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REVIEW ARTICLE

Congenital Anomalies — WILEY

Frequency of gastroschisis and omphalocele and possible influence of maternal folic acid supplementation. A narrative review

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Abstract

There is an increase in the worldwide prevalence of congenital abdominal wall defects (CAWD), with gastroschisis (GS) and omphalocele (OC) being the most common. It is widely accepted that folic acid supplementation (FAS) in the maternal diet decreases the incidence of anomalies such as neural tube defects, but there is controversy regarding the possible beneficial role for other congenital malformations. Several epidemiological studies raise controversy regarding a possible relationship between vitamin supplementation with the occurrence of abdominal wall malformations. The aim of the present study is to obtain an updated review of the global frequency of CAWD in neonates and the relationship with FAS in the mothers. For this we have carried out a systematic search of epidemiological studies in different article databases between 2011 and 2022. The analysis of 25 studies conducted in different countries where cases of OC and/or GS are registered directly or together with other congenital defects shows that 60% inquire into the relationship of FAS with the incidence of CAWD. Half of them proposes a beneficial effect of FAS and the other half find no association, concluding that there is no unanimous evidence that FAS in the maternal diet decreases the incidence of CAWD. However, it seems that an influential factor to take into account is the nutritional habits of the mothers.

KEYWORDS
congenital abdominal wall defects, folic acid supplementation, gastroschisis, omphalocele

1 | INTRODUCTION

The abdominal wall envelops the abdomen constituting a myofascial complex that, together with the diaphragm, resist pressure variations in physiological processes such as breathing, urination, or even childbirth. Its main function is to contain and protect the viscera and internal organs of the abdominal cavity. Anatomically, it is limited by the xiphoid process of the sternum, the costal arches, the spine, the pelvis, and the inguinal ligament. Topographically, it can be divided into the anterolateral areas—containing the external, internal, and transverse oblique muscles of the abdomen, as well as the rectus abdominis and pyramidal muscle—and the posterior region, with the lumbar spine and dorsal muscles.[1]

During embryonic development the abdominal organs are formed before the abdominal wall, therefore, they are found externally until the formation of the abdominal wall begins in the sixth week of gestation. If there is no alteration, the abdominal wall will position the organs in the abdominal cavity and the yolk sac, the connecting stalk and the allantois will herniate. In this way, the lateral folds fuse in the middle zone, passing from the primitive ventral umbilical ring to the formation of the umbilical cord together with the expansion of the amnion. This process of creation of the abdominal wall ends in the twelfth week of gestation, and congenital defects (CD) can be confirmed from that moment on.[2,3]

Congenital abdominal wall defects (CAWD) are usually detected during pregnancy by ultrasound and require postpartum surgery because of concerns that they may affect the development of other vital organs such as the lungs.[1,3]

Globally, gastroschisis (GS) and omphalocele (OC) are the most prevalent CAWD in the world and their incidence has been increasing.[1] GS occurs in approximately 1 in 4000 live births, is more common in males, and in the last 30 years has become the most common abdominal wall defect. This increase is not fully understood, although it has been attributed, among others, to the socioeconomic status of families and/or environmental factors, as well as to the young age of the mother. Besides, the overall incidence of OC is estimated to be between 1 and 2.5 per 5000 live births.[1]

GS is defined by having a diameter of less than 4 cm and is characterized by externalization of the small intestine outside the abdominal cavity and, in some cases, the stomach or gonads, without a covering membrane. Occasionally, it may have a fibrous covering around the intestine (Figure 1A,B). It is not characterized by other associated CD, although it does increase the likelihood of necrosis,

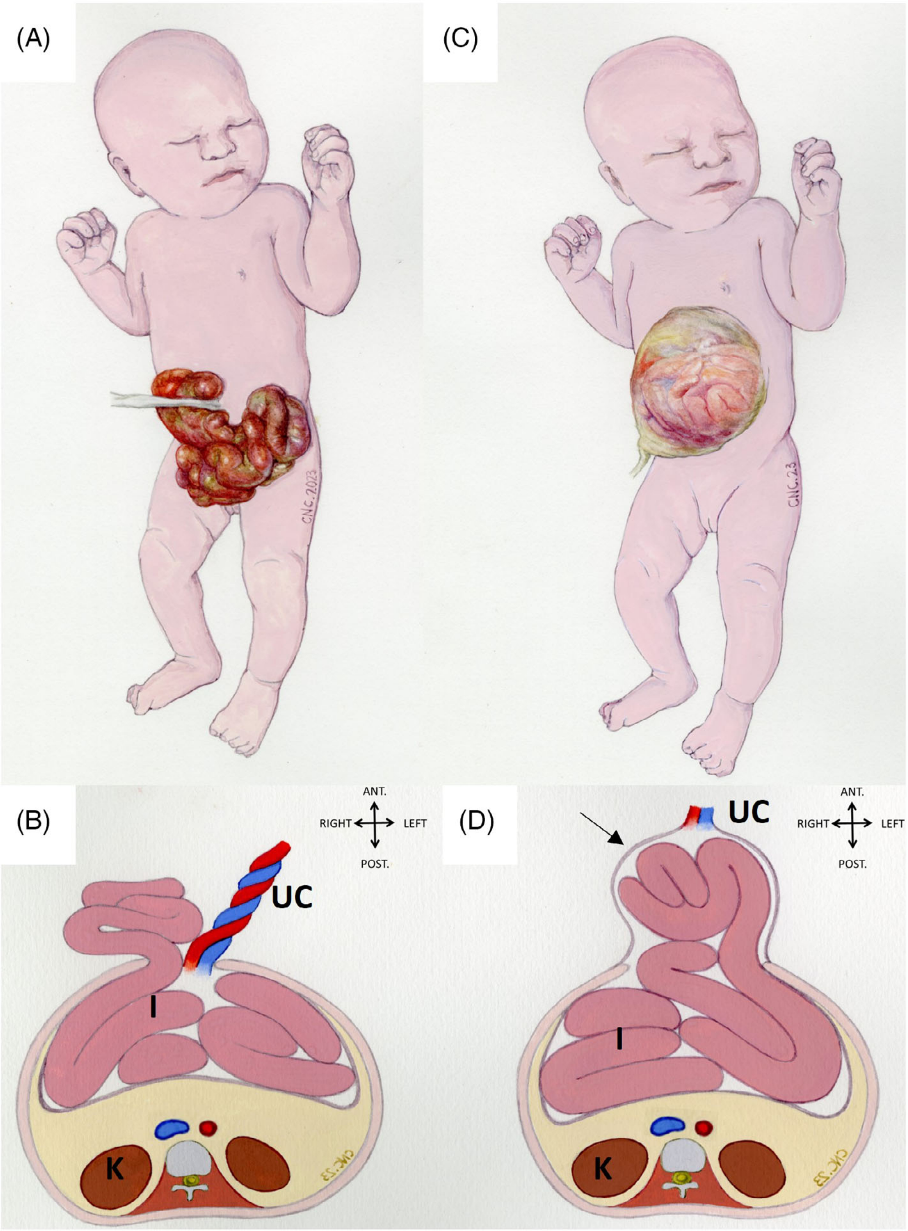

FIGURE 1 (A, B) Gastroschisis. (C, D) Omphalocele. (B–D) Schematic representations of inferior views of axial sections of a case of gastroschisis (B) and omphalocele (D). arrow, membrane; I, intestine; K, kidney; UC, umbilical cord.

perforations, and atresia.[1,3] Cases of OC are defined by externalization of the bowel along with other organs such as liver, spleen, and gonads, appearing on prenatal ultrasound as a hernia within a membranous sac (Figure 1C,D). Commonly, it appears with other associated CD such as pulmonary hypoplasia, bladder exstrophy, imperforate anus, and spinal anomaly. Cesarean section is chosen in cases where the liver is externalized, followed by a staged closure of the abdominal cavity with several surgeries to reduce the abdominal contents and achieve complete closure of the abdomen.[1,3]

Folic acid (FA) is the synthetic form of vitamin B9, also called folate. It is especially important during embryonic development because of its role in DNA methylation and the formation of compounds necessary for the generation of nucleic acids. In addition, the correct functioning of the cycle in which it is involved prevents the toxic accumulation of homocysteine.[4,5]

It is used globally as a supplement in young women of childbearing age and during pregnancy, being important especially during the first trimester of gestation. Folic acid supplementation (FAS) is mainly used to prevent neural tube CD—such as spina bifida—and is widely accepted by professionals, given the available scientific evidence evaluated according to the GRADE (grading of recommendations, assessment, development and evaluations) system.[4,5] In addition, there are countries where certain basic foods are fortified with FA because of its beneficial effects against certain CD.[6,7] FAS usually occurs several months before pregnancy, in the case of planned pregnancies, and during at least the first 3 months of gestation. The most widely accepted guideline to generate a protective effect is to administer orally an amount of 400 μg of FA daily. According to some studies, it seems to increase the risk of CD when taken only after a positive pregnancy test or stopped in the first months of pregnancy.[5]

Although the usefulness of preventive FAS seems clear against neural tube CD and its benefits against the development of orofacial clefts and congenital heart defects are now beginning to be accepted,[6] the possible relationship with CAWD is not well known.

2 | OBJECTIVE

To obtain an updated review of the global frequency of CAWD and its relationship to FAS in the mothers of the neonates.

3 | METHODS

Bibliographic searches were performed, through PubMed/MEDLINE, Dialnet, Google Scholar, Web of Science, and Cochrane Library with the following profiles: (acid folic gastroschisis; acid folic omphalocele; acid folic abdominal wall defects).

The search was performed by three of the authors independently and applying the same criteria. All three obtained the same results.

To obtain updated information, it was decided to include articles only published in the period between January 1, 2011 and December 31, 2022; and that were written in either English or Spanish. In addition, additional filters were selected such as epidemiological studies that included the terms CAWD, GS, and/or OC related to general epidemiological or risk factors and included data on FA consumption in their results or in graphs/tables.

On the other hand, studies related to genetic variants or involved in the metabolism of CAWD-related genes were excluded. Books and theses were also excluded, due to the breadth of their content. Because of the importance of focusing the work on the effect of FA on CAWD, we avoided including studies that directly compared CAWD with other diseases or focused on this association, treatment rather than preventive therapies, pregnant women with a specific disease, reports based on specific cases, and those studies where the purpose was to test how drugs influence folate absorption.

As additional documents, we also consulted pages of interest: the US database Centers for Disease Control and Prevention (CDC[8]), the Spanish Collaborative Study of Congenital Malformations (ECEMC[9]) and the European Registration of Congenital Anomalies and Twins (EUROCAT[10]).

Finally, 25 articles that met the criteria were included (Table 1).

4 | RESULTS

Of the 25 articles selected,[11–35] eight focus on the study of CAWD or specifically OC and/or GS.[11–13,20,25–27,33] That is, 60% ($n = 15$) of the studies analyze the most common CAWD and among them include OC and GS. Of these, six articles reported five or less cases of OC or GS.[14,21,22,30,31,34]

The populations studied belong to different countries and continents, with the highest percentage of studies conducted in the USA, followed by Europeans and Africans, and lastly, Asians and South Americans (Figure 2).

The frequency of OC and GS per 10 000 births was observed in all the articles where it was possible, that is, in those that specified the number of total births in the period studied or that directly provided the prevalence data. In addition, data provided by the CDC,[8] ECEM,[9] and EUROCAT[10] were taken into account (Table 2).

The studies analyzed obtained their samples from databases (36%; $n = 9$) or from cases observed in health centers (64%; $n = 16$). All of them evaluated various habits or characteristics of the mothers, one of which being the intake of a FA supplement. The main objective in four of the studies was maternal FAS.[15,28,33,35] Only two of the studies observed factors other than maternal FAS, such as the blood folate level[25] and the difference between a period of time without fortified foods and another in which fortification was present.[15]

The 64% ($n = 16$) directly related a FAS with the incidence of CAWD, in nine of the studies they observed a beneficial effect[12,16,17,20,26,28,32,33,35] and in seven others no effect.[11,13–15,18,25,27] The remaining 36% ($n = 9$) comment on the possible benefit of FAS against CD in general, without specifying which ones in particular.

TABLE 1 Articles resulting from the search.

Ref. #	Authors	Year of publication	Study location	Study characteristics	Analyzed cases	Analyzed anomalies	CAWD-FAS relationship
11	Feldkamp et al.	2011	10 USA states	National Birth Defects Prevention Study (NBDPS) data on GS during 1997–2005 (8 years).	694 GS (6157 controls)	GS	No
12	Paranjothy et al.	2012	Five regions of the United Kingdom	Isolated GS cases between 2007 and 2010 (3 years).	91 GS (217 controls)	GS	Yes
13	Feldkamp et al.	2014	10 USA states	Data from the National Birth Defects Prevention Study (NBDPS) of OC during 1997–2008 (11 years).	376 OC (8494 controls)	OC	No
14	Eke et al.	2016	A Nigerian Hospital	Gastrointestinal CD cases, where they include OC and GS, in period 2012–2014 (2 years).	59 with CD (five OC and one GS)	CD (OC and GS)	No
15	Yang et al.	2016	California (USA)	Comparison of CD in two periods: 1989–1996 (without FAS) and 1999–2010 (FAS); total: 20 years.	632 GS (1 366 369 births)	CD (GS)	No
16	Almeida et al.	2016	A Brazilian hospital	Study of CD cases between 2011 and 2013 (2 years).	250 with CD (38 with CAWD)	CD (CAWD)	Yes
17	Dawson et al.	2016	USA	National Birth Defects Prevention Study (NBDPS) database. Study of CD in twins in the period 1997–2007 (10 years).	7872 controls and 20 809 CD; 632 OC and 1834 GS	CD (OC and GS)	Yes (OC)/ No (GS)
18	Kovalenko et al.	2017	Two counties in northwest Russia and Norway	Comparison of records between 2006 and 2011 (5 years) of CD, GS, and OC with each other.	23 OC and 17 GS of 58 141 CD; three OC and five GS of 35 417 CD; 30 OC and 79 GS of 243 231 CD	CD (OC and GS)	No
19	Seyoum and Adane	2018	Two hospitals in Northwest Ethiopia	Children with CD between 2015 and 2017 (2 years).	321 total (104 with CD, 21 CAWD)	CD (CAWD)	NE
20	Acosta et al.	2018	A province in Cuba	Pregnant women between 2013 and 2016 (3 years) who had fetuses with any CAWD.	23 cases	CAWD	Yes
21	Ekwochi et al.	2018	A Nigerian Hospital	Children with CD, OC among them between 2013 and 2017 (4 years).	52 controls, 38 CD (three OC)	CD (OC)	NE
22	Singh et al.	2019	A Nepal Hospital	Newborns born between 2015 and 2017 (2 years).	108 with CD (one OC and one GS); 111 controls	CD (OC and GS)	NE
23	Hoyt et al.	2019	10 USA states	National Birth Defects Prevention Study (NBDPS) database, 1997–2011 (14 years).	32 200 with CD (240 OC and 1280 GS); (11 829 controls)	CD (OC and GS)	NE
24	Rehan et al.	2019	A Pakistan Hospital	Pregnant women going for ultrasounds between 2015 and 2017 (2 years).	570 with CD (25 GS and 23 OC); (11 830 controls)	CD (OC and GS)	NE
25	Goodman et al.	2019	An Oklahoma Clinic (USA)	GS cases during 2010–2012 (2 years).	31 GS (76 controls)	GS	No
26	Kapapa et al.	2020	A Hospital in Germany	Children with non-syndromic CAWD between 2000 and 2011 (11 years).	27 438 births (18 OC and 36 GS)	CAWD	Yes

TABLE 1 (Continued)

Ref. #	Authors	Year of publication	Study location	Study characteristics	Analyzed cases	Analyzed anomalies	CAWD-FAS relationship
27	Freitas et al.	2020	A Brazilian hospital	Fetuses that may have gastroschisis after radiography. From 2013 to 2015 (2 years).	57 GS (114 controls)	GS	No
28	Gildestad et al.	2020	Norway	Data from the Medical Birth Registry of Norway (MBRN) database in the period 1999–2013 (14 years).	18 373 with CD (243 GS and 113 OC); 870 182 controls	CD (OC and GS)	Yes
29	Egorov and Barbova.	2021	Republic of Moldova	Comparison data from the registry of congenital anomalies of the republic of Moldova with EUROCAT data, in the period 2011–2018 (7 years).	1/8333 in Moldova with OC and 1/7937 in EUROCAT	CD (OC)	NE
30	Gedamu et al.	2021	An Ethiopian Hospital	Newborns with CD between 2018 and 2019 (1 year).	2218 births, 23 CD (4.3% OC)	CD (OC)	NE
31	Jemal et al.	2021	8 hospitals in one region of Ethiopia	CD cases during 2020.	105 with CD (five GS and four OC); 313 controls	CD (OC and GS)	NE
32	Petersen et al.	2021	10 USA states	National Birth Defects Prevention Study (NBDPS) data from 1997 to 2011 (14 years).	3219 CD (154 GS); 2508 controls	CD (GS)	Yes
33	Liu et al.	2021	Two regions of China	CAWD cases comparing women taking FAS with those not during 1993–1996 (3 years).	180 142 cases with FAS (per 10 000 births: 1.61 OC and 1.61 GS) and 117 689 without FAS (per 10 000 births: 1.70 OC and 2.12 GS)	CAWD	Yes
34	Wojtowicz et al.	2022	Cracow, Poland	CD comparing women taking FAS with those not during 2017–2019 (2 years).	681 women with FAS (OC $n = 2$), and 774 women without FAS (OC $n = 3$)	CD (OC)	NE
35	Che et al	2022	Five regions of China	CD, like OC and GS, associated to NTD. Cases comparing women taking FAS (from 2009) with those not (before 2009) during 2002–2021 (19 years).	296 306 births, 2031 with NTD, 97 non isolated (25 CAWD).	CAWD	Yes

Abbreviations: CAWD, congenital abdominal wall defects; CD, congenital defects; FAS, folic acid supplementation; NE, not specified if there is a relationship of CAWD, OC or GS with FAS; GS, gastroschisis; NTD, neural tube defects; OC, omphalocele.

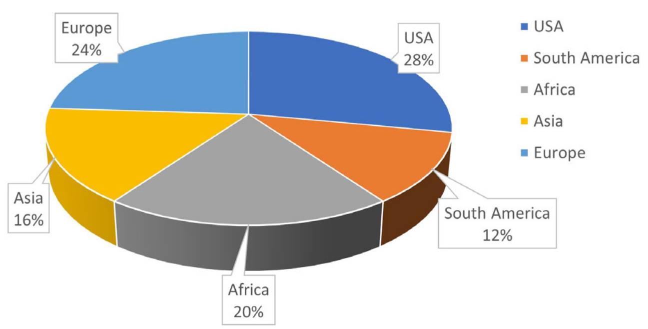

FIGURE 2 Percentage of studies analyzed in each region.

5 | DISCUSSION

The WHO establishes that 303 000 newborns in the world die in the first month of life due to congenital malformations. This is the main reason why, in 2010, at the sixty third World Health Assembly, Member States were informed of the need to establish plans for epidemiological surveillance, primary prevention and promotion of international cooperation to reduce CD.[36] It is estimated that two of the most common CD are GS and OC.[1] For this reason, the studies included in the present work are those whose objective was to analyze the most common CD and always include OC and GS.[14–19,21–24,28–32,34,35]

TABLE 2 Articles from which GS and OC frequency data are extracted along with Centers for Disease Control and Prevention (CDC), the Spanish Collaborative Study of Congenital Malformations (ECEM) and the European Registration of Congenital Anomalies and Twins (EUROCAT) databases. Frequencies are expressed in cases per 10 000 births.

Ref. #	Data source	Region	Period-years of data collection	GS	OC
15	Yang et al.	California (USA)	1989–1996 (without FAS)	3.6	No data
			1999–2010 (with FAS)	5.3	No data
26	Kapapa et al.	Germany	2000–2011	13.12	6.56
28	Gildestad et al.	Norway	1999–2013	2.73	1.27
30	Gedamu et al.	Ethiopia	2018–2019	0	4.50
33	Liu et al.	China	1993–1996 (without FAS)	2.12	1.70
			1993–1996 (with FAS)	1.61	1.61
8	CDC	USA	1999–2001	3.73	2.09
			2021–2022	5.12	2.41
9	ECEM	Spain	1980–1985	0.55	1.70
			1986–2019	0.45	0.73
			2020	0.56	0.28
10	EUROCAT	Europe	2005–2020	2.76	3.63

Abbreviations: FAS, folic acid supplementation; GS, gastroschisis; OC, omphalocele.

The frequencies of these anomalies are variable according to the area and the period of time over which the data were recorded. According to the studies analyzed, the frequency does not exceed five cases per 10 000 births; except for the study developed in a hospital in Germany[26] where 13.12 cases of GS and 6.56 cases of OC per 10 000 births were observed. It is difficult to evaluate these data because of the diversity in the time frame established to carry out each study. Even if we compare the prevalence data in Spain, through the ECEM, and the European data, collected by the EUROCAT, we see certain differences. In Spain, in the period from 1986 to 2019, the prevalence per 10 000 births was 0.73 for OC and 0.45 for GS[9]; while EUROCAT recorded a prevalence of 3.63 OC and 2.76 GS per 10 000 births for the period 2005–2020.[10] Moreover, in Spain there is a decrease in OC cases and the number of GS cases remains stable, while the European study indicates an increase in OC cases and stable data for GS.[9,10] The only explanation is that there must be a large difference in the number of cases between countries. In fact, the behavior of the data collected globally points to an increase in cases, especially of GS.[1] As can be seen from the updated USA data collected by the CDC[8] compared with those for the period 1999–2001,[37] GS cases are increasing but OC cases remain stable.

It should be noted that the studies analyzed were conducted in different regions, the majority being American (28%), followed by Europeans (24%) and Africans (20%). However, the African studies[14,19,21,30,31] provide a smaller sample size than the European ones and none specifically analyze CAWD, but look at more common CD in general. Among the Europeans, the one conducted in the Republic of Moldova[29] also did not specify whether the benefit of FAS was for CAWD, as it attributes it to CD in general. The same observation is seen in studies from two hospitals in Pakistan[24] and Nepal[22] and in Poland.[34]

Of the nine articles showing a beneficial effect of maternal FAS only three specify that it is observable in GS cases,[12,30,32] the others do so on CAWD in general. Particularly interesting is the study conducted in California (USA) by Yang et al. over an 18 year period[15] in which they analyzed the occurrence of CAWD, GS among them, in a period without cereal FAS (1989–1996) versus FAS of this staple food product in the US diet (1999–2010). This large study with a large sample size gives no evidence that FAS influences the occurrence of GS cases. However, the work by Petersen et al.[32] where a large study was conducted in 10 USA states focusing on GS, observed a beneficial effect of FAS when FA is administered as a multivitamin complex. Something similar is reflected in the research of Gidelstad et al. in Norway,[28] where they observed that FAS, as a multivitamin complex or alone, has a protective effect against OC and GS, or that of Paranjothy et al.[12] in the United Kingdom, in which they noted a beneficial effect of FAS against GS. Studies conducted in Brazil[16] and Cuba[20] also show a benefit of maternal FAS against CAWD in general. It should be noted that all of them evaluate maternal FAS, as opposed to the study focused on FAS in staple food products that does not show a specific effect.

Another study with special interest is the one conducted in two regions of China[33] for 3 years with two similar groups in each: one group of women who took a FA supplement and another group where they did not. Interestingly, they observed a decrease in CAWD, especially OC, in the supplemented group, but only in one of the two regions. In the other region they did not observe this effect.

It should be noted that these studies look at whether the mothers have taken the stipulated FAS before and/or during at least the first trimester of pregnancy, but the diet of these women has not been taken into account. The study by Kapapa et al.[26] is the only one that refers to a possible protective role against CAWD that is more effective due to the consumption of whole-grain products, fruits and vegetables, rather than by FAS. Two investigations carried out in the USA[11,25] also point to the possibility of poor maternal nutrition as a main factor for the appearance of GS, together with that carried out by Yang et al.,[15] who highlights maternal obesity as a risk factor for the same anomaly.

It is not only nutrients that may play a role. The effect of mothers being smokers or taking some type of drugs or chronic medication is also important. Although the work of Feldkamp et al.[13] found no association between the appearance of OC and maternal smoking, despite all the toxic components produced by tobacco,[38] they do detect an association of the anomaly with those who are passive smokers. Regarding GS, there are studies that do relate the increase in prevalence to the increase in tobacco consumption.[39,40] The studies that look for a relationship between certain drugs and the increase in cases of GS are not conclusive,[12,25] although there does seem to be a relationship with alcohol consumption.[25]

Another interesting factor highlighted in the study by Petersen et al.[32] is the possible risk of a short period of time (less than 6 months) between pregnancies. This short period causes a "nutritional depletion" that may not be compensated by the mother before the next pregnancy. In fact there is evidence that women with a longer interval between pregnancies tend to require less FAS[17,23] and short periods of time between pregnancies have been associated with a risk for the occurrence of GS.[17]

An interesting concept evaluated by Hoyt et al.[23] is that of acculturation and its relationship with CD. Acculturation is a term that has been widely used to describe the process of cultural and psychological change that follows cross-cultural contact.[41] Among many other factors, they evaluate the influence of the ethnicity of the parents on various CD of children and the length of time they have resided in the USA. They conclude that children of parents born outside the USA and who have resided in the USA for less than 5 years show fewer cases of GS. Petersen et al.[32] also analyze the ethnicity of the mothers in their work, but do not obtain conclusive data.

The study by Hoyt et al.[23] is complex because they observed that this group of foreign parents had lower levels of some risk factors for CD (such as smoking, drug use, and obesity) but higher levels for others, such as lower educational levels and income. This study leads us to believe that in addition to the genetic component, the most influential factor in certain CD, such as GS, is nutritional and substance intake habits. Therefore, we believe that a little studied aspect, which could be more important than the genetic load associated with ethnicity and its relationship with CAWD, could be the differences between the eating habits of each ethnic group, a fact reflected by other researchers.[42] There are also studies that relate an elevated risk of GS associated with a mother's age of under 25 years[12,43] that do not explain, but that we could associate with a worsening of dietary patterns in recent years.[44]

We consider it important to highlight the limitations of the present review, such as the difficulty of establishing comparisons between such diverse studies; both in terms of the number of cases consulted, as well as the periods of observation and the geographical diversity in which they have been carried out. An important bias is the fact that the studies with the largest number of cases and the most exhaustive are those carried out in the USA population, which makes the situation in other geographic regions less clear. In addition, the frequencies recorded may be described in terms of the number of live births or total gestations, which would include stillbirths, spontaneous deliveries, abortions and live newborns. This fact may generate variations in the data that have not been taken into account.

6 | CONCLUSIONS

As we have observed in the present review, studies on factors specifically related to OC are scarcer than those dedicated to GS, possibly because it is an anomaly that does not usually appear in isolation (as opposed to GS, which usually occurs in isolation). Moreover, we have found that there are many possible factors that can be associated with the appearance of CAWD, but it seems that nutritional aspects, FAS among them, may be among the more relevant. Since the possible beneficial role of FAS in pregnant women is not clear in the face of CAWD, we believe that future studies should continue to investigate this aspect.

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CONFLICT OF INTEREST STATEMENT

The authors declare no competing interests. The views expressed in this review do not reflect an official policy or position.

ETHICS STATEMENT

We would like to disclose that as our manuscript comprises a comprehensive literature review, it did not involve any direct research with human subjects, animals, or any other ethical considerations that would necessitate ethics approval. Therefore, no ethics approval statement was required for this submission.

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REFERENCES

1. Bence CM, Wagner AJ. Abdominal wall defects. *Transl Pediatr*. 2021;10(5):1461-1469. doi:10.21037/tp-20-94
2. Moore KL, Persaud TVN. *PhD MGT Msc. Embriología Clínica*. Elsevier Health Sciences; 2020.
3. Gratacós E. *Medicina Fetal*. Ed. Médica Panamericana; 2007.
4. Thakur M, Virk RS, Sangha PS, et al. A review on the role of vitamins in congenital ventral abdominal wall defects; omphalocele and gastroschisis. *Eur J Biomed*. 2020;7(2):66-76.
5. Organización Mundial de la Salud *Directriz: Administración Diaria de Suplementos de Hierro y Ácido Fólico en el Embarazo*. Organización Mundial de la Salud; 2014. Accessed February 3, 2023. https://apps.who.int/iris/handle/10665/124650
6. Wilson RD, O'Connor DL. Maternal folic acid and multivitamin supplementation: international clinical evidence with considerations for the prevention of folate-sensitive birth defects. *Prev Med Rep*. 2021;24:101617. doi:10.1016/j.pmedr.2021.101617

7. Crider KS, Bailey LB, Berry RJ. Folic acid food fortification—its history, effect, concerns, and future directions. *Nutrients*. 2011;3(3):370-384. doi:10.3390/nu3030370
8. CDC. *Data & Statistics on Birth Defects* | CDC. Centers for Disease Control and Prevention; 2022. Accessed February 9, 2023. https://www.cdc.gov/ncbddd/birthdefects/data.html
9. 2021-Boletín del ECEMC-Datos. Memoria Anual | Boletines ECEMC | Fundación 1000. Accessed February 3, 2023 2019 http://www.fundacion1000.es/2021-Boletin-del-ECEMC-Datos-2019
10. European Platform on Rare Disease Registration. Accessed February 6, 2023. https://eu-rd-platform.jrc.ec.europa.eu
11. Feldkamp ML, Carmichael SL, Shaw GM, Panichello JD, Moore CA, Botto LD. Maternal nutrition and gastroschisis: findings from the National Birth Defects Prevention Study. *Am J Obstet Gynecol*. 2011; 204(5):404.e1-404.e10. doi:10.1016/j.ajog.2010.12.053
12. Paranjothy S, Broughton H, Evans A, et al. The role of maternal nutrition in the aetiology of gastroschisis: an incident case–control study. *Int J Epidemiol*. 2012;41(4):1141-1152. doi:10.1093/ije/dys092
13. Feldkamp ML, Srisukhumbowornchai S, Romitti PA, et al. Self-reported maternal cigarette smoke exposure during the periconceptional period and the risk for omphalocoele. *Paediatr Perinat Epidemiol*. 2014;28(1):67-73. doi:10.1111/ppe.12093
14. Eke C, Ezomike U, Chukwu B, Onyire N. Congenital anomalies of the alimentary tract in children: experience in a tertiary health Facility in Enugu, Nigeria. *Br J Med Med Res*. 2016;13:1-823306. doi:10.9734/BJMMR/2016/23306
15. Yang W, Carmichael SL, Shaw GM. Folic acid fortification and prevalences of neural tube defects, orofacial clefts, and gastroschisis in California, 1989 to 2010. *Birth Defects Res A Clin Mol Teratol*. 2016; 106(12):1032-1041. doi:10.1002/bdra.23514
16. Almeida L, Araujo Júnior E, Crott G, et al. Epidemiological risk factors and perinatal outcomes of congenital anomalies. *Rev Bras Ginecol Obstet*. 2016;38(7):348-355. doi:10.1055/s-0036-1586160
17. Dawson AL, Tinker SC, Jamieson DJ, et al. Twinning and major birth defects, National Birth Defects Prevention Study, 1997–2007. *J Epidemiol Community Health*. 2016;70(11):1114-1121. doi:10.1136/jech-2015-206302
18. Kovalenko AA, Brenn T, Odland JØ, Nieboer E, Krettek A, Anda EE. Under-reporting of major birth defects in Northwest Russia: a registry-based study. *Int J Circumpolar Health*. 2017;76(1):1366785. doi:10.1080/22423982.2017.1366785
19. Seyoum G, Adane F. Prevalence and associated factors of birth defects among newborns at referral hospitals in Northwest Ethiopia. *Ethiop J Health Dev*. 2018;32(3):1-12. doi:10.4314/ejhd.v32i3
20. Acosta YR, Pereira MEB, Leyva GM, Ceballos EJL, Arrien JCP, Oviedo JM. Diagnosis of risk factors associated to abdominal wall defects in women with affected descendants. Province of Matanzas, January 2013–January 2016. *Rev Méd Electrón*. 2018;40(4):1059-1069.
21. Ekwochi U, Asinobi IN, Osuorah DCI, et al. Pattern of congenital anomalies in newborn: a 4-year surveillance of newborns delivered in a tertiary healthcare facility in the South-East Nigeria. *J Trop Pediatr*. 2018;64(4):304-311. doi:10.1093/tropej/fmx067
22. Singh SD, Shrestha RPB, Poudyal P, Sradanandha S, Shrestha S. Pattern and risk factor associated with congenital anomalies among young infants admitted in Dhulikhel hospital. *Birat J Health Sci*. 2018; 3(3):548-553. doi:10.3126/bjhs.v3i3.22173
23. Hoyt AT, Shumate CJ, Canfield MA, et al. Selected acculturation factors and birth defects in the National Birth Defects Prevention Study, 1997–2011. *Birth Defects Res*. 2019;111(10):598-612. doi:10.1002/bdr2.1494
24. Rehan N. Frequency of congenital fetal anomalies and associated risk factors among patients of the radiology Department of Frontier Medical and Dental College Abbottabad. *Proceedings*. 2019;33(1):1-7. doi:10.47489/p000s331z698-1-7mc
25. Goodman JR, Peck JD, Landmann A, Williams M, Elimian A. An evaluation of nutritional and vasoactive stimulants as risk factors for gastroschisis: a pilot study. *J Matern Fetal Neonatal Med*. 2019;32(14): 2346-2353. doi:10.1080/14767058.2018.1433657
26. Kapapa M, Rieg T, Henne-Bruns D, Serra A. Risk factors for abdominal wall defects. *Congenit Anom*. 2020;60(2):54-61. doi:10.1111/cga.12336
27. Freitas AB, Centofanti SF, Osmundo-Junior GS, Rodrigues AS, Francisco RPV, Brizot ML. Risk factors for gastroschisis: a case–control study in a Brazilian population. *Int J Gynecol Obstet*. 2020; 149(3):347-353. doi:10.1002/ijgo.13135
28. Gildestad T, Bjørge T, Haaland ØA, Klungsøyr K, Vollset SE, Øyen N. Maternal use of folic acid and multivitamin supplements and infant risk of birth defects in Norway, 1999–2013. *Br J Nutr*. 2020;124(3): 316-329. doi:10.1017/S0007114520001178
29. Egorov V, Barbova N. Rare diseases in monitoring of congenital anomalies. *Bull Perinatol*. 2021;90(1):46-52.
30. Gedamu S, Sendo EG, Daba W. Congenital anomalies and associated factors among newborns in Bishoftu general hospital, Oromia, Ethiopia: a retrospective study. *J Environ Public Health*. 2021;2021:1-6. doi:10.1155/2021/2426891
31. Jemal S, Fentahun E, Oumer M, Muche A. Predictors of congenital anomalies among newborns in Arsi zone public hospitals, Southeast Ethiopia: a case-control study. *Ital J Pediatr*. 2021;47(1):143. doi:10.1186/s13052-021-01093-6
32. Petersen JM, Yazdy MM, Getz KD, Anderka MT, Werler MM. Short interpregnancy intervals and risks for birth defects: support for the nutritional depletion hypothesis. *Am J Clin Nutr*. 2021;113(6):1688-1699. doi:10.1093/ajcn/nqaa436
33. Liu J, Li Z, Ye R, Ren A, Liu J. Folic acid supplementation and risk for fetal abdominal wall defects in China: results from a large population-based intervention cohort study. *Br J Nutr*. 2021;126(10):1558-1563. doi:10.1017/S0007114521000337
34. Wojtowicz A, Babczyk D, Galas A, et al. Evaluation of the prevalence of folic acid supplementation before conception and through the first 12 weeks of pregnancy in polish women at high risk of fetal anomalies. *Ginekol Pol*. 2022;93(6):489-495. doi:10.5603/GP.a2021.0192
35. Che X, Liu J, Galea GL, et al. Non-isolated neural tube defects with comorbid malformations are responsive to population-level folic acid supplementation in northern China. *Biology (Basel)*. 2022;11(9):1371. doi:10.3390/biology11091371
36. Anomalías congénitas. Accessed February 3, 2023. https://www.who.int/es/news-room/fact-sheets/detail/congenital-anomalies
37. Centers for Disease Control and Prevention (CDC). Improved national prevalence estimates for 18 selected major birth defects—United States, 1999–2001. *MMWR Morb Mortal Wkly Rep*. 2006;54(51): 1301-1305.
38. Talhout R, Schulz T, Florek E, Van Benthem J, Wester P, Opperhuizen A. Hazardous compounds in tobacco smoke. *Int J Environ Res Public Health*. 2011;8(2):613-628. doi:10.3390/ijerph8020613
39. Lam PK, Torfs CP. Interaction between maternal smoking and malnutrition in infant risk of gastroschisis. *Birth Defects Res A Clin Mol Teratol*. 2006;76(3):182-186. doi:10.1002/bdra.20238
40. Haddow JE, Palomaki GE, Holman MS. Young maternal age and smoking during pregnancy as risk factors for gastroschisis. *Teratology*. 1993;47(3):225-228. doi:10.1002/tera.1420470306
41. Berry JW. Conceptual approaches to acculturation. *Acculturation: Advances in Theory, Measurement, and Applied Research*. American Psychological Association; 2003:17-37. doi:10.1037/10472-004

42. Rehm CD, Peñalvo JL, Afshin A, Mozaffarian D. Dietary intake among US adults, 1999-2012. *JAMA*. 2016;315(23):2542-2553. doi:10.1001/jama.2016.7491
43. Friedman AM, Ananth CV, Siddiq Z, D'Alton ME, Wright JD. Gastroschisis: epidemiology and mode of delivery, 2005–2013. *Am J Obstet Gynecol*. 2016;215(3):348.e1-348.e9. doi:10.1016/j.ajog.2016.03.039
44. Imamura F, Micha R, Khatibzadeh S, et al. Dietary quality among men and women in 187 countries in 1990 and 2010: a systematic assessment. *Lancet Glob Health*. 2015;3(3):e132-e142. doi:10.1016/S2214-109X(14)70381-X

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