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Risk factors associated with orofacial malformations and neural tube defects in newborns

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Abstract: **Introduction:** Orofacial malformations and neural tube defects, such as cleft lip, cleft palate, and myelomeningocele, affect the health and quality of life of newborns. Their origin is multifactorial, and their presence increases the risk of complications and infant mortality. **Objective:** To determine the frequency of risk factors associated with orofacial malformations and neural tube defects in newborns. **Materials and Methods:** The records of newborns diagnosed with congenital and orofacial malformations registered from January 2018 to June 2022 at the Hospital de la Mujer Zacatecana were reviewed. Likewise, the statistical association between these diagnoses and the identified risk factors was evaluated. **Results:** 33.67% presented orofacial malformations, isolated or associated with syndromes and neural tube defects. Within this group, 34.8% corresponded to cases of cleft lip, both unilateral and bilateral; 36.4% also had cleft palate. Of the neural tube defects and other embryological structures, 25 cases were presented: 48% were myelomeningocele, 16% were mandibular defects, and 12% were hemifacial microsomia. A statistically significant association was observed between neural tube defects and other embryological structures, as well as the presence of urinary tract infections during pregnancy, in individuals with insufficient folate intake ($p < 0.05$). **Conclusions:** The complexity of addressing congenital malformations and implementing multidisciplinary strategies for prevention, early detection, and comprehensive management of associated risk factors is highlighted.

Keywords: Congenital Abnormalities, Cleft lip, Cleft Palate, Neural Tube Defects, Risk Factors

Factores de riesgo ambientales asociados a malformaciones orofaciales y defectos del tubo neural en recién nacidos

Resumen: **Introducción:** Las malformaciones orofaciales y los defectos del tubo neural, como el labio fisurado, paladar hendido y el mielomeningocele, afectan la salud y calidad de vida de los recién nacidos. Su origen es multifactorial y su presencia incrementa el riesgo de complicaciones y mortalidad infantil. **Objetivo:** Determinar la frecuencia de los factores de riesgo asociados a malformaciones orofaciales y defectos del tubo neural en recién nacidos. **Material y Métodos:** Se revisaron expedientes de recién nacidos con diagnóstico de malformaciones congénitas y orofaciales registrados de enero de 2018 a junio de 2022 en el Hospital de la Mujer Zacatecana. Asimismo, se evaluó la asociación estadística entre dichos diagnósticos y los factores de riesgo identificados. **Resultados:** El 33,67% presentó malformaciones orofaciales, ya sea aislada o asociadas a síndromes, así como defectos del tubo neural. Dentro de este grupo, el 34,8% correspondió a casos de labio fisurado, tanto unilaterales como bilaterales; de estos, un 36,4% presentó además paladar hendido. De los defectos del tubo neural y otras estructuras embriológicas, se presentaron 25 casos, donde el 48% fue mielomeningocele, 16% defectos mandibulares y 12% microsomía hemifacial. Se observó asociación estadísticamente significativa entre defectos del tubo neural y otras estructuras embriológicas con el consumo insuficiente de folatos, así como la presencia de infecciones urinarias durante el embarazo ($p<0,05$). **Conclusiones:** Se destaca la complejidad del abordaje de las malformaciones congénitas y la implementación de estrategias multidisciplinarias para la prevención, detección temprana y manejo integral de los factores de riesgo asociados.

Palabras clave: Anomalías Congénitas, Labio Leporino, Fisura del Paladar, Defectos del Tubo Neural, Factores de Riesgo.

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Fatores de risco associados a malformações orofaciais e defeitos do tubo neural em recém-nascidos

Resumo: **Introdução:** Malformações orofaciais e defeitos do tubo neural, como lábio leporino, fenda palatina e mielomeningocele, afetam a saúde e a qualidade de vida dos recém-nascidos. Sua origem é multifatorial e sua presença aumenta o risco de complicações e mortalidade infantil. **Objetivo:** Determinar a frequência de fatores de risco associados às malformações orofaciais e defeitos do tubo neural em recém-nascidos. **Material e métodos:** Foram revisados os prontuários de recém-nascidos com diagnóstico de malformações congênitas e orofaciais atendidos no período de janeiro de 2018 a junho de 2022 no Hospital da Mulher de Zacatecana. Além disso, foi avaliada a associação estatística entre esses diagnósticos e os fatores de risco identificados. **Resultados:** 33,67% apresentaram malformações orofaciais isoladas ou associadas a síndromes, bem como defeitos do tubo neural. Dentro deste grupo, 34,8% corresponderam a casos de fissura labial, tanto unilateral quanto bilateral; Destes, 36,4% também apresentavam fenda palatina. Dos defeitos do tubo neural e outras estruturas embriológicas, foram apresentados 25 casos, onde 48% eram mielomeningocele, 16% defeitos mandibulares e 12% microsomia hemifacial. Foi observada associação estatisticamente significativa entre defeitos do tubo neural e outras estruturas embriológicas com ingestão insuficiente de folato, bem como a presença de infecções do trato urinário durante a gravidez (p<0,05). **Conclusões:** Destaca-se a complexidade do enfrentamento das malformações congênitas e a implementação de estratégias multidisciplinares para prevenção, detecção precoce e manejo integral dos fatores de risco associados.

Palavras-chave: Anormalidades Congênitas, Fenda Labial, Fissura Palatina, Defeitos do Tubo Neural, Fatores de Risco.

Introduction

Congenital anomalies are alterations in morphological, functional, or molecular development that may manifest some time after birth or be present at birth, resulting in defective embryogenesis[1]. According to the World Health Organization (WHO), the term congenital malformation should be limited to structural defects present at birth[2] and are the result of a deviation from normal embryological development[3]. These pathologies, along with prematurity, asphyxia, and sepsis, represent the main causes of mortality during the first year of life[4], affecting 1 in 35 newborns and causing 3.2 million disabilities annually worldwide[1]. Specifically, prevalence rates are estimated at 4.7% in industrialized countries, 5.6% in middle-income countries, and 6.4% in low-income countries. In Latin America, these conditions cause up to 21% of deaths in children under 5 years of age, and specifically in Mexico, until 2019, congenital malformations ranked second as a cause of death in children under one year of age[2]. In the particular case of congenital craniofacial defects, they represent serious diseases with high structural and functional complexity and are very frequent, so knowledge and understanding of the development of the structures of the oral cavity is fundamental to identifying their presence3 since they represent approximately 75% of human congenital defects and affect 0.1 to 0.3% of all births. In Mexico in 2020, 1386 cases were registered per 100,000 newborns. In the third quarter of 2021, this figure was 1099 cases per 100,000 newborns. The states of Morelos (940.31 cases) and Campeche (454.55 cases) had the highest incidence[2]. Among the most common congenital craniofacial anomalies are neural tube defects

(NTDs), including myelomeningocele, anencephaly, encephalocele, macrocephaly, and microcephaly. Orofacial clefts, such as cleft lip and cleft palate, also significantly affect the mortality, health, and quality of life of children. The etiology of these anomalies is markedly heterogeneous. Various interactions occur between the environment and specific genes in their development. For the anterior palate, these include the genes *Msx1*, *Bmp4*, and *Bmp2*; the signaling pathways *Shh*, *Spry2*, *Fgf10*, *Fgf7*, *Shox2*, and *Efnb1*; and the transcription factors of the *TGF-ß* family. For the posterior palate, alterations occur in the genes *Meox2*, *Tbx22*, and *Barx1*[5,6]. Several studies have associated them with drug use during pregnancy, genetic causes such as monosomy X or Arnold-Chiari II and III malformation, viral infections, hypervitaminosis (vitamin B12), neonatal hypoxia, as well as maternal exposure during pregnancy to toxins, teratogens, alcohol, tobacco, or micronutrient deficiencies such as folic acid, which can affect the frequency of their occurrence[5,7]. Craniofacial malformations can occur in isolation or in association with genetic syndromes, resulting from the interaction between environmental and hereditary factors. Cleft lip and palate is one of the most frequent congenital anomalies and has a significant impact, both functionally and aesthetically. It is estimated that 70% of cases are non-syndromic, while the remainder are syndromic. Isolated cleft palate is more frequently associated with genetic syndromes, while combined cleft lip or cleft lip and palate occur in isolation. This suggests that different genes may be involved in each type of alteration, and that different environmental factors may influence it during critical stages of facial development. Among the associated factors described are maternal tobacco and alcohol use, nutritional deficiencies, and other exposures during pregnancy. Although the evidence is not conclusive, understanding the clinical variability of the condition is essential to guide research, prevention, genetic counseling, and comprehensive management[2,7]. For all the above reasons, and given the biological, clinical, and epidemiological characteristics of these anomalies in the population, the present study aimed to determine the frequency of orofacial malformations and NTDs, as well as the associated risk factors, among newborns at a Second-Level Care Hospital in the state of Zacatecas, Mexico.

Materials and Methods

This retrospective, observational, exploratory, descriptive, and cross-sectional study obtained data from a review of the clinical records of newborns registered in both digital and physical archives at the Hospital de la Mujer Zacatecana, part of the Servicios de Salud de Zacatecas, Mexico, between January 2018 and June 2022. The protocol was structured in accordance with the ethical principles established by the Declaration of Helsinki. Furthermore, it was classified as a low-risk study according to Article 17 of the General Health Law of Mexico regarding Health Research and received approval (362/2022) from the institution's Ethics and Research Committee. Birth registration was based on a review of physical and electronic records that met the inclusion criteria and none of the exclusion criteria (Table 1), and assigned them the corresponding identification

Table 1. Inclusion and exclusión criteria

Inclusion criterio	Exclusion criteria
Births occurring between January 2018 and June 2022 that presented orofacial and neural tube malformations	Apparently healthy newborns
Physical or electronic presence of the clinical record	Patients with congenital malformations other than orofacial and neural tube defects
	Patients with syndromes not associated with orofacial and neural tube defects
	Interrupted pregnancies that did not present orofacial malformations associated with neural tube defects

number. The information obtained was recorded on a registration form, including the mother's and the newborn's family's sociodemographic variables, the type of orofacial malformation recorded, NTDs, and the presence of any risk factors reported in the literature associated with this type of alteration. All births registered during the review period were considered, and using consecutive non-probability sampling, the physical and electronic records that met the inclusion criteria were identified. The data obtained were processed and tabulated in a spreadsheet created in Microsoft Excel and subsequently, using SPSS V. 22 software (Statistical Package for Social Sciences, SPSS Inc., Chicago, USA), descriptive statistics were calculated with measures of central tendency and proportional values, as well as inferential statistics by performing cross-tabulations of variables and bivariate correlations through the Chi square test and Fisher's exact test to find statistically significant associations ($p<0.05$).

Results

From January 2018 to June 2022, 23,173 births were registered at the Hospital de la Mujer Zacatecana in Zacatecas, Mexico. Of these births, 196 records reported the presence of congenital malformations, including congenital heart defects, developmental dysplasias, esophageal atresia, syndromes, and malformations of the face and neck. Within these records, 66 cases were reported with specific neural tube and orofacial malformations, representing 33.7% of the total cases. According to sociodemographic characteristics, 68.18% of the cases were from rural areas and 31.82% from urban areas. 26% of the cases occurred in mothers aged 15 to 19, 24% in those aged 20 to 24, 20% in those aged 25 to 29, 18% in those aged 30 to 34, while 3% occurred in those aged 40 to 44. Regarding education, 54.5% of the pregnant mothers had a secondary education, and 22.7% had a high school diploma; regarding occupation, 60% were exclusively homemakers. In the cases analyzed, no family history of neural tube defects (NTDs) or cleft lip and/or palate was reported, and no information was found regarding genetic counseling received by the parents. Regarding the number of pregnancies, 50% reported having had

one previous pregnancy, 33% three, and 17% two. Regarding the consumption of dietary supplements during pregnancy, 84.8% did not consume them, and 15.2% reported having consumed iron. Furthermore, 86.3% of the mothers reported consuming folate (folic acid), of whom 24.2% started taking it in the first trimester of pregnancy, 56.1% in the second, and 4.5% in the third. Of the 100% of mothers whose newborns had some type of orofacial malformation or neural tube defect (NTD) and other embryological abnormalities, 48% reported having experienced infections during pregnancy, and of these, 47% were urinary tract infections. Likewise, 66% reported having taken some medication during pregnancy, among which the combination of cephalexin with nitrofurantoin, hematinic acid, and metformin was the most frequently used, and 3% reported having been exposed to harmful substances such as tobacco smoke. Regarding prenatal checkups by trimester of pregnancy, 50% attended most frequently in the second trimester, 45.5% in the first trimester, 1.5% in the third trimester, and the remainder did not attend any prenatal checkups. Regarding the sex of infants born with orofacial malformations, neural tube defects (NTDs), and other embryological abnormalities, 58% were male, and 42% were female. Of all cases, 34.8% presented with cleft lip, of which 65.21% were unilateral, and 34.79% were bilateral (Table 2). Cleft palate was present in 36.4% of cases; of these, 83.4% involved both the hard and soft palate, and 12.5% involved only the hard palate (Table 3). Twenty-five cases of NTDs and other embryological abnormalities were present. Of these, myelomeningocele was the most frequent, with a prevalence of 48%, followed by mandibular defects at 16% and hemifacial microsomia at 12% (Table 4). Likewise, combinations of several NTDs were presented, of which 7.6% corresponded to microcephaly, 6.1% to macrocephaly, and 3% to hydrocephalus combined with myelomeningocele. Returning to the presence of syndromes associated with NTDs, Patau syndrome (Trisomy 13) was present in 4.5% of cases, while Treacher Collins syndrome and Arnold-Chiari Type II syndrome each accounted for 3%. Table 5 shows that, using the Chi-square test and Fisher's exact test, a statistically significant association exists between the combination of orofacial malformations

Table 2. *Frequency of cases of cleft lip and its classification.*

Type of Cleft Lip	Frequency	Percentage value
Unilateral	14	63.70%
Bilateral	8	36.30%
Total	22	100%

Table 3. *Frequency of cleft palate cases and their classification*

Cleft palate	Frequency	Percentage value
Hard palate	3	12.5%
Soft palate	1	4.1%
Hard and soft palate	20	83.4%
Total	24	100%

Table 4. Frequency and type of neural tube defects and other embryological structures

Neural Tube Defects and other embryological structures	Frequency	Percentage value
Mandibular defects	4	16%
Hemifacial microsomia	3	12%
Craniosynostosis	2	8%
Myelomeningocele	12	48%
Encephalocele	2	8%
Anencephaly	2	8%
Total	25	100%

and NTDs with the presence of urinary tract infections, as well as with insufficient folate intake during pregnancy (p<0.05).

Table 5. Association of risk factors with the presence of NTDs and other embryological structures.

	NTDs and other embryological structures		
	Frequency	(%)	Xi^2 or Fisher
Urinary Tract Infections	21	31,8%	0.03*
Insufficient folate (folic acid) intake	38	57,5%	0.000*

*(p < 0,05)

Discussion

Congenital anomalies continue to be a significant cause of childhood illness and mortality in developing countries. Many of these conditions are compatible with life; however, some can lead to irreversible, untreatable consequences[8]. This investigation found that the proportion of births with congenital malformations in the analyzed period is higher than that reported by Navarrete-H et al.[9]. Likewise, regarding the prevalence of orofacial malformations and NTDs, the results of this study coincide with the study by González et al.[10], which, despite being a study carried out in the same geographical area where the causes could be related to specific environmental factors, to date there is no evidence or a specific study that allows establishing any association with these factors. Regarding maternal age, most cases in this study occurred in women aged 15 to 19. However, other studies, such as the one by Tsehay et al., conducted in Ethiopia[11], indicate that women over 35 are five times more likely to have newborns with congenital defects. Similarly, they indicated that women residing in urban areas have a six times greater risk of their newborns developing congenital defects, in contrast to the findings of this study, where rural women had a higher incidence of cases. This demonstrates that demographic context and levels of urbanization vary significantly across countries, reflecting that rural women face barriers such as a lack of information and prenatal care, generally attributable to difficulties in accessing health services due to distance from medical centers. In Ethiopia, urban areas are reported to have high levels of environmental pollution, which could also contribute to the development of congenital malformations. Both contexts highlight

the influence of environmental factors on the prevalence of these conditions. The low level of education among mothers and their direct involvement in household duties, as reported in this study, may limit access to prenatal information and make it difficult to attend prenatal checkups at hospitals. This coincides with the findings of Escofié-R[12], who indicates that this population segment faces significant limitations. Furthermore, based on the results of this research, there are differences in supplement and folate (folic acid) intake during pregnancy. Studies such as Mendonca[13] describe that 49.2% of women consumed folic acid exclusively. Furthermore, although the proportion of women exposed to tobacco smoke in the present study was low, a factor reported as a risk for congenital malformations,[5,6,14] the results differ from the study by Hoyt et al.[15], who reported that exposure to secondhand tobacco smoke is significantly associated with neural tube defects. Regarding infectious processes during pregnancy, the present study reported that mothers whose newborns were affected by orofacial malformations, neural tube defects, and other embryological structures primarily suffered from urinary tract infections (UTIs). This is relevant compared with other studies, such as that by Howley et al.16, which found that UTIs were less frequent. However, their research mentions that UTIs are significantly associated with congenital defects such as encephalocele, cataracts, cleft lip, and esophageal atresia, among others. The administration and consumption of medications during pregnancy was a condition present in more than half of the mothers in this study, highlighting the importance of this factor. As García M. et al.[17] point out, it is essential to understand not only the properties and indications of medications, but also the individual characteristics of patients and the gestational stage at which they are prescribed. They emphasize that congenital defects are closely related to the mother's health history. Chronic diseases such as diabetes mellitus, hypertension, and obesity are relevant risk factors[18]. In this study, the results revealed a statistically significant association between the presence of urinary tract infections (UTIs) and congenital malformations. Torres et al.[19] report that urinary tract infections during pregnancy are linked to a higher risk of preeclampsia, preterm births, and low birth weight, as well as congenital defects.[16] Furthermore, they are more frequently associated with diabetic women.[20] This finding underscores the importance of comprehensive and careful management of maternal conditions during pregnancy to prevent neonatal complications.

Limitations

It is necessary to note that among the limitations of this study are its retrospective and observational nature, as well as the fact that the only source of information was medical records. This suggests insufficient information and precise data to establish an accurate diagnosis without bias and without the possibility of clarifying exact causality, since only possible associations between the pathologies and the risk factors cited in the literature were established.

Furthermore, the reported sample size may limit the possibility of establishing, with objective criteria, the generalizability of the results. Additionally, there is a limitation in evaluating genetic or environmental factors, as factors such as environmental exposure to toxins, family history, consanguinity, genetic mutations, or pesticides were not considered. Additionally, the possibility of underdiagnosis of the detected conditions should be considered, given that during the review period, medical records were prepared by different pediatricians, without evidence of standardized clinical procedures for detecting abnormalities at birth. Similarly, future studies of this nature should consider other related factors, such as the mother's nutritional status prior to pregnancy, contraceptive use, and the quality of prenatal care, which could confound results and were not controlled for in this study.

Conclusion

This study highlights the prevalence and complexity of orofacial congenital malformations and neural tube defects (NTDs) in newborns in a geographic area of north-central Mexico, identifying cleft lip, cleft palate, and myelomeningocele as the most common, respectively. These malformations, with a multifactorial etiology significantly influenced by genetic and environmental factors, showed a strong association in this study with insufficient folate intake and urinary tract infections during pregnancy, identified as the main risk factors. The results underscore the urgent need to implement prevention strategies focused on prenatal care and timely risk management in vulnerable populations. Furthermore, the importance of multidisciplinary medical and gynecological care is emphasized to optimize the prevention, management, and control of these conditions, with the aim of reducing their impact on infant morbidity and mortality, improving the quality of life of affected patients, and continuing research into congenital malformations and their prevalence in different populations.

Conflict of interest

The authors declare no conflict of interest with respect to the publication of this article.

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Referencias Bibliográficas

1. Zambrano M, Hernandez E. Prevención de Defectos Congénitos en Atención Primaria de Salud. Ateneo. 2022; 24(1):123-148.
2. Solorio-Fosado J, Martínez-Martínez J, Peñuelas-Romero J, Ibarra-Chaidez J, Chávez-Mondragón E, Arenas-Sordo M. Malformaciones del primero y segundo arcos branquiales. Conceptos embriológicos y genéticos y pautas de seguimiento de los pacientes. An Orl Mex. 2023; 68(3):107-138.
3. Magreni A, May JG. Embryology of the oral structures. Operative Techniques in Otolaryngology-Head and Neck Surgery. 2015; 26(3):110-4.
4. Muñoz M, Kilchemmann C, Román A, Baeza B. Prevalencia de malformaciones congénitas en recién nacidos de la región de la Araucanía. Andes pediatr. 2022;93(3):383-391.
5. Ni W, Tian T, Zhang L, Li Z, Wang L, Ren A. Maternal periconceptional consumption of sprouted potato and risks of neural tube defects and orofacial clefts. Nutr J. 2018;17:112.
6. Lema RA, Godoy MJ, Rodríguez R, Martínez JE, Jadán AM. Aproximación integradora a la etiología genética de labio y paladar hendido. Archivos Venezolanos de Farmacología y Terapéutica. 2019;38(2): 93-100.
7. Ostia-Garza P, Luna-Ríos E, Plaza-Benhumea L. Exencefalia: diagnóstico prenatal y reporte de caso. Perinatol. Reprod. Hum. 2022;36(1): 25-29.
8. Santiago-Sanabria L, Morales-Martínez O, Alonso-León M, Sanabria-Villegas L, Sánchez-Alquicira B, Ignacio-García M. Defecto del tubo neural: encefalocele occipital. Reporte de caso. Rev Fac Med UNAM. 2024;67(5):29-36.
9. Navarrete-HE, Cnún-S S, Reyes-PA, Sierra-RM, Valdés-H J. Prevalencia de malformaciones congénitas registradas en el certificado de nacimiento y de muerte fetal en México. Bol Med Hosp Infant Mex. 2013;70(6):499-505.
10. González A, Luna F, Sotelo MS, Hernández M, Díaz C. Estudio retrospectivo de la prevalencia de labio y paladar hendido en el Hospital de la Mujer Zacatecana de 2013 a 2015. Revista Latinoamericana de Ortodoncia y Odontopediatría. 2020;42(1):42-48.
11. Tsehay B, Shitie D, Lake A, Abebaw E, Taye A, Essa E. Determinants and seasonality of major structural birth defects among newborns delivered at primary and referral hospital of East and West Gojjam zones, Northwest Ethiopia 2017–2018: case–control study. BMC Res Notes. 2019;12(1):495.
12. Escoffié-RM. Asociación de labio y/o paladar hendido con variables de posición socioeconómica: un estudio de casos y controles. Rev Bras Saúde Matern Infant. 2010;10(3):323–9.
13. Mendonca J. Maternal Folic Acid Intake and Risk of Nonsyndromic Orofacial Clefts: A Hospital-Based Case-Control Study in Bangalore, India. The Cleft Palate Craniofacial Journal. 2020;57(6):678–686.
14. Martelli DR, Coletta RD, Oliveira EA, Serts MS, Rodrigues LA, Oliveira MC, Martelli Júnior H. Association between maternal smoking, gender, and cleft lip and palate. Brazilian Journal of Otorhinolaryngology. 2015;81(5):514-519.
15. Hoyt T, Canfield A, Romitti A, Botto D, Anderka T, Krikov V, et.al. Associations between maternal periconceptional exposure to secondhand tobacco smoke and major birth defects. Am J Obstet Gynecol. 2016;215(5):613.e1-613.e11.
16. Howley M, Feldkamp M, Papadopoulos E, Fisher S, Arnold K, Browne M, et.al. National Birth Defects Prevention Study. Maternal genitourinary infections and risk of birth defects in the National Birth Defects Prevention Study. Birth defects Res. 2018;110(19):1443–1454.
17. García M, García M, Jiménez L, Armada Z. Padrón, R, Chala, JM. Factores maternos y el consumo de medicamentos durante el embarazo asociados a la aparición de alteraciones neonatales. Acta Médica del Centro. 2023;17(1):145-153.
18. Álvarez Y, Lantigua P, Benítez Y, Pérez O, Collazo E. Defectos congénitos presentes en la descendencia de mujeres diabéticas, obesas e hipertensas, Artemisa 2016. Revista Cubana de Genética Comunitaria. 2021;13(1):e92.
19. Torres O, Hernández I, Meneses C, Ruvalcaba J. Infección urinaria como factor de riesgo para parto pretérmino. JONNPR. 2020;5(11):1426-1443.
20. López OP. Infección de vías urinarias en mujeres gestantes. Revista Médica Sinergia. 2021;6(12):e745.

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