

ΠΑΝΕΠΙΣΤΗΜΙΟ ΔΥΤΙΚΗΣ ΑΤΤΙΚΗΣ ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ ΚΑΙ ΠΡΟΝΟΙΑΣ ΤΜΗΜΑ ΜΑΙΕΥΤΙΚΗΣ ΠΜΣ ΠΡΟΗΓΜΕΝΗ ΚΑΙ ΤΕΚΜΗΡΙΩΜΕΝΗ ΜΑΙΕΥΤΙΚΗ

ΦΡΟΝΤΙΔΑ

Μεταπτυχιακή Διπλωματική Εργασία

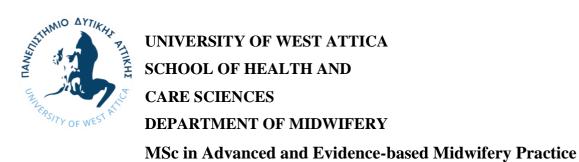
Πρακτικές Θηλασμού μητέρων νοσούντων από Covid-19. Συστηματική Ανασκόπηση και Μετανάλυση της πρόσφατης βιβλιογραφίας

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Diploma Thesis

Breastfeeding Practices for COVID-19 Infected Mothers. A Systematic Review and Metaanalysis of the Current Literature.

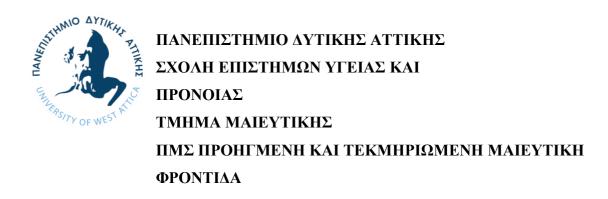
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«Είμαι συγγραφέας αυτής της μεταπτυχιακής εργασίας και ότι κάθε βοήθεια την οποία είχα για

την προετοιμασία της, είναι πλήρως αναγνωρισμένη και αναφέρεται στην εργασία. Επίσης, οι

όποιες πηγές από τις οποίες έκανα χρήση δεδομένων, ιδεών ή λέξεων, είτε ακριβώς είτε

παραφρασμένες, αναφέρονται στο σύνολό τους, με πλήρη αναφορά στους συγγραφείς, τον

εκδοτικό οίκο ή το περιοδικό, συμπεριλαμβανομένων και των πηγών που ενδεχομένως

χρησιμοποιήθηκαν από το διαδίκτυο. Επίσης, βεβαιώνω ότι αυτή η εργασία έχει συγγραφεί από

μένα αποκλειστικά και αποτελεί προϊόν πνευματικής ιδιοκτησίας τόσο δικής μου, όσο και του

Ιδρύματος.

Παράβαση της ανωτέρω ακαδημαϊκής μου ευθύνης αποτελεί ουσιώδη λόγο για την ανάκληση του

πτυχίου μου».

Η Δηλούσα

Μπούκουρα Μαρία-Ελένη, Μαία.

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(Υπογραφή)

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4

Πρακτικές Θηλασμού μητέρων νοσούντων από Covid-19.

Συστηματική Ανασκόπηση και Μετανάλυση της πρόσφατης βιβλιογραφίας

ПЕРІЛНЧН

Εισαγωγή: Καθώς η πανδημία συνεχίζεται, όλο και περισσότερες γυναίκες γεννούν ενώ δίνουν μάχη με τον κορονοϊό.

Σκοπός: Ο στόχος αυτής της συστηματικής ανασκόπησης είναι η διερεύνηση του κινδύνου μετάδοσης του κορονοϊού από μητέρα που νοσεί, στο νεογνό της κατά τη διάρκεια του θηλασμού, της επαφής δέρμα με δέρμα και της συν διαμονής μητέρας νεογνού (Rooming-in).

Μέθοδος- Υλικό: Πραγματοποιήθηκε συστηματική αναζήτηση της βιβλιογραφίας σε διάφορες βάσεις δεδομένων και συγκεκριμένα στην Cochrane Library, στο PubMed Central και στο Scopus. Επίσης πραγματοποιήθηκε μεταανάλυση της εκτίμησης της μόλυνσης των νεογνών από μητέρες με SARS-CoV-2 που θήλαζαν, έρχονταν σε επαφή δέρμα με δέρμα και έκαναν Rooming-in.

Αποτελέσματα: Συμπεριελήφθησαν συνολικά 18 μελέτες στην ανασκόπηση. Το ποσοστό των νεογνών που ήταν θετικό για τον ιό ήταν 2,8%. Οι πρακτικές που χρησιμοποιούνταν στις μελέτες διέφεραν από την απευθείας αποχωρισμό των μητέρων μέχρι την άμεση επαφή δέρμα με δέρμα, τη συνδιαμονή (rooming in) και τον αποκλειστικό θηλασμό. Μόνο μία μελέτη εξέτασε τους παράγοντες που σχετίζονται με τα θετικά τεστ των νεογνών. Αυτή η μελέτη έδειξε ότι ο μόνος παράγοντας που σχετίζεται με θετικό sars-cov-2 ήταν ο μητρικός δείκτης κοινωνικής ευπάθειας>90. Ο τύπος τοκετού, το Rooming-in, και το αν η μητέρα είναι συμπωματική ή όχι δεν συσχετίστηκαν με θετικά αποτελέσματα στα νεογνά.

Συμπεράσματα: Το ποσοστό περιγγενητικής λοίμωξης είναι χαμηλό. Ο θηλασμός, η επαφή δέρμα με δέρμα και το Rooming-in συνίσταται τηρώντας προστατευτικά μέτρα όπως η αυστηρή υγιεινή των χεριών, η χρήση μάσκας και ο καθαρισμός του στήθους όταν χρειάζεται και όχι μετά από κάθε θηλασμό.

Λέξεις κλειδιά: covid-19, SARS-CoV-2, κορονοϊός, θηλασμός, πρακτικές, δέρμα με δέρμα επαφή, συνδιαμονή.

Abstract:

Introduction: As the COVID-19 pandemic continues, more and more women are giving birth while battling SARS-CoV-2.

Aim: The aim of this review is to investigate the risk of transmission of the coronavirus from mother to infant during breastfeeding, skin-to-skin contact, and Rooming-in and to explore ways of managing covid-19 positive maternal-infant dyads. Maternity care practices such as skin-to-skin care, rooming-in, and direct breastfeeding are recommended, but it is unclear if these practices increase the risk of clinically significant COVID-19 in newborns, and if disruption of these practices adversely affects breastfeeding.

Methods: searches were accomplished in various databases and specifically in Cochrane Library, PubMed Central and Scopus up to 30th November 2021, using the Matrix Method and guided by the PRISMA, to identify studies involving mothers infected with COVID-19 and their infants in the early postpartum period. Criteria included English Language, broad search terms, full-text reviews and articles published from December of 2019 as well as the first case that appeared then. A meta-analysis was also performed to estimate the infection of infants from infected mothers who breastfed, had Skin to skin contact and did Rooming-in.

Findings: A total of 18 studies were included in this review. The rate of infected infants was 2,8%. The maternal practices were used in these studies varied from the direct separation of the dyad to direct skin-to-skin contact, Rooming-in and exclusive breastfeeding. One study examined the factors associated with positive tests in newborns. This study showed that the only factor was the maternal social vulnerability index>90. The type of delivery, Rooming-in, and if the mother had symptoms or not were associated with positive neonatal outcomes.

Conclusion: The rate of perinatal infection is low. Breastfeeding, skin-to-skin contact, and Rooming-in are recommended to follow all protective measures such as strict hand hygiene, the use of masks and breast cleaning when it is necessary and not after each breastfeeding.

Keywords: covid-19, coronavirus, SARS-CoV-2, breastfeeding, maternal practices, skin-to-skin contact, rooming in.

Περιεχόμενα

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ΚΑΤΑΛΟΓΟΣ ΣΥΝΤΟΜΟΓΡΑΦΙΩΝ

CI: Confidence Interval

NR: No Reply

OR: Odds Ratio

PICOST: Population Intervention Comparison Outcome Study Timely

PRISMA: Preferred Re-porting Items for Systematic Reviews and Meta-analysis

SARS-Cov2: Severe Acute Respiratory Syndrome Coronavirus 2

RCOG: Royal College of Obstetricians and Gynecologists

WHO: World Health Organization

ΕΥΧΑΡΙΣΤΙΕΣ

Η συγγραφή της διπλωματικής μου εργασίας παρόλη τη δυσκολία που είχε ήταν επιτυχής λόγω της διαρκούς καθοδήγησης που είχα από τους καθηγητές μου.

Αρχικά, θα ήθελα να ευχαριστήσω την επιβλέπουσα μου αναπληρώτρια καθηγήτρια του Τμήματος Μαιευτικής του Πανεπιστημίου Δυτικής Αττικής, κα Αντιγόνη Σαραντάκη, για την πολύτιμη βοήθεια της και τη συνεχή καθοδήγησή της κατά τη διάρκεια της συγγραφής της παρούσας διπλωματικής εργασίας. Μέσω της διαρκούς στήριξής, της πολλής υπομονής, ενθάρρυνσης και πίστης σε έμενα όλα αυτά τα χρόνια έπαιρνα δύναμη για να συνεχίσω και να καταφέρω να ολοκληρώσω τις μεταπτυχιακές μου σπουδές παρά τις πολλές δυσκολίες που υπήρξαν. Αν δεν ήταν εκείνη δεν θα τα κατάφερνα για αυτό το ευχαριστώ είναι πολύ λίγο.

Θα ήθελα να εκφράσω ειλικρινείς ευχαριστίες επίσης, στα μέλη της τριμελούς εξεταστικής επιτροπής, την Καθηγήτρια & Πρόεδρο του Τμήματος Μαιευτικής του Πανεπιστημίου Δυτικής Αττικής, κα Αικατερίνη Λυκερίδου, και την Αναπληρώτρια καθηγήτρια του Τμήματος Μαιευτικής του ΠαΔΑ, κα Δάγλα Μαρία για την ουσιαστική συμμετοχή τους στην ολοκλήρωση και επιτυχή διεκπεραίωση αυτής της προσπάθειας.

Τέλος, θα ήθελα να ευχαριστήσω τον σύντροφό μου και την οικογένεια μου και ιδιαίτερα την αδελφή μου, που όλο αυτό το χρονικό διάστημα στάθηκαν στο πλευρό μου με αγάπη και πολύ κατανόηση. Η υποστήριξη της αδελφής μου ήταν άκρως απαραίτητη για να φέρω εις πέρας την παρούσα διπλωματική εργασία.

1.INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by SARS-Cov2 and first appeared in December 2019 in China, specifically in Wuhan. This disease can occur from without symptoms or very mild to a life-threatening respiratory infection or a severe cardiac disorder [1]. The infection can appear at any age and anyone may become severe ill or die from this disease [2]. The virus can be transmitted from person to person when an infected person speaks, sneezes or coughs and a healthy person may inhale these droplets. Furthermore, if anyone comes in contact with surfaces or things of an infected person and then touches his eyes, nose or mouth can be infected with COVID-19 [3].

Pregnant women and young children are susceptible to COVID-19 [4]. The newborns are more vulnerable to SARS-CoV-2 infection due to do not have antibodies against coronaviruses [5]. The mode of transmission and potential effects of COVID-19 on pregnant mothers and their newborns are uncertainty. Data is still insufficient regarding if women with COVID-19 can transmit the virus to her newborn during labour or through breast-feeding [6]. The guidelines for taking care of maternal-newborn dyads have changed significantly during the pandemic [7].

The concern of possible transmission of the virus from an infected mother to her infant led to the disruption of some practices recognized as crucial for maternal bonding and breastfeeding initiation, such as skin-to-skin and rooming-in [8]. Breastmilk is rich in nutrients, bioactive molecules, antibodies, and microorganisms, which contribute to infants for their growth and development, maturation of immune, development of organs, and microbial colonization [9]. The active and passive immunity provided by breastmilk plays an important role in strengthening the infant's response to infectious diseases [10]. More-over, breastfed babies are less likely to be overweight as children or teenagers and have better tests IQ [11]. Breastfeeding has many positives for mothers. In particular, a me-ta-analysis showed that women who breastfeed for more than twelve months have a reduced risk of breast and ovarian cancer. Furthermore, breastfeeding was related with low-er risk of type 2 diabetes. In contrast, less breastfeeding time was related with a higher danger of postpartum depression [12]. Also, Skin to skin contact and Rooming in have multiple benefits for the dyad mother-infant. Skin to skin contact

helps the initiate of breastfeeding, stabilizes the levels of infant glucose and maintains newborn temperature [13].

RNA of virus has found in breastmilk, but this does not mean to infectivity from viable virus. Breast milk contains antibodies with a neutralizing capacity in the case of a mother infected with the virus [14]. Due to the heterogeneity of studies concerning the possibility of mother-to-child transmission, many scientific societies have recommended that SARS-CoV-2 positive mothers adopt practices of distancing themselves from their babies and use personal protective equipment, such as masks and gloves during rooming-in or breastfeeding [15]. So, it is urgent to examine all possible effects which can be caused in the newborn not only by breastfeeding but also by other practices related to the care of newborn as well as the contact and development of the mother's bond with the infant such as skin to skin contact.

2. MATERIAL AND METHODS

2.1 Aim

We aimed to examine the risk of transmission of SARS-CoV-2 from infected mother to neonate during the breastfeeding, the skin-to-skin contact, and the rooming-in.

2.2 Design

The systematic review and meta-analysis were conducted following Preferred Re-porting Items for Systematic Reviews and Meta-analysis (PRISMA) 2020 standards [16].

2.3 Search Strategies

PubMed, Scopus, and Cochrane Library were searched on 30th November 2021, and we removed duplicates. We used the following keywords: "COVID-19", "SARS-CoV-2", "Breastfeeding", "skin to skin contact", "rooming in", "transmission". These were used both separately and in combination with the help of the Boolean administrators (OR, AND, NOT). Since Covid-19 is a contemporary issue, records published since 2019 were identified in the primary search stage.

2.4 Inclusion and exclusion criteria of studies

We used the acronym PICOST to determine the eligibility criteria of the articles. More specifically:

- 1. Population: We included studies which the sample consisted of mothers infected from SARS-CoV-2, as well as, and their newborns. SARS-CoV-2 infection had to be ascertained by a nasopharyngeal swab through a molecular test. We excluded studies which including < 20 infected mothers.
- 2. Intervention: We included studies that applied maternal practices such as breastfeeding, or skin to skin contact, or rooming in. Rooming-in was defined as allowing the mother and infant to remain together 24 hours per day during the birth hospitalization. We defined the skin-to-skin care as the practice of placing the infant directly on the mother to maximize surface-to-surface contact. Exclusive breastfeeding was defined as giving no other food or drink not even water except breast milk.
- 3. Comparison: The studies assessed mother-to-infant transmission of the SARS-CoV-2 during maternal practices.
- 4. Outcome: The prevalence of SARS-CoV-2 infection in infants, which had to be ascertained by a nasopharyngeal swab through a molecular test during the first 30 days after birth.
- 5. Study: We included only primary quantitative studies, such as prospective observational studies, retrospective observational studies, intervention studies, and descriptive studies. We excluded secondary studies (systematic review, meta-analysis), qualitative studies, letter to editor, editorial, protocols, and opinion articles. We excluded studies where the full text was not available.
- 6. Timely: We included studies that had been published up to 30th November 2021. The studies were published in the English language. We excluded studies where they were not written in the English language, or where the full text was not available.

2.5 Search outcomes and data extraction

Two independent researchers separately identified and screened the titles and abstracts of the retrieved articles. Next, individual papers were subjected to full-text review. Conflicts in opinion between the two authors were resolved by the third.

Data on the following variables were extracted from the eligible studies: authors, publication year, country, number of mothers with SARS-CoV-2 infection, mother age, type of delivery, gestational age, number of infants with and without SARS-COV-2 infection, and frequency of maternal practices (breastfeeding, rooming in, skin-to-skin). Also, we recorded the measures that hospitals were taking to limit the spread of the virus from mothers to children.

2.6 Data synthesis and analysis

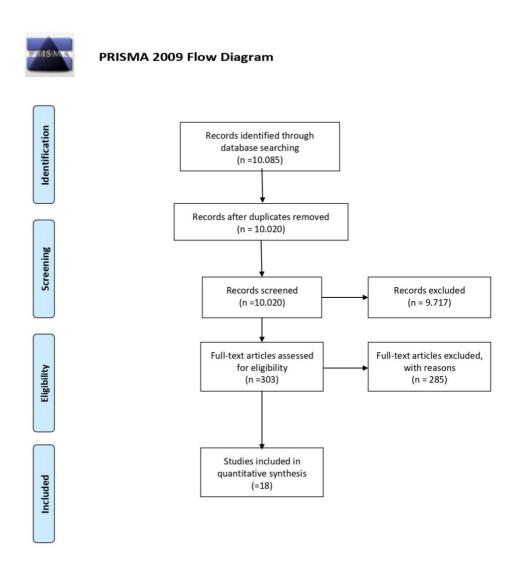
The main outcome measure was the estimate of infected infants born to mothers with SARS-CoV-2 infection. Random-effects models were used. Pooled data were given with 95% confidence interval values (95% CI) and showed by forest plots. We used I2-index to assess between-studies heterogeneity and values > 50% were considered as significant. We used a funnel plot and the Egger's test to assess the publication bias with a p-value <0.05 indicating publication bias. We performed subgroup meta-analyses for rooming-in, breastfeeding, and skin-to-skin contact as the independent variable. Statistical analysis was performed with STATA.

3. RESULTS

Results

After the search in three databases a total of 10.085 records was identified, specifi-cally 9.746 in PubMed Central, 154 In Scopus and 185 In Cochrane Library. 65 records were removed because they were duplicates. Thus, 10.020 records were examined about their eligibility for inclusion. Finally, it was proved that 9.717 records were excluded be-cause after reading their titles and abstracts were not relevant. Both authors read the full text of 303 records and only 18 met the criteria and were comprised in this study (Figure 1: Flow Diagram).

Figure 1: Flowchart of the literature search according to the Preferred Reporting Items for Systematic Reviews and Meta- Analysis.



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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From 18 studies, 6 studies were conducted in Spain [17-22], 4 in USA [23-26], 4 in It-aly [27-30], and form 1 study in France [31], India [32], Israel [33], Portugal [34]. Four studies were retrospective [25,29,31,34]. Table 1 represents the main characteristics of included studies.

Table 1: Main characteristics of the studies included in this systematic review.

First Author (publication year)	Type design	Study period	Country	Number of mothers with SARS- CoV-2 infection	Age of mothers (years) Mean (±SD)	Asymptomatic COVID-19 illness, N (%)	Gestational age (weeks) Mean (±SD)	Route delivery, N (%)	Number of infants	
Angelidou et al (2021)	Multicenter cohort study	March 1, to July 31, 2020	USA	250	30.4 (±6.3)	170 (68,0%)	37.9 (±2.6)	113 (45,2%)	255	
Congdon et al (2021)	Case-series study	March to May, 2020	USA	70	NR	NR	39.0 (36.3- 41.6)**	25 (35,7%)	70	
Conti et al (2021)	Observational study	April 1, 2020, to March 18, 2021	Italy	37	31 (17 - 45)*	10 (27,0%)	39 (32-42)*	18 (48.5%)	37	
Dumitriu et al (2021)	Retrospective cohort study	March 13 to April 24, 2020	USA	100	28.5 (24.0 - 34.0)**	NR	39.0 (37.0 - 40.0)**	46 (45.5%)	101	
Donati et al (2021)	Prospective cohort study	February 25, to July 31, 2020	Italy	525	31.8 (±5.69)	235 (44,8%)	NR	177 (33.7%)	538	
Ferazzi et al (2020)	Retrospective study	March 1 to March 20, 2020	Italy	42	32.9 (21- 44)*	NR	NR	18 (42.8%)	42	
Jiménez et al (2020)	Prospective observational study	March 1 to May 31, 2020	Spain	403	NR	291 (72,2%)	NR	136 (26.0%)	403	
Marin Gabriel et al (2020)	Descriptive study	March 13 to May 31, 2020	Spain	242	32.1 (±6.3)	98 (40,5%)	39 (38- 40)**	63 (26.0%)	248	
Marín Gabriel et al (2020)	Descriptive study	March 13 to May 31, 2021	Spain	42	33.6 (±4.9)	NR	38 (±3.1)	20 (47.6%)	42	
Martenot et al (2021)	Retrospective study	March 15 to April 24, 2020	France	26	30.6 (±7.9)	NR	39 (±2)	10 (38.6%)	26	
Nayak et al (2021)	Prospective observational study	May 1 to October 20, 2020	India	162	39 (19 - 41)*	NR	37.5 (25 - 41)*	103 (63.6%)	165	
Pereira et al (2020)	Retrospective case series study	March 14, to April 14, 2020	Portugal	22	34 (19 - 43)*	11 (50.0%)	38 (31-41)*	4 (18.2%)	22	
Ronchi et al (2020)	Prospective, cohort study	March 19 to May 2, 2020	Italy	61	32 (28 - 36)**	34 (55.7%)	39 (35- 41)**	15 (24.6%)	62	
Salvatore et al (2020)	Observational cohort study	March 22 to May 17, 2020	USA	78	NR	20 (25.6%)	38 (27-41)*	36 (43.9%)	82	
Sánchez García et al (2021)	Prospective case-control study	April to July, 2020	Spain	37	33.9 (±5.4)	16 (43.2%)	39.1 (±1.8)	10 (27.0%)	37	
Sánchez- Luna et al (2021)	Prospective cohort study	March 8 to May 26, 2020	Spain	497	33	245 (49.3%)	49 (±3.7)	164 (33.0%)	503	
Shlomai et al (2021)	Observational cohort study	March 5 to May 30, 2020	Israel	53	29.7 (±7.3)	40 (75,5%)	39 (±1.0)	10 (18.9%)	55	

Solis-Garcia et al (2021)	Prospective cohort study	March 15 to August 17, 2020	Spain	73	34 (27- 37)**	32 (43,8%)	38 (37- 40)**	26 (35.6%)	75					
*Median (Min	*Median (Min – Max); **Median (IQR)													

A total of 2763 neonates, 79 (2,8%) had positive COVID-19 test. According to the ma-ternal practices, 54,7% of neonates (440/804) separated early from mothers [18,24,27,28,30,33], 56,0% (564/1007) neonates was dried and laid directly on the mother's bare chest after birth (skin-to-skin) [19,20,21,24,31], 66,69% (1199/1798) neonates stay with mothers the same room for 24 hours a day from the time they arrive in mothers room after delivery (rooming in), and 51,5% (971/1886) breastfed exclusively [17,18,22,23,24,25,27,29,30,31,35].(Table 2)

Table 2: Rate of infected infants and the practices who used by mothers.

First Author (publication year)	Number (%) of infected infants	Skin- to-skin, N(%)	Early separation, N(%)	Rooming in with mother, N(%)	Exclusive breastfeeding, N(%)	Breastfeeding (exclusive or complementary), N (%)
Angelidou et al (2021)	6 (2,7%)	NR	NR	167 (66,8%)	152 (66,8%)	230 (90,2%)
Congdon et al (2021)	0 (0,0%)	NR	33 (47,1%)	33 (47,1%)	21 (30,0%)	33 (47,1%)
Conti et al (2021)	1 (2,7%)	NR	37 (100,0%)	NR	1 (2,7%)	10 (27,0%)
Dumitriu et al (2021)	0 (0,0%)	NR	NR	82 (81,2%)	41 (40,6%)	91 (90,1%)
Donati et al (2021)	18 (3,4%)	NR	279 (51,9%)	379 (72,2%)	NR	428 (79,6%)
Ferazzi et al (2020)	3 (7,1%)	NR	NR	NR	11 (26,2%)	NR
Jiménez et al (2020)	6 (1,5%)	251 (62,3%)	NR	NR	249 (61,8%)	NR
Marin Gabriel et al (2020)	13 (5,2%)	NR	NR	NR	103 (41,5%)	179 (72,2%)

Marín Gabriel et al (2020)	0 (0,0%)	NR	37 (88,1%)	NR	6 (14,3%)	19 (45,3%)
Martenot et al (2021)	1 (3,9%)	10 (38,5%)	NR	NR	11 (42,0%)	23 (88,5%)
Nayak et al (2021)	9 (5,5%)	NR	NR	138 (83,4%)	NR	125 (75,8%)
Pereira et al (2020)	0 (0,0%)	NR	NR	13 (59,1%)	11 (50,0%)	17 (77,3%)
Ronchi et al (2020)	3 (4,8%)	NR	7 (11,3%)	55 (87,1%)	45 (72,6%)	59 (95,2%)
Salvatore et al (2020)	0 (0,0%)	NR	NR	68 (82,4%)	NR	64 (78,0%)
Sánchez García et al (2021)	0 (0,0%)	NR	NR	NR	NR	NR
Sánchez- Luna et al (2021)	18 (3,6%)	252 (50,0%)	NR	264 (52,3%)	272 (54,1%)	393 (78,1%)
Shlomai et al (2021)	0 (0,0%)	NR	47 (85,5%)	NR	NR	41 (74,5%)
Solis-Garcia et al (2021)	1 (1,3%)	51 (68,0%)	NR	NR	48 (64,0%)	55 (73,3%)

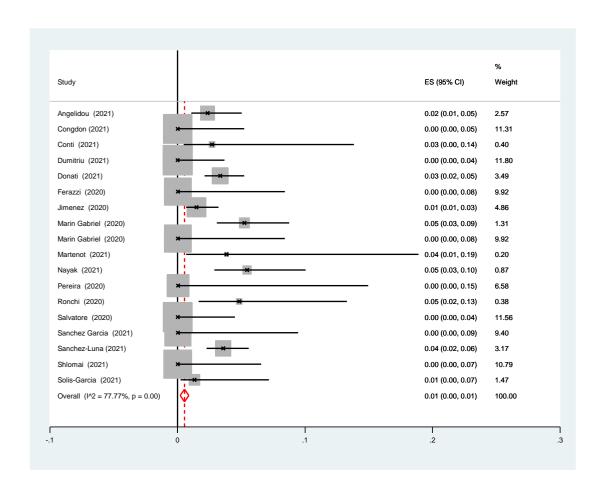
Only one study examined the factors associated with positive sars-cov-2 results among neonates [23]. This study showed that the only factor associated with positive sars-cov-2 was maternal SVI >90th percentile vs other (OR=4.95; 95% CI: 1.53 - 16.01; p=0.008). The type of delivery (vaginal vs cesarean delivery: OR=0.47; 95% CI: 0.16 - 1.40; p=0.18), rooming-in (any vs no: OR=0.29; 95% CI: 0.04 - 2.29; p=0.24) and maternal symptoms (symptomatic vs asymptomatic: OR=0.71; 95% CI: 0.49 - 1.02; p=0.07) were not associated with positive sars-cov-2 results among neonates [23].

For the spread of the disease the hospitals had taken measures such as the infected mothers were separated from their newborns immediately after birth and during the entire hospitalization [27,33,34], mothers wear surgical face masks [21,26,28,30,31,32], disinfect their hands [26,30,31], and wash their nipples with odorless soap during breastfeeding [26,31], and newborns placed at least 2m away from mothers bed during sleeping [30,31,32], use personal protective equipment [25].

4. Meta-analysis

The pooled proportion of SARS-CoV-2 infection among infants born to infected mothers of 1.0% (95% CI: 0.0 - 1.0%) (Fig. 2).

Figure 2: Proportion metanalysis of the overall estimate of SARS-CoV-2 infection among infants born to infected mothers



The I2-test was 77.77%, demonstrating a high heterogeneity. The sub-analysis showed that the proportion of infected neonates was similar between the studies with (1%, 95% CI: 0.0%-1%, I2-test 36.94%) and without (0.0%, 95% CI: 0.0%-1.0%, I2-test 74.61%) (Fig. 3) data for rooming-in, with (1%, 95% CI: 0.0%-1%, I2-test 85.36%) and without (0.0%, 95% CI: 0.0%-1.0%, I2-test 63.23%) (Fig. 4) for skin-to-skin, and with (1%, 95% CI: 0.0%-1%, I2-test 75.52%) and without (1.0 %, 95% CI: 0.0%-1.0%, I2-test 85.43%) for exclusive breastfeeding (Fig.5).

Figure 3: Proportion of the estimate of SARS-CoV-2 infection among infants born to infected mothers in subgroups analyses from studies with and without rooming-in.

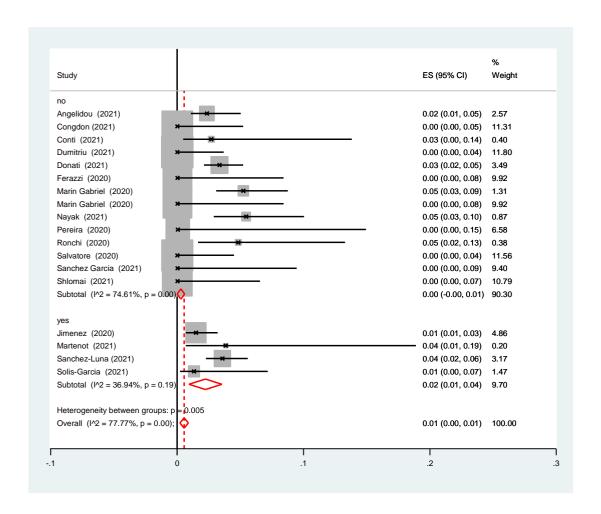


Figure 4: Proportion of the estimate of SARS-CoV-2 infection among infants born to infected mothers in subgroups analyses from studies with and without skin-to-skin.

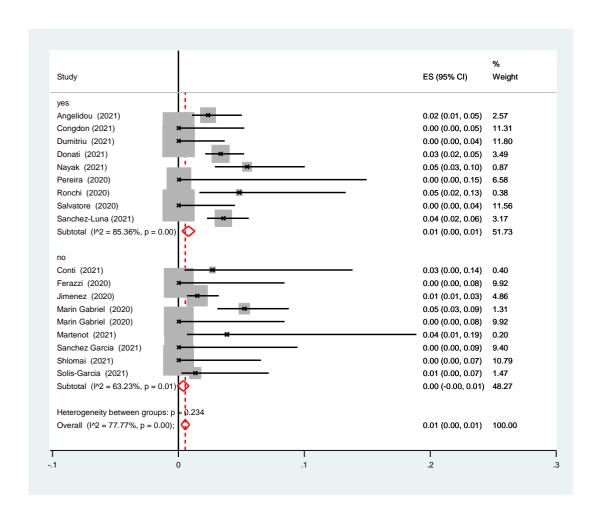
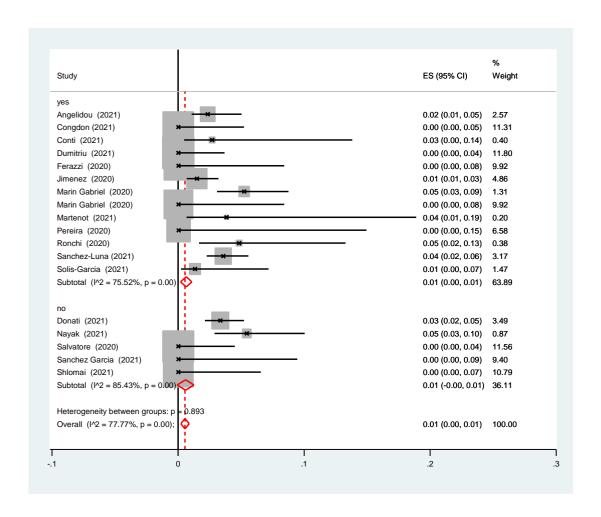


Figure 5: Proportion of the estimate of SARS-CoV-2 infection among infants born to infected mothers in subgroups analyses from studies with and without exclusive breastfeeding.



5. DISCUSSION

The objective of this systematic review and meta-analysis was to examine the risk of transmission of SARS-CoV-2 from infected mother to neonate during the breastfeeding, the skin-to-skin contact, and the rooming-in. We found that the SARS-CoV-2 infection among neonates born to infected mothers was found to be 1.0%. This indicate that mother-to-child transmission in the neonatal period is low.

Concerning breastfeeding, it is well known that covid-19 is transmitted mainly through horizontal transmission and specifically through aerosols. In our review, the most articles referred that the vertical transmission through breastmilk cannot be excluded/or limited as well as there are searches which the virus was detected in breastmilk and the infants were diagnosed with covid-19 but it was unclear, the exact way of transmission. However, the benefits of breastfeeding outweigh the potential transmission. Because of this, the major organizations such as WHO and RCOG support the direct breastfeeding following protective measures such as strict hand hygiene and wearing mask [36]. In addition, it is

important that anti-SARS-CoV-2 antibodies have found in breastmilk and these might offer protection in infants [37].

Since the beginning of COVID-19 until the moment of the writing of this review have adopted various recommendations for breastfeeding. Most researches and international organizations such as WHO, RCOG (Royal College of Obstetricians and Gynecologists) and the American Academy of Pediatrics support direct breastfeeding following individual protective measures such as strict hand hygiene, wearing mask and breast cleaning when it is necessary such as when mother coughs or sneezes on breast [36]. For mothers who are not in condition to breastfeed immediately or it is not their desire, it is recommended the expression of milk following not only protection measures but also the thorough pump cleaning and feeding of breastmilk to the infant by a caregiver without boiling or pasteurizing breastmilk [38]. In case, breastmilk is not available or sufficient, it is suggested the use of pasteurized human milk from bank milk against using formula [39]. The study by Salvatore et al. reports on a cohort of neonates born to SARS-CoV-2 positive mothers and follows the outcomes of staying and breastfeeding up to one month after birth. All newborns tested negative for SARS-CoV-2, either immediately after birth or fourteen days later. This shows that staying and breastfeeding can be safe when the necessary precautions are taken, including hand hygiene and the use of surgical masks [26].

The early separation of the dyad adopted in our management negatively affected the percentage of women who were able to breastfeed, with only a mild recovery in total breastfeeding rate being observed after the mother-infant reunification probably due to the decrease in breastfeeding support that occurred during the pandemic [40]. The WHO recommends breastfeeding of infants and young children also in case of suspected or con-firmed maternal SARS-CoV-2 infection. The beneficial properties of breastfeeding including the practice of skin-to-skin care and the transfer of protective maternal antibodies via breast milk (especially secretory IgA (sIgA) and, to a lesser extent, IgM and IgG isotype immunoglobulins) are well established [41]. Recent evidence indicates that breastfeeding does not seem to be associated with neonatal SARS-CoV-2 infection because viral trans-mission through the milk, if

any, should be rare and because a robust sIgA-dominant SARS-CoV-2 antibody response is detectable in human milk soon after infection in a significant majority of individuals [42].

There are some limitations to this review. As the pandemic continues the data is rapidly changing. As our search for this review ended on November 30,2021, it is potent that some of these suggestions may be outdated by the moment this review is published. However, the summary of all suggestions is important as we can understand ways of managing covid-19 from the beginning of pandemic until the moment of writing this re-view as well as how the suggestions could be modified in the future. Furthermore, the study period ended few months after the appearance first vaccine. Therefore, further re-search is needed for women who are with covid-19 in early post-partum period and were previously vaccinated during or before pregnancy.

6. Conclusion

The results of this study show a low rate of perinatal infection, support the rooming-in and skin-to-skin confirm the effectiveness of preventive measures in reducing the risk of mother-to-child viral transmission. We suggest the encouragement of direct breast-feeding as well as breastmilk may provide specific antibodies to infants, the immediate skin-to-skin and rooming in when the condition of mother and newborn permits it and following all protective measures and specifically strict hand hygiene, wearing a mask and breast cleaning when need it and not before every breastfeeding. The literature indicates that while vertical transmission cannot be excluded however, if it exists, it might be rare and we should focus on horizontal transmission. For this reason, it is utmost im-portance that women strictly observe personal protection measures. In addition, in case if these practices are avoided, breastfeeding is adversely affected. With these practices and following mothers all protection measures the potential of transmission of covid-19 in infant is almost impossible. However, even if newborns have covid, they have no or mild symptoms and recover well. We hope that the findings of this review could help medical staff and government officials making protocols for patient care. Authors should discuss the results and

how they can be interpreted from the perspective of previous studies and of the working hypotheses. The findings and their implications should be discussed in the broadest context possible. Future research directions may also be highlighted.

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	Author(year)	Study design	Study period	Country	Study place	, ta	Sample of Infected Mother, N	As getomatic CO VID-19 Bluess	Symptomatic COVID-19 Illness	Age (jean)	Getational age	Neomie Simple ₊ N	Route of delivery: constrain N	Route of delivery: centreata N	Number of meante who had positive result during hospitalization, N		Number of recente who lad positive result in the first 30 Bays after hospital discharge, N	had positive result in the	Early separation, N	Eady separation, N	Sinto-kin, N	Slinteslin, S	Rooming in with mother, ?	Receive in with mether, N	Breastferding (Greet OR exclusive), N	Brassfeeding N	Number of neonite who fed with breast milk, N	Number of nemate who fed with breast milk, W	Masure to link be transision of ovid then make to nebro	RSA fizion forzonsole infection	Codules
1	Angdidos d al (1011)	Malticator calori study	March 1, 2020, and July 31, 2020	USA	11 hagink	To assertain the portionage of moments who were born to make to the poster SARSCOVE test results during the first things planters, the chieval and sociology planters associated with moment for several testinately positive.	259	170	79	30.4 (+6.3)	319(4.6)	255	113	45,7%	Š	2,22%	1	Ville	NE.		NR	6	16	6,3%	152	55,66	230	90,2%	Program women were track for SAPSCeV-2 according to the guide faces of formal vidual lamptade	15 astran & Bray, OR +0.47; 95% CE 0.16-1.40; p=0.18),	The endy aboved thinks makered so had velocability vacance. Southfur mound are treat positivity, whose makered COVID— Mayangara, Adin oy not dual recently de practice were not applicate favor.
2	Congdon ct at (2021)	Carestric study	Nard to May, 2000	USA	BORN member hespital	To describe early neutral outcomes and inputent to management in US hospitals.	70	NR.	NR	SSN of motions had 20 to <40 years	39.0 (6.3 - 41.6)	70	25	2,71%	0	0,00%	NR		33	थ1क	NR		33	47,146	1	30,00%	E	47,1%	NZ.		Of the scenarios who were tratedy neutrated positive for SARS- CoV-2 during the birth heapthal cation.
3	Comi et al (2021)	Obscriptional study	April 1, 2000,to March 18, 2021	hdy	Thogist	To describe the effect of the early separation of the material fishin dyad, in our of material SARS- Coll-1 indiction.	37	В	21	31 (17 - 42)	39 (N - Q)	31	B	4,1%	1	2,70%	NR		37	10,50%	NR		NR		1	2,7%	10,50	27,0%	All bruite de mbors wer, square d'un bor acubem immelie by after birhand durig de cuite begin birate. At déclarge, de épai was reconpead, and breat deling wer cenarqui by melieul stall afor appopriate counciling enthe safery condition—handha shing and as cof surgiol mark		Ocepie carly separation of the dyall promoting the non-berm from possible betiment transmission of SASPC (VII.) is required justice to be affecting during the first months of the
4	Demitrie at al (2021)	Retrospective cohort analysis	March 13 to April 24, 2020	USA	2 hapial	To amby in the processage of victical reasons size from infrared modern to infrare and to describe infrared experience and control (PAC) mode about the results.	160	NR.	NR	285 (240- 240)	39.0 (01.0 - 40.0)	161	46	@\$4#	0	0,00%	NR		NR.		NR		52	\$1,196	q	40,39%	91,50	9,1%	Withite co-caption of implementation of appropriate transmission processions and some dipersonal processive conference command per usual standard modern-train takes to a literate, and direct be sufficielly after appropriate lead and brown beautic.		No chinal ordene of votal transision variatisficial (I) m vibras of mobile posite for a vish agence SARS-GNU infection, depte met m vibras remains and direct breaster diagram tex.
5	Donat d al (2021)	National population based prospective cohort study		ldy	All hogists	To explain how claimed gravitic model protect the labour physiology and the mother-child band at first water of pandemic in July	525	235	30	31.5 (45.69)	NR	SI	177	11,76	18	3,5%	NR		279	51,56%	NR		379	72,9%	M		425	79,6%	95% of the women wore a surgical mask during labour		The infants repeated and not repeated from their SARS-CeV-2 per live methors but had good outcomes.
6	Fernani et al (2009)	Ratesparine study	March I to March 20, 2000	bily	Dhospitals	To report mode of éditivery and immediate normal outcome in women in éte é vi in COVED-19.	42	NR.	NR	329(21-44)	10 materstad >01 weeks of gestation	42	ı	Q36%	1	7,14%	NR		NR		NR		NR		п	26,19%	NR		When the positive infected state of the moder was known at thirtopy broadfording was allowed according to increational guide their Si if the moder was asymptomic or had only niter symptoms. During		Vaginal delivery is associated with a low risk of integratum SASS-Cor-2 transmission to the sewborn.
7	Américacial (2009)	Prospective observational study	March 1 to May 31, 2000	Spain	70 contens	To doministrate that delayed cored champing (DCC) is suffer in mathers with continue of SARS-CoV-1 in Edition	46	291	112	214 matters had age between 20- 34 years	NR	465	126	E,75%	6	1,49%	NR		NR		251	62,35%	NR		249	61,79%	NR		NR.		Nebasinface with arms income confine had shinned in amount and they broaded seen, no increase in actual tempolisies was decorded by this study.
8	Maria Gabrid et al (2029)	Malacana dacriptivestudy	March 13 to May 31, 2000	Spán	Bhogish	To amby the clinical distriction from their with on ideal fidning programs; or labour and the penalthill of visital remannion. Moreover to investigate the penalthilly of best and transition after height little labour.	10	98	364	32.1 (#63)	39 (3840)	248	6	261	13	5,24%	0	0,00%	NR.		NR		NR		163	41,53%	179	72,2%	NZ.		Nacofidate v a feed CVIO-8 transisionésingédicty o trophot ik foi mob d'il k ink ne konsindat é a or stép, Euleis e brasifedignet a de drug ad a 1 mob of ag wat beer ha a pad.
9	Maria Gabrid a al (2029)	Multicator docriptivestally	March 13 to May 31, 2021	Spain	Kheqiab	To do only the clinical features of makes mit and with COVID-19 and comments promited vortical moder to newbornings resiston.	42	NR.	NR	33.6(+4.5)	38 (41.1)	42	2	G _A IN.		0	NR		37	55,1 0 6	NR		NR		6	14,25%	В	6,3%	NΣ		No transmission of COVID-19 was descreed during birth. So, the way of labour should be dependent on general grid of terms. At deschape, the permanages of transferding more reduced because of the operation of the measure of the operation of the operation.
10	Martinototal (2021)	Retrospective study	March 15 to April 24, 2000	France	Two load II pointed control	To assess the softey of the current management of dyadic models - infantin two periodal contents.	26	NR.	NR	30.6(47.9)	39(4)	26	10	18,9%	1	3,55%	0		NR		10	38,5%	NR		n	42%	z	88,5%	Sin-to-sin omar tand brandre dag required specific beginnin measure. Nichters had to wear surgeal face make, dismit or boir hands, and weah their night with other loss sage. When makes were slooping, creates had be given at least 1 m away from their had?		As feet thins at very racely influent and, if inflicted, here only mild by replaces, it agrees as it is contact providing family-control providing area of contaging bending the two trials and feet SARS-Co-V-Spatistics of our during the COVID-18 participate.
11	Najaketal (2021)	Prayedine observational study	May 1 to October 20, 2000	India	1 CONID hespital	To investigate disitual characteristics and results in selected modern and their revisions. Moreover, to show the selected forces flooding and Receiving in.	16	NR.	NR	39 (19 - 41)	37.5 (25 - 41)	165	103	6317	9	5,45%	NR		NR		NR	62%	128	17,646	NR.		125	75,5%	Any optimate names was allowed to room in with their methors and to be settled with a thinguar dample and coming procession. Subjects were kept in a repeate their control of their settled in th		Next of the menter developed sign and symptoms of SARS-CoV-I refer to during receiving a said force infecting
12	Perdiract al (2000)	Romagazáva czac soricz study	March 14, to April 14, 2020	Potagi	1 University Regulat	To describe the different kinds of lactation of women with COVID-19, to show the possible difficulties and to assess the infant infloring misk	22	11	11	34 (19-43)	38(31-41)	22	Ł	15,2%	0	0,00%	NR		NR		NR		13	9,1%	п	50,0%	n	17,3%	Temperary separation of mothers with COVID-19 was considered when monthly indicated occur and or skin- to-skineconted was avoided.		Browleding in a views of motion with COVID-19 is safe with the adequal infection control measure to avoid motion-budy contagion.
13	Ronchi etal (2020)	Prospedine, multicoter educt study	March 19 to May 2, 2020	ldy		To assess the peach disty of postural of SARS- CoV-2 transmission from makes with covid-19 to their new borns after they have Recombiginated breastfeeding.	61	34	27	32 (28-36)	29 (2541)	62	15	24,59%	1	1,61%	2	3,2%	7	11,29%	NR		55	89,77%	6	72,58%	S-j.0	95,2%	Hadvesting, surject for mak dans d deing brassfoding or what providing carefor the india, and observing physical distancing (2 m) from the india.		The possibility of tractics in through protective Receiving-in war and no case war not division medicas had no or mild a program. It is suggested, receiving in and breat facility after following all appropriate precessions no cases.
14	Salvatoro d al (2026)	Obscriptional cohort study	March 22 to May 17, 2020	USA	3 New York Probyterian Haspitals in New York City		78	2	78	NR	18(27 - 4)	12	36	6,90%	0	0,00%	NE		NR.		NR.		69	12,97%	NZ.		61		Notices denet a surgical mask whencur their remate and practiced proper hand higher before skin- te-skin contact, breatheding and resine care. All remates who researed in with their markers were held		The possibility of perimal transists acros to be impossible following all agreepine processions measure. Recently-in and detect the activation to suggested provided of the treatment of parties about infinity rotes for.
15	Sánchiz Gerdia d al (2021)	Malicata, prospedire as e- cartal study	April to July 2000	Spain	4 kmc13 institutions of the health system of the Madrid region		37	¥	21	339(45.4)	39.1 (4.8)	37	H	TAIN	0	open			NR.		NR		NR		M		NE		NE NE		According to the constant's SWS-Co-VI states, this received apports the abstract of viral RNA and additional immunological grafic internation is.
16	Sánche » Luna etal (2021)	Prospective cohart study	March S to May 26, 2000	Spain	9 loogitals	To investigate the material and most all calculations of infant from infected medium.	ধ্য	245	252	В	49 (+2.7)	503	164	2,0%	18	1,58%	NE		NR.		252	50%	264	52,49%	272	54,08%	393	78,1%	Ck-godi in malars used far emaks when having skin to-disk context.		There is no and for separation of makers framewater, allowing distribution contentioning with maintainer of the self-colling in a high processor (or whom some moders with COND-19.
17	Shiomai et al (2021)	Obscriptional cohort study	March Sto May 30, 2000	iral	11 pointed-scoratel costos	To calcut factate of transmission of coronavirus through broaderding before and a for the discharge of a where where continue were indicated and who were expended after labour and standard.	53	4	13	29.7 (47.3)	39 (±1.0)	55	В	11,1%	0	0,00%			47	15,4%	NR		NR		NR.		٩	74,5%	Malkes with positive SARS CoV-2 test results works quarted from the continues.		No vial infection vasidatified in menatishemic and separated from biolistatis-GNA-positive mobiles at lark and subsequently fed separational breast milk
15	Solis Garciactal (2021)	Obscriptional, prospective and single contor cohortstudy	March 15 to August 17, 2020	Spán	éprinatef	To docribe the characteristics and externors of normality form to method with SARS-Cell-2 y infortion did word disa baggiall with a loved IDC normal distoration concernit (NICC)	73	2	41	34 (27-97)	38 (3740)	75	ä	BAIN	0	0,00%	1	13%	NR		51	65%	NR		ē	64%	5	73,3%	We provided becased using other access support to the markers, explaining the baceless and potential mide known to date, and recommending maternal mile over demails based on the recommendations of the SENson and the most reconstructions.		Risk of SARS-CaV-2 reasonimients less when complete public recommendates inseed by Sackad Egy melade Normalistic, allowing receive in and promoting be self-cline.