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Variation in incidence of type 2 diabetes mellitus: time series of Mexican adolescents

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ABSTRACT

Purpose: To study temporal changes in the cumulative incidence (CI) of type 2 diabetes mellitus during early and late adolescence from 2003 to 2013.
Methods: This was an ecologic, analytical study of trends over time. Data were weekly reports of new cases (General Directorate of Epidemiology). Specific CI was calculated and standardized by age using the direct method (WHO). Autoregressive Integrated Moving Average models offering a better fit to the observed series were calculated and controlled by intentional screening. Structural break point analysis was performed.
Results: The CI was lower in younger adolescents than in older adolescents. In early adolescence, the incidence was similar in both sexes and stable over time [Autoregressive Integrated Moving Average female: (2,0,2)(0,0,0), male: (1,0,1)(0,0,0); $P < .001$], whereas in late adolescence, the female incidence was higher than the male incidence and showed a linear increase [female: (1,1,2)(1,0,0), male: (1,0,1)(0,0,0); $P < .001$)]. The female series showed two structural break points, in 2010 and 2012. The male early adolescent series showed one break point in 2011.
Conclusions: Although there was an increase in the CI of type 2 diabetes mellitus during the study period, only the female late adolescence series showed an epidemiologically significant linear trend. There was also a brief, limited rise between 2010 and 2012 that affected all adolescents. This suggests that the disease may be triggered by specific events.

Introduction

Juvenile-onset type 2 diabetes mellitus (T2DM) has become a very important global health problem in recent years and is an emerging health problem in Mexico [1–3]. The General Directorate of Epidemiology reports the annual cumulative incidence (CI) of T2DM in adolescents, calculated with a population size of inhabitants aged over 10 years. Mexico's Morbidity Yearbook 2016 reports 2.05 cases of T2DM in adolescents aged 10–14 years. In adolescents aged 15–19 years, the corresponding figure was 5.81. The CI in the prior decade varied considerably. For example, in 2003, the CI was 1.98 for younger adolescents and 6.67 for older adolescents. The greatest CI was seen in 2012, when it was 2.6 and 9.2 for these age groups, respectively [4].

In relation to the detection of T2DM cases, the screening is regulated by NOM-015-SSA2-2010 in those adolescents with clinical suspicion who attend a first-level consultation [5]. The Ministry of Health promotes the Prevention Strategy and Health Promotion of the Lifeline (PSHPL) that offers care only to adolescents considered at risk and carries out the secondary prevention of DM2 [6]. The registration of care in this program is the only ecological measure that can be used to reveal variations in detection of the disease.

The context in which this problem has emerged has not escaped the attention of social epidemiologists [7]. It is likely that this alteration in metabolism occurs at earlier ages due to

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developmentally pervasive changes in lifestyle related to social changes and health contexts. The decade under study was a one in which there were particular changes in the secular trend. It should be noted that the changes in the epidemiology of diabetes that took place in this period occurred against a background of changes in social determinants of health that may involve causal factors that can explain the phenomenon [8–11]. The life course approach used in social epidemiology can help us to understand these variations. This theory posits that people become ill, especially with chronic conditions, once sufficient risk has accumulated. We are exposed to various risks throughout life, from gestation until the onset of a disease. We are all exposed to risk factors and social determinants that can influence the development of any illness; however, the sudden action of one unusual event can increase this risk sufficiently enough to cause illness. The trigger model in the life course approach suggests that there is a chain of risks throughout one's life and then an acute exposure that takes the cumulated risk over the threshold required to trigger disease [12–18].

Historically, adolescents have constituted a vulnerable population group in Mexico due in part to the poverty they experience [19]. A broad sector of the adolescent population has high levels of inequality and poverty, persistent over time, compared to the rest of population. These adolescents belong to households with social deprivation, food insecurity, and low incomes, which all contribute to the difficulty in meeting their basic needs and properly managing their health. There are insufficient studies in Mexico that distinguish the variations in socioeconomic backgrounds with respect to the incidence of diabetes in adolescents. Nevertheless, it has been widely suggested that diabetes is a disease strongly associated with poverty [20–22]. This situation increases stress, which, combined with the lack of a healthy diet and a sedentary lifestyle, leads to the difficulty of adolescents experiencing healthy and safe environments [23].

This article aims to study temporal changes in the CI of T2DM during early and late adolescence from 2003 to 2013.

Material and methods

Design

This was an analytical, ecologic study of trends over time.

Population

Adolescents aged between 10 and 19 years were segmented by sex (men and women) and age early adolescence (10–14 years) and late adolescence (15–19 years).

Information sources

Cases of T2DM

The data were obtained from weekly reports of new cases issued by the General Directorate of Epidemiology of the Ministry of Health [24]. Epidemiological calendars, published by the same institution, were used to calculate monthly totals of new cases. Data were reported by the same health units throughout the period. The diagnostic criteria used by clinicians are the same throughout the nation and are noted in the official Mexican norms for the diagnosis, treatment, and control of diabetes mellitus [5,25]. These criteria are consistent with the international criteria based on norms produced by the WHO [26–28].

Population size

The population size was that reported by the National Council of Population with the projections and retro-projections produced by the National Population and Housing Census of 2010, conducted by the National Institute of Statistics, Geography and Informatics [29,30].

Screening

The intentional screening data were obtained from the registry of newly enrolled cases under the PSHPL strategy, which is the Mexican government's secondary prevention strategy for T2DM in adolescents and involves actively searching for new cases [6,31,32].

Variables. The dependent variable was the standardized CI of T2DM for adolescents, defined as the number of cases of T2DM per 100,000 adolescents for the projected annual Mexican population during the study period. The independent variable was time (monthly measures were calculated). The variable used to control the effect of diagnosis, by intentional screening, was the new enrollment under PSHPL strategy during the studied period.

Method. CI was calculated separately by sex and for early and late adolescence. Population sizes were obtained from the 2010–2050 projections of National Council of Population [30]. Once the measures were calculated, they were standardized by age using the WHO's direct method to eliminate the effect of deaths due to war, famine, or epidemics [33].

Statistical analysis

Autoregressive Integrated Moving Average models

The Autoregressive Integrated Moving Average (ARIMA) models were chosen to determine any temporal dependence of the data to evaluate the order of differentiation and the seasonality of the CI series by sex and age. As a secondary analysis to control the screening, we modeled the series of new cases of diabetes mellitus predicted by the series of cases of adolescents attending the PSHPL strategy. To evaluate the fit of the models, the important parameters considered are their structure orders, seasonal orders, and their goodness of fit indexes.

A. Structure orders (p, d, q) and seasonal orders (p', d', q') refer to (1) autoregressive order (p) that describes the temporal dependence, (2) order of the difference (d) that may well be stationary when it maintains the magnitude of the measure at the usual levels or shows a linear or even exponential increase or decrease, (3) order of the moving average (q) that is useful for making predictions. Seasonal orders (p', d', q') are the same, but their analysis is in relation to seasonal cycles.

B. Goodness of fit indexes: These indexes tell us that the model can reproduce the observed data; insofar as they are equivalent, they will not show statistically significant differences. (1) R2 and R2 stationary tell us that both data are reproduced in terms of percentage and (2) Ljung–Box index is an index of the overall fit of the model.

C. Residuals analysis: This analysis determines if the model has a good fit, showing a normal distribution and a variance close to zero [34].

Time series were constructed from the standardized measures. Best fit equations for these series were explored with ARIMA models [34]. The analysis assumes the application of general formula of ARIMA models:

$$Y_t = -\left(\Delta^d Y_t - Y_t\right) + \varphi_0 + \sum_{i=1}^{p} \varphi_i \Delta^d Y_{t-i} - \sum_{i=1}^{q} \theta_i \varepsilon_{t-i} + \varepsilon_t$$

where

$$\Delta Y_t = (Y_t - Y_{t-1})$$

Table 1
Cumulative incidence and % change per year grouped by phase of adolescence and sex*

Year	T2DM cumulative incidence—early adolescents				T2DM cumulative incidence—late adolescents			
	Female		Male		Female		Male	
	Incidence	% of change	Incidence	% of change	Incidence	% of change	Incidence	% of change
2003	0.21	—	0.13	—	0.68	—	0.49	—
2004	0.20	−0.05	0.13	0.00	0.61	−0.10	0.37	−0.24
2005	0.25	0.25	0.18	0.38	0.66	0.08	0.47	0.27
2006	0.23	−0.08	0.18	0.00	0.72	0.09	0.46	−0.02
2007	0.18	−0.22	0.16	−0.12	0.74	0.03	0.47	0.02
2008	0.24	0.34	0.18	0.10	0.78	0.05	0.45	−0.04
2009	0.14	−0.41	0.14	−0.20	0.61	−0.22	0.36	−0.20
2010	0.24	**0.71**	0.16	**0.14**	0.81	**0.33**	0.44	**0.22**
2011	0.31	**0.30**	0.26	**0.66**	0.95	**0.17**	0.56	**0.27**
2012	0.26	*−0.19*	0.19	*−0.27*	1.01	**0.06**	0.54	*−0.04*
2013	0.13	*−0.48*	0.21	*0.08*	0.56	*−0.45*	0.39	*−0.28*

Bold—increase in variable; italics—decrease in variable.
* Cumulative incidence (per 100.000), phase of adolescence (early and late).

Structural break

The structural break point analysis determines if, in a series of data observed during a period, there are significant differences between the magnitudes of the variable in an observation of the series with respect to the subsequent observation [35].

The analysis of time series was performed using the statistical software SPSS, version 21.0, and the detection of structural breaks was carried out with R.

Results

Population

The entire Mexican population of adolescents was studied. At the beginning of the study period, the female early adolescent population was 5,557,805 and at the end of the period, it was 5,534,420; the corresponding figures for the male early adolescent population are 5,587,610 and 5,746,298. At the beginning and end of the study period, the figures for the female late adolescent population were 5,242,068 and 5,547,538, respectively; the corresponding figures for the male late-adolescent population are 5,129,833 and 5,623,359.

Temporal CI change in early and late adolescents

There was an increase in annual cases among early adolescents during 2010–2012 in the case of females and during 2011–2012 in the case of males. The annual new cases interval during the study period was 85–194 cases for female adolescents and 85–169 for male adolescents. The annual standardized CI ranged from 0.13 to 0.31 cases per 100,000 female adolescents and 0.13 and 0.26 cases per 100,000 male adolescents (Table 1).

In older adolescents, there was an increase in cases over the period between 2010 and 2012 in the case of females and 2011 to 2012 for male adolescents. The annual new cases interval was 364–664 in the case of females and 223–365 in the case of males. Annual incidence variation comprises between 0.56 and 1.01 per 100,000 female adolescents and between 0.36 and 0.56 per 100,000 male adolescents during the study period (Table 1).

ARIMA models

Analysis of series revealed that the ARIMA models specified in Table 2 had the best fit. The autoregressive components of the series of male early adolescence and of late adolescence in both sexes corresponded to estimates of the adjusted series, which necessitated the use of CI values from a previous month for calculation of the values for the whole model. In addition, both early adolescent series and the male late adolescent series do not show any order of differentiation. The female late-adolescent series was characterized by a linear tendency. For all models, estimates were made with one and two deviations of the moving average. The significant predictor analysis to control by diagnosis by intentional screening showed

Table 2
Goodness fit indexes for ARIMA models by phase of adolescence and sex

Indexes		Early adolescence		Late adolescence		Significant predictor
		Female (2,0,2)(0,0,0)	Male (1,0,1)(0,0,0)	Female* (1,1,2)(1,0,0)	Male† (1,0,1)(0,0,0)‡	PSHPL (0,0,2)(0,0,0)
Index of fit	R2 Stationary	0.210	0.212	0.525	−0.329	0.366
	R2	0.210	0.190	0.360	0.065	0.360
	Root mean square error	0.007	0.007	0.016	.011	18.63
	Mean absolute percentage error	35.92	36.34	22.5	27.9	17.29
	Ljung–Box	15.45 ($P = .348$)	22.44 ($P = .129$)	10.063 ($P = .758$)	10.72 ($P = .826$)	36.02 ($P = .003$)
Model Parameters	Autoregressive Lag 1	0.153 ($P = .526$)	0.868 ($P = .000$)	−1.000 ($P = .000$)	1.000 ($P = .000$)	—
	Lag 2	0.659 ($P = .001$)	—	—	—	—
	Difference	—	—	1	—	—
	Mobile average Lag 1	−0.166 ($P = .483$)	.603 ($P = .000$)	−0.331 ($P = .000$)	0.813 ($P = .000$)	−0.180 ($P = .061$)
	Lag 2	0.588 ($P = .000$)	—	0.659 ($P = .000$)	—	−0.327 ($P = .001$)
	Autoregressive (seasonal)	—	—	0.218 ($P = .022$)	—	—
Residuals	Kolmogorov-Smirnov	$P = .000$	$P = .200$	$P = .195$	$P = .200$	$P = .200$
	Variance	0.000	0.000	0.000	0.000	0.100

* Innovative outlier March 2011.
† Additive outlier March 2011.
‡ Square-root transformation.

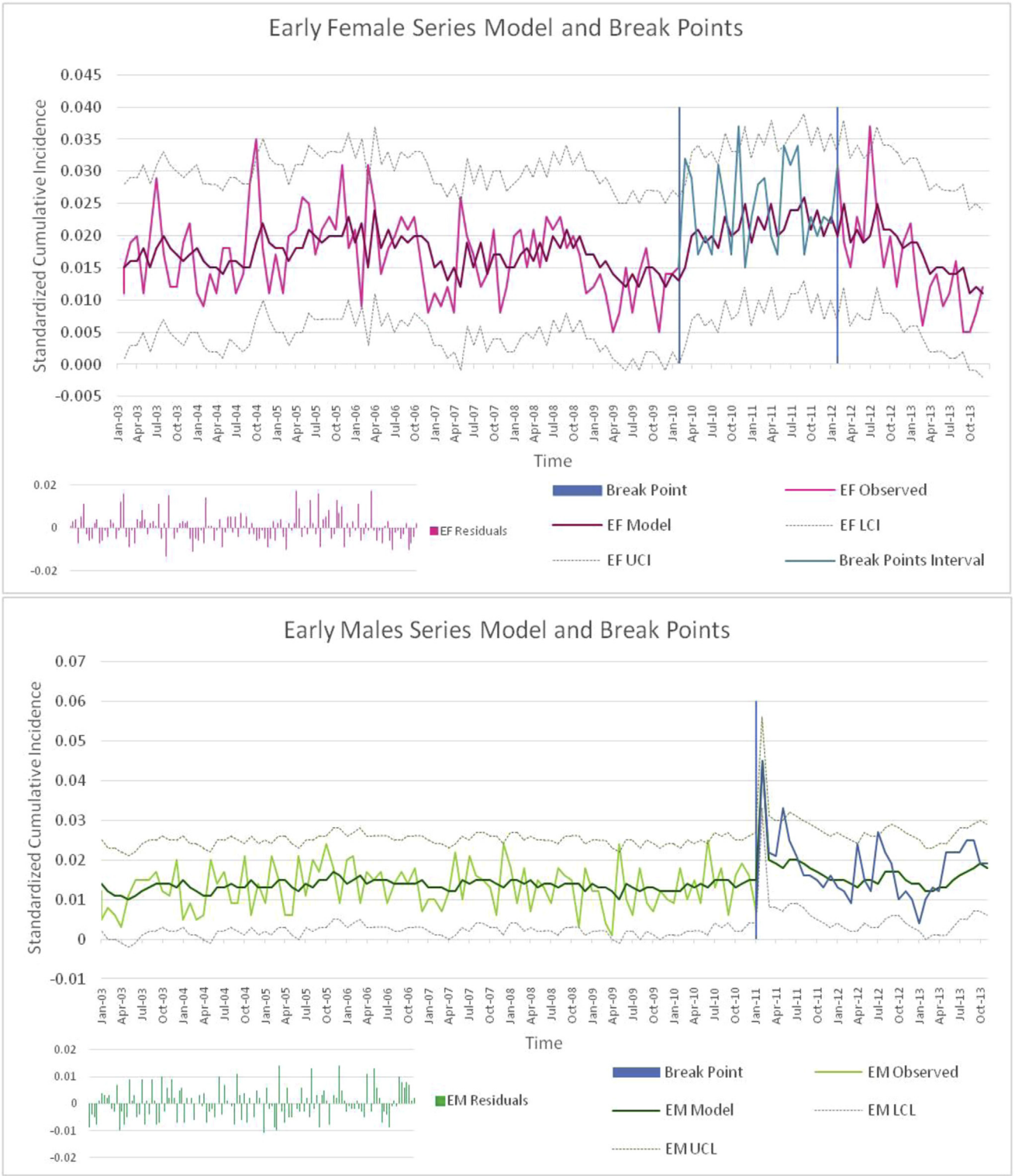

Fig. 1. Structural break points in separate time series for males and females in early and late adolescence. EF = early females; EM = early males; LF = late females; LM = late males; LCL = low confidence limit; UCL = upper confidence limit.

that the best model failed to adjust the series of diabetes mellitus cases predicted by participation in the PSHPL strategy and showed a poor fit. The parameters of the models, goodness of fit indices, and residue analysis are shown in Table 2.

The CI of diabetes was greater in female adolescents than in male adolescents and greater in late adolescence than in early adolescence. All series show an increase in CI during the first months of 2010, with CI reaching its maximum between the years of 2011 and 2012. Likewise, there is a decrease in incidence in all groups from 2012 to 2013. The male series did not show any order of differentiation. In late-adolescent females, an order of differentiation was obtained, confirming the linear tendency (Fig. 1).

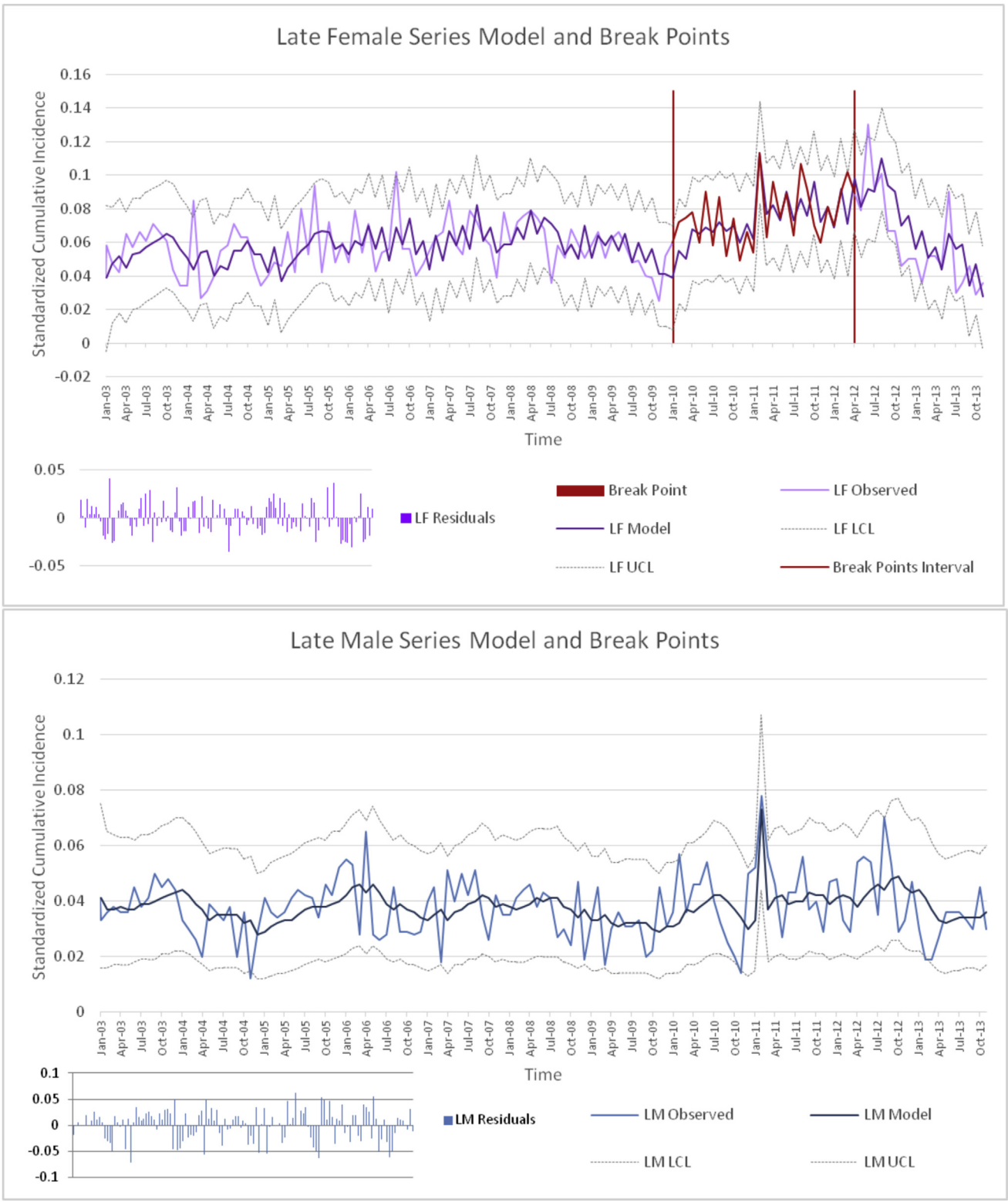

Fig. 1. (*continued*).

Structural break analysis

Analysis of structural breaks identified two change points in young female adolescents, the first, in February 2010, corresponds to an increase in incidence, which remained constant until February 2012 when appears the second point of change, which represents a decrease in the usual values. There were no change points in the male series, but there was a significant atypical figure, representing an increase in incidence, during February 2011. In the case of older adolescents, there were two change points in the female series, the first, in February 2010, representing an increase in the indicator that remained until the second, in May 2012. There

were no significant breaks detected in the older male adolescent series (Fig. 1).

Discussion

Period of generalized increase

In general, the results of the time series analyses indicate that the increase in T2DM morbidity varies with age group and sex. In addition, during the years 2010–2012, there was a generalized increase in both the number of cases and incidence that was followed by a return to the secular trend for 2013 (these years, we will mark them as a period of general rise for both age groups and both sexes).

Both male and female early-adolescent series were found to be stationary, which implies that variations in incidence were within the parameters for secular variation in the disease. Adjustment of the models does not reproduce the temporal behavior of both series with the best solutions; this is probably because the incidence in early adolescence varied randomly, as expected in this age group in which the CI has low values.

In late adolescence, there was a more clearly defined, consistent temporal pattern. The sex differences are important. The CI figures were higher in older female adolescents, and this group showed the greatest increase in incidence of all the groups during the study period. This increase was of sufficient magnitude that we can assert that the morbidity increased in this group. It is remarkable that during the first years of the series, the incidence of diabetes in female adolescents was stable, with the increase in incidence during 2010–2012 being of such magnitude that it was sufficient to result in identification of a linear trend. The incidence was stable in male adolescents, but with a better-defined temporal pattern that meant the models reproduced the series better. There was also a period of increase in the male series for this group, although it was brief.

It is very important to note that the period of increase we have described was observed in all the groups, although it varied in magnitude and temporal boundaries. It should be pointed that this period of increase was brief and well defined, which reduces the probability that it represents a transition in the disease. Generally, epidemiological transitions are more gradual and remain a trend [36,37].The patterns we have described do not seem to be related to the intentional search for cases or health promotion strategies implemented in Mexico. The Mexican government's PSHPL strategy rules the secondary prevention for adolescent T2DM and involves actively searching for new cases [6,31].

Gender differences in T2DM detection

It is notable that in late adolescence, females become ill with T2DM more frequently than males; this is consistent with reported national data. According to the literature, there are no sex differences in the pathophysiology of T2DM [1]; however, the differences in the measures are related to the differentiated identification of cases by gender roles. It is probable that there are in fact no sex differences in T2DM morbidity and that the figures reflect underdiagnosis in male adolescents. In Mexico, adults older than 20 years are screened as a secondary diabetes prevention strategy [38]. The General Directorate of Health Information records show that during the study period, the proportion of eligible women who were screened was almost twice the proportion of men, although the proportion of screening tests, which produced a positive result, was similar in both sexes (12%, author's analysis of General Directorate of Health Information data) [32,39].

This pattern, of sex proportion in diagnosis, appears to be general to the whole Mexican population, so we postulate that these sex differences in late adolescence are due to cultural factors. It has been documented that women make more use of health services than men [32]. Among the factors involved are gender differences in socialization, recognition of need for care and demand for care, health involvement, and other structural factors such as labor barriers, which mean that Mexican men have less time to attend health services than their female counterparts [40–42]. The effect of sex differences in workforce participation extends to adolescents, especially older adolescents [43]. In those adolescents who refer been working, women use health services more frequently than men [39,43].

Structural breaks: ¿is it a trigger event?

The analysis of structural breaks in early adolescents showed that the breaks in the female series coincided with the period of general increase in incidence. In the case of males, only the incidence increase in 2011 was significant, and variations during the period of the general increase were not sufficient to imply a change in secular variation in the disease. In late adolescence, the structural breaks suggest that among females, there was a brief, very clearly defined period of significantly higher incidence that was followed by another significant decrease that returns to normal at the end of the study period. No structural changes were observed in the male series, so we suggest that the stationary behavior is related to the secular trend of the disease.

The results suggest that there may be socially determined environmental factors that influenced incidence during these years. This explanation is the more plausible because the discussed period is very clearly delimited and has an abrupt start, as well as a decrease, which is also immediate and abrupt toward the end of the series. In addition, the period of increase corresponds to a moment in history during which Mexico went through a social and economic crises that had repercussions for levels of violence, poverty, deprivation, displacement, service provision, and access to food [8,10,44–47]. These factors may have acted as triggers for early onset of T2DM as one would not have expected sufficient risk accumulation at this age, although the exposure to risk starts during gestation [12,14,15,17,48–52].

In conclusion, we suggest that the CI of T2DM remained stable throughout the period, and there was no real increase in epidemiological terms. There was a period of generally increasing incidence between 2010 and 2012, but only in late-adolescent females that was of sufficient magnitude to be regarded as a significant increase in incidence and spoken of as a trend.

Limitations

This ecological study was based on population-level secondary sources, so it is not possible to draw inferences at the individual level. The incident cases data presented are national, obtained from the registry of all new cases reported by all health institutions. The most reliable data available for the secondary analysis of the health promotion strategy are those reported by the health services of the Ministry of Health and are limited to the population that uses these services.

Perspective

It is important to develop new research on the short-term participation of social determinants of health, especially gender, related to the social crisis, in the onset of T2DM in adolescence. In addition, there are emerging barriers to health promotion that are linked to this type of crisis. Both factors can increase the risk of diabetes, which for some children could represent the trigger of the disease.

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