

## ORIGINAL ARTICLE

# New diagnoses of type 1 diabetes mellitus in children during the COVID-19 pandemic Regional multicenter study in Spain



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## KEYWORDS

Type 1 diabetes mellitus;  
Paediatric age;  
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COVID-19

## Abstract

**Introduction:** The aim of this study is to determine whether during the year 2020, coinciding with the COVID-19 pandemic, there has been an increase in the incidence of diabetes mellitus in children compared to the previous 2 years. It is also to find out if lockdowns and the difficulty providing face-to-face care in the health system have led to children showing more severe symptoms at the time of diagnosis.

**Material and methods:** Retrospective observational multicenter study of the province of Tarragona where data is collected from new diagnoses of type 1 diabetes mellitus in patients under the age of 15 during the year 2020 and compared with years 2018 and 2019.

**Results:** The number of new diagnoses of type 1 diabetes during 2020 was 37 cases compared to 2019 and 2018 which was 23 and 29 respectively. The median age at onset was 9 years, 54% males. There was an increase in new diagnoses in the range of 10 to 14-year-olds, with a decrease in the range of 0–4 year-olds. In 2020, the incidence in the group of patients with families from the Maghreb area rose from 52.2 cases per 100,000 population/year ( $c/10^5$  p-y) in 2019 to 135.8 in 2020. Compared to the previous year, 2020 showed a significant decrease of ketoacidosis at the onset. None of the patients was diagnosed with COVID-19 during admission.

**Conclusion:** During the year 2020 concurring with the COVID-19 pandemic, there was an increase in the number of new diagnoses of type 1 diabetes mellitus in pediatrics. Contrary to expectations, the presentation did not worsen by decreasing the proportions of ketoacidosis at onset. This data would suggest that, although attendance in the different health facilities dropped drastically during the year 2020 at the expense of virtual consultations, health systems and families were able to detect the symptoms of the disease early.

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## PALABRAS CLAVE

Diabetes mellitus tipo 1;  
Edad pediátrica;  
Cetoacidosis;  
COVID-19

## Nuevos diagnósticos de diabetes mellitus tipo 1 en niños durante la pandemia COVID-19. Estudio multicéntrico regional en España

### Resumen

**Introducción:** El objetivo de este estudio es determinar si durante el año 2020 coincidiendo con la pandemia COVID-19 ha habido un incremento en la incidencia de diabetes mellitus en la infancia respecto a los últimos 2 años. Debido al confinamiento domiciliario y la dificultad en la asistencia presencial en los centros de salud se analiza si han debutado con síntomas más graves.

**Material y métodos:** Estudio retrospectivo observacional multicéntrico de la provincia de Tarragona donde se recogen los datos de los nuevos diagnósticos de diabetes mellitus tipo 1 en pacientes menores de 15 años durante el año 2020 y se comparan con los años 2018 y 2019.

**Resultados:** El número de nuevos diagnósticos de diabetes mellitus tipo 1 durante el año 2020 fue de 37 casos en comparación con los años 2019 y 2018 que fueron de 23 y 29 respectivamente. La mediana de edad al debut fue de 9 años, 54% varones. Hubo un incremento de debuts en la franja de 10 a 14 años con una disminución en el rango de 0 a 4 años. En el año 2020 hubo un aumento de la incidencia en el grupo de pacientes con familias procedentes de la zona del Magreb, desde 52,2 en 2019 a 135,8 casos/100,000 habitantes y año ( $c/10^5$  h-a) en 2020, especialmente en el subgrupo de 10 a 14 años. Respecto al año anterior, en 2020 se evidenció una disminución importante de niños al debut con cetoacidosis. Ninguno de los pacientes fue diagnosticado de COVID-19 durante el ingreso.

**Conclusión:** Durante el año 2020 coincidiendo con la pandemia COVID-19 hubo un incremento en el número de nuevos diagnósticos de diabetes mellitus tipo 1 en pediatría. Al contrario de lo esperado, la forma de presentación no empeoró, disminuyendo las presentaciones en forma de cetoacidosis. Este dato sugeriría que, aunque la presencialidad en los diferentes centros de salud bajó de manera drástica durante el año 2020 a expensas de las consultas virtuales, los sistemas de salud y las familias supieron detectar de manera precoz los síntomas de la enfermedad.

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## Introduction

The year 2020 has been marked by the COVID-19 pandemic. From 21 March to 26 April, Spain was under strict lockdown. This was followed by a progressive easing of restrictions until the state of alarm ended on 21 June. From October, regional lockdown restrictions of territorial confinement were reintroduced. The fear of going out into the street and getting infected, added to the restrictions on face-to-face care in health centres, led to a drastic drop in consultations in the different paediatric emergency services.<sup>1,2</sup>

Previous publications have not documented a significant increase in new diagnoses of type 1 diabetes mellitus (DM1).<sup>3-5</sup> However, a German study on a national scale reported an increase in the incidence of new cases in 2020. Still, it did not differ significantly from that predicted according to the trend observed between 2011 and 2019.<sup>5,6</sup>

Regarding the severity of presentation at the onset of DM1, most publications report a significant increase in diabetic ketoacidosis (DKA) and severe DKA, predominantly at younger ages.<sup>2-5,7</sup>

The objectives of this study were to describe the incidence and severity of the onset of DM1 in the province of Tarragona during the first year of the COVID-19 pandemic compared to previous years.

## Material and methods

The study was an analytical, observational, retrospective, multicentre study in the province of Tarragona (Spain) of the newly diagnosed cases of DM1 in children up to 15 years of age during the years 2018–2020. The Clinical Research Ethics Committee approved the study.

There are three paediatric diabetes units in the province of Tarragona, at Joan XXIII Hospital in Tarragona/Pius Hospital in Valls, Sant Joan Hospital in Reus and Verge de la Cinta Hospital in Tortosa.

All patients under 15 years of age who attended a hospital in the province of Tarragona with an initial diagnosis of DM1 during the years 2018–2020 were included.

The following data were obtained from the medical records: age, sex, origin, severity at onset according to analytical parameters, PCR COVID-19. The same data was obtained (except PCR COVID-19) for the beginning of 2018 and 2019. For the calculation of the incidence rates, the demographic data of the general population of the Institut d'Estadística de Catalunya (IDESCAT) [Institute of Statistics of Catalonia] were accessed.

DM1 and DKA criteria were defined according to the International Society for Pediatric and Adolescent Diabetes (ISPAD) criteria.<sup>8,9</sup> For the comparison of quantitative varia-

**Table 1** Characteristics of paediatric patients newly diagnosed with DM1 in the province of Tarragona from 2018 to 2020.

	2020	2019	2018	p
<i>Total cases</i>	37	23	29	0.190
Cases at Joan XXIII/Pius de Valls hospitals	21	10	7	<b>0.013</b>
Cases at Sant Joan de Reus Hospital	7	6	12	0.289
Cases at Verge de la Cinta de Tortosa Hospital	7	7	8	0.956
<i>Overall incidence rate</i>	29.1	18	22.7	0.189
<i>Total population</i>	126,983	127,293	127,636	
<i>Incidence rate in the Maghrebi population</i>	132	52.2	74.5	0.125
<i>Maghrebi population</i>	9,842	9,570	9,386	
<i>Age, median (IQR)</i>	9 (1–14)	9 (1–14)	8 (0–14)	0.729
<i>Age groups</i>				
0–4 yrs	7 (18.9)	5 (21.7)	9 (31.0)	0.564
5–9 yrs	14 (37.8)	10 (43.5)	8 (27.6)	0.416
10–14 yrs	16 (43.2)	8 (34.8)	12 (41.4)	0.263
<i>Maghrebi</i>				
Total	13 (35.1)	5 (21.7)	7 (24.1)	0.125
0–4 yrs	3 (8.1)	2 (8.6)	2 (6.8)	0.866
5–9 yrs	3 (8.1)	2 (8.6)	3 (10.3)	0.882
10–14 yrs	7 (18.9)	1 (4.3)	2 (6.8)	<b>0.004</b>
<i>Gender</i>				
Male	20 (54.1)	9 (39.1)	18 (62.1)	
Female	17 (45.9)	14 (60.9)	11 (37.9)	
<i>DKA</i>				
Total	12 (32.4)	13 (56.5)	9 (31.0)	0.111
0–4 yrs	4 (10.8)	7 (30.4)	2 (6.9)	0.253
5–9 yrs	6 (16.2)	2 (8.7)	3 (10.3)	0.864
10–14 yrs	2 (5.4)	5 (21.7)	4 (13.8)	0.162

Data are expressed in n (%).

Statistically significant data ( $p < 0.05$ ) are in bold.

DKA: diabetic ketoacidosis; IQR: interquartile range.

bles, the Kruskal–Wallis ANOVA H test was used; for the comparison of qualitative variables, Fischer's exact test was used.

The level of statistical significance used was 0.05.

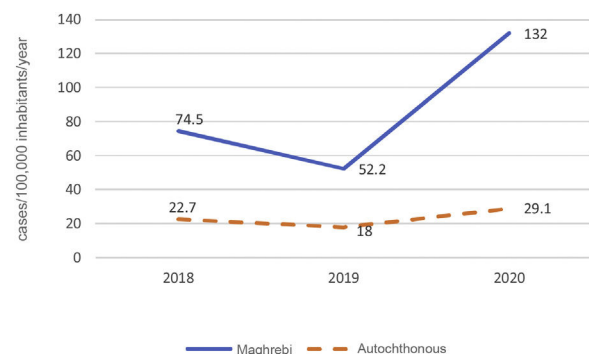
Statistical analysis was performed with the SPSS Statistics 21 program.

## Results

**Table 1** describes the general characteristics of the sample. Between 1 January 2020 and 31 December 2020, 37 children between 0 and 14 years old were diagnosed with DM1; 60.8% and 27.6% more than in 2019 and 2018, respectively ( $p = 0.190$ ). This increase mainly occurred at one of the units (Hospital Joan XXIII/Pius Hospital de Valls) with 23 cases ( $p = 0.013$ ).

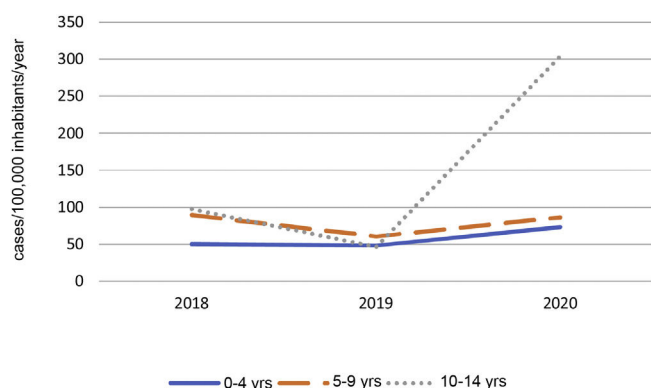
The incidence rate in the province of Tarragona in 2020 increased compared to previous years, being 29.2 cases per 100,000 inhabitants in 2020, 18.1/100,000 in 2019 and 22.9/100,000 in 2018 (95% CI: 17.1–29.7) ( $p = 0.189$ ).

The incidence rate in children with families from the Maghreb area was 132.1 per 100,000 inhabitants in 2020; 52.2/100,000 in 2019, and 74.6/100,000 in



**Figure 1** Evolution of the incidence rate of DM1 in the province of Tarragona in the Maghrebi population compared to the autochthonous population.

2018 (95% CI: 39.7–133). In the native population, it was 22.7 per 100,000 inhabitants in 2020; 18/100,000 in 2019 and 29.1/100,000 in 2018 (95% CI: 15.1–21.1) (**Fig. 1**). In the Maghrebi population, this incidence increases and is statistically significant ( $p = 0.004$ ) in the subgroup aged 10–14 years: 303.8 per 100,000 inhabitants in 2020; 46.9/100,000 in 2019; 98/100,000 in 2018 (95% CI: –4.32 to 303.47), remaining stable in the group aged



**Figure 2** Evolution of the incidence rate of DM1 in the province of Tarragona in the Maghrebi population by age group.

5–9 years (86.9/100,000 in 2020; 61/100,000 in 2019; 89.7/100,000 in 2018; 95% CI: 61.32–97.08) and children under 4 years of age (73.4/100,000 in 2020; 48.1/100,000 in 2019; 50/100,000 in 2018; 95% CI: 41.21–73.13) (Fig. 2).

If we analyse the sum of onsets in the three years in Maghrebi children and compare it with the sum of onsets in autochthonous children, we can observe a greater risk in the Maghrebi population of developing DM1 ( $p=0.00$ ).

Median age at onset was nine years in 2020 (interquartile range: 1–14 years), nine years in 2019 (interquartile range: 1–14 years), and eight years in 2018 (interquartile range: 0–14 years) ( $p=0.729$ ). If we separate the children by age groups, we can see that the onsets have progressively decreased in the subgroup of 0–4 years while increasing in the range of 10–14 years, which accounted for 43% of new diagnoses in 2020.

In 2020, 54.1% of onsets of DM1 were in the male sex and 45.9% in the female sex.

DKA as a form of presentation was observed in 12 of 37 patients (32.4%) in 2020, 13 of 23 patients (56.5%) in 2019, and nine of 29 patients (31%) in 2018. If we compare the onsets with DKA with those without DKA, there are no statistically significant differences ( $p=0.111$ ), even comparing the years 2020 and 2019 with a decrease in DKA at onset from 56.5% to 32.4% ( $p=0.066$ ). In the different age groups, we can observe that the rate of onset with DKA decreases both in the group from 0 to 4 years old (10.8%, 30.4% and 6.9% in the years 2020, 2019 and 2018, respectively) and the group from 10 to 14 years old (5.4%, 21.7% and 13.8% in 2020, 2019 and 2018, respectively), rising in the intermediate range from 5 to 9 years old (16.2%, 8.7% and 10.3% in 2020, 2019 and 2018, respectively).

During 2020, no patients with the onset of DM1 were diagnosed with COVID-19.

At diagnosis, anti-glutamic acid decarboxylase, membrane tyrosine phosphatase, anti-pancreatic islet cell and anti-insulin autoantibodies were all analysed. Data were obtained from two hospitals where a decrease in positive results was observed in the last year (96% in 2018, 100% in 2019 and 84% in 2020), with a non-statistically significant result.

## Discussion

Our study shows an increase, albeit not significant, in the absolute number and the incidence rate of DM1 onset in 2020 in the province of Tarragona during the first year of the COVID-19 pandemic, with presentations in the form of DKA decreasing overall and more specifically in young children under four years of age.

Part of our results regarding the increase in cases coincides with the German publication by Kamrath et al.<sup>5</sup> and the British publication by Unsworth et al.<sup>8</sup> However, in a second publication by the same German group,<sup>6</sup> they refer to the fact that the increase observed in 2020 was what was expected according to the trend in recent years.

In the German publication by Kamrath et al., data were collected from the German diabetes registry of new diagnoses of DM1 in children and adolescents between March 2020 and May 2020, when most kindergartens and schools were closed to reduce social contact. They compare the number of DKA cases during the 2020 lockdown period to the same time period in previous years. They conclude that during the COVID-19 period of 2020, the frequency of DKA cases was significantly higher than in the previous two years. Severe DKA cases were also higher. Children younger than six years old had a higher risk of severe DKA.

Like Kamrath, Unsworth et al. collected data from five paediatric hospitals in the same region in England from 23 March to 4 June 2020, coinciding with the total lockdown. They observed an increase in cases at two of the hospitals. In all of them, there was a greater number of cases of DKA, and more cases of severe DKA.

Contrary to our results are those of the diabetes group of the Italian Society of Paediatric Endocrinology and Diabetology,<sup>3</sup> which published the results obtained by survey in 68 hospitals with cases of childhood diabetes in Italy. They compared new diagnoses of DM1 in children under 15 between 20 February 2020 and 14 April 2020 and in the same period in 2019. They observed a lower overall incidence in the absolute number of cases and a lower amount of DKA cases, but these were more severe than in the previous year. In this study, they looked at acute complications in patients already diagnosed and did not find a greater increase than in the previous year. They diagnosed eight COVID-19 patients by PCR, of which one was a new diagnosis, and the others were already known patients. All of them had mild or asymptomatic symptoms.

Finally, Lawrence et al.<sup>4</sup> reviewed the incidence at the John Hunter Children's Hospital in Australia. They compared the number of onsets of DM1 in patients under 18 between 1 March 2020 and 31 May 2020 and the same period in the previous five years. Contrary to our data, they did not detect a higher incidence or changes in terms of predominance of sex or age. But they did observe, like the Kamrath and Unsworth groups, a higher frequency of DKA and severe DKA. They had no diagnosed cases of COVID-19.

In the last nine years in Catalonia, we observed a non-statistically significant increase ( $p=0.07$ ) in the incidence rate of DM1 in children under 15 years of age, which went from 14.6 per 100,000 inhabitants in 2011, to 16.3 in 2018 and 18.4 in 2019, before the pandemic (source: IDESCAT). The data for 2020 has not yet been published. In our region,

we have collected the data for these last three years and have observed this increase, but with a very striking increase during 2020. We cannot relate this increase to COVID-19 infection since none of the cases in which a PCR test was performed for COVID-19 was positive.

Some authors, such as Unsworth, hypothesise that SARS could act as a trigger due to its involvement at the level of the pancreatic beta cell, especially after finding some publications on small localised outbreaks of diagnoses. Marchand<sup>9</sup> reaches this same conclusion, pointing to COVID-19 infection as a possible trigger for the onset of DM 1, as well as other viral infections, such as enteroviruses and other coronaviruses, which have already been described in the literature as environmental agents that trigger the development of DM1.<sup>10</sup>

Other authors, such as Tittel et al.<sup>6</sup> state that psychological stress is known as a potential risk factor for DM1 and that COVID-19 and its social-distancing consequences have affected biological, psychological, economic and social aspects of people's lives.

On the contrary, the Italian group that reported a lower incidence of cases during the 2020 lockdown justifies this finding by claiming that social distancing would have reduced exposure to seasonal viruses that could trigger DM1.

The possible causes of the decrease in the number of diagnoses of DKA could be explained since, during the year 2020, due to lockdowns and social distancing, families have spent more time together, thus being able to detect the initial symptoms of diabetes in their children earlier. In addition, although health centres drastically reduced face-to-face visits for several months and switched to mostly telephone consultations, the cases diagnosed in our areas were quickly identified and treated. Other authors who have accumulated more DKA cases attribute it to the restriction in medical services and/or people not going to health centres due to fear of COVID-19 infection.

Our study shows a very marked increase in the incidence of new DM1 onsets in the Maghrebi population, as well as the increased risk from being of Maghrebi origin to begin with. These results coincide with the data published by Torrabias-Rodas et al.,<sup>11</sup> who reviewed the incidence of DM1 onset in two regions of Catalonia between 2000 and 2012. Their results show an incidence of 37.1 cases per 100,000 inhabitants in Maghrebis, compared to 12.2/100,000 in the autochthonous population. Contrary to our results, they found a higher incidence in the population under five years of age. These data indicate that there is possibly a greater genetic predisposition that interacts with environmental factors and thus makes Maghrebis more susceptible to developing DM1 than the native population.

The limitations of this study include the small sample size and the fact that our data is only compared with the previous two years, which is why we cannot rule out variations in the results in the following months and years. Another limitation would be the methodology used for the diagnosis of COVID-19 infection. A PCR test for SARS-CoV was performed on patients at admission, which cannot assess whether the patient had contact with the virus prior to the DM1 onset or not.

## Conclusion

In this study, we wanted to determine if, during 2020, coinciding with the COVID-19 pandemic, there was an increase in the incidence of diabetes mellitus in childhood compared to the previous two years in our area.

In 2020, we had 60.8% more new cases compared to 2019. A single unit was responsible for the increase. We observed an increase in cases in the Maghrebi population compared to the autochthonous population, primarily in the group aged 10–14 years, and a slight increase in the mean age at diagnosis. Contrary to what we would have expected due to mobility restrictions, there was a decrease in cases of DKA at diagnosis.

A longer observation time is required to see if the upward trend in the number of new diagnoses is maintained over time or if some triggering factor, such as a sedentary lifestyle, diet or psychological stress, could have influenced and explained the increase in cases.

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No funding was received for this study.

## Conflicts of interest

The authors declare that they have no conflicts of interest.

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