ORIGINAL ARTICLE

Maternal factors and the consumption of drugs during pregnancy associated with the development of neonatal disorders

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ABSTRACT

Introduction: drug consumption has increased in the last decades and precisely pregnancy represents a situation of maximum risk related to its use.
Objective: to describe maternal factors and drug consumption during pregnancy associated with the appearance of neonatal alterations.
Methods: a retrospective longitudinal descriptive study was conducted in the period from September 2015 to September 2018 to describe maternal factors and medication consumption during pregnancy associated with the appearance of neonatal alterations. The study population consisted of 779 pregnant women recruited during this period and the sample consisted of 518 randomly selected pregnant women. We worked with two groups: one group of pregnant women who did not consume drugs during pregnancy and the other who did. The data obtained made it possible to analyze maternal variables such as the consumption of drugs during pregnancy, the area of origin of those who consumed them, the drugs prescribed or not and the trimester of pregnancy in which they were consumed and, for the newborn, the presence or absence of neonatal alterations.
Results: the frequency of medication consumption during pregnancy was 55.21%.
Conclusions: in the sample studied, the consumption of drugs during pregnancy prevailed, mainly in the first trimester, mostly by self-medication in women from rural areas, and neonatal alterations were significantly associated with all the above mentioned.
Key words: pregnancy; drugs; teratogens; risk category; neonatal

RESUMEN

Introducción: el consumo de medicamentos se ha incrementado en las últimas décadas y precisamente el embarazo representa una situación de máximo riesgo relacionado con su uso.
Objetivo: describir los factores maternos y el consumo de medicamentos durante el embarazo asociados a la aparición de alteraciones neonatales.
Métodos: se realizó un estudio descriptivo longitudinal retrospectivo en el período de septiembre de 2015 a septiembre de 2018 para describir los factores maternos y el

consumo de medicamentos durante el embarazo asociados a la aparición de alteraciones neonatales. La población de estudio la constituyeron 779 gestantes captadas durante ese período y la muestra quedó conformada por 518 gestantes seleccionadas de forma aleatoria. Se trabajó con dos grupos: uno de gestantes que no consumieron fármacos durante el embarazo y otro que si. Los datos obtenidos permitieron analizar variables maternas como el consumo de medicamentos durante el embarazo, la zona de procedencia de las que consumieron, los medicamentos prescritos o no y el trimestre del embarazo en que los consumió y, del neonato, la presencia o no de alteraciones neonatales.
Resultados: la frecuencia del consumo de medicamentos durante el embarazo fue del 55,21%.
Conclusiones: en la muestra estudiada prevaleció el consumo de medicamentos durante la gestación, principalmente en el primer trimestre, en su mayoría por automedicación en mujeres procedentes de zonas rurales, y las alteraciones neonatales estuvieron asociadas significativamente a todo lo mencionado.
Palabras clave: embarazo; medicamentos; teratógenos; categoría de riesgo; neonatal

INTRODUCTION

The use of drugs during pregnancy has increased in the last decades and is such a frequent circumstance that it requires a correct knowledge of the properties of the drug and its indications, the characteristics of the persons to whom it is prescribed and the stages of pregnancy, which has differential particularities that require special considerations because it can have serious consequences for both the mother and the fetus or infant.[1,2]
Pregnancy represents a situation of maximum risk related to the use of drugs because the use of some drugs has been associated with the development of neonatal alterations.[3]
Almost 3% of all newborns have a congenital anomaly that requires medical attention. One third of these defects are life-threatening. Prevention of neonatal defects and investigation of risk factors are key objectives. Since the thalidomide disaster all attention has been focused on the drugs and environmental chemicals to which a pregnant woman may be exposed. Some reports suggest that a large number of pregnant women take three or four prescribed or non-prescribed drugs.[4,5,6]
In developed countries, congenital malformations are the leading cause of infant mortality. The World Health Organization estimates that, worldwide, 276,000 newborns die each year during the first four weeks of life due to neonatal alterations, specifically congenital anomalies, which can also cause chronic disabilities, with great impact on the cost of their care and follow-up. In Latin America and the Caribbean, congenital malformations represent 21% of infant mortality in children under five years of age. In Cuba, during 2019, neonatal alterations and congenital defects constituted the second cause of death in children under one year of age with 89 deaths (rate of 0.8 per 1 000 live births); very similar results are found in the Province of Villa Clara, so that it has a primordial place in the country's medical and social programs.[4,7,8]
The information about the security of drugs in gestation is abundant, but there is little scientific evidence and, for ethical reasons, very few clinical trials have been carried out and published; most of the published researches are case-

control studies, registry of the exposure of patients to certain drugs or preclinical trials carried out with animals. All this has led to the overestimation of the danger of drugs in pregnancy and to limit their reasonable use in chronic diseases in pregnant women, and, at the other extreme, to prescribe medication freely without knowing the true risk involved in administering them at the wrong time and in the wrong dose.[9]

It was decided to carry out the present investigation with the purpose of describing maternal factors and the consumption of medications during pregnancy associated with the appearance of neonatal alterations.

METHODS

Design and population

A retrospective longitudinal descriptive study was conducted to describe the maternal factors and the consumption of medications during pregnancy associated with the appearance of neonatal alterations, in the Municipality of Santo Domingo, Villa Clara Province, in the period from September 2015 to September 2018, in the study sample and in the period mentioned above.

The study population was constituted by all the pregnant women registered in the period (779). The sample consisted of 518 pregnant women selected randomly, by simple random probability sampling, in which two out of three were selected and two groups were worked with: one group of pregnant women who did not consume drugs during pregnancy and another that did.

Study variables

The information was obtained from the Linear Registry of risk factors of the Municipal Genetics Department, which analyzed maternal variables such as the consumption of medications during pregnancy, the area of origin of those who consumed them, the medication prescribed or not and the trimester of pregnancy in which they were consumed, and, for the neonate, the presence or absence of neonatal alterations.

Statistical analysis

The study data were stored in a database in Microsoft Excel and then exported to SPSS 20.0 software. For the statistical analysis, descriptive statistics were used with the calculation of absolute and relative frequencies, Chi-square and binomial statistical tests as required. A $p<0.05$ was used as the level of statistical significance. A 95% confidence interval was used. The results were shown in graphs and tables.

Ethical considerations

Ethical considerations were taken into account in the research and the commitment to use the data obtained strictly for the proposed objectives was respected, maintaining the anonymity of the participants' personal data.

RESULTS

A total of 518 pregnant women were studied, of whom 286 (55.21%) consumed some medication during pregnancy and 100% were from rural areas.

When a binomial test was applied, a pα=0.000 was obtained, which shows that rural residence is significant for the consumption of medications during pregnancy in the sample studied (Figure 1).

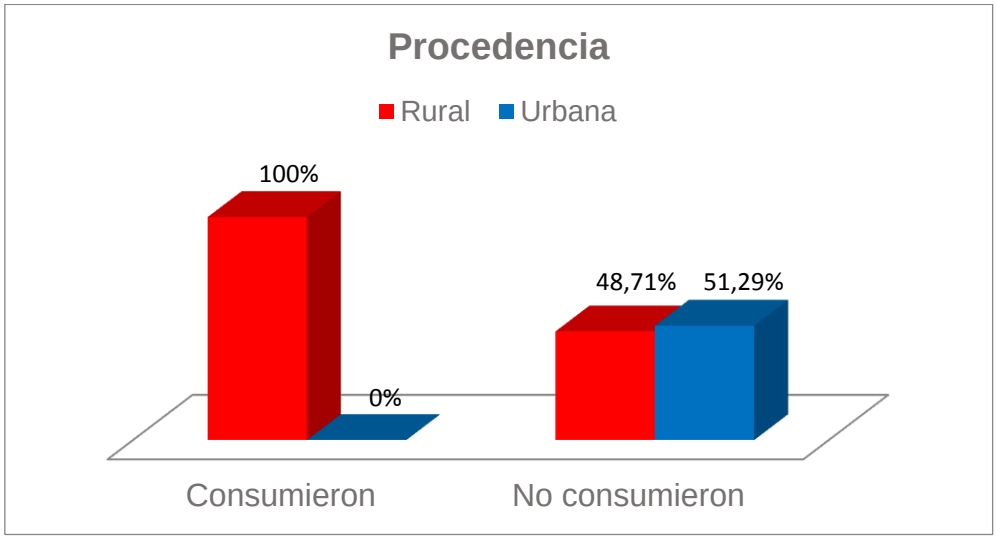

Figure 1. Distribution of the sample according to the area of origin and the consumption of drugs by pregnant women
pα=0.000
Source: Linear Registry of risk factors of the Municipal Genetics Department

The distribution of the pregnant women according to the origin of the consumption of medications during pregnancy showed that 224 (78.32%) consumed medications by self-medication and not by medical prescription. A binomial test was performed in which a pα=0.000 was observed, showing that self-medication is significant within the consumption of medications during pregnancy in the sample studied (Figure 2).

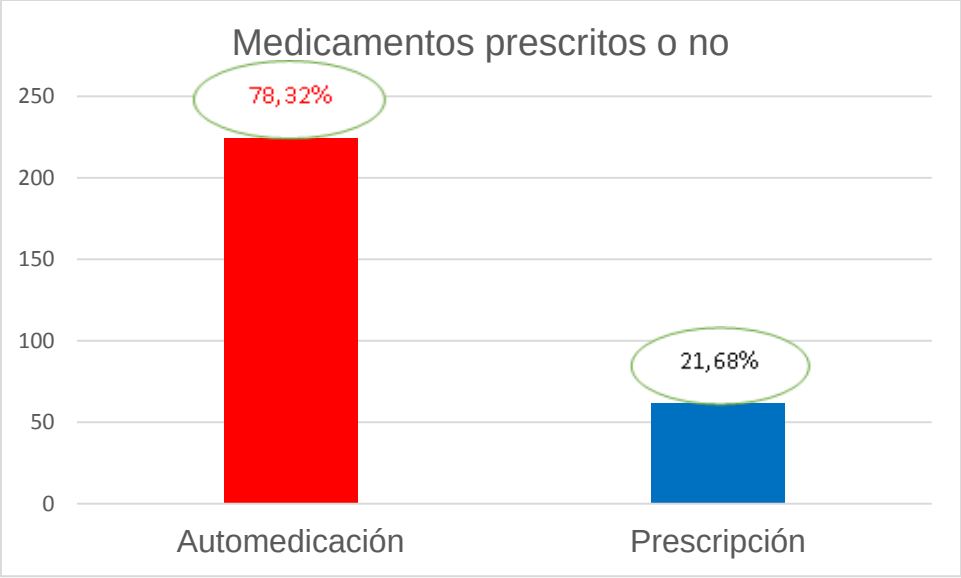

Figure 2. Distribution of the sample according to drugs prescribed or not during pregnancy
pα=0.000
Source: Linear Registry of risk factors of the Municipal Genetics Department

The greatest number of pregnant women who consumed medications did so in the first trimester of pregnancy (222, 77.62%); they were followed, in order of frequency, by those who consumed medications in all trimesters (18.53%). When a Pearson's Chi-square test was applied, a $p<0.05$ was obtained, which showed that the consumption of medications in the first trimester marked a significant difference with respect to the rest of the trimesters (Figure 3).

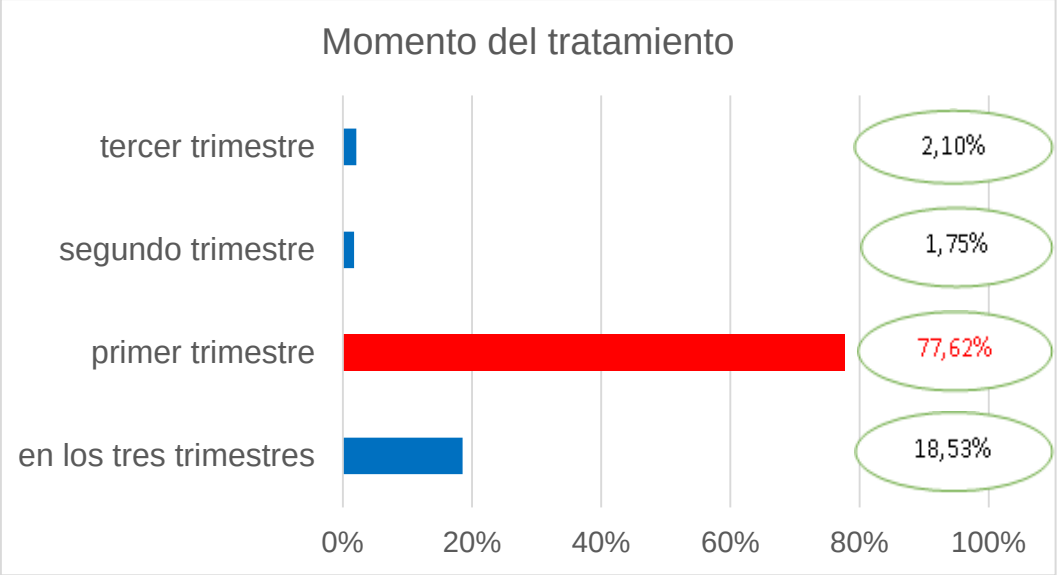

Figure 3. Distribution of the sample according to the trimester of pregnancy in which drugs were consumed
$X^2=3.020$; pα=0.032
Source: Linear Registry of risk factors of the Municipal Genetics Department

Neonatal alterations were mostly in newborns of pregnant women who consumed drugs during gestation (0.77%), with a significant statistical relationship. Nonsteroidal anti-inflammatory drugs and sulfas antibiotics were the most consumed drugs. The main neonatal alterations were closed fontanel, brachial palsy, Felot's tetralogy and ureterocele (Table 1).

Table 1. Distribution of the sample according to the presence of neonatal alterations

Neonatal disorders	No consumption		Consumption		Total	
	No.	%	No.	%	No.	%
No	224	43,24	289	55,80	513	99,04
Yes	1	0,19	4	0,77	5	0,96
Total	**225**	**43,43**	**293**	**56,57**	**518**	**100**

T=0.10; pα=0.163
Source: Linear Registry of risk factors of the Municipal Genetics Department

DISCUSSION

During pregnancy, approximately four to ten medications are consumed, either to improve the conditions that accompany it or to prevent complications; self-medication and dosage errors on the part of the patient should not be underestimated, which is why adequate follow-up and control by the basic health care team is timely.[2,10]

Similar results to those shown in Figure 1, which showed that more than 50% of pregnant women consumed some medication during pregnancy, were obtained in a study conducted in a health area of Bayamo, Cuba, which showed that more than half of the study sample (70%) also did the same thing.[11]

As shown in Figures 1 and 2, 100% of the pregnant women who consumed medications during pregnancy were from rural areas and 78.32% self-medicated, respectively. A study carried out in Sucre, Colombia, on the surveillance of the use of medications during pregnancy differs from these results, in which only 32% of the sample that consumed medications during gestation resided in rural areas and only 21% of the sample analyzed did so by self-medication.[12]

The results shown in Figure 2 are very similar to those obtained in a study in Peru on predisposing factors to self-medication, in which it was concluded that 77% of the sample analyzed consumed the medications consumed by pregnant women through self-medication.[13]

Similar results to those shown in Figure 3 were obtained in a study carried out in Santiago de Cuba, which showed that the time of gestation when the highest consumption of drugs occurred was in the first trimester of pregnancy (92.3%), which is the most critical period for causing a teratogenic effect on the embryo.[14] There is a tendency to prescribe and consume drugs in the first trimester of pregnancy, a finding that coincides with different authors, due to the fact that in prenatal screening and evaluation a series of risk factors and conditions are identified that lead to timely and early treatment, with the aim of avoiding future complications; however, it is advocated that these patients should be adequately followed up and genetic counseling.[14]

The results of this study do not coincide with one conducted in Sao Paulo, Brazil, where it was found that the highest consumption of medications during pregnancy occurred in the second trimester (55.84%).[15]

Most neonatal alterations, specifically congenital defects, are of unknown cause. Exposure to chemical substances, including drugs, is the main cause that produces these alterations in about one and 1.5% of cases. Results similar to those shown in Table 1 are those of a study conducted in Lima, Peru, which showed that 1.1% of the births presented neonatal alterations.[16]

Neonatal alterations can be caused by genetic or environmental factors or by a combination of both. Approximately 5% of clinically significant congenital structural defects in humans are caused by environmental agents, including drugs. Unfortunately, animal studies are not predictive of human outcomes in teratology research. Genetic variability results in differences in drug absorption, distribution and metabolism. Extrapolating results from animal data to humans is problematic because pharmacokinetic profiles vary in dependence on the drug and species.[17,18,19,20]

CONCLUSIONS

In the sample studied, the consumption of medications during gestation prevailed, mainly in the first trimester, mostly due to self-medication in women from rural areas, and neonatal alterations were significantly associated with all of the above.

BIBLIOGRAPHIC REFERENCES

1.Vera Carrasco O. Uso de fármacos en el embarazo. Rev Méd La Paz [Internet]. 2015 [cited 04/21/2021];21(2):60-76. Available at: http://www.scielo.org.bo/scielo.php?script=sci_arttext&pid=S1726-89582015000200010
2.Valdes Silva Y, Sánchez Ramírez E, Fuentes Arencibia S. Malformaciones congénitas relacionadas con los agentes teratógenos. CCM [Internet]. 2018 [cited 04/21/2021];22(4):652-66. Available at: http://scielo.sld.cu/pdf/ccm/v22n4/ccm11418.pdf
3.Motta IM. Promoción de salud. La importancia de conocer los factores teratogénicos que afectan el SN. Rev Digit Prospect Psicol [Internet]. 2019 [cited 04/21/2021];3(2):33-43. Available at: https://www.kennedy.edu.ar/wp-content/uploads/2019/10/2019_07_Revista-Prospectiva_carta.pdf#page=33
4.Ministerio de Salud Pública. Dirección de Registros Médicos y Estadísticas de Salud. Anuario Estadístico de Salud 2019. La Habana: MINSAP; 2020 [cited 07/14/2022]. Available at: https://files.sld.cu/bvscuba/files/2020/05/Anuario-Electr%c3%b3nico-Espa%c3%b1ol-2019-ed-2020.pdf
5.Florez J. Farmacología Humana.3a ed. Barcelona: Masson S.A; 1997 [cited 07/14/2022]. Available at: https://clea.edu.mx/biblioteca/files/original/3233e9fb8d4c9c4419774a62e7d587c6.pdf
6.Brunton LI. Goodman y Gilman. Las Bases farmacológicas de la terapéutica. 13 ed. Buenos Aires: Mc Graw Hill Castellanos; 2018.
7.Aguilar G, Mazariegos E, Arriola C, Peralta S. Caracterización de pacientes con hijos diagnosticados con malformaciones congénitas. Rev Cienc Multidiscip CUNORI [Internet]. 2019 [cited 07/14/2022];3(1):19-28. Available at: http://revistacunori.com/index.php/cunori/article/view/76/76. https://doi.org/10.36314/cunori.v3i1.76
8.Alvarez Gavilán Y, Lantigua Cruz PA, Benítez Cordero Y, Pérez Grenier O, Collazo Acosta E. Defectos congénitos presentes en la descendencia de mujeres diabéticas, obesas e ipertensas, Artemisa 2016. Rev Cubana Genét Comunitaria [Internet]. 2020 [cited 07/14/2022];13(1):e92. Available at: https://revgenetica.sld.cu/index.php/gen/article/view/92/155
9.Toapanta Guamán AR, Gamboa Santana KE. Efecto teratogénico de la exposición a fármacos u otras sustancias químicas en niños con defectos congénitos nacidos en el Hospital Matilde Hidalgo de Prócel [thesis]. Guayaquil: Universidad de Guayaquil; 2019 [cited 04/20/2021]. Available at: http://repositorio.ug.edu.ec/handle/redug/40985
10.Silva González GK, Rodríguez Peña Y, Muñoz Callol JL, Carcases Carcases E, Romero Portelles LC. Incidencia de los defectos congénitos asociados al uso de medicamentos en Las Tunas. Rev Electrón Dr Zoilo E. Marinello Vidaurreta [Internet]. 2015 [cited 07/16/2022];40(5):[aprox. 7 p.]. Available at: http://revzoilomarinello.sld.cu/index.php/zmv/article/view/61/pdf_1
11.Verdecia Torrez L, Pérez Domínguez IR, Guerra Torrez RA. Uso de medicamentos durante el embarazo en un área de salud en Bayamo [Internet]. Cibamanz 2020. I Congreso Virtual de Ciencias Básicas Biomédicas en Granma. Manzanillo: Universidad de Ciencias Médicas de Granma; 2020 [cited 07/16/2022]. Available at: http://www.cibamanz2020.sld.cu/index.php/cibamanz/cibamanz2020/paper/view/290/334
12.Oliu Bosch SB, Bosch Núñez AI. Prevalencia de gestantes consumidoras de medicamentos con diagnóstico prenatal de defectos congénitos. Rev Cient Estud

Unimed [Internet]. 2020 [cited 07/16/2022];2(1):6-17. Available at: https://revunimed.sld.cu/index.php/revestud/article/view/14/pdf
13.Márquez Gómez MA; Gómez Díaz GM. Vigilancia del uso de medicamentos en el embarazo en el municipio de Los Palmitos, Sucre, Colombia: una contribución para la prevención y reducción de la mortalidad materna y perinatal. Nova [Internet]. 2017 [cited 07/16/2022];15(28):115-124. Available at: http://www.scielo.org.co/pdf/nova/v15n28/1794-2470-nova-15-28-00115.pdf
14.Hoyos Rojas JJ. Factores predisponentes a la automedicación en un Centro de Salud en la Ciudad de Huancayo [thesis]. Huancayo: Universidad Peruana de los Andes; 2017 [cited 07/12/2022]. Available at: https://repositorio.upla.edu.pe/handle/20.500.12848/169
15.Satie Kassada D, Inocenti Miasso A, Pagliarini Waidman MA, Silva Marcon S. Prevalence and factors associated with drug use in pregnant women assisted in primary care. Text Context Nursing [Internet]. 2015 [cited 07/12/2022];24(3):713-721. Available at: http://www.scielo.br/pdf/tce/v24n3/0104-0707-tce-2015002770013.pdf. https://doi.org/10.1590/0104-07072015002770013
16.Vásquez Bereche DP, Zelaya Sánchez PA. Relación entre medicamentos prescritos durante el embarazo y defectos congénitos en recién nacidos atendidos en el Centro de Salud "Santa Fe Totorita" del distrito de San Juan de Lurigancho-Lima en el año 2018-2019 [thesis]. Lima: Universidad María Auxiliadora; 2021 [cited 07/16/2022]. Available at: https://repositorio.uma.edu.pe/handle/20.500.12970/465
17.Hidalgo Collazos MM, Salas Frías S, Cazorla Luque C. Anomalías congénitas de origen ambiental y consecuencias: Teratógenos. In: Molero Jurado MM, coord. Salud y cuidados durante el desarrollo. Vol 1. Almería: ASUNIVEP; 2017 [cited 07/13/2022]. Available at: https://dialnet.unirioja.es/servlet/libro?codigo=703193
18.García Algar O, Mendoza R, coords. Consumo de alcohol en el embarazo. Prevención, diagnóstico y atención temprana de los Trastornos del Espectro Alcohólico Fetal (TEAF). Madrid: Ediciones Díaz de Santos; 2021 [cited 04/13/2021]. Available at: http://www.editdiazdesantos.com/wwwdat/pdf/9788490521519.pdf
19.Morales García B, Moya Toneut C, Blanco Balbeito N, Moya Arechavaleta N, Moya Arechavaleta A, Moya Toneut R. Trastornos hipertensivos durante el embarazo en gestantes del Policlínico Universitario "Santa Clara" (2015-2016). Rev Cubana Obstet Ginecol [Internet]. 2017 [cited 04/13/2021];43(2):1-14. Available at: http://scielo.sld.cu/pdf/gin/v43n2/gin06217.pdf
20.Acero Viera O, Ticona Rendon M, Huanco Apaza D. Resultados perinatales del recién nacido con Apgar bajo en el Hospital Hipólito Unanue de Tacna, 2002-2016. Rev Peru Ginecol Obstet [Internet]. 2019 [cited 04/13/2021];65(1):21-26. Available at: http://www.scielo.org.pe/pdf/rgo/v65n1/a04v65n1.pdf. https://doi.org/10.31403/rpgo.v65i2147

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTION OF THE AUTHORS

MaiyGA: Conceptualization, research, data curation, validation.
MailGA: Data curation, validation, writing the original draft, writing (reviewing and editing).
LJF: Formal analysis, research, writing original draft.
ZAE: Formal analysis, research, methodology, writing the original draft.
RPO: Data curation, writing the original draft, writing (reviewing and editing).
JMCT: Research, methodology, writing the original draft.