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Pharmacognosy Journal, Vol 14, Issue 6 (Suppl.), Nov-Dec, 2022

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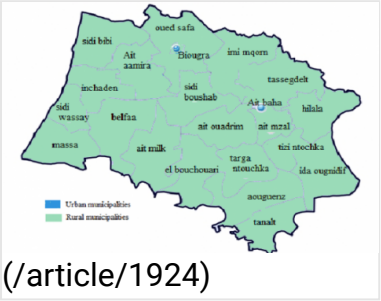

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Medicinal Plants Adopted to Treat Children's Diseases by Traditional Pediatrics ''Women Healers'' In The Souss Massa Region (Agadir Idaoutanan, Inzegane Ait Meloul and Chtouka Ait Baha) Morocco (/article/1924)

Taleb Ali Khalid,Aarab Ahmed

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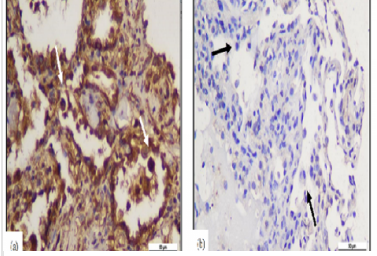
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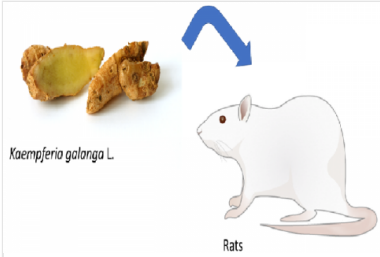
Fajar Herbowo Niantiarno,Agus Turchan,Myrna Adianti,Budi Utomo,Muhammad Arifin Parenrengi,Abdul Hafid Bajamal



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Effect of Pomegranate Extract On N-Terminal Pro Brain Natriuretic Peptide and Asymmetric Dimetylarginine Levels in Children with Pulmonary Artery Hypertension in Acyanotic Congenital Heart Disease (/article/1927)

Sari Yunita Suk Noer,Mahrus A. Rahman,Budi Utomo

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Evaluation of Experimental Cerebral Malaria of Curcumin and Kaempferol in Plasmodium berghei ANKA-Infected Mice (/article/1928)

Maulana Yusuf Alkandahri,Afiat Berbudi,Anas Subarnas

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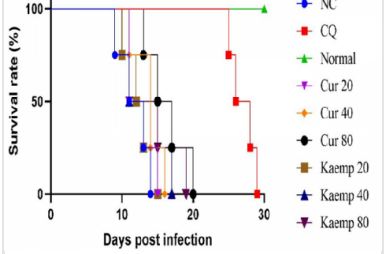

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Puja Adi Priatna,Rizki Rahmadi Pratama,Retno Widyowati,

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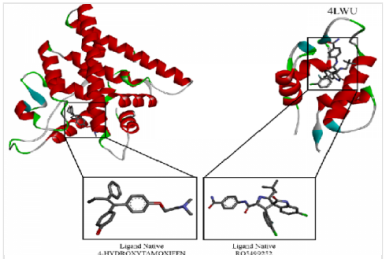
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Left Atrial Myxoma Presented with an Obstructive Shock, Right Ventricle Dysfunction and Pulmonary Hypertension (/article/1930)

Wisda Medika Valentidenta,Agus Subagjo,Dandy Hertriwibowo

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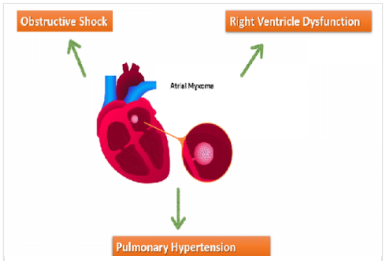

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Original Article

Risk Factors for Hepatotoxicity From L-Asparaginase Chemotherapy In Children With Acute Lymphoblastic Leukemia (/article/1931)

Agniya Ali Fahmi Hikmat,Mia Ratwita Andarsini,Bagus Setyoboedi,Maria Christina Larasati,Andi Cahyadi,Dewa Gede Ugrasena

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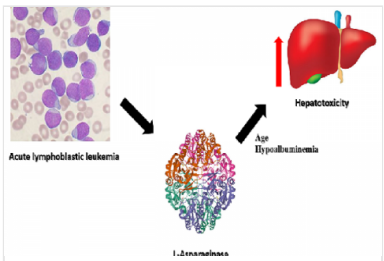

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Mohammed Wasel Matar,Shahad Mohammed N. Alqahtani,Duaa Adnan Alghafli,Abdullah Abdulhamid Altaweel,Abdullah Jalal Alasoom,Hussein Ali Burshed,Marwan Mohamed Alshawush,Hany Ezzat Khalil


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Cichorioside a biocoumarin modulates lipid and glucose storage on 3T3-L1 cell lines: In vitro and in silico approach (/article/1895)

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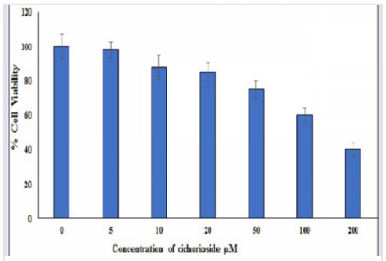

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Relationship Histopathology Grading of Meningioma with the Use of Medroxyprogesterone Acetate (MPA) as A Hormonal Contraceptive (/article/1932)

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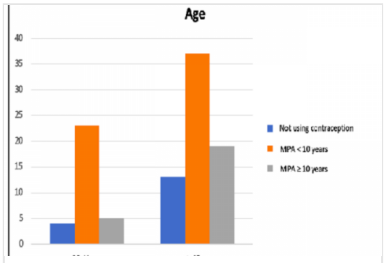

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Nafdzu Makhmudatu Muna,Ni Made Mertaniasih,Pepy Dwi Endraswari

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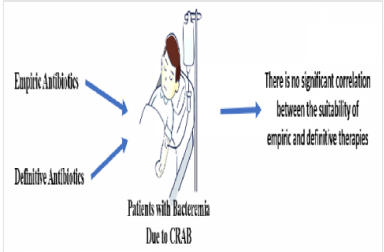

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GC-MS Analysis of Volatiles Present in Pappea Capensis Extracts (/article/1934)

Makhoahle PM

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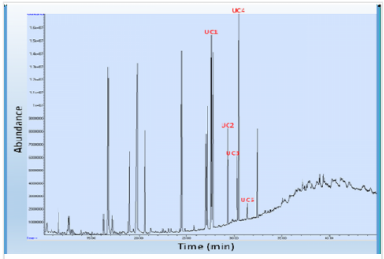

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Phytochemical Analysis and Antioxidant Activity of Water Hyacinth Flowers (Eichhornia Crassipes) Extract (/article/1935)

Ace Baehaki,Shanti Dwita Lestari,Wiwira Agustina,Sintya Dwika Putri

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Research on External Signs and Chemical Composition of Medicinal Plant Raw Material -Leaves of Ficus Elastica (/article/1936)

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Antiparasitic effect of Psidium guajava on promastigotes and axenic amastigotes of Leishmania (/article/1937)

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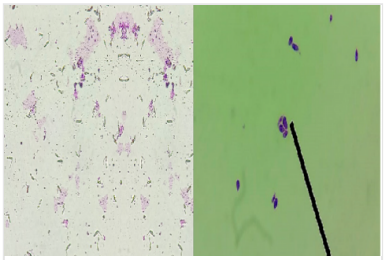
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The Serum Formulation of Hati Tanah Tuber Ethanol Extract from Central Kalimantan (/article/1938)

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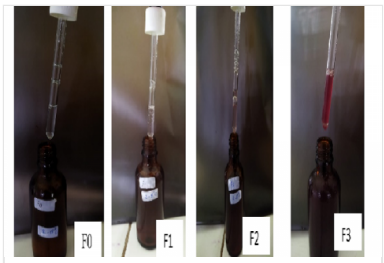

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Job fulfilment and its related variables among pharmacy certificate holders in Jordan: A Cross-sectional Study (/article/1939)

Noha Abd Alkare Younis

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Chemical Profiling of Nonpolar Compounds of Onopardum Acanthium using GCMASS (/article/1940)

Amjad I. Oraibi,Hayder M. Abdulhamza

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Antioxidant, Antimicrobial, and Antiplasmodial Activities of Sonchus arvensis L. Leaf Ethyl Acetate Fractions (/article/1941)

Dwi Kusuma Wahyuni,Anindya Nariswari,Agus Supriyanto,Hery Purnobasuki,Hunsa Punnapayak,Wichanee Bankeeree,Sehanat Prasongsuk,Wiwied Ekasari

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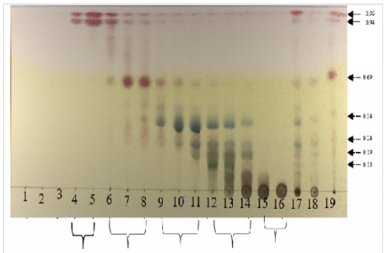
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Senna Siamea Hexane Extract: Potent Antifungal Activity Against Candida albicans, Candida Krusei and Identification of Its Chemicals Content (/article/1942)

Diny Kamilah,Berna Elya,Robiatul Adawiyah,Annysa Ellycornia Silvyana

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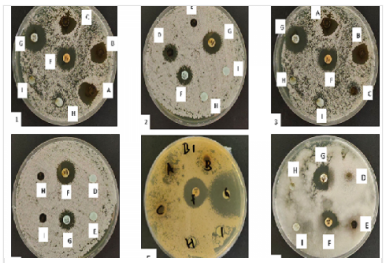
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DFT and Pharmacokinetic Study of Some Heterocyclic Aspirin Derivatives as The Cyclooxygenase Inhibitors: An In-Silico Approach (/article/1943)

Emranul Kabir,M. R.O.Khan Noyon,Md. Amjad Hossain,Pranta Acharjee

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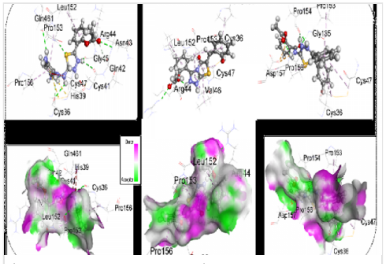
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Fingerprint and Multivariate Analysis of Apium Graveolens L. From Different Geographic with Spectroscopic ATR-FTIR (/article/1944)

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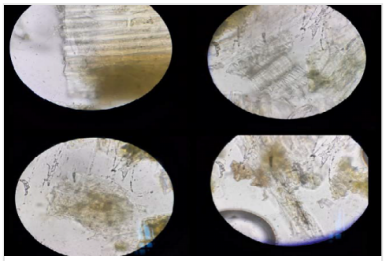
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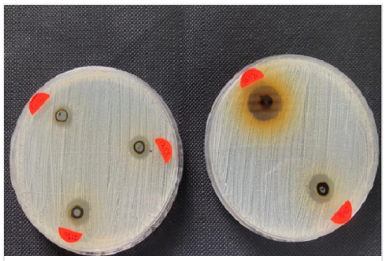
Antibacterial Effect of Nigella sativa L. Seed from Indonesia (/article/1945)

Em Sutrisna,Sri Wahyuni,Aris Fitriani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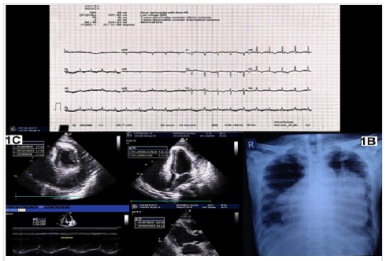
Research Article

Successful Intrapericardial Fibrinolysis on Acute Recurrent Purulent Pericarditis with Impending Cardiac Tamponade during Pandemic Situation: A Rare Case Report (/article/1946)

Muhammad Dedy Pratama,Budi Baktijasa Dharmadjati,Muhammad Rafdi Amadis,Ahmad Faisal Dwi Raharja,Muhammad Ramadhan,Dwika Rasyid Firmanda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Bio-Evaluation, In-Vitro and In-Vivo Anti-Inflammatory Activity, Therapeutic Efficacy, and Genotoxicity of the Potentials of the Green Seaweed Valoniopsis Pachynema using Zebra Fish Larvae (Danio Rerio) as an Animal Model (/article/1947)

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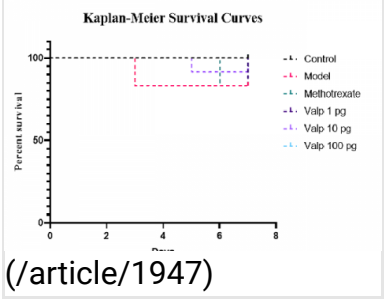

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Aquaporine 4 Expression on End Feet Astrocyte Before and After Cerebrospinal Fluid Drainage of Hydrocephalus Mice Model (/article/1948)

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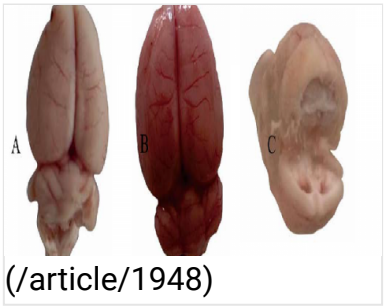

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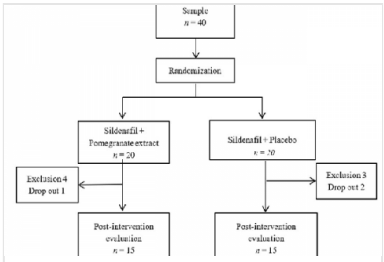
Research Article

Effects of Pomegranate Extract Supplementation (Punica granatum L.) on Clinical Manifestations of Pulmonary Arterial Hypertension in Children with Acyanotic Congenital Heart Disease (/article/1949)

Audylia Hartono,Mahrus A. Rahman,Budi Utomo



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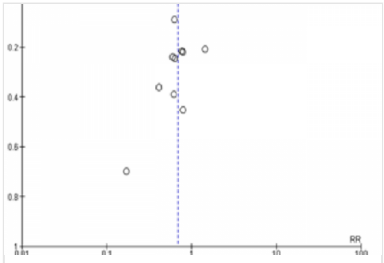
Review Article

The Role of Breast Milk on Reducing the Risk of Neonatal Sepsis in Preterm and Low Birth Weight Infants: A Systematic Review and Meta-Analysis (/article/1950)

Tita Natalia Manurung,Citrawati Dyah Kenco Wungu,Martono Tri Utomo



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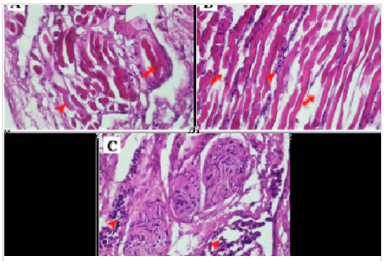
Case Report

Histopathological Perspectives of Multiple Organs in a Red- Footed Tortoise (Chelonoidis carbonaria) with Suspected Metabolic Bone Disease: A Case Report (/article/1951)



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Hani Plumeriastuti,Annise Proboningrat,Djoko Legowo,Bilqisthi Ari Putra,Gracia Angelina H,Agung Budianto Achmad

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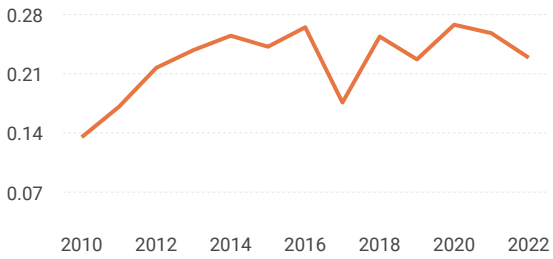

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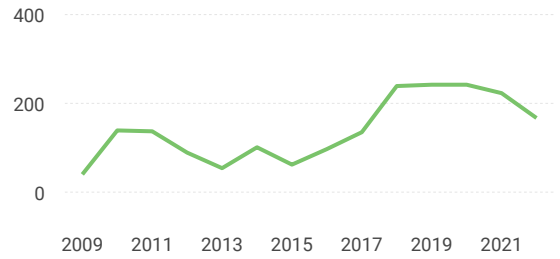

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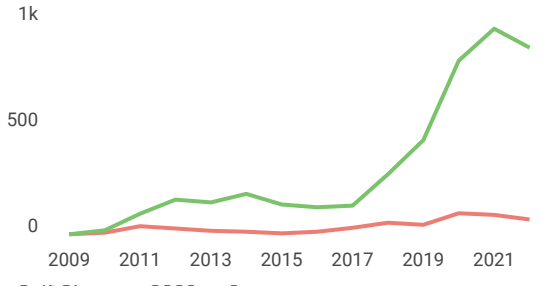

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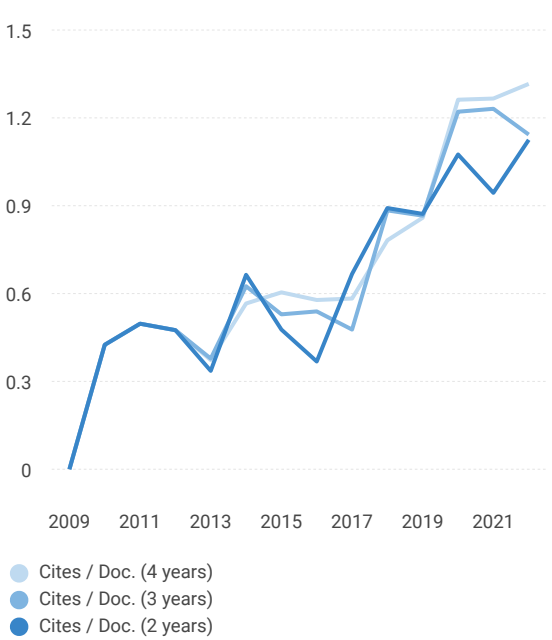

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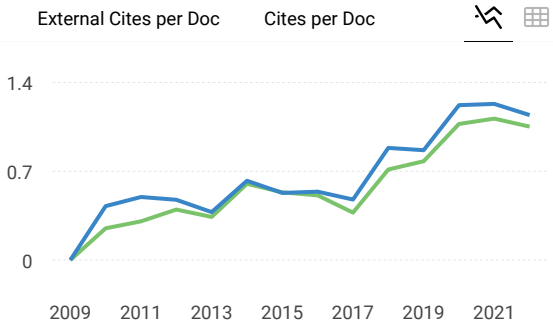

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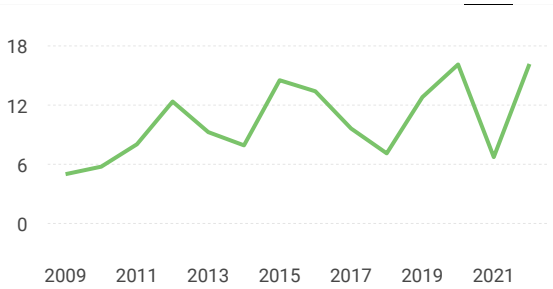

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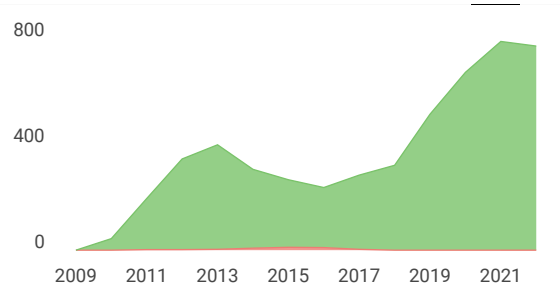

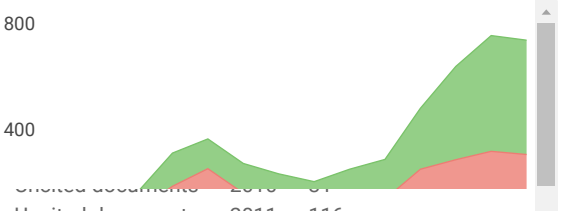

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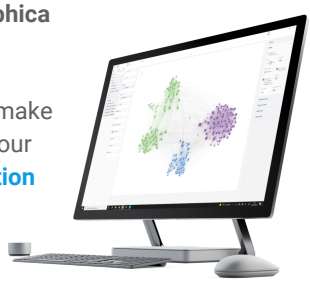

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Review Article

The Role of Breast Milk on Reducing the Risk of Neonatal Sepsis in Preterm and Low Birth Weight Infants: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: High mortality and morbidity rates are associated with neonatal sepsis in preterm and low birth weight infants. Aside from controlling the nosocomial infection, intervention for reducing the risk of sepsis is demanded. The best nutrition for preterm infants is breast milk. Bioactive compounds found in it, such as antibacterial, antiviral, and anti-inflammatory activities not only for immunity against the infection but also for growth, and development. **Objective**: To investigate the effect of breast milk against the risk of neonatal sepsis in preterm and low birth weight infants. **Methods**: We conducted an electronic search through several databases including PubMed, Web of Science, Science Direct, and Scopus. We performed an analysis on nutritional feeding and volume of breast milk and late-onset sepsis from ten potential observational studies. **Results**: Breast milk significantly reduced the risk of sepsis in preterm and low birth weight infants (pooled RR 0.70; 95 % CI 0.55 - 0.88, p = 0.002). In addition, when we performed subgroup analysis, we found that breast milk volume > 50ml/kgbw/day also reduce the risk of sepsis with pooled RR 0.61(95% CI 0.46-0.8, p=0.0004). **Conclusion**: Low birth weight and preterm infants had a lower risk of neonatal sepsis when they got breastmilk. To preserve the supply of breastmilk, health professionals should support and encourage mothers who were breastfeeding.

Key words: Breast milk, Neonatal sepsis, Preterm infant, Low birth weight.

INTRODUCTION

Neonatal sepsis, which affects infants in their first month of life, is a dysregulation of the immune system's response to infections that leads to organ damage.[1,2] Neonatal sepsis was the main cause of neonatal deaths in low- and middle-income countries and without a considerable decrease to 12 per 1,000 live births by 2030, the Sustainable Development Goals would not be met.[3,4] Preterm and low birth weight infants needed intensive and invasive treatment during hospitalization that put them at risk for sepsis. Culture-proven sepsis mostly occurred in preterm and low birth-weight neonates.[5] To lower mortality and morbidity rates, interventions were being developed to lower the risk of sepsis in preterm and low birth weight infants.[6] In wealthy nations, the prevalence of neonatal sepsis ranges from 1 to 4 out of every 1,000 live births, while in low-middle-income countries, it ranges from 10 to 50 out of every 1,000 live births.[7] Preterm babies have highly vulnerable and immature organ systems. They are postnatally confronted with drastically altered antigen exposure including hospital-specific microbes, artificial devices, drugs, nutritional antigens, and hypoxia or hyperoxia. Hence, preterm infants are predisposed to sepsis but also to several injurious conditions that can contribute to the onset or perpetuation of sustained inflammation.[8]

Breast milk provides immunity and physiological and economic benefits by including proteins, lipids, carbs, minerals, vitamins, enzymes, growth factors, and hormones.[7]9 Preterm infants who are fed mother's milk are less likely to suffer from late-onset sepsis and the mortality rate is lower compared to formula.[10,11] Human milk is the optimal nutrition for preterm and low birth weight infants and decreases the risk of complications of prematurity.[12] It contains bioactive substances that play a role in the immune system such as immunoglobulin, anti-inflammatory, anti-oxidant, and microbiota that are expected to have an influence on reducing the incidence of neonatal sepsis. Preterm infants have a high risk for necrotizing enterocolitis, sepsis, retinopathy, abnormalities of brain development, metabolic syndrome, and repeated hospitalizations in premature infants.[13,14] Infants who receive breast milk greater than 50 ml per kilogram per day have a decreasing chance of developing necrotizing enterocolitis and late-onset sepsis and every 10 ml per kilogram per day decrease the re-hospitalization.[15] The challenge of providing breast milk for a preterm infant is that mothers who cannot provide enough breast milk for their own baby's needs should get breast milk donor and mothers who cannot breastfeed directly can express the breast milk. Difficulties in breastfeeding infants, techniques, and insufficient milk output were the predominant challenges. Mothers play an important role in the success of breastfeeding.[16] Interventions targeting the improvement of early postpartum lactation and training may increase breastfeeding mothers in preterm infants.[17] The American Academy of Pediatrics recommends exclusive breastfeeding in premature babies. If the mother's breast milk is not available, the babies can be given pasteurized donor milk.[12] Breastfeeding can begin immediately after childbirth when the baby is in a stable condition, however, if the baby is not stable, the mother should express the milk.[18]

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There are many studies found along the contradiction about breast milk and whether it reduces infection. Several studies revealed that late-onset sepsis in preterm infant was derived from contaminated breastmilk expression.[19,20] However, there is still limited evidence regarding the role of breast milk's effects on neonatal sepsis. Therefore, this systematic review and meta-analysis aimed to determine the role of breast milk on neonatal sepsis in preterm and low birth weight infants.

METHOD

Protocol and registration

The systematic review evaluation was conducted on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.[21] The detailed protocol in this study had been registered on PROSPERO with registration number CRD42022306263.

Searching strategies

Two persons separately did the literature searching on electronic database including PubMed, Science Direct, Web of Science, and Scopus up to August 2022. The Boolean operators AND and OR must be used to integrate concepts and keywords that were expressed as related keywords and index terms, such as Medical Subject Headings (MeSH). "Low birth weight", "preterm infant", "human milk", "breastfeeding", "formula milk", and "neonatal sepsis" were the search phrases utilized. These two reviewers were separately did the extracting data and if there was a misunderstanding, it could be reviewed by another reviewer.

Study selection

The articles that were in this review's qualification included: 1) English literature, 2) including preterm and low birth weight infants, 3) Evaluated the association between breast milk and neonatal sepsis compared to formula milk or compared the volume between administered breast milk to the risk of neonatal sepsis, 4) Available full text and 5) Observational studies. We excluded conference papers, book chapters, case reports/case series, review articles, studies with incomplete data and duplicated.

Risk of bias assessment

The Newcastle-Ottawa Scale for observational studies was used to evaluate the research's quality and publication viability. This scale aims to assess the quality of observational studies to construct a good meta-analysis outcome. The quality of included articles or studies was classified as high (9 stars), medium (7-8 stars) and low quality (less than 7 stars).[21]

Data extraction

The following data were extracted from each study: author, publication year, sample count, population, birth weight, gestational age, infection status, amount of breast milk, length of breastfeeding and results were the details that needed to be noted.

Data analysis

All analysis was conducted using Review Manager 5.4 software. We compared between breast milk and formula milk administration and calculated the pooled risk ratio of neonatal sepsis with a 95 percent confidence interval (CI) as the main outcome. A p value of < 0.05 was considered as statistically significant. The Cochrane's Q statistic and Higgin's I^2 were used to determine heterogeneity between studies. If the heterogeneity is low, fixed-effects model was used. Otherwise, random-effects models was used. Sensitivity analysis was carried out by leave-one-out method. Funnel plot asymmetry was used to analyze the possibility of publication bias. Subgroup analysis was performed for studies conducted on different volume of breast milk (>50ml and exclusive breast milk)

RESULTS

From the initial electronic database, we found 10,789 studies that matched up with our keyword (Figure 1). Subsequently, 313 studies were identified as duplications and removed. After the screening the title and abstract, we found 33 potentially relevant studies, in which 19 studies did not match with our criteria. Four studies were excluded because the outcome was not sepsis and incomplete data. Ten observational studies were included in this study's systematic review and meta-analysis.

The characteristic of the included studies is presented in table 1. The included studies yielded 3,414 preterm and low birth weight infants. The included studies were published from 1998 to 2019 in which each study had a sample size ranging from 80-1,587 participants. Of all studies included in this meta-analysis, the population were majorly from America and only one study from Asia. All of the participant were preterm 26-35 gestational age and very low birth weight < 1,500g.

From ten studies, there were five studies we analyzed the volume of breast milk above 50 ml/kgbw/day and exclusive breast milk associated with neonatal sepsis. We also checked the quality of studies using NOQS. We found three studies had high quality while five studies had medium quality and two studies had low quality.

Relationship between breast milk and neonatal sepsis in preterm and low birth weight infants

In the present study we found that breast milk significantly reduced the risk of sepsis in low birth weight and preterm infants by 0.70 times compared to formula milk, according to ten included studies (95% CI 0.55-088, p=0.002) with random effect model analysis. By removing one leave one out study the results of the sensitivity analysis revealed that the result was still significant.

Publication bias was evaluated using plot funnels (see Figure 2). As the funnel plot shows no asymmetry, it suggests that there was no publication bias found.

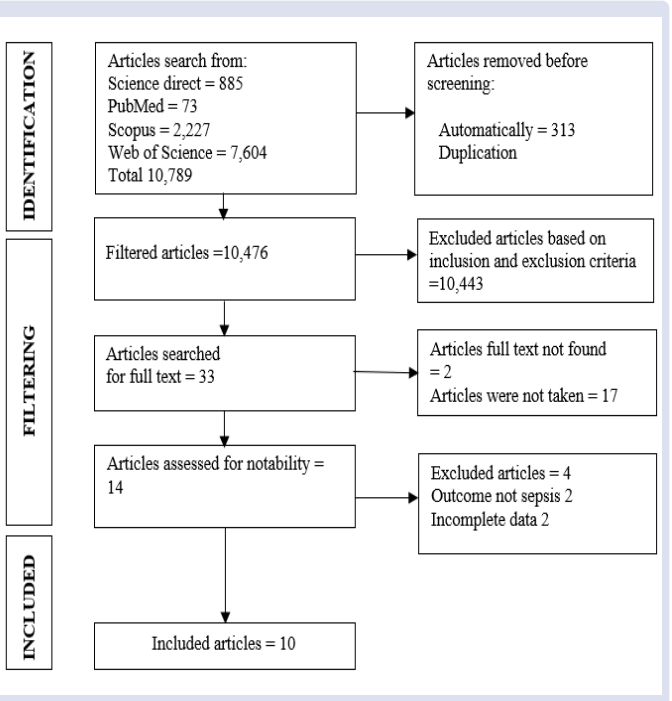

Figure 1: PRISMA study selection diagram.

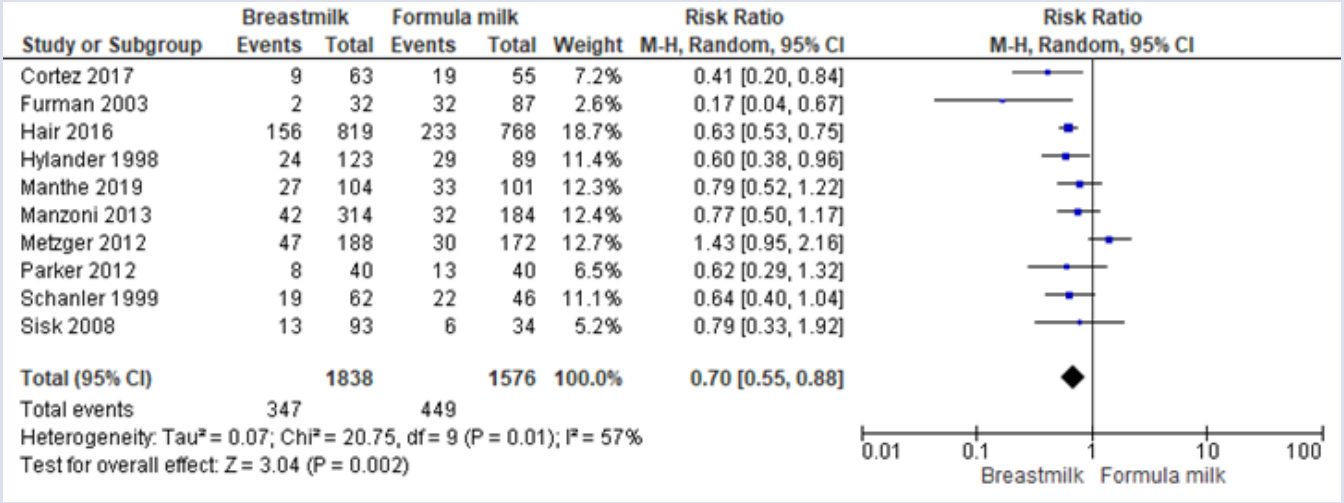

Figure 2: Forest plot of the effect of breast milk and preterm formula reducing the risk of neonatal sepsis.

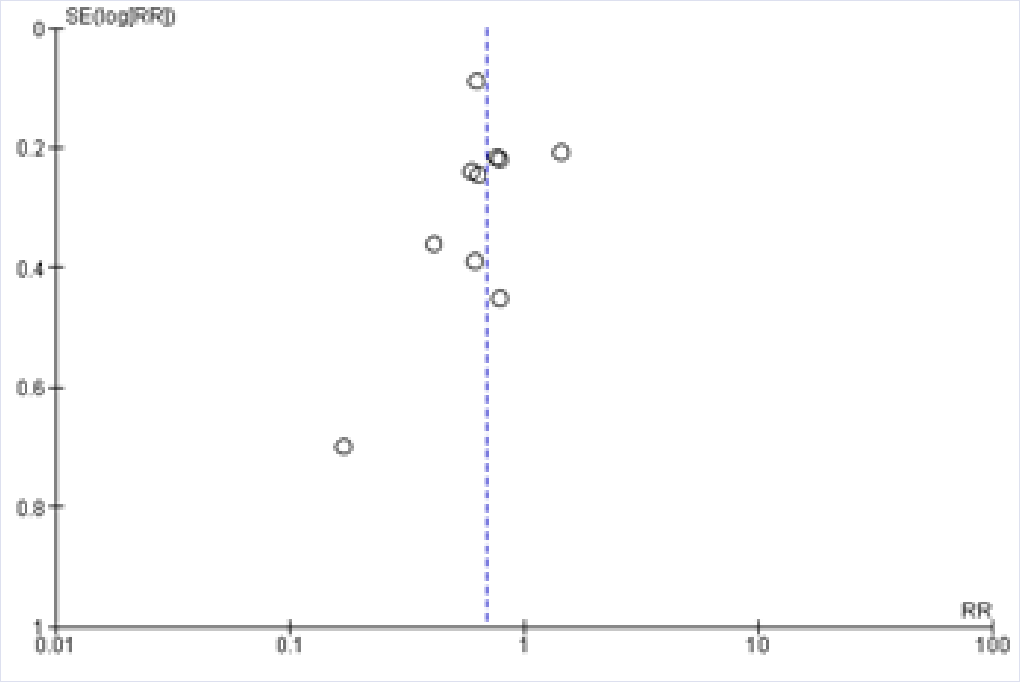

Figure 3: Funnel plot of the effect of breast milk and preterm formula reducing the risk of neonatal sepsis.

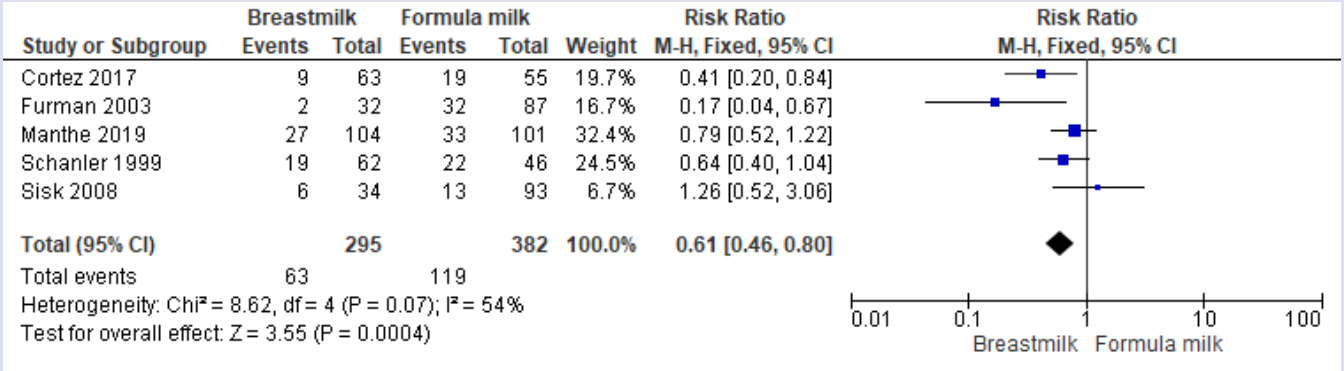

Figure 4: Forrest plot of volume breast milk more than 50ml/kgbw in reducing the risk of neonatal sepsis.

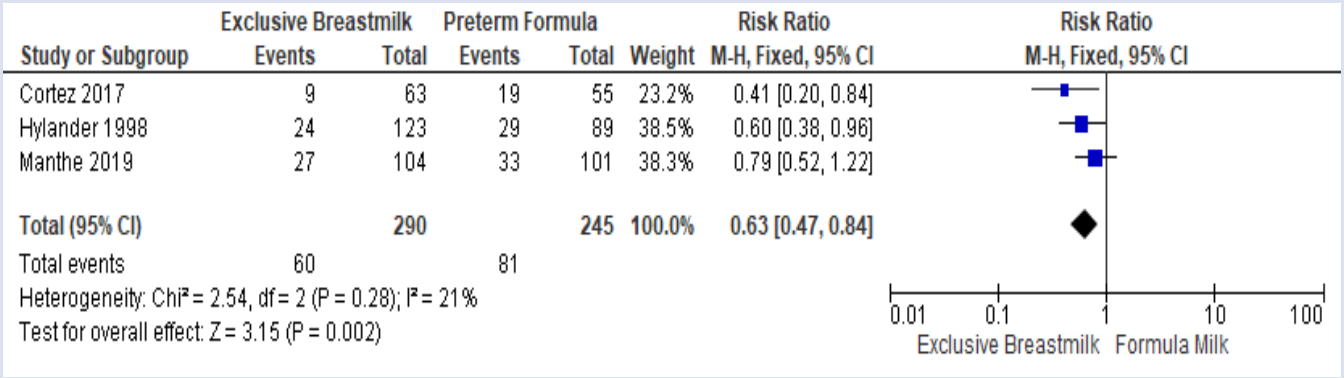

Figure 5: Forrest plot of exclusive breast milk in reducing the risk of neonatal sepsis.

Table 1: New castle ottawa quality scale of the studies.

Study	Selection				Comparability	Outcomes			Total
	Representativeness of exposed cohort	Selection of non exposed cohort	Ascertainment of exposure	Outcome not Present at the start of the study		Assessment	Length of follow up	Adequacy of follow up	
Cortez *et al.*	*	*	*	*	**	*	*	*	9
Furman *et al.*	*	*	*	*	**	*	*	*	9
Hair *et al.*	*	*	*	*	**	*	*		8
Hylander *et al.*	*	*	*	*	**	*			7
Manthe *et al.*	*	*	*	*	**	*	*	*	9
Manzoni *et al.*	*	*	*	*	**	*	*		8
Metzger *et al.*	*	*	*	*	*	*	*		8
Parker *et al.*	*	*	*	*	**	*	*		8
Schanler et al.	*	*	*	*	**	*	*		8
Sisk *et al.*	*	*	*	*	*		*		6

Relationship between volume breast milk and neonatal sepsis in preterm and low birth weight infants

Additional analysis showed that breast milk volume more than 50ml/kgbw significantly reduced the risk of sepsis in preterm and low birth weight infants and preterm infant by 0.61 times, according to five included studies (95% CI 0.46-0.80, p= 0.0004). The findings of the sensitivity analysis by leaving out one study at a time revealed that the results were still significant.

Relationship between exclusive breast milk and neonatal sepsis in preterm and low birth weight infants

We also analyzed exclusive breast milk in reducing the risk of sepsis in preterm and low birth weight infant 0.63 (95% CI 0.47-0.84). Exclusive breastmilk in these studies were differs in volume such as 80ml/kgbw, more than 80% and more than 95%. According to WHO exclusive breastfeeding was that the infant only receives breast milk without any additional food or drink not even water. We suggest that more volume of breast milk can reducing more risk of sepsis. Exclusive breastfeeding infants transition to full feeding more quickly were taken off parenteral nutrition more quickly. This might be because breast milk was simpler to digest and improved enterohepatic circulation and gastrointestinal motility in preterm infants.[25]

DISCUSSION

Neonatal sepsis was linked to prematurity by a lack of humoral and cellular immunity.[32] Infants who were born prematurely and with low birth weight needed more time in the hospital for care, which rose the possibility of nosocomial sepsis.[33] Because they do not have enough IgG antibodies, premature infants have undeveloped immune systems.[32] At the end of pregnancy, when these antibodies were not transferred from the mother to the fetal blood through the placenta, the risk of infection after birth rose until it eventually turned into sepsis.[34]

Breast milk as nutrition had positive effects on the immune system, the brain, and the economy.[35] Components of breast milk served as nutrients for infants as well as enzymes, antimicrobial peptide proteins, anti-inflammatory, growth factors, chemokines, and antioxidants.[36] The mechanism of anti-infective effect of maternal milk is thought to be *via* its high immunoglobulin. Secretory IgA as a main immunoglobulin that plays a critical role in the biological specificity of breast milk in infants that effectively coats the intestinal mucosa and prevents the entry of microorganisms into the tissue.[37] IgA levels are highest in colostrum and gradually decrease to during breastfeeding.[38] IgA active throughout the newborn's gastrointestinal tract and impact the binding of commensal or pathogenic microorganisms, toxins, viruses, and other antigenic materials, such as lipopolysaccharide, preventing their adherence and penetration into the epithelium without triggering inflammatory reactions that could be harmful to the newborn.[39] Breast milk oligosaccharides served as prebiotics that aided in the development of the baby microbiota and function in the binding of direct pathogens.[40] By enhancing phagocytosis, breast milk glycoproteins like cadherin could inactivate viruses and decrease inflammation. Living cells such as secretory cells, myoepithelial cells, mammary gland stem cells, and epithelial cells were also present in a mother's milk. The establishment of the gut microbiota could inhibit the growth of pathogenic bacteria.[39] Because of breast milk had positive immunological effects, the American Academy of Pediatrics (AAP) advised breastfeeding for a brief period of time and for the first time in premature neonates.[41]

Table 2: Literature characteristics of included studies.

No	First Author	Year	Country (State)	Study Design	Sample size	Population	Breast milk		Formula		Nutrition Data	Data Invasive tool	Sepsis Criteria	Research results
							Sepsis	No sepsis	Sepsis	No sepsis				
1.	Furman, *et al.*[22]	2003	United States (Ohio)	Prospective	119	VLBW < 1500g and gestational age 33 weeks	2	30	32	55	Breast milk was fortified more than 50ml/kgbw for the breast milk group. Breast milk started on the second day until enteral nutrition > 110ml/kgbw and until 4 weeks of age, infants got parenteral feeding.	Ventilator. Other data were not available.	Based on clinical and blood culture	The group of infants who got breast milk more than 50ml/kgbw had a smaller risk with an RR of 0.27(0.08-0.95)
2.	Schanler, *et al.*[23]	1999	United States (Texas)	Prospective	108	VLBW < 1500g and gestational age 26-30 weeks	19	43	22	24	Breast milk was fortified. The breast milk group received more than 50ml/Kgbw. Started on the third day	No data	Based on clinical and blood cultures.	Lower incidence of sepsis in the breast milk group r- 0.26 p<0.007
3.	Sisk, *et al.*[24]	2008	United States (North Carolina)	Prospective	127	VLBW < 1250g and gestational age <= 30 weeks	13	80	6	28	Fortified breast milk more than 50% in group of breastmilk. Started on the third day until returning home. Parenteral nutrition was started on the first day.	Central access intravenous and umbilical catheter.	Blood culture	There was no risk difference between the breast milk and non-breast milk groups.
4.	Cortez, *et al.*[25]	2017	United States	Prospective	118	VLBW < 1500g and gestational age < 32 weeks	9	54	19	36	The exclusively fortified breast milk group received 95 percent breast milk during treatment. Breast milk started on the first day or when it was stable and continued until full fed.	Intavenous access.	Sepsis based on blood culture and clinical	Exclusive breastfeeding groups had a lower risk of sepsis.
5.	Manthe, *et al.*[26]	2019	United States (Virginia)	Prospective	205	VLBW < 1250 g and gestational age < 34 weeks	27	77	33	68	The exclusive breast milk group got fortified breast milk > 80ml/kgbw until the baby left the hospital.	No data	Sepsis based on clinical and blood culture and urine culture	Lower sepsis risk in the exclusive breast milk group p < 0.027
6.	Hylander, *et al.*[27]	1998	United States (Washington)	Retrospective	212	VLBW < 1500g and gestational age <32 weeks	24	99	29	60	The exclusive breast milk group obtained 80 percent >fortified breast milk. It was not explained when the beginning entered administration of nutrients and followed by how long.	Ventilator Intravenous access has no data.	Sepsis based on clinical and blood culture and cerebrospinal fluid culture	The risk of sepsis increased in the infant formula milk group by 32.6 vs 19.5% OR 0.43.95% CI (0.23-0.81)
7.	Metzger, *et al.*[28]	2012	Israel (Tel Aviv)	Retrospective	360	VLBW <1376g and gestational age 32 weeks	47	141	30	142	The breast milk group received more than 7 of 8 times the fortified breast milk. Breast milk was given from the first day and seen in the next one month.	Ventilator. Intravenous access	Sepsis based on blood culture	There was no difference in the risk of the sepsis in the breast milk and formula groups.
8.	Parker, *et al.*[29]	2012	United States (Florida)	Retrospective	80	VLBW < 1500g and gestational age < 32 weeks	8	32	13	27	The breast milk group got >50% breast milk and start from the beginning until returning home.	No data	Not explained what blood cultures are based on	There was no difference in the risk of neonatal sepsis in both groups.
9.	Manzoni, *et al.*[30]	2013	Italian	Retrospective Studies Secondary data from previous RCTs	498	VLBW < 1500g and gestational age <35 weeks	42	272	32	152	The breast milk/donor group got more than 50ml/kgbw of breast milk.	Ventilators. Intravenous access has no data.	Sepsis based on blood culture	There was no difference in the risk of neonatal sepsis in both groups.
10.	Hair, *et al.*[31]	2016	United States	Retrospective	1587	VLBW < 1250g and gestational age < 30 weeks	156	663	233	535	The breast milk group got fortified breast milk/donor breast milk and comparing group got bovine milk. There was no data about volume or frequency.	No data.	Sepsis based on blood culture	There were differences in the incidence of sepsis in the breast milk group 30.3% Vs 19% p < 0.0015

Parker *et al* (2012) stated that there were no appreciable changes in the risk of neonatal sepsis between the breast milk group and the formula milk group.[29] This can be attributed to the prolonged length of stayed, which increases the risk of nosocomial infections. A similar result was also observed by Sisk *et al* (2008), of which the results showed that no differences between the two groups could cause the small sample size. Metzger *et al* (2011) revealed that sepsis was 25 % more common in the breast milk group and 30% more common in the formula milk group were not statistically significant (p = 0.09). The study was limited by the lack of accurate information regarding the amount of breast milk administered.[28] Most of the study came from developed countries, eight studies were conducted in the United States, one in Italy, one in Brazil, and one in Israel contrast with Milton *et al* (2022) revealed more prevalent in low and middle-income countries in developing countries.[3] Other studies suggested that the incidence of neonatal sepsis increases in high-income countries in mothers cause of hypertension and diabetes.[42]

Furman *et al* (2003) stated that the impact of breast milk on morbidity in very low birth weight infants who received more breast milk than 50 ml per kilogram per day for four weeks had a 0.27-fold lower risk of neonatal sepsis than those who received less breast milk.[15,22,23] We examined the subgroup analyzed in exclusive breast milk which volume more than volume in other studies which suggest that there is a dose response effect of maternal milk in reducing sepsis.

All of this study were fortified breast milk that was advised by the American Academy of Pediatrics for infants and fortified breast milk was the best source of nutrition for low-birth-weight infants. The European Society for Pediatrics Gastroenterology Hepatology and Nutrition (ESPGHAN) advised using human milk fortifiers or nutritional supplements to prevent development failure because the nutritional demands of neonates could not be met by breast milk alone.[43] The American Academy of Pediatrics advised using donor milk in the absence of breast milk with pasteurization of donor breast milk before usage resulted in a decrease in the activity of bioactive compounds that helped protect infants from illnesses.[44] The pasteurization, mixing, and distribution of donor breast milk were all steps in the safe and efficient donor breastfeeding bank processing method.[45] A non-profit organization in North America called the Human Milk Banking Association of North America (HMBANA) contained policies and guidelines for breastfeeding banks, including the procedure for gathering donor milk.[46] The breast milk bank also processed donor breast milk to be safe when given to infants.[47]

In this systematic meta-analysis study, breastfeeding reduced the risk of neonatal sepsis in preterm and low birth weight infants who got critical care in the NICU and were susceptible to nosocomial infections while hospitalization. The limitation of this study was there were only just ten studies in this meta-analysis study, which was a small number. To get better findings, meta-analysis studies of randomized controlled trials with all components under control were required maternal milk in reducing sepsis.

CONCLUSION

In conclusion, the administration of breastmilk compared to formula reduced the risk of neonatal sepsis in low birth weight and preterm infant. Moreover, higher dose of breast milk also significantly reduced the risk of neonatal sepsis. Therefore, breastfeeding should be improved by encouraging mothers with holistic comprehensive assistance to maintain the sustainable supply of breast milk and through a breast milk bank. However, a study with larger, more precise, and diverse population should be conducted to fully elucidate these findings.

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DISCLOSURE STATEMENT

The author reports no conflicts of interest in this work.

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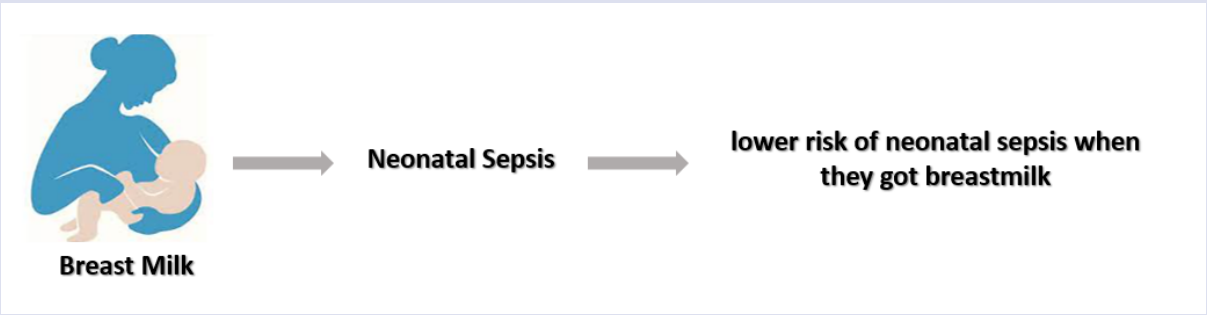
GRAPHICAL ABSTRACT



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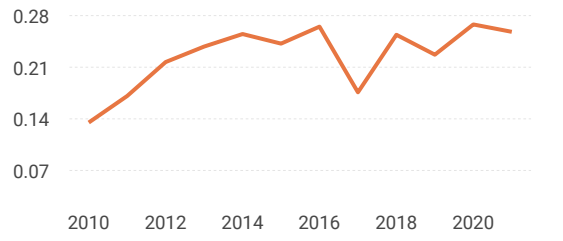

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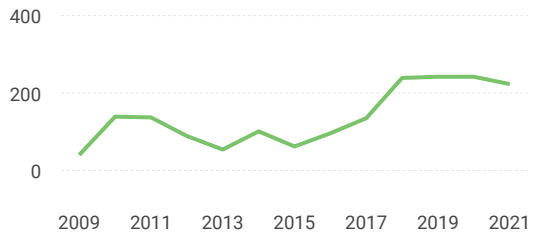

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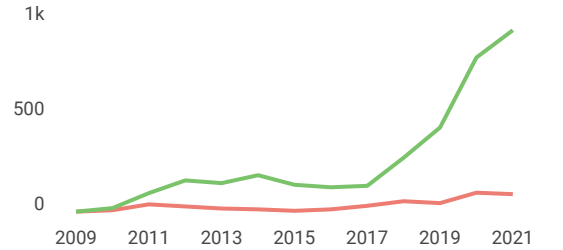

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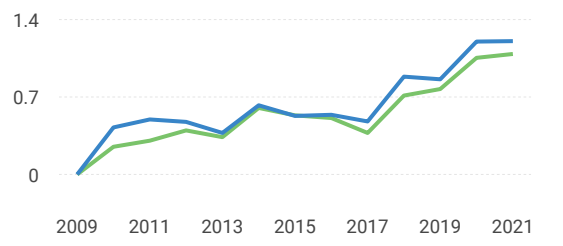

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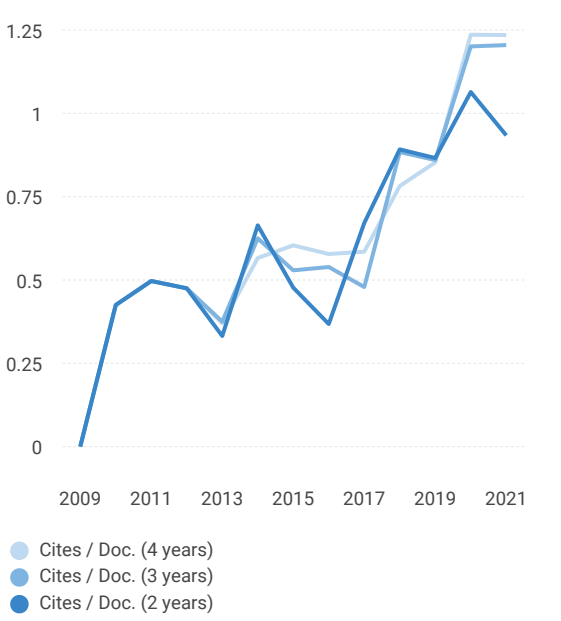

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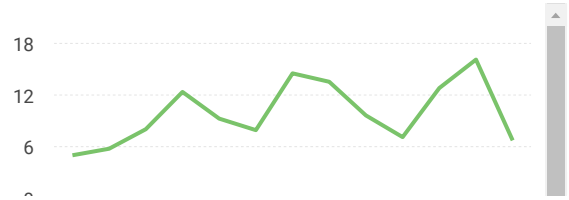

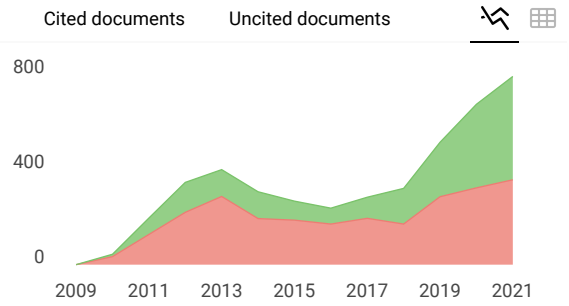

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