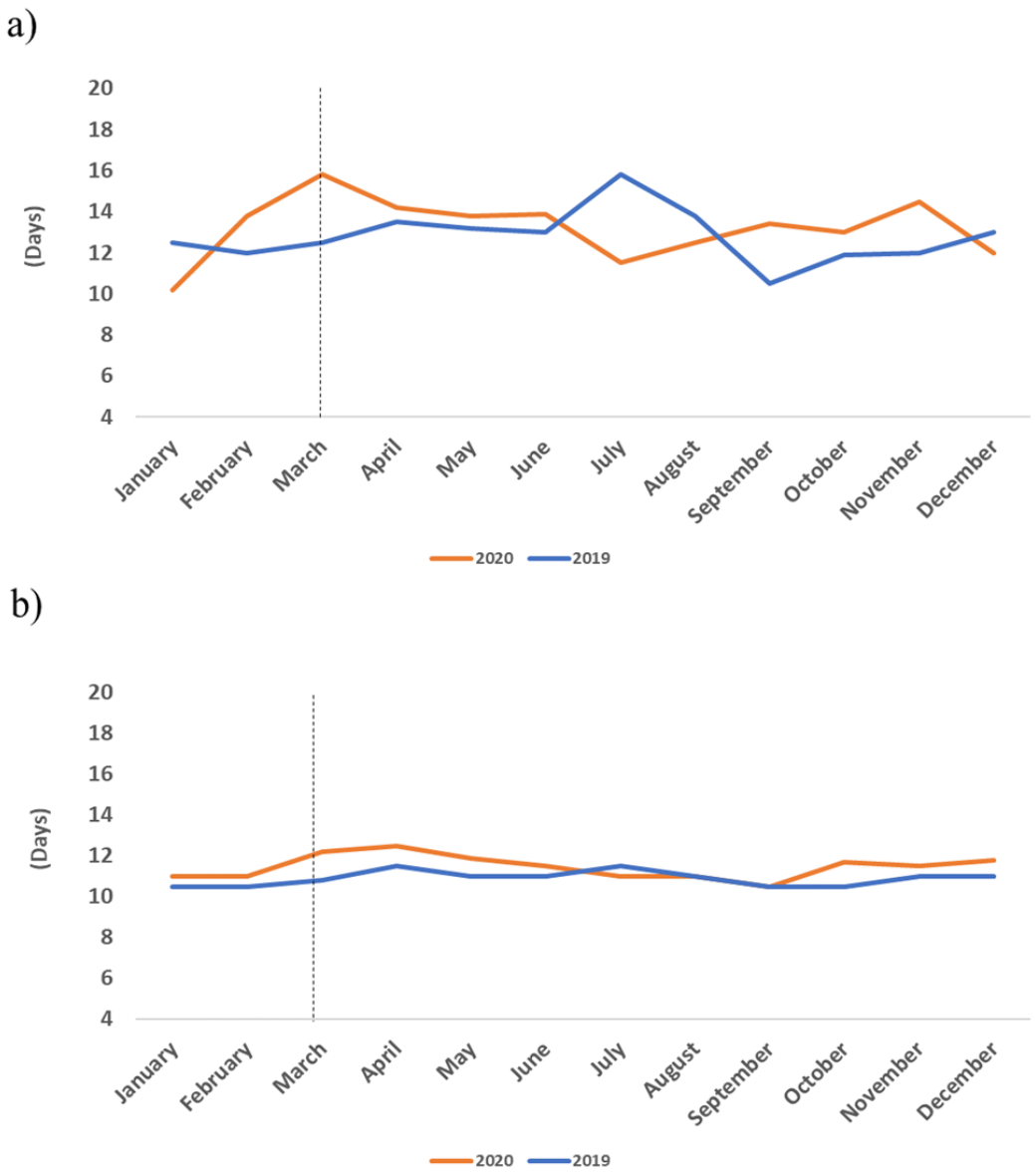

Figure 11. Average hospitalisation period, in days, of DM patients from 2019 and 2020. a) Average hospitalisation period for MD patients; b) Average hospitalisation period for SD patients. The dashed line corresponds to March 18th, the beginning of COVID induced lockdown in Portugal.

The total number of deaths in SNS decreased 2.2% in 2020 when compared to 2019. The relative weight of DM deaths to total deaths in SNS suffered an increase of 9.3% and 7.4% in 2020, in MD diabetes and SD diabetes, respectively (41). Those values mean a higher mortality resultant of DM in the pandemic period.

Associated to the number of deaths from DM, the numbers of in-hospital lethality, shown in Figure 12, emphasizes the severity of the average DM hospitalisation, with a major

increase in lethality between 2019 and 2020. On MD patients, a 24.9% of increase in lethality (6.0% to 7.4%, Figure 12), and a 22.6% increase on SD patients (9.8% to 12.1%, Figure 12).

5.5. Complications 2019 versus 2020

In 2020, according to the study (41), there was an increase of total complications in SNS hospitals by 3.3%. To further describe the severity of DM patients, an analysis was made of the number of hospitalisations due to diabetic foot and the number of minor and major amputations of lower members on DM patients. In 2020, there was a decrease of 18.6% in MD patients, from 102 to 83 patients; however, there were more SD patients in 2020 when compared to 2019, 1409 to 1335, respectively, translating into a 5.5% of improvement (41), with an overall increase of 3.7%.

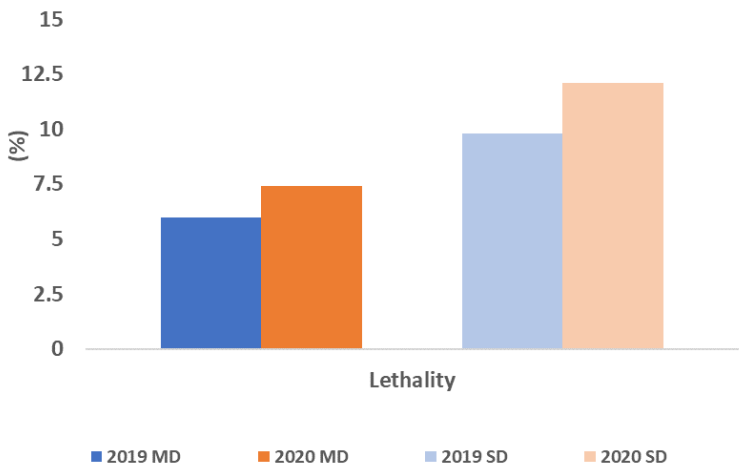

Figure 12. In-Hospital Lethality of DM comparison of 2019 and 2020 MD and SD patients.

The analysis of the number of amputations showed a decrease in the level amputations, either minor or major, in all patients, with a decrease of 11.7% on the total amputations, and reductions of 15.4% and 8.1%, in minor and major amputations, when compared to the homologous period of 2019 (41). Table 4 depicts the absolute numbers.

Table 4. Number of minor and major amputations on MD and SD diabetes patients

	Minor		Major	
	MD	SD	MD	SD
2019	673	999	415	867
2020	597	877	423	801

As Table 4 shows, either minor or major, and MD or SD patients, there is a reduction in the number of these types of procedures, apart from major amputations on MD patients, with an increase of 1.9%. The variation in SD patients' number of total amputations was of -10.1%, while the MD patients showed -6.3% in total number of amputations. Even though there was a decrease in amputations in DM patients, when compared to the total amount of amputations in SNS, there was an actual increase in the comparative weight of amputations in DM patients.

Other pathologies were studied, in the number of hospital discharges, number of deaths, in-hospital lethality, hospitalisation days and average hospitalisation days.

Relative to stroke there was an insignificant increase in the number of patients with diabetes as MD and stroke as SD, 35 to 36 patients, and an actual decrease of patients with diabetes as SD and stroke either as MD or SD, from 7 556 to 6 654, from pre-COVID to COVID (34). The number of deaths changed by a two-factor, from 6 to 11, on diabetes as MD and stroke as SD patients, an 83.3% increase, but a small increase in patients with diabetes as SD and stroke, either as MD or SD, 938 to 1019, in 2019 and 2020, respectively (41). This fact results in a growth of in-hospital lethality of diabetes as MD patients and stroke either as MD or SD, from 17.1% to 30.6%, 78.2 percentual points change. This means an increase of severity, and loss of controlled diabetes in an increasing number of patients. The total days of hospitalisation and average days of hospitalisation to these patients, support this claim, with an increase from 866 to 1385 days, with the average growing to 38.5 days, from 24.7 days in 2019. Meanwhile, in patients with diabetes as SD and stroke, either as MD or SD, there was a decline from 2019 to 2020 in total amount of days (41), from 144 590 to 103 597 days. The average had a negligible variation, from 15.2 to 15.6 days (41).

MI patients were also analysed, and contrary to stroke patients, in both types of patients, diabetes as MD and MI as SD, and diabetes as SD and MI either as MD or SD, there was a decline in numbers. Specifically, it changed from 2019 to 2020, 74 to 73, and 6 316 to 5 375, respectively. The decrease in patients with DM as MD and MI as SD was insignificant when

compared to the total amount of patients with DM and MI. In contrast, death counts were different, with an 81.8% increase in deaths on diabetes as MD and MI as SD patients, from 11 to 20, while the number of deaths on diabetes as SD and MI either as MD or SD patients, suffered a non-significant change, from 736 to 727 (34). Meaning, an increase in lethality of 84.3% in patients with DM as MD and MI as SD. The total days of hospitalisation decreased in both types of patients, from 1 280 to 1 167, and 68 013 to 55 667, respectively (41). The variations between years were, in percentage, of 8.8 and 18.2 respectively. The average days of hospitalisation of MI and DM patients also decreased, from 16.3 days to 16.0 days, 7.6% decline, in diabetes as MD and MI as SD patients, and 10.8 days to 10.4 days, a 3.8% decline.

6. Discussion

The first lockdown brought a decrease in the number of hospitalisations and ambulatory care, provided to DM patients between March and April 2020 in SNS hospitals. This fact was due to 3 main factors. A shift of focus of SNS resources to COVID-19 patients, the lockdown in itself, reducing the ability of people to search for healthcare, and a general apprehension by the population to look for healthcare when needed. However, DM patients still needed medical follow-up to manage their disease. But with several restrictions on SNS hospitals, DM patients suffered, with a higher percentage of activity in hospitalisations. This meant that DM patients were not able to do a proper management of DM in larger numbers.

An increase in complexity and severity on the average DM patient is supported by the data shown. The increase of case mix index by 15%, meaning a higher allocation of resources in hospitals to DM patients, translates to a higher average cost per patient, also registering an increase of 30%. Higher resources spent, means more procedures, which results from the higher severity of DM. Although there were less patients, they were in a worse state when hospital care was sought.

With a decrease in total patients, a decrease in number of hospitalisation days was also observed. However, the increase in average hospitalisation days of the DM patient, further corroborates the higher severity and complexity of the patients looking for healthcare. With the relative weight of hospitalisation days of DM related cases also increasing, evidencing the impact of COVID on DM patients.

The severity of DM resulted in a higher mortality and lethality, despite the decrease in general mortality in the SNS. The reasons for the general decrease in mortality must be further studied to better understand this phenomenon, whether it resulted from an actual decrease in total mortality, or simply due to the decreased search for hospital care and consequent home deaths. In-hospital lethality grew almost by a quarter in both MD and SD diabetes patients, 24.9% and 22.6%, respectively. This significant increase clearly suggests, once more, an increase of severity in DM.

Further complications were analysed; DF showed a higher increase, when compared to the total surge of complications in SNS, resulting in a growth in relative weight of DM associated complications. Despite a suggestive decline in amputations in SNS, either total amputations or DM related ones, the decrease of 6.3% and 10.1% in MD and SD diabetes patients, when compared to a decrease of 11.7% in total amputations, point to an actual increase in relative weight of DM related amputations. Once again, DM patients suffering from a worse follow-up in primary care, resulting in an uncontrolled disease management.

DM associated stroke mortality, with DM as MD, almost doubled in 2020, while the total amount of cases stayed relatively the same. A similar conclusion can be made through the data shown of DM as SD and stroke patients. Even though the increase in mortality was much smaller, closer to 9%, and the total amount of cases saw a decline. This conclusion being the higher severity of DM patients' complications, resulting in higher lethality of stroke associated to DM. MI with DM patients showed a very similar result, with the mortality rate almost doubling, with lethality of DM as MD and MI patients jumping almost 90%.

The data from this research allows for a first evaluation of the impact of the COVID pandemic in the diabetic patient in Portugal. Taking the described results and conclusions into consideration it unveils a grim reality. To sum-up, the data points to a decrease in quality of primary care of diabetes patients.

In a systematic review regarding outcomes of patients with DM during COVID-19 worldwide, in Far and Middle East regions, a higher mortality rate was reported (42). It is also highlighted in this study, that patients with overall better control of diabetes had significantly improved outcomes in terms of mortality (42).

As seen in other studies, throughout Europe, COVID-19 had a negative impact on DM patients, In Switzerland, a primary care cohort study, 49% of DM patients did not consult their general practitioner, with a decrease of patients able to reach target HbA1c (43). In Spain, a

study comparing HbA1c in DM patients before and during COVID-19, showed a decrease in half in HbA1c testing during lockdowns, and, to a lesser extent, a decrease in testing HbA1c in partial lockdowns (44). In Italy, a comparison between older population either healthy or with DM, showed an increase in exercise, reduced alcohol consumption and better nutrition, which might have led to better outcomes (45). Despite this, an increase in hospitalisations, diagnostic tests, examinations with specialist prescription suggest a decrease in primary care accessibility (45). With a lack of testing, glycaemia levels might have destabilized in these patients, leading to either acute or long-term complications, increasing a secondary healthcare necessity. Reinforcing the main conclusion of this dissertation.

However, this study lacks any information about the primary care of DM patients, an important aspect of diabetes treatment, mainly focusing on secondary care in hospitals. Also, only information regarding to the first COVID-19 year, an adaption period to the pandemic, with a lack of long term follow up is shown.

On a contrary note, some studies have shown a stabilisation or even improvement in HbA1c levels, during the lockdowns, especially in younger T1DM patients. In Portugal, a study showed that patients with ages comprised between 3 and 18 years, no significant change was reported in HbA1c levels (46). While in the UK, HbA1c levels were shown to drop, possibly being related to a more predictable routine during COVID-19 lockdowns (47).

This analysis should lead us to further studies to better understand and describe this complex problem. The continuous lack of released official data can only lead to a deteriorating medical care for DM patients. Considering only the first pandemic year has yet been analysed, with no data released from 2021. The DM landscape maybe be significantly worse than described in this master dissertation. COVID degraded the outcomes in DM patients, and apparently the policy makers are yet to take note. It is imperative to prospectively evaluate all diabetic patients in SNS, to help recuperate the healthcare once provided, and even improve it.

Luckily, there are moves being made, with the release of *Um PRR para a Diabetes – A Oportunidade é Agora* by the APAH (48). This report delineates a future plan to improve primary care, follow-up, resource allocation, and prevention, with the goal to improve health outcomes of DM patients. Still, it is up to the policy makers to further develop and implement strategies to this end.

7. Conclusion

In sum, the data presented regarding the Portuguese diabetic patient, points to a decrease in these patients' health during the first year of the pandemic. This is supported by higher activity of diabetic patients in SNS hospitals. An increase in complexity of each case of diabetes mellitus related hospitalisation, with higher case mix index, higher per patient cost coupled with higher average hospitalisation period, which ultimately lead to a higher mortality and lethality for hospitalised diabetic patients. Further complications were noted on these patients. With more diabetic foot appointments, higher lethality for both stroke and MI in diabetic patients.

Many studies in different European countries showcased a decline in health outcomes in diabetic patients during the pandemic, either decreases in primary care outputs, with lower health outcomes, or an increase in hospitalisations in certain populations, stressing the negative impact of the COVID pandemic on diabetes mellitus patients.

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