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Presentation of Content

In the first article we present Plasma glucose, triglycerides, cholesterol and dietary levels in inhabitants of a Mayan community of Campeche, by AKÉ-CANCHÉ, Baldemar, SARABIA-ALCOCER, Betty, LÓPEZ-GUTIÉRREZ, Tomás Joel and GUTIERREZ-ALCÁNTARA, Eduardo Jahir, as the following article we present, *Main sources of exposure to environmental risks in pregnant women from Kinil, Yucatan, Mexico*, by HEREDIA-ALLEGRETTI, Yazmín, RODRÍGUEZ-ANGULO, Elsa, ANDUEZA-PECH, Guadalupe and OJEDA-RODRÍGUEZ, Ricardo, with adscription in the Universidad Autónoma de Yucatán, as the following article we present, *BDNF expression in blood. Study in iron deficient females*, by VIEYRA-REYES, Patricia & GÓMEZ-LAGUNAS, Néstor G., with adscription in the Universidad Autónoma del Estado de México, as the following article we present, *Metabolic control with diet vs insulin in patients with gestational diabetes and obesity*, by AKÉ-CANCHÉ, Baldemar, LÓPEZ-GUTIÉRREZ, Tomás Joel, SARABIA-ALCOCER, Betty and CANUL-RODRÍGUEZ, Pedro Gerbacio, with adscription in the Universidad Autónoma de Campeche.

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Plasma glucose, triglycerides, cholesterol and dietary levels in inhabitants of a Mayan community of Campeche

Niveles plasmáticos de glucosa, triglicéridos, colesterol y dietéticos en habitantes de una comunidad de Maya de Campeche

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Abstract

Objective of this work was to study the blood levels of glucose, cholesterol and triglycerides, and their association with eating habits in inhabitants of the community of Tenabo, Campeche, Mexico. Methodology Anthropometric measurements were made to the inhabitants who ranged in age from 10 to 80 years old. Mean glucose levels were 132.86 mg/dL, cholesterol 139.640 mg/dL, and triglycerides 189.2 mg/dL. According to the applied survey, the diet of this population consists of the consumption of meat from wild animals in the region, as well as foods with a high fat content such as pork, in addition, a low consumption of vegetables and fruits is reported among the inhabitants. Results: In this population, glucose and triglyceride levels are elevated compared to the reference values; however, it is necessary to investigate other biochemical parameters that help the timely diagnosis of this type of disease.

Glucose, Triglycerides, Cholesterol

Resumen

Objetivo de este trabajo fue estudiar los niveles sanguíneos de glucosa colesterol y triglicéridos, y su asociación con los hábitos alimenticios en habitantes de la comunidad de Tenabo, Campeche, México. Metodología Se realizaron mediciones antropométricas a los habitantes que oscilaron en un rango de edad de 10 a 80 años de edad. La media de los niveles de glucosa fue de 132.86 mg/dL, los de colesterol 139.640 mg/dL, y triglicéridos 189.2 mg/dL. De acuerdo con la encuesta aplicada, la alimentación de esta población consiste en consumo de carne de animales silvestres de la región, así como alimentos con alto contenido de grasa como el cerdo, además se reporta un escaso consumo de verduras y frutas entre los habitantes. Resultados: En esta población los niveles de glucosa y triglicéridos se encuentran elevados en comparación con los valores de referencia; sin embargo, es necesario investigar otros parámetros bioquímicos que ayuden al diagnóstico oportuno de este tipo de enfermedades.

Glucosa, Triglicéridos, Colesterol

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Introduction

Diabetes and cardiovascular disease are major public health problems worldwide¹. Epidemiological studies in developed and developing countries have shown that cardiovascular diseases resulting from atherosclerosis are among the leading causes of mortality, and that dyslipidemias and diabetes are among the main risk factors¹. These diseases are associated with alterations in the balance of plasma levels of glucose, cholesterol and triglycerides. Although lipids such as cholesterol and triglycerides are important in the body's normal physiology, when altered they can trigger disorders such as atherosclerosis. Plasma lipid profile values are the result of complex metabolic processes influenced by genetic and environmental factors.

Lifestyle, including dietary habits, can affect parameters such as individual weight and thus plasma cholesterol levels in the body, eventually leading to obesity and cardiovascular disease². Excess weight tends to increase low-density lipoprotein (LDL) and triglyceride cholesterol, and conversely can reduce high-density lipoprotein (HDL) levels. In cases of overweight, weight loss is helpful in regulating plasma levels of these lipids; thus, under conditions of proper nutrition and exercise, elevated cholesterol and LDL levels can be reduced while HDL levels increase, supporting the functioning of the body's biochemistry. Recently, a study in Mexico City found that 34.1 % of the population studied (833 men and 889 women) had cholesterol levels ≥ 200 mg/dL. Triglyceride levels were also found to be altered in 29.9% of the population. However, the prevalence of dyslipidemias in rural communities has received less attention.

On the other hand, in Mexico, diabetes mellitus is the leading cause of mortality in general. Pharmacological treatment of this metabolic syndrome is lifelong, and focuses on controlling clinical manifestations and preventing complications in patients. Unfortunately, for many patients this is not achieved, and the drugs are not freely available, so they need to be purchased with their own resources. In rural populations with few job opportunities, limited income and limited health services, the diagnosis and treatment of this disease is less efficient than in large metropolises such as Mexico City.

Another problem among patients with diabetes is that they do not follow a strict dietary plan, so their diets continue to contain foods high in sugar. This condition is worsened in rural communities where the economy is scarce and the health culture is poor, leading to a lack of strict dietary regimen and proper dosage of medications.

Methodology to be developed

A cross-sectional study was conducted among inhabitants of the rural community of Tenabo, located in the municipality of Tenabo in the state of Campeche. Fifty participants ranging in age from 10 to 80 years, who had not consumed alcohol for at least 5 days prior to the study and who had read and signed the informed consent letter, were included. This population was surveyed about dietary habits and the presence of a family history of cardiovascular disease and diabetes. Anthropometric measurements of weight and height were taken. Blood samples were obtained by venous puncture under adequate conditions of asepsis and antisepsis in an 8-hour fasting period without modification of dietary habits.

Serum glucose, cholesterol and triglyceride (TG) determinations were performed by automated methods on the clinical chemistry analyser, MINDRAY model BS120.

Statistical analysis

Data analysis was performed with conventional statistics by calculating mean, mode, median and standard deviation in age stratified groups.

The association between glucose and cholesterol values, as well as glucose and triglyceride values were done by linear regression using GraphPad Prism software version 5.0.

Results

In this study, 50 individuals from the Tenabo community were studied (Figure 1), of which 44 % were in the age range 41-60 years, being the majority group. In contrast, the minority group was the 10 to 20 year age group, accounting for only 8 % of the total. The 21-40 age range accounted for 36 % of the population, while 61-80 years of age accounted for 12 % (Figure 2).

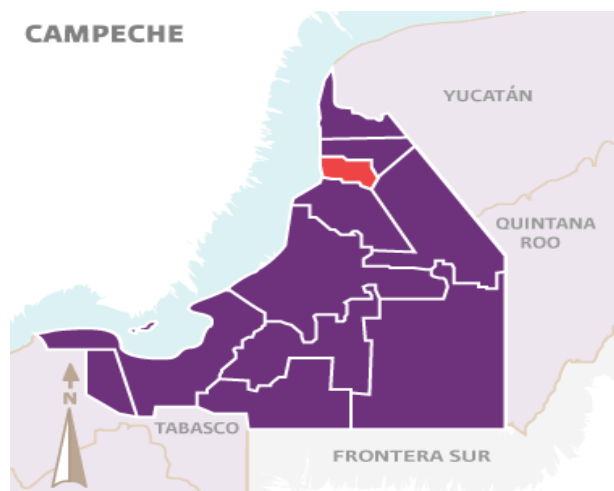
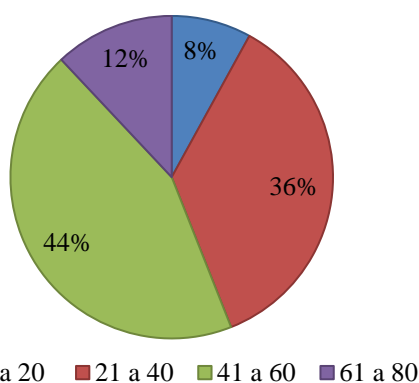


Figure 1 Municipality of Tenabo in the state of Campeche



Four age ranges are presented: 10-20, 21-40, 41 to 60 and 61-80. The % of the population that falls into each range is expressed

Figure 2 Age range of the population studied

Blood glucose, cholesterol and triglyceride measurements are presented in table 1. Glucose levels in this population were 132.86 mg/dL, which is above the reference values (70-100 mg/dL). With regard to cholesterol, a mean of 139.64 mg/dL was found, which is within the established reference values (≤ 200 mg/dL). For triglycerides, a mean of 189.2 mg/dL was found, which is above the reference values (≤ 150 mg/dL). Concerning plasma glucose levels, the affected groups were in the age ranges 21-40, 41-60 and 61-80 years. For cholesterol no group appears to be altered, while for triglycerides it is observed that the groups that are above the reference values are 41-60 and 61-80 years of age (figure 3).

Table 1 Statistical data on plasma glucose, cholesterol and triglyceride levels. Mean, standard deviation, mode and median are presented

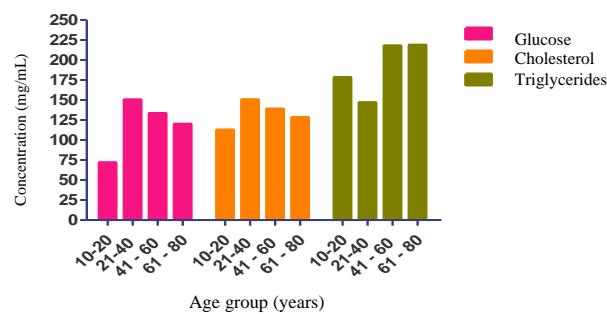


Figure 3 Plasma levels of glucose, cholesterol and triglycerides according to age range

In the linear regression analysis a positive association was found between glucose and cholesterol levels with a value of $r^2=0.1267$ (Figure 4), likewise a positive correlation was found between plasma glucose and triglyceride levels, showing a value of $r^2=0.03732$ (Figure 5).

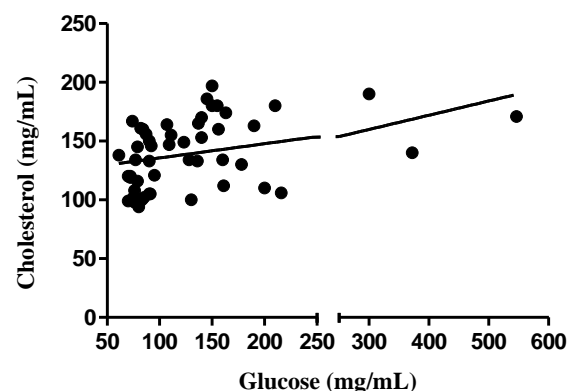


Figure 4 Linear regression analysis between cholesterol and blood glucose levels. Glucose and cholesterol values from 50 blood samples were analysed. The r^2 value obtained was: 0.1267

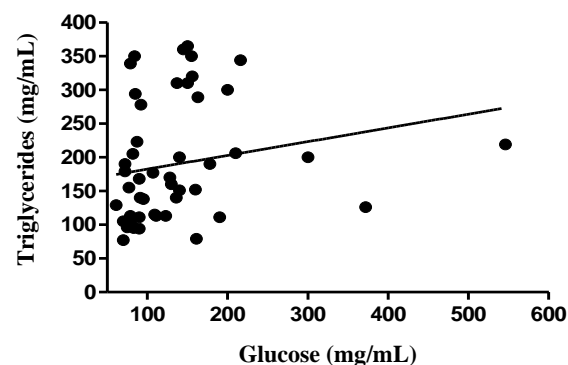


Figure 5 Linear regression analysis between cholesterol and blood glucose levels. Glucose and cholesterol values from 50 blood samples were analysed. The r^2 value obtained was: 0.03732

Tenabo is a rural community in the state of Campeche, which suggests that its diet is significantly different from urban communities such as the city of Campeche. In the survey it was determined that the diet of this population is mainly based on wild animal meat such as wild pig, armadillo, deer and pizotes (38% of the population consumes it). However, they also consume traditional foods with a high fat content, such as tamales, panuchos, pan de cazón, pan dulce (36 % of the population consumes it). 9 % of the population consumes pork, while only 17 % of the population consumes fruits and vegetables.

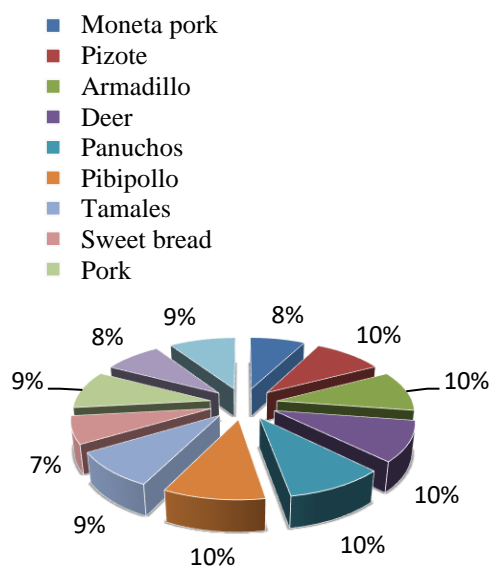


Figure 4 Type of diet of the population studied. The % of the population that consumes each of the foods is expressed as follows

Conclusions

The glucose and triglyceride levels of the inhabitants of Tinun, Campeche are above the reference values established for the Mexican population. Although the diet of these people relies heavily on bushmeat, fruit and vegetable consumption is low, this coupled with limited access to health services could increase the risk of developing cardiovascular disease and/or diabetes. Further studies in rural communities are needed to get a better picture of the current health of this vulnerable group, as well as the implementation of prevention programmes to inform them about the importance of a healthy diet and sports activities.

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Main sources of exposure to environmental risks in pregnant women from Kinil, Yucatan, Mexico

Principales fuentes de exposición a riesgos ambientales en embarazadas de Kinil, Yucatán, México

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Abstract

Objective. To identify main environmental hazards to which pregnant women in Kinil, Yucatan are exposed. **Methodology.** Cross-sectional study consisting of two parts: 1) review of clinical archives of women who received prenatal care from 2015 to 2017, registered in the Pregnancy Census of the Kinil Health Center, to obtain prenatal medical records, data on babies and perinatal conditions of their births; 2) the patients were visited in their homes to explain the objective of the study and request the pertinent permits with informed consent, as well as the caregivers in the case of minors. The frequency of major diseases during pregnancy was determined, as well as the prevalence of adverse perinatal outcomes. **Contribution.** Approach to environmental diagnosis, identify potential sources of risks of disease, characterize positive or negative situations to detect groups in vulnerable situations

Potential source, Risks, Pregnant women

Resumen

Objetivo. Identificar principales peligros ambientales a los que están expuestas las mujeres embarazadas de Kinil, Yucatán. **Metodología.** Estudio transversal constituido en dos partes: 1) revisión de expedientes de mujeres que recibieron atención prenatal del 2015 al 2017, registradas en el Censo de Embarazadas del Centro de Salud de Kinil, para obtener las historias clínicas prenatales, datos de los bebés y condiciones perinatales de sus nacimientos; 2) se visitaron a las pacientes en sus hogares para explicar el objetivo del estudio y solicitar los permisos pertinentes con los consentimientos informados, así como a los tutores en caso de menores de edad. Se determinó la frecuencia de las principales enfermedades durante el embarazo, así como la prevalencia de los resultados adversos perinatales. **Contribución.** Aproximación del diagnóstico ambiental, identifica fuentes potenciales de riesgos de enfermedad, caracteriza situaciones positivas o negativas para detectar a grupos en situación de vulnerabilidad.

Fuentes potenciales, Riesgos, Mujeres embarazadas

Citation: HEREDIA-ALLEGRETTI, Yazmín, RODRÍGUEZ-ANGULO, Elsa, ANDUEZA-PECH, Guadalupe and OJEDA-RODRÍGUEZ, Ricardo. Main sources of exposure to environmental risks in pregnant women from Kinil, Yucatan, Mexico. ECORFAN Journal-Republic of Guatemala. 2022. 8-15:5-11.

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Introduction

Environmental health is the area of public health dedicated to the evaluation of health risks and damages caused by environmental degradation and pollution, as well as to the design of programmes and strategies for their reduction (Pan American Health Organization. Area of Sustainable Development and Environmental Health; 2003).

From Alma Ata in 1978 to the Millennium Declaration in 2005, there have been numerous global meetings expressing proposals to improve environmental health (Bulacio, J., De Grandis, S., Fernández, R., Gomila, A., Sfaello, I., Sosa-Boye, I., et al; 2006).

The World Health Organisation (WHO) has defined the environment as one of the most decisive factors influencing the global toll of ten million child deaths per year and a very important one for the health and well-being of mothers (Pan American Health Organisation; 2003).

Similarly, the WHO points out that high rates of mortality and disability worldwide are a consequence of fetal developmental disorders. Optimal foetal development requires that the mother enjoys good physical and emotional health before and during pregnancy, as her ability to meet the needs of foetal development is related to her diet and depends on her lifestyle, and exposure to toxins has an impact on the health of mother and child. Exposure to environmental pollution facilitates the incorporation of toxic agents, which move easily into the blood, brain and other tissues of the developing foetus (Pan American Health Organization; 2017).

In the last 20 years, studies have been conducted worldwide to assess the consequences of prenatal exposure to environmental pollutants and their effects on the resolution of pregnancy and subsequent development of the infant to determine the level of pre- and post-natal impact of the environment on the health of individuals (Pan American Health Organization; 2017), (Kim, B., Ha, M., Park, H., Lee, B, Kim, Y. J., & Hong, Y.; 2009).

In the Region of the Americas there is inequality in environmental health, areas in different states of development have been characterised, so that groups with greater vulnerability have been identified. Some of these inequalities are observed in rural areas with relatively preserved ecosystems, where indigenous populations live, or in more developed areas with agricultural populations. In urban areas, there is inequality between marginalised groups which tend to be closer to polluted areas or working populations in industrialised sectors (Pan American Health Organization; 2009).

In a study carried out in 2009 in Yucatan, it was determined that due to its geohydrological characteristics it has a high vulnerability to water contamination, and almost 4000 potential sources of hazardous waste were found, of which 73.4% were concentrated in the municipality of Merida and the ten most populated municipalities in the state. Polanco et al. 2014, demonstrated the presence of organochlorine pesticide residues in water from 20 cenotes in the so-called "ring of cenotes" (Polanco, A., Navarro, J., Solorio, J., Mena, G., Marrufo, J., & Del Valls, T.; 2014).

Even with the evidence of exposure to environmental hazards, no studies have been conducted in Yucatan to determine their impact on maternal and perinatal health in rural areas.

Therefore, we pose the following question: What is the situation of maternal and perinatal environmental health, as well as what are the main potential sources of environmental risk faced by pregnant women in the commissariat of Kinil, Yucatan?

General objective

To determine the situation of maternal and perinatal health, as well as the main potential sources of environmental risks to which pregnant women in Kinil, Yucatan are exposed.

Specific objectives

- To describe the main maternal and perinatal health problems such as: abortion, premature birth, low birth weight products.

- To describe the characteristics of pregnant women's environment.
- To identify the main sources of exposure of pregnant women to environmental risks such as exposure to biomass, pesticides and contaminated water.

Type and general design of the study

Observational, descriptive, cross-sectional

Definition of the universe

All women who attended prenatal care at the Rural Health Centre of Kinil, Yucatan, during the period 2015-2017.

Selection and sample size

A survey was conducted among 64 women who were the total population of pregnant women registered according to the Pregnancy Census of the Rural Health Centre of Kinil, who attended prenatal control during the period from 2015 to 2017 and who concluded their gestational period.

Conceptual definition of variables

- Age: Years and months of life since birth, at the time of pregnancy.
- Gestational age: Weeks and days calculated from the onset of conception to the time of delivery, according to the birth record.
- Low birth weight: Product of conception with a body weight at birth of less than 2,500 grams, regardless of gestational age, according to the record.
- Preterm: Product of conception from 28 weeks to 37 weeks of gestation, which is equivalent to a product from 1,000 grams to less than 2,500 grams according to the file.
- Illnesses suffered during pregnancy: Illnesses recorded in the maternal medical record during the prenatal check-up visit.

- Suspected cases of vector-borne disease during pregnancy: Patients with the following signs and symptoms during pregnancy: fever greater than 39°C with no other source, with any of the following: Irritability, arthralgia, headache, arthralgia, myalgia or oral intolerance.

- Overcrowding: The presence of 2.5 or more persons per room within the dwelling.

- Household construction material: The material of which the pregnant woman's dwelling is constructed.

- Person assigned to cook the food: Person who performs daily food preparation.

- Location of the kitchen: Space intended for the location of the kitchen.

- Fuel used for cooking: Resource used for cooking food.

- Water used for drinking: Water intended for consumption by the pregnant woman.

- Exposure to pests: Presence of animals carrying diseases that may affect the pregnant woman.

- Presence of pets in the home: Animals that are in contact with the pregnant woman during her pregnancy.

- Use of pesticides: Contact with chemicals used to treat pests.

- Presence of agricultural activity near the dwelling: Farm or orchard that is less than 5 minutes away from the pregnant woman's dwelling.

Methodology

The research work consisted of two parts: The first was the review of the files of women who received prenatal care during the years 2015 to 2017 and who had completed their gestational period and were registered in the Pregnancy Census of the Kinil Health Centre. Prenatal medical records were obtained from these files, as well as data on the babies and perinatal conditions of their births.

In the second part, the homes of the registered patients were visited and the patients were given an explanation of the purpose of the research study, the aims of the study and the potential benefits of the study results as feedback for their participation. Subsequently, the pertinent permissions were requested with the signing of the informed consent forms, as well as from the caregivers in the case of a minor patient. After obtaining acceptance to participate, the surveys were administered; the estimated duration was 20 minutes.

The variables referring to the gynaecological-obstetric data, as well as the follow-up of prenatal control and product data, were obtained from the file, while the variables referring to the environmental conditions were collected from the surveys applied to the mothers.

Measuring instrument

For the elaboration of the maternal environmental clinical history, an instrument was used whose parts are made up of two instruments in turn: the Maternal Clinical History for Prenatal Control of the Yucatan Ministry of Health, and the questionnaire "Evaluation of the maternal environment" belonging to the INTERBIO 21st study protocol, which has been applied in homogeneous populations in 8 countries. This questionnaire can be used to identify subpopulations for further analysis to identify areas requiring intervention, education or policy change such as environmental health (Valls-Llobet, C.; 2010). The frequency of the main diseases during pregnancy was determined, as well as the prevalence of adverse perinatal outcomes in patients.

The data obtained were collected in tables in the Office Excel programme version 2016, and then entered into the Epi Info programme version 7.0.1.0 for statistical analysis.

For quantitative variables, mean and standard deviation were calculated, and for qualitative variables, percentages were calculated.

Permission for the study was requested from the authorities of the Rural Health Centre of Kinil, Yucatan.

Information provided to and obtained from patients was treated in strict confidence. Participants, as well as caregivers of minor patients, were given a letter of informed consent detailing the benefits and objectives of the study.

Results

The age range of the women surveyed was from 15 to 34 years, with a mean of 24.03 years and a standard deviation of 5.11. Out of a total of 58 births, 8 (13.79%) were preterm and 19 (32.76%) were low birth weight (Table 1).

Gestational age	Number	Porcentaje
Mature	50	86.21
Premature	8	13.79
TOTAL	58	100
Birth weight		
Normal	39	67.24
Low birth weight	19	32.76
TOTAL	58	100

Table 1 Percentage of adverse gestational events by gestational age and birth weight

According to the medical records and medical histories reviewed, it was determined that 46 (79.31%) of the women in this study suffered from at least one illness during their pregnancy and the majority of this percentage had two or more illnesses during gestation; on the other hand, none of the women surveyed had eclampsia, mild or severe pre-eclampsia (Table 2).

	Number	Percentage (%) *
Urinary tract infection	35	60.34
Vaginal infection	24	41.38
Upper airway infection	34	58.62
Disease diarrheal disease	23	39.66
Threat of abortion	1	1.72
* Each in relation to the total number of pregnant women n=58		

Table 2 Most frequent illnesses during pregnancy

The environmental setting of the pregnant women was defined, where only 12.07% lived in overcrowded conditions according to CONEVAL parameters. The main sources of exposure to environmental risks were also identified, the main pest detected was mosquitoes (77.59%), for which periodic nebulisations have been carried out, most of the women were in contact with animals (75.86%), with dogs being the main ones (41.38%) (Table 3).

Pests		
Mosquitoes	45	77.59
None	9	15.52
Other	4	6.90
Total	58	100
Presence of animals		
No	14	24.14
Yes	44	75.86
Total	58	100
Type of animals		
Poultry	15	25.86
Cats	5	8.62
None	14	41.38
Dogs	24	41.38
Total	58	100

Table 3 Environmental setting of the dwellings

It was also observed that most of the women bought bottled water (62.07%), cooked with firewood (60.34%), lived near crops (58.63%) and did not use agro-industrial pesticides (77.59%) as sources of environmental exposure (Table 4).

Water consumption	Number	Percentage
Well	22	37.93
Bottled	36	62.07
Total	58	100
Fuels used for cooking	Number	Percentage
Gas	23	39.66
Firewood	35	60.34
Total	58	100
Housing next to crops	Number	Percentage
No	28	41.37
Yes	30	58.63
Total	58	100
Pesticide use	Number	Percentage
No	45	77.59
Yes	13	22.41
Total	58	100

Table 4 Main sources of exposure to environmental risks

Discussion

In Mexico, environmental and perinatal risk factors have been studied in paediatric cancer patients (Martínez, M., Talavera, G., Benítez, M. L., Noguera, J., & Mesquita, M. 2022). In Yucatan, environmental problems have been detected without adequate intervention by governmental public health programmes to solve them. This exploratory study aims to describe the main maternal and perinatal health problems.

According to the national average of teenage pregnancies, it was found that Kinil is below since according to figures from the National Institute of Statistics and Geography (INEGI), the national percentage of teenage pregnancies in 2016 was 17.08%. In Mexico, there are reports of association of preterm birth with vehicular emissions of PM10 and CO in pregnant women (González, D., & Aristizabal, B. H. 2022).

The percentage of preterm births was 13.9%, in contrast to the percentage recorded from 2007 to 2012 in Yucatan of 7.2%, likewise the percentage of children with low birth weight recorded in Kinil was 32.76% compared to the percentage recorded by INEGI in the state in 2014 which was 11.5%.

The main health problems were Urinary tract infection (60.34%), upper airway infection (58.62%) and vaginal infection (41.38%) compared to those recorded by the National Survey of Demographic Dynamics (ENADID), which mentions that the main illnesses during pregnancy are pre-eclampsia/eclampsia, which occurs between 2% and 10% of pregnancies and urinary tract infection, particularly asymptomatic, which is observed between 17% and 20% of pregnant women. In terms of housing construction quality, most women reside in houses built with recycled material, and the percentage of overcrowding found was 12.07%, below the state average recorded in 2016 in Yucatan by the National Council for the Evaluation of Social Development Policy (CONEVAL) of 15.8%. The information collected allowed an approximation towards an environmental diagnosis of the main sources of exposure to environmental risks in pregnant women in Kinil, Yucatan, both in their positive and negative factors, but only in a cross-sectional manner. It is therefore necessary to implement analytical studies that allow for the study of associations between risks and disease, in order to propose intervention strategies for their reduction and control.

Conclusions

The main maternal health problems are urinary tract infection (60.34%), upper airway infection (58.62%) and vaginal infection (41.38%).

The prevalence of low birth weight and prematurity were 32.76% and 13.79% respectively and no neonatal deaths were recorded.

The percentage of women living in overcrowded conditions is 12.07%, 37.93% are exposed to potentially contaminated sources, 60.34% use biomass as fuel and 22.41% of them were exposed to pesticides used in agriculture.

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BDNF expression in blood. Study in iron deficient females**Expresión de BDNF en sangre. Estudio en hembras deficientes de hierro**

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Abstract

Iron deficiency is a public health problem that greatly impacts women and children, especially at the neurological level, being BDNF a relevant factor involved in such pathogeny. Objectives: To determine in females suffering from chronic iron deficiency, from the perinatal stage to adulthood, the levels of peripheral BDNF in blood. In addition, the effect of iron supplementation after weaning. Methodology: female Wistar rats with chronic iron deficiency and rats supplemented from weaning to adulthood (70 postnatal days) were euthanized to analyze BDNF levels in blood samples. Contribution: we demonstrate that in the presence of chronic iron deficiency, BDNF levels decrease peripherally and supplementation normalizes them. In addition, hemoglobin-bound iron (Fe-Hb) levels correlate positively with BDNF levels in blood. This could indirectly indicate a possible restoration or contribution to the improvement of the patient's cognitive or behavioral processes.

Resumen

La deficiencia de hierro es un problema de salud pública que impacta sobremanera a mujeres y niños, sobretodo a nivel neurológico, siendo el BDNF un factor relevante implicado en tal patogenia. Objetivos: Determinar en hembras que padecen deficiencia de hierro crónica, desde la etapa perinatal hasta la edad adulta, los niveles de BDNF en sangre. Además, el efecto de la suplementación de hierro a partir del destete. Metodología: ratas Wistar hembras con deficiencia de hierro crónica y ratas suplementadas desde el destete hasta la edad adulta (70 días-posnatales) fueron eutanasiadas para analizar en muestra sanguínea los niveles de BDNF. Contribución: demostramos que ante una deficiencia de hierro crónica, los niveles de BDNF disminuyen periféricamente y la suplementación los normaliza. Además, los niveles de hierro unido a hemoglobina (Fe-Hb) se correlacionan positivamente con los de BDNF en sangre. Lo anterior podría indicar indirectamente un posible restablecimiento o aporte a la mejora de procesos cognitivos o conductuales del paciente.

BDNF, iron, sex, deficiency, neurological, perinatal**BDNF, hierro, sexo, deficiencia, neurológico, perinatal**

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Introduction

Iron is a trace element that plays a key role in muscle metabolism, DNA synthesis and oxygen transport. Iron deficiency (DFe) is the most common micronutrient deficiency worldwide; it affects 614 million women and 280 million children worldwide (WHO, 2020a). Iron deficiency is the leading cause of anaemia, the most prevalent nutrient deficiency worldwide, affecting 33% of non-pregnant women, 40% of pregnant women and 42% of children (WHO, 2020a). Iron deficiency in foetal life and in children under two years of age can have significant and irreversible effects on brain development, leading to negative repercussions on affective, cognitive, memory, learning and school performance (Burden et al., 2007; Lozoff, 2011; Lozoff & Georgieff, 2006; Riggins et al., 2009). In adults, iron deficiency can also cause negative effects such as fatigue, reduced physical performance and decreased work productivity, as well as affecting socialisation and neurocognitive function. DFe occurs mainly when iron needs increase during periods of rapid growth and development, such as early childhood, adolescence and pregnancy, but can also occur at other stages of life. In pregnant women, iron deficiency can lead to anaemia, low birth weight and shortened gestation (WHO, 2020b).

Brain development during foetal and early postnatal life is an energy-intensive process (Fukumitsu et al., 2016; Kuzawa, 1998; Li et al., 2004) and is impaired in a rat model of foetal-neonatal ID (Brunette et al., 2010; Carlson et al., 2009; Fretham et al., 2012). Various neurocognitive disorders such as those related to iron deficiency, both in humans and in animal models, have been shown to be linked to alterations in neurotrophic factors, such as brain-derived neurotrophic factor (BDNF). BDNF is a polypeptide that acts as a growth factor and plays an important role in neuronal integrity; modulating neurotransmitter synthesis, metabolism and release (Crump et al., 2014), survival, differentiation and synaptic plasticity in the central and peripheral nervous systems (Lu & Figurov, 1997; Morse et al., 2015; Texel et al., 2011).

Long-term low expression and activity of BDNF at the hippocampal level has been demonstrated in subjects with DFe (Tran et al., 2009); in addition to changes in histone methylation at the BDNF locus in hippocampus of adult subjects who suffered fetal-neonatal DFe (Blegen et al., 2013; Tran et al., 2015); in addition to persistent dysregulation of JARIDs (members of the dioxygenase family that require iron as a cofactor to remove methyl groups from histone lysine residues); which was recently shown to be compensated or normalised following iron supplementation (Liu et al., 2021).

An important feature of BDNF is its ability to cross the blood-brain barrier; therefore, serum and cerebrospinal fluid levels are strongly correlated with brain levels (Gururajan et al., 2014; Harris & Barraclough, 1997; St Laurent et al., 2013). It is relevant to consider that an estrogen response element (ERE) is present in the BDNF gene, so estrogens increase the expression of this neurotrophic factor (Singh et al., 1995; Sohrabji et al., 1995), making its expression sex-dependent. As for iron, BDNF is known to increase its accumulation by inhibiting the expression of IRP1 (iron-responsive element-binding protein 1) and DMT1+IRE (divalent metal transporter 1 + iron-responsive element) (Zhang et al., 2014).

Few studies have been conducted in females, and with respect to iron deficiency, it is not known whether chronic iron deficiency in females affects BDNF levels in blood, an indirect determinant of brain levels. It is also unknown whether in females that suffered from perinatal iron deficiency and that after weaning were supplemented with iron, BDNF levels in blood are restored, which would indirectly indicate at the level of the central and peripheral nervous system, the benefits of the incorporation of iron in the diet.

Methodology

Ethical considerations

The study was conducted according to approved institutional protocols in accordance with the Principles and Procedures described by the National Institute of Health, Guide for the Care and Use of Laboratory Animals of the National Institutes of Health, in accordance with the guidelines of NOM-062-ZOO-1999; technical specifications for the production, care and use of laboratory animals. For sample collection, sacrifice was induced with CO₂ to minimise suffering.

Animals and diet

Wistar rats were maintained under standard conditions in the vivarium: 12:12 light/dark cycle (lights were switched on at 05:00 hours), temperature controlled at 22 ± 2°C and free access to food and water.

Twenty 3-month-old or 250-gram female foal rats were used to obtain study subjects. Fourteen days prior to mating conditions, ten rats were subjected to an iron-deficient diet consisting of 10 ppm FeSO₄ (Lab diet AIN-76W/10). The other ten rats received a control diet containing 100 ppm FeSO₄ (Lab diet AIN-76W/100). Twenty-five days after mating, the offspring were obtained. At weaning, 21 days postnatal (DPN), ten female offspring from iron-deficient dams and ten female offspring from the control group were randomly separated and fed the same diet as their dams until adulthood at 70 days postnatal day 70. Another group of female offspring from iron-deficient dams from 21 to 70 PND were supplemented with 100 ppm FeSO₄ iron (Lab diet AIN-76W/100).

Sample collection

At 70 PND, rats were euthanised in a CO₂ chamber with a gradual release of O₂ at a rate of 0.5 L CO₂/min/10 min. Subsequently, two mL of blood was withdrawn by intracardiac puncture using an EDTA syringe. For Fe-Hb measurement, one mL of blood was used. The other mL was used to determine the amount of circulating BDNF; thirty minutes after blood collection, it was centrifuged for 10 minutes at 1000 rpm. The plasma was extracted and kept cold (-80°C) until processing.

Haemoglobin-bound iron (Fe-Hb)

To demonstrate the presence of ID, Fe-Hb levels were indirectly measured in each study group using the following formula (Hernandez et al., 2006; Wienk et al., 1999):

$$Fe - Hb(mg) = \frac{\left(\frac{Hb}{L}\right) * (body\ weight) * 6.7 * 0.335}{10000}$$

Where Hb (g) contains 0.335% iron. The blood volume in growing rats is 6.7% of body weight (g).

To determine Hb, 1 mL of blood was taken from the subjects studied; its concentration was determined in triplicate by the cyanomethaemoglobin method using Drabkin solution (Radox Mexico SA de CV) (Prohaska & Gybina, 2005; Unger et al., 2007).

Determination of BDNF

Blood samples were analysed according to the immunoassay procedure, Milliplex Map Kit, Rat Pituitary Magnetic Bead Panel, Cat. # RPTMAG-86K. Results were expressed in pg/mL.

Statistical analysis

SPSS 22® statistical software was used for statistical analysis; initially a descriptive statistical analysis was performed for each variable considered. The results were presented as means ± standard deviation (mean±SD). To compare differences between two groups (e.g. "Control" and "DFe" or "DFe+S" groups), the Mann-Whitney U-test was used. Results of p<0.05 were considered statistically significant, with a 95% confidence interval.

Results

Iron bound to haemoglobin (Fe-Hb)

When studying the ID group with respect to the control group, it was found that the former had 10.9% less Fe-Hb and 3.8% less than the ID+S group, see Table 1.

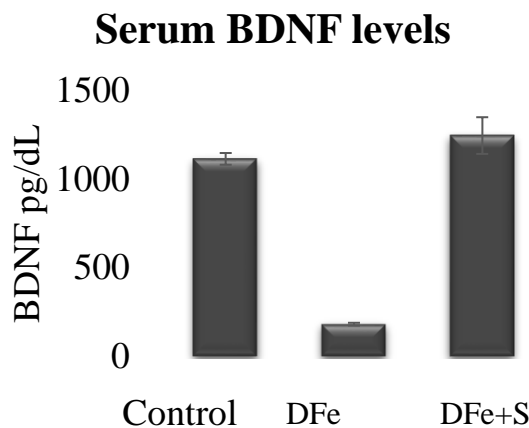
Group	Fe - Hb
Control	3.71±0.11
Iron deficient+supplementation	3.47±0.11
Iron deficient	3.18±0.23*

* Female of control group (p≤0.05).

Table 1 Levels of iron bound to haemoglobin "Fe-Hb". All values are expressed as mean ± standard deviation

Determination of BDNF

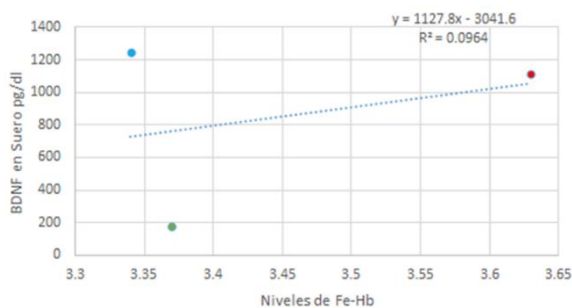
BDNF levels at the peripheral (serum) level were decreased in iron-deficient subjects compared to control subjects; however, iron supplementation resulted in an increase in BDNF levels at the peripheral level, even above the levels of control females (Graphic 1)



* vs. control group female (p≤0.05)
 **Female from Iron Deficient+Supplemented group (p≤0.05)

Graphic 1 BDNF levels in blood. Values indicate mean ± standard error

Graphic 2 shows the correlation between serum BDNF levels and haemoglobin-bound iron levels.



Graphic 2 Correlation between BDNF and haemoglobin-bound iron levels. Red dots indicate control females; green DFe and blue DFe+S

Discussion

Iron deficiency during pregnancy has been associated with a high risk of developing schizophrenia (Insel *et al.*, 2008) and autism (Schmidt *et al.*, 2014) in infants; and in later life with Alzheimer's disease (Faux *et al.*, 2014; Lee *et al.*, 2020). A child's cognitive development may also be affected if the mother is iron deficient during the last trimester of pregnancy (WHO, 2020a). Long-term behavioural deficits in hippocampal-dependent learning and memory have been demonstrated in murine models of iron deficiency (Pisansky *et al.*, 2013; Schmidt *et al.*, 2012), which is associated with altered expression of genes critical for neural development (Brunette *et al.*, 2010; Carlson *et al.*, 2007; Tran *et al.*, 2009) and gene networks implicated in schizophrenia, autism and mood disorders (Tran *et al.*, 2016). The neurological alterations mentioned above have also been observed in animal models of foetal-neonatal iron deficiency (Barks *et al.*, 2018; Barks *et al.*, 2019; Fretham *et al.*, 2011). It should be noted that brain development during these stages is an energy intensive process (Fukumitsu *et al.*, 2016; Kuzawa, 1998; Li *et al.*, 2004) that has been shown to be altered in a rat model of DFe (Brunette *et al.*, 2010; Carlson *et al.*, 2007; Fretham *et al.*, 2011).

Brain Derived Neurotrophic Factor (BDNF) is the most widely distributed neurotrophin in the central nervous system. In the adult brain, BDNF fulfils certain functions such as regulating neuronal integrity, promoting brain plasticity, modulating synthesis, metabolism and release of neurotransmitters, and intervening in neuroplasticity processes (Crump *et al.*, 2014). Importantly, BDNF crosses the blood-brain barrier and serum levels correlate strongly with brain levels (Harris & Barraclough, 1997). Serum BDNF levels have been shown to increase after three months on a reduced-calorie diet (Araya *et al.*, 2008) but it is not known what happens in the face of chronic iron deficiency, a situation experienced by a large proportion of the population mainly in developing countries. There is evidence that BDNF levels can undergo short-term changes in response to external stimuli.

For example, it has been shown that serum levels of the factor increase after three months on a reduced-calorie diet (Araya *et al.*, 2008), and decrease in the hippocampus after iron deficiency during the prenatal period and up to 7 days postnatal (Tran *et al.*, 2008). However, it has also been found that under dietary restriction there is an increase in BDNF levels (Lee *et al.*, 2002). So far, it was not known what happens in females with chronic iron deficiency. It is worth mentioning that BDNF as well as estrogens share parallel effects in terms of neuroprotection in the processes of neuronal excitotoxicity, enhanced learning (Scharfman & MacLusky, 2006), modulation of synaptic transmission and increased synaptogenesis (McAllister *et al.*, 1999). In the present study, iron deficiency over a prolonged period of time was shown to negatively affect BDNF levels. In addition, the impact of iron supplementation on BDNF levels, especially in females, was unknown, although research reports data on BDNF elevation in serum of subjects with Zinc monotherapy, a bivalent element that has similar functions to iron (Solati *et al.*, 2015). Our results could demonstrate that iron-supplemented females reestablish homeostatic mechanisms that allow the passage of BDNF back to the peripheral level.

Therefore, the findings of the present research are of great importance for the medical field, since it is known that subjects suffering from iron deficiency have memory and emotion problems that impact on their reasoning and quality of life, which may be associated with alterations in BDNF levels in the central nervous system, data that coincide with previous reports. In addition, it was shown that adequate iron supplementation can balance BDNF levels at the peripheral level, reflecting levels in the central nervous system, which could be applied in the clinic as a prognostic marker to help indicate early improvement or recovery of brain function in patients suffering from iron deficiency from an early age.

Conclusions

- A. In chronic iron deficiency, BDNF levels decrease peripherally.
- B. Iron supplementation in iron-deficient subjects normalises BDNF levels peripherally.
- C. Haemoglobin-bound iron levels correlate positively with BDNF levels in the blood.

Suggestions

Mexico is a nation with risk factors predisposing to iron deficiency. Based on the results obtained, it is recommended to emphasise the determination of haemoglobin values to indirectly identify iron values and thus supplement with this trace element only in the indicated cases. If low iron levels in the infant are determined at an early age, closely monitor the adequate intake of this trace element and continue supplementation during postnatal development until it is deemed necessary, as this prevents cognitive, behavioural and emotional deterioration, entities associated with low BDNF levels.

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Metabolic control with diet vs insulin in patients with gestational diabetes and obesity

Control metabólico con dieta vs insulina en pacientes con diabetes gestacional y obesidad

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Abstract

Objective: To identify the degree of metabolic control achieved in pregnant patients diagnosed with Gestational Diabetes and Obesity treated with diet, compared to those treated with insulin. Methodology: Observational, retrospective, longitudinal and descriptive study, carried out from January to December 2021. Metabolic control was evaluated monthly during pregnancy based on the treatment received (diet vs insulin with 23 patients in each group). Results: Of the 23 patients who started on the diet, only 30.4% finished in a controlled manner under the same diet-only regimen. In contrast, of the 23 who started with insulin, 86.9% ended up controlled.

Metabolic Control, Gestational Diabetes, Obesity

Resumen

Objetivo: Identificar el grado de control metabólico logrado en las pacientes embarazadas con diagnóstico de Diabetes Gestacional y Obesidad tratadas con dieta, comparadas con aquellas tratadas con insulina. Metodología: Estudio observacional, retrospectivo, longitudinal y descriptivo, realizado de enero-diciembre de 2021. Evaluándose mensualmente el control metabólico durante la gestación con base en el tratamiento recibido (dieta vs insulina con 25 pacientes en cada grupo). Resultados: De las 25 pacientes que iniciaron con dieta, sólo el 30.4% terminaron en forma controlada bajo el mismo régimen de solo-dieta. En cambio, de las 25 que iniciaron con insulina, el 86.9% terminaron controladas.

Control Metabólico, Diabetes Gestacional, Obesidad

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Introduction

Gestational diabetes is defined as carbohydrate intolerance of variable severity, which is first recognised during pregnancy, and which may or may not resolve after pregnancy, whatever the necessary treatment and postpartum course. Pre-gestational diabetes is established in patients already known to have type 1 or 2 diabetes who become pregnant [1].

The products of mothers with poorly controlled gestational diabetes have an increased risk of macrosomia leading to an increased risk of dystocia and caesarean section to prevent it, and these products require special care and even hospitalisation in neonatal therapy areas. Therefore, metabolic control of gestational diabetes is essential to prevent complications and reduce maternal and foetal morbidity and mortality and thus the number of days of hospitalisation and costs. Obesity itself is a factor of metabolic dyscontrol, so it is important to determine which type of treatment has a favourable impact on metabolic control and obstetric outcome: diet or insulin.

Physiological changes in pregnancy

During pregnancy, the pancreas is subject to a greater demand for adaptation, so there may be varying degrees of alterations in carbohydrate metabolism; these would be genetically determined and may manifest for the first time during pregnancy (GD) or be aggravated in patients with pre-existing diabetes. It must be considered that these metabolic alterations will be accentuated in a state of insulin resistance, such as pre-pregnancy obesity, due to increased abdominal fat or uncontrolled excessive weight gain during the course of pregnancy [2]. Decreased insulin sensitivity in women during pregnancy and inadequate response to insulin secretion are the pathophysiological mechanisms that cause gestational diabetes, with abnormalities in glucose transport by insulin-sensitive tissues and in the affected sensitivity of the b-cells of the pancreas, which synthesise the hormone. Insulin-regulated carbohydrate, protein and lipid metabolism is also affected. Decreased maternal sensitivity to insulin increases the availability of nutrients to the fetus, which increases the risk of excessive growth and increased adiposity.

Diagnosis of gestational diabetes

There are four ways to diagnose Gestational Diabetes according to the Clinical Practice Guideline [1]:

1. Fasting glucose greater than or equal to 126 mg/dl on two occasions
2. Casual blood glucose of ≥ 200 mg/dl
3. Screening test with 50 g of glucose with a result greater than or equal to 180 mg/dl (170 mg/dl in women over 30 years of age).
4. Oral Glucose Tolerance Curve with 75 g with two abnormal results, ≥ 95 in fasting, ≥ 180 in the 1st hour, ≥ 155 in the 2nd hour.

Medical treatment

When diet and exercise do not achieve target numbers with fasting glycaemia less than 95 mg/dL and 120 mg/dL two hours postprandial within 2 weeks, pharmacological management should be initiated. Metformin is recommended in patients with gestational diabetes and pregnancy greater than 20 weeks when the patient refuses insulin therapy and does not have metabolic dyscontrol that puts the pregnancy at risk.1 Approximately 25% of patients with GD require medical management with insulin. Some are treated with a single dose of neutral protamine Hagedorn (NPH) insulin before bedtime (usual starting dose 0.2 units/kg body weight) in response to elevated fasting glucose levels; while other women may need only short-duration insulin injections to cover postprandial hyperglycaemia¹⁰. In cases where both fasting and post-meal hyperglycaemia are evident, a multiple injection regimen combining intermediate- and short-duration insulin is administered. The total starting dose is usually 0.7 to 1.0 units/kg daily. Approximately 50% of the total daily insulin is given as NPH (at breakfast and before bedtime) and the remainder may be insulin lispro or aspart, both rapid-acting insulin analogues, before meals as needed. Short-acting analogues are safe and superior to regular insulin in reducing postprandial glucose spikes. Long-acting insulin analogues (insulin glargine and detemir) have been designed to more closely mimic basal insulin secretion, but neither has yet been extensively studied in women with gestational diabetes.

Methodology to be developed

Observational, retrospective, longitudinal and descriptive study. We studied patients admitted with a diagnosis of gestational diabetes during the study period from January to December 2021, with associated obesity, evaluating metabolic control during pregnancy based on the treatment received with diet or insulin.

A sample of 50 patients was estimated and divided into two groups:

Group 1 (D) were the patients starting with diet, n = 25.

Group 2 (I) were patients starting with insulin, n = 25.

According to laboratory parameters, in the following determinations

Glucose (mg/dL) Glycosylated haemoglobin (%).

Results

A total of 50 patients with a diagnosis of Gestational Diabetes (GD) were selected, however, when calculating BMI, 4 of them (2 from each group) were found not to be obese and were therefore discarded from the study. Therefore, the total sample was 46 patients: 23 in the group that received "Diet" and 23 in the group that received "Insulin" as initial treatment. The mean age of the patients was 28.7 ± 6.5 years, BMI was 34.4 ± 5.2 kg/m² and gestational age was 29.8 ± 3.9 weeks of gestation. The analysis by groups with respect to maternal age, gestational age and BMI is presented in table 1. Significant differences were observed only for gestational age. The Mann-Whitney U test was used because the distribution of this variable did not fit a Normal curve.

Variable	Diet group N: 23 M (DE)	Insulin group N: 23 M (DE)	p-value
Maternal age (years)	30 (7.4)	27.4(5.4)	0.179
Gestational age (weeks)	29.0 (3.2)	30.7 (4.4)	0.017
IMC (Kg/m ²)	37.5 (5.6)	37.3 (4.8)	0.956

Table 1 Mean (M) and standard deviation (SD) of maternal and gestational ages and BMI according to groups

Although it was observed that baseline blood glucose values in group I were higher than in group D, this difference was not significant. In contrast, and contrary to expectations, significance between groups was observed with respect to HbA1c, where it was higher in group D than in group I. These data are presented in table 2.

Variable	Group I M (DE)	Group D M (DE)	p-value
Blood glucose Basal (mg/dL)	177.5 (22.2)	160.1 (40.3)	0.076
HbA1c (%)	6.8 (1.1)	7.3 (1.1)	0.039

Table 2 Mean (M) and standard deviation (SD) of baseline blood glucose and HbA1c according to the groups

Diet group

Of the 23 patients who started on a diet, only 7 concluded the diet in a controlled manner. Twelve (52.2%) patients who started on diet were switched to insulin due to metabolic dyscontrol. This occurred between weeks 32 and 38 with an average of 34.7 ± 2.1 . Nine patients showed glucose values of 140 mg/dL or higher in the first month of starting treatment. This group had an average glucose value of 147.7 ± 5.6 mg/dL. One patient had normal glucose values in the first month (119 mg/dL) but higher values (198 mg/dL) in the second month, so her treatment was also changed. Two patients were found to have blood glucose values below 140 mg/dL at all times and their treatment was changed. The remaining 11 (47.8%) patients concluded their treatment with diet. This group showed an average of 139.5 ± 33.9 mg/dL. These patients were kept on diet throughout the treatment and no high numbers (≥ 140 mg/dL) were observed in the subsequent months. However, this was not the case in 6 of them (mean: 162.1 mg/dL). Of these six, three were controlled in the second month, the other three remained with inadequate metabolic control. One of the patients who was controlled in the first month (133.0 mg/dL) increased to 140 mg/dL in the second month. Finally, these four patients had values below 110 mg/dL in the third month of their treatment. It is important to note that patients who did not show up for their evaluation in that month, or who had already completed their pregnancy, were grouped as "Non-assessed".

Insulin group

No change was found in the 23 patients who received insulin as initial treatment. This group had an average of 144.9 ± 23.7 mg/dL in the first month from the start of treatment. This value is high because 13 patients remained uncontrolled. In the second month, 8 patients showed uncontrolled values; only one in the third month (144 mg/dL) and also one in the fourth month (150 mg/dL). The latter had shown acceptable values in the previous month (135 mg/dL) and is the only one who ended the pregnancy with abnormally high blood glucose levels. Two patients in this group could not be assessed at the end of pregnancy.

Conclusions

1. Of the 23 patients who started on a diet, only 30.4% (n=7) finished in a controlled manner on the same diet-only regimen. In contrast, of the 23 who started with insulin, 86.9% (n=20) ended up controlled.
2. 52.2% (n=12) of the patients who started on diet had to switch to insulin due to their metabolic dyscontrol. Of these, 10 ended up in a controlled manner. The change of treatment occurred between weeks 32 and 38 with an average of 34.7 weeks.
3. The degree of metabolic control in the patients was better in those who received insulin compared to those who were on diet alone.
4. Initial treatment with insulin in patients with Gestational Diabetes and Obesity is associated with better metabolic control than that obtained with diet.

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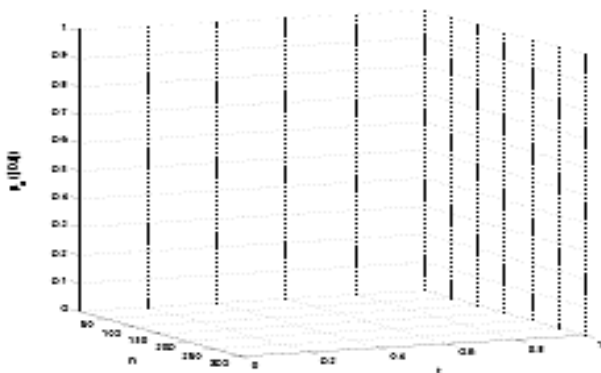
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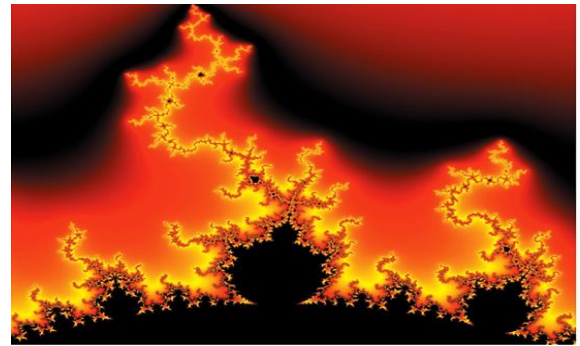


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