

Perinatal mental health in Chilean mothers

Salud mental en madres en el período perinatal

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Received: November 25, 2020; Approved: April 25, 2021

What do we know about the subject matter of this study?

Levels of depression and anxiety symptoms are highly prevalent in the pregnancy and postpartum periods. These can negatively impact mother-child health and interaction.

What does this study contribute to what is already known?

To present updated information on prevalence of depression and anxiety symptoms in perinatal Chilean women. Additionally, it presents evidence on the relevance of perceived social support for women's mental health during the transition to motherhood.

Abstract

Pregnancy and postpartum are periods of increased vulnerability for the development of maternal mental health disorders, that have a negative impact on maternal-infant interaction and health. Most studies have focused on depression, with anxiety being less studied, despite its high prevalence. **Objectives:** to evaluate the prevalence of positive screening for anxiety and depressive symptoms in a sample of women seen in public primary health centers in Chile, and the association of these symptoms with specific risk factors. **Subjects and Method:** 158 women completed self-report questionnaires (Edinburgh Scale and Perinatal Anxiety Scale) during the third trimester of gestation and at 3 and 6 months postpartum. The prevalence and evolution of symptoms were analyzed, as well as possible differences in mental health associated with sociodemographic variables. **Results:** During the perinatal period, there was a prevalence between 41.3% and 44.3% of elevated anxiety symptoms and 13.9% to 20.9% for elevated symptoms of depression at 3 and 6 months, respectively. The study highlights the associations between perceived support, maternal educational level, and history of spontaneous abortion with maternal mental health during the transition to motherhood. **Conclusions:** Maternal perinatal symptoms of anxiety and depression are prevalent. Initiatives to identify women at risk and to promote protective factors, such as social support, are necessary to increase the well-being of women and their families.

Keywords:

Postpartum;
Anxiety;
Depression;
Perinatal Mental
Health

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Introduction

The transition to motherhood involves major emotional, social, and physiological changes, making it a period of increased risk for developing mental health problems in women. In biological terms, gestation and postpartum expose the mother to several hormonal and brain changes that can increase the sensitivity of a woman's emotional processing. For example, during gestation, altered activation of the prefrontal cortex has been identified, which is associated with increased sensitivity to threatening stimuli in pregnant women. Although these changes may be an evolutionary adaptation to prepare women for the protective needs of motherhood by increasing their overall emotional sensitivity and vigilance to emotional cues of threat and aggression, these alterations may also account for an increased vulnerability to experiencing anxiety in pregnancy^{1,2}.

Similarly, postpartum hormones and sensory signs from the newborn modify the maternal brain; they may make women more vulnerable or resistant to anxiety and depression. For instance, increased activity at the GABAA receptor suppresses postpartum anxiety through physical contact with the newborn. In contrast, altered GABAergic signaling is associated with impairments in maternal care and increased anxious and depressive symptoms².

During pregnancy, depression has a 7-15% prevalence in high-income countries and 19-25% in middle- and low-income countries^{3,4}. In the postpartum period, this prevalence is close to 10% in high-income countries and 20% in middle and low-income ones⁵. In Chile, recent studies indicate that at eight weeks of postpartum the prevalence of depression is 20.5%⁶, and 41.3% of women would present depressive and/or anxious symptoms between 2 and 3 months postpartum⁷.

Postpartum depression has several negative consequences, such as a higher prevalence of risk behaviors in mothers, alterations in mother-child interaction, and problems in the cognitive and socioemotional development of the child⁸. Given the relevance of maternal mental health in the perinatal period, the Chilean Ministry of Health has issued guidelines for the early detection and treatment of depression during pregnancy and the postpartum period. Screening for depressive symptomatology with the Edinburgh Postnatal Depression Scale reaches 89% of pregnant women nationwide^{9,10}.

Despite their high prevalence, anxiety disorders have been less studied in the perinatal period. In a recent meta-analysis, Fawcett et al describe an estimated prevalence of 20.7% of one or more anxiety disorders in this period¹¹. This is especially relevant

since high levels of maternal anxiety during pregnancy have been associated with obstetric complications, low birth weight, and preterm delivery, as well as emotional and behavioral problems in childhood and adolescence⁹⁻¹¹. In the postpartum period, maternal anxiety has been associated with increased use of health services and decreased breastfeeding, especially in new mothers¹⁴.

There is a high rate comorbidity among anxious and depressive disorders. Both in general population and pregnant women¹⁵. In addition, anxious symptoms constitute a risk factor for the development of depressive symptomatology in the postpartum period¹⁶. This indicates that both conditions are related and highlights the need to study them together.

One of the factors that affect the risk of presenting anxious and/or depressive symptoms in the perinatal period is the support that the mother receives and her social network's capacity to provide emotional and instrumental support, which may come from family members and other people close to her, as well as from health institutions and their professionals¹⁷. In pregnancy, higher levels of social support have been associated with decreased anxiety, greater perceived self-control, and lower rates of postpartum depression¹⁸. Likewise, smaller social networks, perception of low social support, especially from partners, and domestic violence have been recognized as risk factors for mental health in the perinatal period^{17,18}.

This study aims to evaluate the prevalence of a positive screening for depression and anxiety in a sample of mothers from two public primary health centers in two cities of Chile, during the third trimester of gestation and at three and six months postpartum. Although special attention is given to anxious symptomatology, which has not been thoroughly studied in Chilean cohorts, the evaluation of depressive symptomatology was included due to the high comorbidity between both types of symptoms. Additional objectives include exploring the association between sociodemographic risk factors and depressive and anxious symptomatology and evaluating the differences in depressive and anxious symptomatology in the three assessment periods.

Subjects and Method

Quantitative study of repeated measures design, which included 158 pregnant women selected by convenience sampling, chosen through non-probabilistic sampling in two public primary health care centers in Santiago and Concepción, Chile, between May 2018 and August 2019. Inclusion criteria were women older

than 18 years, Spanish-speaking, in their third trimester of gestation (pregnancy > 24 weeks). Exclusion criteria were the presence of cognitive disability or serious illness of the mother, multiple pregnancy, and preterm delivery. These criteria were used to define a representative community sample, thus excluding those cases that might have low prevalent risk factors that were not analyzed in this study.

Procedure

A team of trained psychologists evaluated that each of the potential participants met the inclusion criteria, in addition to explaining the study and clarifying any doubts. Subsequently, the subjects signed the informed consent form and filled out the questionnaires. The participants completed questionnaires of demographic variables, report on degree of satisfaction with their social support network and instruments of mental health self-report during the third trimester of gestation. The anxious and depressive symptomatology screening instruments were applied again at 3 and 6 months postpartum. At 3 months postpartum, participants also completed a questionnaire about their childbirth experience and information about the birth. Participants completed the instruments by telephone or at the health centers. Women who reported above cut-off scores on depressive and/or anxious screening instruments or other risk factors were referred to the health care team for evaluation and treatment.

This study was approved by the Ethics Committees of the *Universidad del Desarrollo* and the Concepción Health Service and was carried out in coordination with the authorities and professional teams of the health centers involved.

Instruments

The Edinburgh Postpartum Depression Scale (EDPE)²¹ was used. This is a 10-item self-report instrument with a 4-point Likert scale (0 to 3). A score greater than or equal to 13 is considered an indicator of risk of depression during gestation and the cut-off point during postpartum is 10. This scale has been validated in Chile for use during pregnancy and the postpartum period and reports high reliability (Cronbach's alpha: 0.77) and 67% specificity²¹.

Perinatal Anxiety Screening Scale (PASS)²², was also used. This is a 31 items self-report questionnaire divided into four subscales: 1) acute anxiety and adaptive symptoms, 2) worry and specific fears, 3) perfectionism and trauma symptoms, 4) social anxiety. The items have a Likert scale from 0 to 3 and the score of each subscale is obtained by adding the mentioned items. Each item asks about the presence of different feelings or experiences, such as "Fear

of harm to the baby", "Repetitive thoughts that are difficult to stop or control" or "I have felt restless or easily irritable".

The authors of the scale have reported high reliability for the subscales and the global score (Cronbach's alpha: 0.96 to 0.86)²³. This instrument is currently under validation in Spanish. This scale was chosen because it is one of the few screening instruments for anxious symptomatology in the perinatal period.

Sociodemographic and obstetric variables

Two questionnaires designed by the research team were applied to gather information on the sociodemographic profile of the sample and the birth experience of the participants. The sociodemographic variables questionnaire provided information on age, marital status, occupation, gestational age, level of education, type of housing, number of previous pregnancies, history of miscarriage, mental health history, and health difficulties during pregnancy. In addition, participants were asked to identify the person(s) in their close circle who they expected to provide the most emotional and instrumental support and to report their satisfaction with the support received from members of their close network on a Likert scale from 0 to 7, being 7 the highest level of satisfaction.

Finally, the questionnaire on the birth of the baby collected information on the sex of the newborn, gestational age at delivery, birth weight and length, type of delivery, place of birth of the baby, health complications in the mother and/or baby, and satisfaction with the birth experience.

Analysis

Non-parametric analyses were performed since the normality criteria of the measured variables were not met. To evaluate possible changes in mental health during the three measurement times, a Friedman Test was used. The Kruskal-Wallis test was used to explore differences in mental health according to the marital status of the participants and their level of education and Spearman's correlation analysis was used to evaluate the association between mental health and satisfaction with support.

The Mann-Whitney test was used to compare the averages of the mental health variables according to the demographic characteristics of the participants. Possible differences in the satisfaction level with the level of support received during gestation and postpartum were evaluated with the Wilcoxon test. The chi-square test was used to explore the association between categorical variables and the participants' mental health reports, which were categorized as above or below the cut-off point corresponding to each instrument used.

Results

Participants

In the first phase, 161 women were evaluated of which 7 were excluded because they did not meet the inclusion criteria (4 due to preterm delivery and 3 due to severe maternal illness). Of the remaining 158 women, 119 participated in phase 2 (3 months postpartum) and 110 in phase 3 (6 months postpartum).

Regarding the percentage of mothers who agreed to participate in the study, only one of the health centers had information on the total number of registered pregnant women. In this center, 71.3% of the mothers who could be contacted and who met the inclusion criteria agreed to participate in the study. Table 1 shows the demographic characteristics of the participants.

Prevalence of positive screening for depressive and anxious symptomatology

Of the 158 mothers assessed with the PASS scale in the third trimester of gestation, 44.3% (N = 70/158) reported moderate or severe anxiety symptoms. This percentage was 46.9 (N = 54/115) at 10-12 weeks postpartum and 41.3 (N = 45/109) at 6 months postpartum.

13.9% (N = 22/158) of the participants reported levels of depression above the EDPE cut-off scores during gestation. Of these women, 13.6% (N = 3) were undergoing treatment at the time of assessment. At three and six months postpartum, 16.5% (N = 19/115) and 20.9% (n = 23/110) of mothers reported elevated depressive symptoms, respectively.

Stability of emotional difficulties between gestation and postpartum

Results of the Friedman test indicated that participants' symptoms of depression and anxiety at 3 months postpartum were significantly lower than those reported during the third trimester of gestation. At six months postpartum, symptoms remained lower than those measured during gestation, but there were no significant differences between the two postpartum measurements (Table 2).

Socio-demographic and health variables

There were significant differences in the positive screening for anxiety symptomatology in relation to the participants' educational level at three months postpartum. Women who reported having completed higher education reported fewer anxiety symptoms than women who reported incomplete elementary or high school education (Table 3).

When exploring differences in mental health according to participants' obstetric characteristics, analyses with the Mann Whitney test showed that, during the

third trimester of gestation, mothers with history of miscarriage reported significantly more symptoms of depression and anxiety than participants without such a history (Table 4).

No significant differences were observed in participants' reports of mental health according to employment status, type of housing, and previous mental health history.

Social support and maternal mental health

Regarding satisfaction with the support received, most mothers reported high levels of satisfaction during the third trimester of gestation and at six months postpartum [6.54 (SD = 1.0, Mdn = 7) and 6.63 (SD = 0.84, Mdn = 7), respectively]. No significant differences were observed between these measurements according to the Wilcoxon test ($z = 1.16$, $p < .05$, $r = .11$).

When mothers were asked to identify the significant others in their lives who provide the most emotional and instrumental support, 60.7% (N = 96/158) reported two or more significant others, the rest of the mothers only identified one person. 78.5% (N = 124/158) reported their significant others as their partner and 44.3% (N = 70/158) their mother.

Spearman's correlation analysis showed a significant association between satisfaction level with the support received and symptoms of depression ($\rho = -0.34$, $p < 0.01$) and anxiety ($\rho = -0.32$, $p < 0.01$) of the participants during the third trimester of gestation. In all cases, greater satisfaction with the support received was associated with less symptomatology.

According to the Kruskal-Wallis test, participants' reports of mental health did not vary according to their marital status. However, according to the Mann-Whitney test, during the third trimester of pregnancy, participants who live with their partner reported fewer symptoms of depression (X = 5.77, Mdn = 6, N = 105) than participants who did not (X = 7.43, Mdn = 5, N = 47), U = 1948, $z = -2.08$, $p = .038$, $r = 0.17$. Similar results were observed for anxiety symptoms between these groups [lives with partner (X = 21.55, Mdn = 17, N = 105)]; [does not live with partner (X = 25.74, Mdn = 21, N = 47)] at the same measurement time, U = 1904.5, $z = -2.25$, $p = .025$, $r = 0.18$.

Moreover, according to the Mann-Whitney test, participants who identified their partners as significant provider of emotional and instrumental support reported significantly fewer symptoms of depression and anxiety during the third trimester of gestation and at 3 months postpartum than women who did not (Table 5). Likewise, participants who identified their mothers as a significant other reported fewer symptoms of depression and anxiety during the third trimester of pregnancy than women who did not (Table 5).

Table 1. Sociodemographic characteristics of the participants. (N = 158)

Characteristics	n (%)
<i>Age (years)</i>	
18 a 24	36 (23%)
25 a 34	97 (61%)
≥ 35	25 (16%)
<i>City of residence</i>	
Santiago	65 (41.1%)
Concepción	93 (58.9%)
<i>Nationality</i>	
Chile	130 (83.3%)
Venezuela	16 (10.3%)
Other	10 (6.4%)
<i>Marital status</i>	
Live together un married	63 (40.1%)
Married	42 (26.8%)
Single	21 (13.4%)
Separated/divorced	2 (1.3%)
Other	29 (18.5%)
<i>Health prevision</i>	
Fonasa A y B	79 (50.3%)
Fonasa C	28 (17.8%)
Fonasa D	38 (24.2%)
Other	12 (7.6%)
<i>Highest educational level achieved</i>	
Incomplete school education	17 (10.8%)
Complete high school education	27 (17.1%)
Incomplete technical formation	10 (6.3%)
Complete technical formation	39 (24.7%)
Incomplete university studies	21 (13.3%)
Complete university studies	44 (27.8%)
<i>Paid job</i>	
Yes	93 (58.9%)
No	65 (41.1%)
<i>Housing type</i>	
Owner	25 (15.8%)
Rental	60 (38.0%)
Shared home	63 (39.9%)
Other	10 (6.3%)
<i>Previous pregnancies</i>	
First pregnancy	63 (39.8%)
1 previous pregnancy	64 (40.5%)
2 previous pregnancy	15 (9.4%)
≥ 3 previous pregnancy	16 (10%)
<i>Previous miscarriage history</i>	
No	126 (79.7%)
Yes	32 (20.3%)
<i>Previous mental health history</i>	
No mental health history	122 (70.9%)
Depressive symptoms	11 (7%)
Depressive disorder	18 (11.4%)
Anxiety symptoms	3 (1.9%)
Anxiety disorder	3 (1.9%)
Other	11 (7%)
<i>Type of birth</i>	
Vaginal	47 (39.9%)
Assisted	9 (7.6%)
Cesarean section	63 (52.9%)
<i>Feeding at 3 months</i>	
Exclusive breastfeeding	73 (61.9%)
Formula	8 (6.8%)
Mixed formula and breastfeeding	37 (31.4%)

Table 2. Friedman ANOVA de Friedman assessing changes in mental health during pregnancy and postpartum (N = 158)

	Third trimester Mdn (Ranking)	3 months PP Mdn (Ranking)	6 months PP Mdn (Ranking)	χ^2 (df)	p
Depression (EDPE)	5 (2.30)	4 (1.80)**	1.89 (5.0)+	16.03 (2)	0.00
Anxiety (PASS)	19 (2.31)	19 (1.79)**	17 (1.91)**	14.89 (2)	0.00

Note. Mdn = median, * = $p < 0.5$, ** = $p < 0.1$, ++ indicates significant difference with T1 $p < 0.1$. EDPE: Edinburgh Postnatal Depression Scale. PASS: Perinatal anxiety scale.

Discussion

This study describes the prevalence of positive screening for anxiety and depression during pregnancy and postpartum in a sample of women attending two public primary health centers in Santiago and Concepción, Chile. Approximately, anxious symptomatology was identified in 40% of the participants.

Regarding depressive symptomatology, 13.9% of women in the third trimester of gestation reported intensified symptoms, a percentage that increased to 16% and 20% at three and six months postpartum, respectively. Previous national studies in Santiago have reported a prevalence of depressive symptomatology of 34.5% in the postnatal period in a sample of 542 mothers of diverse socioeconomic status⁷. More recently, Rojas et al have described a probable rate of postpartum depression of 24.1% assessed with the EDPE scale in a sample of 305 women at 2-3 months postpartum, similar to that reported in this study⁹.

Of the women who reported depressive and/or anxious symptoms, only a few were in treatment at the time of the evaluation. In relation to this phenomenon, Rojas et al observe that, although universal screening strategies for the detection of depressive symptoms in postpartum women are highly effective in the Chilean public health system, access to treatment is very low²². This would be associated with barriers that include a misconception of treatment alternatives, lack of knowledge of the severity of symptoms, and characteristics of the health systems, including long waiting lists and lack of coordination between professionals²⁰.

Given the negative impact of mental health symptoms for both women and their families, improving access to treatment is an important challenge for the

Table 3. Kruskal Wallis analysis evaluating differences in mental health according to the educational level of the participants

	Incomplete high school education (N = 17)	Complete high school education (N = 27)	Higher education (N = 114)	χ^2 (df)	p
Third trimester	Mdn (Ranking)	Mdn (Ranking)	Mdn (Ranking)		
Depression (EDPE)	12 (102.32)	6.5 (78.72)	5 (76.28)	4.84 (2)	0.09
Anxiety (PASS)	39 (100.38)	20 (82.17)	19 (75.75)+	4.4 (2)	0.11
3 months PP					
Depression (EDPE)	9 (85.94)	4 (58.5)	3 (55)+	7.13 (2)*	0.03
Anxiety (PASS)	37 (84.67)	19 (55.53)	16.5 (55.78)+	6.25 (2)*	0.04
6 months PP					
Depression (EDPE)	8 (67.9)	5 (52.52)	5 (55.54)	0.96 (2)	0.62
Anxiety (PASS)	35 (84.3)	22 (56.11)	16 (52.91)	4.68 (2)	0.09

Note. Mdn = median, * = $p < 0.5$, ** = $p < 0.1$, + indicates significant difference with T1 $p < 0.5$. EDPE: Edinburgh Postnatal Depression Scale. PASS: Perinatal anxiety scale.

Table 4. Mann Whitney test to assess differences in mental health according to history of previous pregnancy loss

Variables	Previous spontaneous miscarriage		U	z	r
	Yes (Mdn) Ranking	No (Mdn) Ranking			
Third trimester	N = 32	N = 126			
Depression (EDPE)	7.5 (101.36)	5 (73.95)	2715.5**	3.04	0.24
Anxiety (PASS)	25 (96.52)	17 (75.18)	2560.5*	2.36	0.19

Note. Mdn = median, * = $p < 0.5$, ** = $p < 0.1$. EDPE: Edinburgh Postnatal Depression Scale. PASS: Perinatal anxiety scale.

public and private mental health network in our country, where the general population has a perception of low effectiveness in the treatment of mental health conditions²⁴.

When exploring the evolution of anxious and depressive symptomatology during the three measurement times, it was observed that this decreases significantly from the third trimester of gestation to the postpartum period. Previous studies have observed this trend, which could be explained by the decrease in worries associated with delivery and childbirth, which are positively resolved in the postpartum period with the birth of a healthy child²⁵. Despite the decrease in symptomatology throughout the perinatal period, the percentage of mothers reporting scores above the cut-off point for the anxiety scale remained stable. This

could indicate that, despite the decrease in symptoms, there is a group of women who maintain a risk profile.

Regarding the risk factors for the development of depressive and/or anxiety symptoms, the low educational level of the participants stands out, which is consistent with both national and international studies^{14,18}. This suggests that higher education levels would be associated with a better ability to cope with challenging situations, either by the possible development of individual resources or by a lower exposure to stress due to the socioeconomic vulnerability that is commonly associated with low levels of education. Likewise, a history of miscarriages stands out. In relation to this, Chojenta et al describe similar results in a sample of 584 women with history of previous pregnancy losses, who reported high anxiety and depressive symptoma-

Table 5. Mann Whitney test to evaluate differences in mental health according to who was reported as a significant person

Variables	Woman's couple					Woman's mother				
	Yes Mdn, (Ranking)	No Mdn, (Ranking)	U	z	r	Yes Mdn, (Ranking)	No Mdn, (Ranking)	U	z	r
Third trimester	N = 124	N = 34				N = 70	N = 88			
Depression (EDPE)	5 (74.4)	9 (98.21)	1.472**	-2.70	0.21	5 (72.81)	6 (84.82)	2.611.5	-1.65	0.13
Anxiety (PASS)	17 (75.1)	27 (95.56)	1562*	-2.31	0.18	18 (71.09)	27 (86.19)	2.491*	-2.06	0.16
10-12 weeks PP	N 87	N 28				N 52	N64			
Depression (EDPE)	3 (51.51)	8 (78.2)	653**	-3.71	0.03	3 (52.51)	2 (62.4)	1.352	-1.59	0.15
Anxiety (PASS)	14.5 (52.33)	26 (75.61)	725**	-3.22	0.03	17 (56.4)	21 (59.3)	1.550	-0.46	0.04
6 months PP	N 86	N 23				N54	56			
Depression (EDPE)	5 (54.5)	5 (58.79)	1.006.5	-0.61	0.06	5 (57.4)	5 (53.7)	1.614.5	0.62	0.06
Anxiety (PASS)	16 (54.72)	18.5 (55.9)	1.055.5	-0.17	0.02	16.5 (54.08)	19 (55.9)	1.435.5	-0.3	0.03

Note. Mdn = median, * = $p < .05$, ** = $p < .01$ EDPE: Edinburgh Postnatal Depression Scale. PASS: Perinatal anxiety scale.

tology during subsequent pregnancies, but not in the postpartum period²⁶.

The results of this study show the relevance of the support available to women during the transition to motherhood and its impact on maternal mental health. As in previous studies, both high satisfaction with the emotional and practical support received and living with a partner are associated with greater emotional well-being^{27,28}.

A novel contribution of this work is to recognize the protective effect, at the level of perinatal mental health, of having one's mother as a source of support during the transition to motherhood. This is consistent with the motherhood constellation model which indicates that having the support of other mothers, especially one's mother, contributes significantly to women's well-being during the perinatal period²⁹. On the other hand, most of the participants reported satisfaction with the support they received, and a large proportion described being accompanied during childbirth and supported in parenting, especially by their partner. This could reflect the effect of initiatives that promote respectful childbirth and the participation of fathers in parenting, which have been promoted in the country by the national early childhood program *Chile Crece Contigo* in recent years³⁰.

Among the limitations of this study are the characteristics of the participants, whose voluntary participation may have biased the sample through the self-selection of women with a certain mental health profile. In addition, the fact of having a non-proba-

bilistic sample limits the generalization of the results to similar groups, since they are not representative at a national level. On the other hand, anxious and depressive symptomatology was assessed by self-report and does not allow us to distinguish the presence of clinical mental health conditions. Future studies could use diagnostic interviews to define the prevalence of depressive and anxious disorders, in addition to symptomatology.

Regarding the instruments used, the PASS scale, which assesses anxious symptomatology, has not been validated for use in Latino populations. The lack of questionnaires to assess perinatal anxiety explains the use of this instrument; however, the results obtained through this scale should be carefully considered. Future research could focus on the validation of instruments that allow the detection of anxiety symptoms in our country.

Conclusion

Despite its limitations, this study presents an update on the prevalence of anxious and depressive symptomatology during the perinatal period in a diverse sample of women in Chile. The results highlight the relevance of perceived support for women's emotional well-being in the perinatal period and could provide useful information for health professionals working with women and their children in this meaningful period of life.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

This study was supported by CONICYT (Fondecyt N°11170338).

Aknowledgments

The authors would like to thank the families who participated in this study and the Santa Julia (Santiago) and Víctor Manuel Fernández (Concepción) family health centers support.

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