

Review

Psychopathology Present in Women after Miscarriage or Perinatal Loss: A Systematic Review

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Abstract: Miscarriage or perinatal loss constitutes one of the most important emotional stressors a woman can experience and can be associated with bereavement. This mourning is a way of adapting and coping with the circumstances. However, inadequate management of this process can lead to the development of complicated grief and psychopathologies such as anxiety, depression, and post-traumatic stress disorder. The aim of this systematic review was to evaluate the prevalence of psychopathology (anxiety, depression, and post-traumatic stress disorder) in women with a history of miscarriage or perinatal loss in the year prior, and to compare these results with women without this history. A peer review was conducted in PubMed, Cochrane, Scopus, and Web of Science databases. We included (1) articles that included women of any age who had had a miscarriage or perinatal loss in the year prior, and (2) articles with a longitudinal cohort design with a comparison group of women without a history of miscarriage or perinatal loss. After the screening process, three articles met these inclusion criteria and were included in this study. Psychopathology in women after miscarriage or perinatal loss was higher than in the control groups. In addition, it was observed that these psychopathologies gradually decreased over the first year from the loss. In conclusion, abortion and perinatal loss pose a risk factor for the development of psychopathology. Therefore, we emphasize the importance of implementing a mental health plan for these women.

Keywords: abortion; anxiety; bereavement; depression; perinatal loss; post-traumatic stress



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1. Introduction

In the literature, there are up to 80 classifying systems for pregnancy or neonatal loss, all with widely varying characteristics [1]. Among these classification systems, we can find terms such as perinatal loss, stillbirth, fetal death, abort, or miscarriage, some meaning the same and others contradicting each other. This incompatibility between the terms of different systems may complicate understanding the type of death we are referring to and its prevalence.

For example, the term perinatal loss has been used to encompass all types of loss during the pregnancy and neonate's first days of life (ectopic pregnancy, miscarriage, stillbirth, neonatal death, etc.), but without clarifying what period of time corresponds to each type of loss or which losses should actually be included in the term.

According to the World Health Organization (WHO), stillbirth is defined by a birth weight of 1000 g or more; if birth weight is unknown, by gestational age equal to or greater than 28 weeks of gestation; and if both criteria are unknown, by crown-heel length of 35 cm or more. However, the ICD refers to fetal deaths, not stillbirths, which are defined by a birth weight of 500 g or more; if birth weight is unknown, by gestational age of 22 completed weeks or more; and if both criteria are unknown, by crown-heel length of

25 cm or more. Even in some high-income countries, the definition of stillbirth can start as early as 18 weeks [2].

Another term that varies between countries and international organizations is miscarriage, which is usually defined as the loss of an intrauterine pregnancy before viability. However, the concept of “viability” is controversial: the WHO defines it as the expulsion of a fetus weighing less than 500 g, or approximately 22 weeks of gestation; the American Society for Reproductive Medicine as a clinical pregnancy loss of less than 20 weeks of gestation; and the European Society of Human Reproduction and Embryology as the loss of pregnancy before 22 weeks of gestation [3]. It is also remarkable to highlight the difference between a miscarriage and abortion, the latter term being commonly used to refer to a voluntary interruption of pregnancy. In fact, with an approximate prevalence of 15%, miscarriage is the most common type of pregnancy loss [4].

In turn, pregnancy is understood by many authors as a process of mature life crisis for the mother [5]. Indeed, among the various changes that take place, Raquel Soifer highlighted the increase in fears and anxieties expecting mothers experience around the risk of miscarriage [6]. When this fear becomes a reality, it means the abrupt and unexpected rupture of all the woman’s affective bonding with the unborn baby, as well as a break with the fantasies, ideas, and plans she had developed around her child since the beginning of pregnancy [7], usually ending in a mourning process.

The 4th Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) defines mourning as a reaction to the death of a person with whom there was an affective bond. The circumstances surrounding this experience vary according to the psychological, biological, cultural, and social characteristics of the mother, which is why it impacts each woman in a unique and personal way. Some will grieve for a brief period, while others require a longer time; however, some will not even experience grief [8]. Although certain symptoms are associated with perinatal grief [9] (Table 1), the development of psychopathology is common if certain risk factors are present [10].

Table 1. Symptoms associated with grief.

Physical	Empty stomach; chest and throat tightness; shortness of breath; weakness; fatigue; and sweating.
Behavioral	Difficulty sleeping; nightmares; poor appetite; social withdrawal; substance use and abuse; avoidance of health situations, pregnant women and children; and limited social and occupational functioning.
Emotional	Shock; guilt; emptiness; anger; anxiety; sadness; reproach; confusion; disbelief; derealization; depersonalization; and loneliness.
Cognitive	Re-experiencing the trauma with intrusive ideas and fantasies about the fetus; “phantom” fetal movements; auditory and/or visual hallucinations with the fetus; difficulties concentrating and making decisions.

Retrieved from Moscarello, 1989 [9].

Previous studies have documented how miscarriage affects the mental health of women in the short term, increasing the risk of anxiety, depression, and post-traumatic stress disorder (PTSD) [11]. Although this psychopathology can persist in some women, the symptoms of anxiety and depression usually decrease in the first two months after the loss [11].

Despite the fact that several academic publications have documented the impact of miscarriage or perinatal loss in terms of mental health, these articles do not always distinguish between the different terms mentioned above. In addition, existing reviews include both longitudinal and cross-sectional studies that make it difficult to assess whether psychopathology in these women actually corresponds to this loss or how this psychopathology may evolve over time. Thus, there is a gap in the literature over the past years on this topic.

With this systematic review, we aimed to: (a) evaluate the prevalence of anxiety, depression, and post-traumatic stress disorder in women with a history of miscarriage

or perinatal loss and compare it with that of women without such a history; and (b) to examine the evolution of the prevalence of psychopathology in women with and without a history of miscarriage or perinatal loss during the first year.

2. Materials and Methods

We conducted this systematic peer review in accordance with the PRISMA statement guidelines [12]. First, we used the PICO system (criteria for determining which populations, interventions, comparators, and outcomes qualify for each analysis) to pose the following structured question: do women who suffer a miscarriage or perinatal loss have more psychopathologies (anxiety, depression, or PTSD) than those who do not?

In this work, PubMed, Cochrane Library, Scopus, and Web of Science databases were analyzed in December 2021. To search for articles, we used the Medical Subject Headings (MeSH) system to identify the corresponding terms for the concepts under study and joined them using the AND or OR Boolean operators. The MeSH terms we used were “anxiety”, “depression”, “post-traumatic stress disorder”, “miscarriage”, and “perinatal loss”. According to the search system of each database, we used the following syntax: “anxiety” OR “depression” OR “post-traumatic stress disorder” AND “miscarriage” OR “perinatal loss”. In the advanced search terms, we limited the search period to articles published between 2016 and 2021 in order to fill the current gap in the literature. The articles were selected by considering the following inclusion and exclusion criteria:

Inclusion criteria:

- Studies that included women of any age who had had a miscarriage or perinatal loss in the last year;
- Studies with a longitudinal cohort design with a comparison group comprising women who had not had a miscarriage or perinatal loss.

Exclusion criteria:

- Studies focused on women who had had a recurrent miscarriage, recurrent perinatal loss, or an abortion;
- Studies that included women who had had a miscarriage or perinatal loss more than one year ago;
- Studies that referred to psychopathology present in the non-pregnant partner;
- Studies published in a language other than English or Spanish;
- Book chapters, conference communications, opinion articles, or documents other than scientific articles;
- Meta-analyses, case-controlled studies, studies with qualitative designs, or design types other than longitudinal cohorts.

To screen the articles obtained according to the inclusion/exclusion criteria, first, we filtered according to the title, followed by filtering based on the abstract, and then by reading the entire article, discarding any articles that did not meet the aforementioned parameters. In each phase of the process, the decisions of each reviewer were shared, with joint discussion in the case of any differing opinions. The initial search yielded 1324 potentially useful articles. In addition, the bibliographic references of the excluded meta-analyses and/or reviews were examined to incorporate relevant articles that might have been omitted in the search. First, duplicate articles were eliminated, reaching a total of 793 articles. Next, applying the selection criteria and evaluating the title and abstract, 764 articles were eliminated, leaving 29 articles. Finally, applying the selection criteria and reading the full text of the article, 26 articles were eliminated, obtaining a final result of 3 valid articles for the review. This procedure is shown in the work flowchart displayed in Figure 1.

The quality of the articles included in this review was assessed using the Spanish Critical Appraisal Skills Program (CASP) criteria [13].

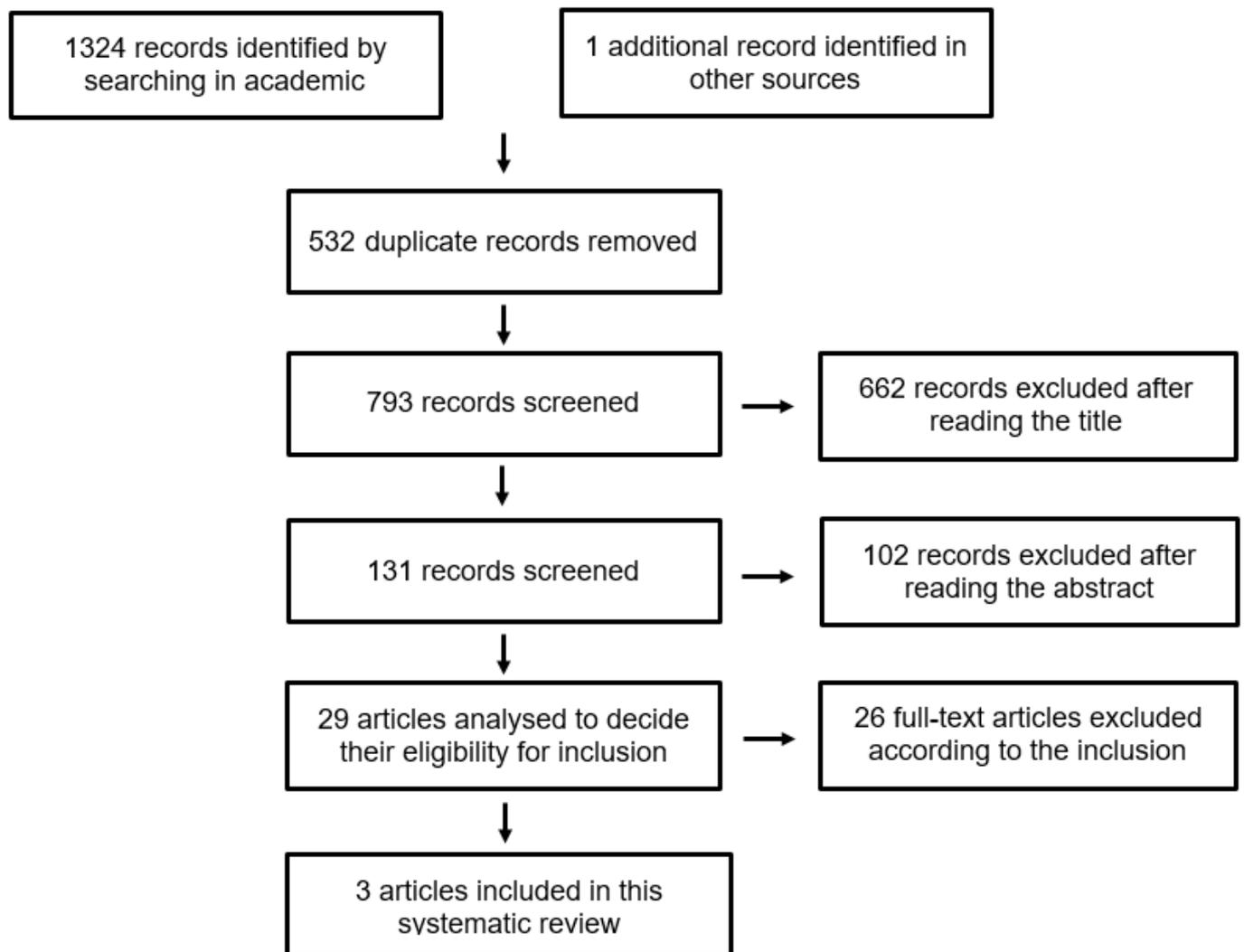


Figure 1. Flowchart of the screening process.

3. Results

3.1. Characteristics of the Studies Included

Three studies were included in this systematic review:

- Jacob, et al., 2017 [14], analyzed 24,316 German women aged 19–54 years and the impact of miscarriage on the occurrence of anxiety and depression over 12 months;
- Farren, et al., 2019 [15], analyzed 908 British women aged 16–45 years and the impact of miscarriage on the occurrence of anxiety, depression and PTSD over 9 months;
- Lewkowitz, et al., 2019 [16], analyzed 1,206,050 US women aged 13–54 years and the impact of perinatal loss on the occurrence of anxiety, depression, and PTSD over 12 months.

In total, 21,564 women with a history of miscarriage/perinatal loss and 1,207,319 women without such a history were counted. The main characteristics of the research articles included in this work are shown in Table 2.

3.2. Presence of Psychopathology

3.2.1. Anxiety

Anxiety was analyzed in all three studies included in this work (Table 2).

Table 2. Characteristics of the studies included in this review.

Author	Year	Country	Age	Type of Loss	Psychopathology	Miscarriage/ Perinatal Loss Sample Size	Control Sample	Monitoring
Jacob, et al. [14]	2017	Germany	16–45	Miscarriage	Anxiety, depression	12,158	12,158	12 months
Farren, et al. [15]	2019	United Kingdom	19–54	Miscarriage	Anxiety, depression, PTSD	737	171	9 months
Lewkowitz, et al. [16]	2019	United States	13–54	Perinatal loss	Anxiety, depression, PTSD	8292	1,194,758	12 months

Abbreviations: PTSD, post-traumatic stress disorder.

Jacob, et al., 2017 [14], and Lewkowitz, et al., 2019 [16], made this diagnosis using the International Classification of Diseases (ICD), while Farren, et al., 2019 [15], administered the Hospital Anxiety and Depression Scale (HADS).

Jacob, et al., 2017 [14], showed that 2.4% of women who had suffered a miscarriage presented anxiety after one year, while this prevalence was 2.1% in the control group, corresponding to 1.49 times more risk of suffering from anxiety after miscarriage (OR = 1.49; 95% CI [1.30, 1.70]).

In turn, Farren, et al., 2019 [15], found that 24% of women presented anxiety one month after suffering a miscarriage compared to 13% of the control group, representing 2.14-fold more risk of suffering from anxiety because of miscarriage (aOR = 2.14; 95% CI [1.14, 4.36]). In addition, the prevalence among the group with a history of miscarriage decreased to 22% at 3 months and 17% at 9 months. In fact, for each month that passed, the risk of miscarriage anxiety decreased by 0.69 times (OR = 0.69; 95% CI [0.50, 0.94]).

Finally, Lewkowitz, et al., 2019 [16], showed that 2.1% of the women who had suffered a perinatal loss presented anxiety at one year compared to 0.8% in the control group. In other words, there was 2.29 times more risk of suffering anxiety because of perinatal loss (aOR = 2.29; 95% CI [1.93, 2.70]).

3.2.2. Depression

Depression was also noted in all three studies analyzed (Table 2).

Again, Jacob, et al., 2017 [14], and Lewkowitz, et al., 2019 [16], used the ICD, while Farren, et al., 2019 [15], used the HADS to diagnose depression.

Jacob, et al., 2017 [14], indicated that 3.1% of women who had had a miscarriage presented depression at one year, while in the control group, this figure was 1.2%. That is, women who had suffered a miscarriage had a 1.66-fold greater risk of suffering from depression for this reason (OR = 1.66; 95% CI [1.46, 1.89]).

Farren, et al., 2019 [15], found a higher percentage of depression among women who had had a miscarriage (12%) than in the control group (2%), with the risk of suffering from depression in the former group being 3.8 times higher (aOR = 3.88; 95% CI [1.27, 19.2]). Again, this group observed how this prevalence decreased both at 3 months (8%) and 9 months (6%), with the risk decreasing by 0.87-fold for each month that passed (OR = 0.87; 95% CI [0.53, 1.44]).

For their part, Lewkowitz, et al., 2019 [16], showed that the prevalence of depression among women who had had a perinatal loss was 1.7%, while in the control group, it was 0.6%, meaning that perinatal loss was associated with 2.75-fold more risk of suffering depression (aOR = 2.75; 95% CI [2.31, 3.26]).

3.2.3. Post-Traumatic Stress Disorder

PTSD was studied by Farren, et al., 2019 [15], and Lewkowitz, et al., 2019 [16] (Table 2).

Farren, et al., used the Post-traumatic Stress Diagnostic Scale (PDS), while Lewkowitz, et al., used the PTSD Checklist (PCL).

Farren, et al., recorded that 29% of women that had suffered a miscarriage had PTSD. It was impossible to know the prevalence of this disorder in the control group because these women had not suffered a traumatic event related to miscarriage. Among women who had had a miscarriage, the prevalence of PTSD decreased both at 3 months (21%) and 9 months (18%), with the risk for each month that passed decreasing by 0.80 times (OR = 0.87; 95% CI [0.72, 0.89]).

Finally, Lewkowitz, et al., 2019 [16], showed a prevalence of PTSD of 0.03% among women who had suffered a perinatal loss, meaning that this event was associated with a 4.23 times greater risk of suffering from PTSD (aOR = 4.23; 95% CI [1.98, 9.04]).

Table 3 presents a summary of the prevalence and odds ratios of each disorder found in each of these three studies.

Table 3. Prevalence of psychopathology and the associated odds ratio.

Study	Psychopathology	Miscarriage/Perinatal Loss Group	Control Group	Odds Ratio
Jacob, et al., 2017 [14]	Anxiety	2.4%	2.1%	OR = 1.49; 95% CI [1.30, 1.70]
	Depression	3.1%	1.2%	OR = 1.66; 95% CI [1.46, 1.89]
Farren, et al., 2019 [15]	Anxiety	24% (1 month)	13%	aOR = 2.14; 95% CI [1.14, 4.36]
		22% (6 months)		
		17% (9 months)		
	Depression	12% (1 month)	2%	aOR = 3.88; 95% CI [1.27, 19.2]
		8% (6 months)		
		6% (9 months)		
PTSD	29% (1 month)			
	21% (6 months)			
	18% (9 months)			
Lewkowitz et al., 2019 [16]	Anxiety	2.1%	0.8%	aOR = 2.29; 95% CI [1.93, 2.70]
	Depression	1.7%	0.6%	aOR = 2.75; 95% CI [2.31, 3.26]
	PTSD	0.03%		aOR = 4.23; 95% CI [1.98, 9.04]

Abbreviations: aOR, adjusted odds ratio; OR, odds ratio; PTSD, post-traumatic stress disorder.

3.2.4. Psychopathology, Age and Psychiatric History

Jacob, et al., 2017 [14], showed that there was a significant relationship between miscarriages and the presence of psychiatric disorders in the groups of 21–30 years [OR 1.57 (1.42–1.74); $p < 0.001$, 95% CI], 31–40 years [OR 1.52 (1.37–1.70); $p < 0.001$, 95% CI], but not at 16–20 years nor 41–45 years.

For their part, Lewkowitz, et al., 2019 [16], notes that women with perinatal loss have more history of anxiety (1.3% vs. 0.9% $p < 0.001$), depression (2.4% vs. 1.4% $p < 0.001$) and PTSD (0.2% vs. 0.06% $p < 0.001$) than those without perinatal loss.

4. Discussion

In this work, we evaluated the psychopathology present in women after a miscarriage or perinatal loss compared to women without such antecedents. As these previous studies showed, women with a history of miscarriage or perinatal loss had higher levels of anxiety, depression, and PTSD [11,17] than women without this history. Among the main reasons for

this psychopathology is suffering from loss [18,19] or physiological grief, with a correlation being observed between a higher level of grief and increased PTSD symptoms [20,21].

In addition, another possible explanation would be the complication of this physiological mourning resulting from social disavowal. Indeed, Cacciatore suggested that, unlike any other death, fetal or perinatal loss behaves as an invisible loss because of the exclusive dyad that occurs between mothers and their children [21]. Dyads are complementary relationship systems of two people who pay attention to each other, constituting a source of socializing ties [22]. Thus, the social group out of this dyad could exert more pressure on the grieving mother in an attempt to get her to assimilate the loss more quickly [23]. Therefore, not only the mourning process but also the dyad rupture and subsequent loss of the mother's individuality, along with several other elements that take place in the complex process of the pregnancy and child loss, such as psychological stressors [18], could lead to the pathologization of this grief and the consequent development of psychopathology [24].

The characteristics and circumstances within which the loss occurs could also be considered a determining factor. Therefore, perhaps a factor that should be analyzed is the type of loss, and this could help us to understand the higher prevalence of depression in the study by Farren, et al., 2019 [15], which analyzed miscarriage, compared to that of Lewkowitz, et al., 2019 [16], which addressed perinatal loss. Other studies have suggested that the greater the gestational age at the time of the loss, the more prevalent the depressive symptoms [19,25], given that perinatal loss is thought to be more difficult to manage than miscarriage [26]. It has also been observed in studies that mothers whose children lived, even briefly, show more grief and anger [27].

Although it may be surprising that women without a history of psychopathology also present these symptoms, it must not be forgotten that pregnancy and childbirth is a vulnerable, stressful, and sometimes even traumatic time for women [14], with a demonstrated impact on maternal mental health [16]. Moreover, during pregnancy, so that the mother can bond effectively with her child, she undergoes a process of 'psychic transparency' during which she goes through a period of introspection whereby she reviews her primary ties (father, mother, grandparents, etc.) and psychobiography and which may reactivate unresolved conflicts, mourning, or traumas [7,28]. This process spans from the beginning of pregnancy and can last up to a month after delivery. For John Bowlby, alterations in this relationship with the child are key to the development of psychopathology [29]. Moreover, it is consistent with Gálvez-Toro, et al. [30], who state that medical technology has given the possibility for the mother to see and hear the child even before the birth, contributing to a closer emotional bonding (mother-child dyad) but also to the development of the fear of loss and thus a higher vulnerability.

Also noteworthy is the hospitalization and substance use disorder in both women with and without perinatal loss and no psychiatric history one year after shown in Lewkowitz, 2019. Because of this lack of prior psychiatric morbidity, this phenomenon may be subsequent to the pregnancy itself, reinforcing the idea that this is a stressful event with a demonstrated impact on maternal mental health, whether full-term or not [16].

Similarly, in women with a history of fetal or perinatal loss, the time elapsed since the said event also influences the presence of psychopathology. As shown in the literature [30,31], the more time that passes after the miscarriage or perinatal loss, the lesser the psychopathology tends to be. In this way, it is understood that the occurrences provided by Farren, et al., 2019 [15], at 9 months are higher than those cited by Jacob, et al., and Lewkowitz, et al., 2019 [16], at 12 months. This phenomenon could be because of the progressive natural recovery from the traumatic process of miscarriage or perinatal loss [32] and its subsequent mourning [32,33].

On the other hand, it has been shown that the presence of anxious or depressive symptomatology in the mother may favor miscarriage [34], thus explaining the results of Lewkowitz, et al., in which women with perinatal loss have a greater history of psychopathology than those without perinatal loss.

Given the results of this study and previous literature, it may be advisable to establish screening protocols for implementation after pregnancy as a means of secondary prevention of psychopathology [35], as well as providing specific training in perinatal mental health to healthcare professionals so that they can better treat these cases [11,36]. It would also be beneficial to promote initiatives that facilitate mourning when a loss of this type occurs. This could include the provision of rooms for parents who want to say goodbye to their baby [37,38], physical contact with the deceased child, and/or the creation of boxes of tangible memories of the baby (photos, the umbilical cord, and the baby's medical certificates, etc.) [39].

Regarding the limitations of this work, first, we only included studies written in Spanish or English. Likewise, only studies published between the years 2016 and 2021 were considered. Second, this review does not include studies with women who had had a recurrent miscarriage, recurrent perinatal loss, or abortion. Third, depressive symptoms sometimes overlap with those of grief, which could lead to the underdiagnosis of said psychopathology. Fourth, the lack of data on PTSD in the control group is a limitation that must be considered, as it prevents further study of this aspect. Fifth, since the role of cultural, racial/ethnic, and gender identities could not be assessed, it can also be considered a weakness.

In terms of terminology, there is a gray area on the concept of perinatal loss, which includes the entire spectrum of losses during pregnancy and even the first days of the neonate. Since this study attempts to simplify the current terminology, we have focused on miscarriage and perinatal loss, understood as all types of loss during pregnancy except miscarriage. Unfortunately, due to the lack of data on the impact of the loss of a child already born or about to be born (both included in the term perinatal loss), we have not been able to analyze and discuss the impact of these situations in comparison with pregnancy loss. This is evidence that more efforts are needed by international institutions, countries, and researchers to agree on a common definition of pregnancy and neonatal loss.

Finally, the number of times a particular questionnaire was delivered in each study could have also had an impact. This is because the more times it is administered, the more mourning is expedited by generating greater awareness among patients, thereby meaning that they show lower psychopathology results.

5. Conclusions

This study evidences that miscarriage and perinatal loss are risk factors for the appearance of anxiety, depression, and PTSD in women who have experienced this type of loss. Furthermore, grief plays a key role in the development of these psychopathologies, with these mental disorders gradually yielding as a progressive and natural recovery from grief occurs. Therefore, we would like to highlight the importance of implementing a plan focused on perinatal mental health for the secondary prevention of these psychopathologies and their effective resolution if they do occur. Finally, more efforts are needed by international institutions, countries and researchers to agree on a common classification system that unifies terms used to define pregnancy and neonatal losses.

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